

## 1

## Accelerometer

### Purpose

Accelerometers are widely used as sensors for wearable medical devices to measure and assess physical activity (PA) in clinical/laboratory settings or free-living environments. They are, however, mostly employed for ambulatory monitoring for continuously measuring long-term activities of subjects in a free-living environment. From the recorded activity data, it is possible to identify daily movements that are associated with an individual's functional status and also to detect adverse activity, such as falls, through signal analysis and appropriate algorithm. In addition, energy expenditure is the most commonly found application of the accelerometers.

### Principle

Any bodily movement produced by skeletal muscles that results in an energy expenditure can be regarded as PA. Various techniques and devices have been used to measure physical activities that employ wearable or body-fixed motion sensors. These include gadgets ranging from simple switches, pedometers, goniometers, actometers, accelerometers, and gyroscopes. The measurement of physical activity employing accelerometers is the most preferred technique because the acceleration is proportional to external force and, as a consequence, can reflect intensity and frequency of human movement. Also, it is easy to obtain velocity and displacement information by integrating accelerometer data with respect to time. The accelerometers are also designed to respond to gravity, thereby providing tilt sensing with respect to reference planes when accelerometers rotate with objects on which they are mounted. The resulting inclination data from accelerometers help to classify body postures or orientations, thus providing sufficient information for measuring physical activity and a range of human routine activities.

Accelerometers are sensors that are designed to measure the acceleration of an object in motion along reference axes. These sensors are basically force sensors that sense linear acceleration along one or several directions, or angular motion about one or several axes. The former is called an accelerometer, while the latter is referred to as gyroscope. The principle on which an accelerometer operates is based on a mechanical sensing element that consists of a proof mass or seismic mass attached to a mechanical

suspension system with respect to a reference frame. Inertial force due to acceleration or gravity causes deflection of the proof mass according to Newton's second law. The acceleration is measured electrically based on the physical changes in displacement of the proof mass with respect to the reference frame. The most common type of sensors used to measure acceleration are based on the principle of piezoresistivity, piezoelectricity, or differential capacitive measurement.

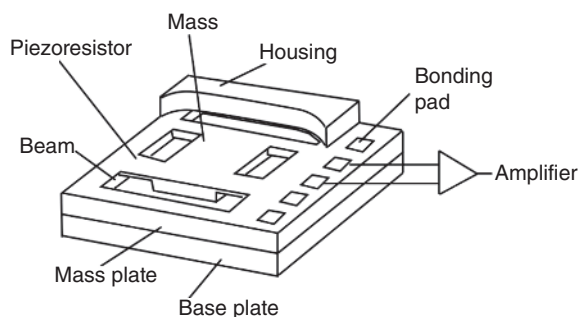
### ***Piezoresistive Accelerometers***

Piezoresistive accelerometers, also termed as strain gauge accelerometers, operate by measuring the change in electrical resistance of a piezoresistive element when mechanical stress is applied to it. Figure 1.1 shows the principle of piezoresistive accelerometer. The sensing element consists of a cantilever beam and its proof mass is determined by bulk micromachining. The acceleration causes the motion of the proof mass that can be detected by piezoresistors in the cantilever beam and proof mass. The piezoresistors are placed as two arms of a Wheatstone bridge that produces a voltage proportional to the applied acceleration.

In practice, a piezoresistive accelerometer is structurally quite stable. This is because it is composed of a silicon chip formed by the semiconductor production technology. An electrical bridge is formed by piezoresistors representing a mass and a beam which are fabricated on a silicon chip. The electrical bridge so formed by such piezoresistive resistors generates electrical signals that are proportional to the applied acceleration. The piezoresistive accelerometers can measure constant acceleration with respect to gravity as they are responsive to DC voltage. The piezoresistive accelerometers are simple and low cost but have lower level of the output signals and suffer from the temperature-sensitive drift. Though they have a limited high frequency response, they are preferred in high shock applications.

### ***Piezoelectric Accelerometers***

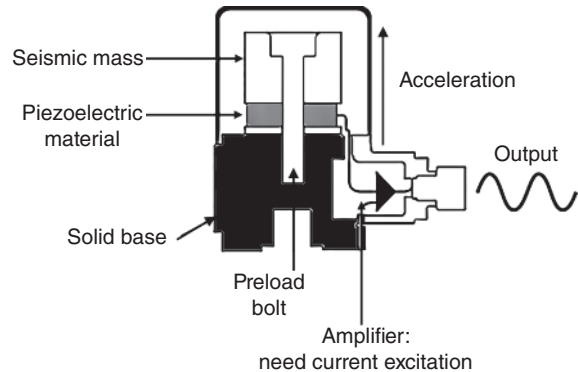
This type of sensor is based on the piezoelectric effect. When certain types of crystals are compressed by application of some force, charges of opposite polarity accumulate on opposite sides of the crystal. Figure 1.2 shows a simplified schematic of a piezoelectric accelerometer. The accelerometer uses an internal piezoelectric element that is coupled with a proof mass to form an accelerometer system. Here, the sensing element



**Figure 1.1** Principle of piezoresistive accelerometer.



**Figure 1.2** Cross section of a piezoelectric accelerometer.



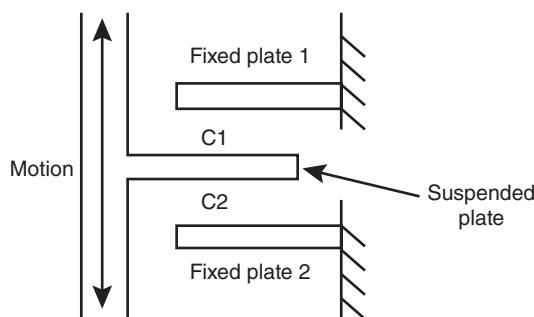
bends due to applied acceleration, which causes a displacement of the proof mass, that results in an output voltage proportional to the applied acceleration. The accelerometer is a charge-sensitive device in which an instantaneous change in stress on the piezoelectric element produces a voltage at the accelerometer's output terminals that is proportional to the applied acceleration. Piezoelectric or charge mode accelerometers require an external amplifier or built-in charge converter to amplify the generated charge, lower the output impedance for compatibility with measurement devices, and minimize susceptibility to external noise sources and crosstalk. These devices are usually integrated circuit piezoelectric (ICP) sensors.

A piezoelectric accelerometer's sensitivity is specified in picocoulombs per gram (pC/g). Typical sensitivities are in the range of 0.5–1000 pC/g. Piezoelectric accelerometers only respond to AC phenomenon such as vibration or shock, rather than DC phenomenon such as the acceleration of gravity. The accelerometers can be applied to measure acceleration levels ranging from 4 g to greater than 100 g. The useful measurement range of a given system is often limited by its signal conditioning and measurement system.

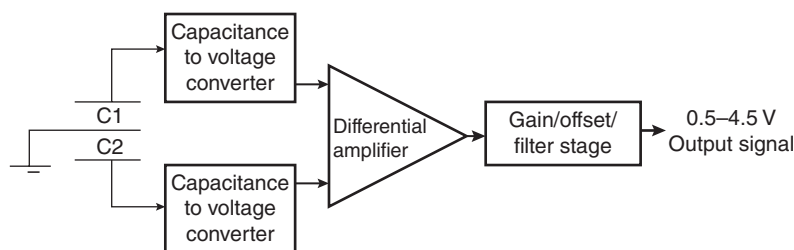
### ***Differential Capacitive Accelerometers***

The displacement of the proof mass due to acceleration can also be identified by measuring changes in capacitance. Capacitive sensing accelerometers produce a voltage dependent on the distance between two planar surfaces or plates. One or both of these 'plates' are charged with an electrical current. When there is a change in the gap between the plates due to application of force, it changes the capacitance of the system, which can be easily measured in terms of voltage. There are several advantages of using capacitive accelerometers which include larger bandwidth, low power dissipation, faster response to motion, high accuracy and stability in operation. They are also less prone to noise and variation with temperature. Differential capacitive accelerometers are also responsive to static forces.

Figure 1.3 illustrates the working of the differential capacitive accelerometers. The sensing element of the accelerometer consists of two fixed plates attached to the substrate and a suspended plate. When the unit moves in the direction as shown in the diagram, the displacement of the suspended plate with respect to the two fixed plates changes, resulting in a change in capacitance of C1 and C2. An increase in C1 will result



**Figure 1.3** Principle of differential capacitance-based accelerometer.



**Figure 1.4** Circuit diagram for signal conditioning of differential capacitance-based accelerometer.

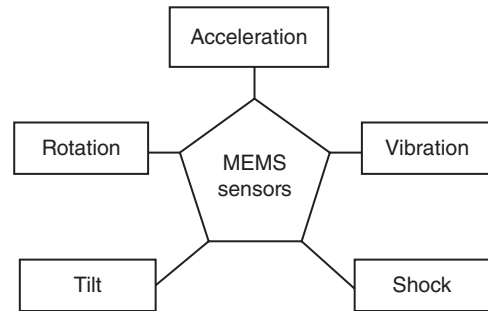
in a decrease in  $C_2$  and vice versa which can be sensed as a voltage signal. A simplified circuit diagram of the signal conditioner of the differential capacitance circuit is shown in Figure 1.4. The signal from the sensor is processed to obtain a filtered and amplified linear output. Due to the small capacitances involved and in order to reduce noise and thermal drift and increase the resolution, a differential capacitance system is employed.

### **Microelectromechanical Sensors (MEMS)-based Accelerometers**

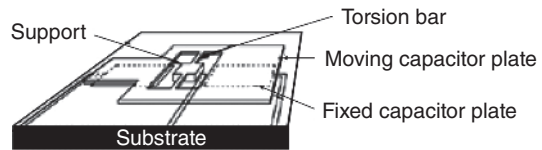
Most of the modern accelerometers are based on microelectromechanical sensors (MEMS). All the above-mentioned technologies for converting acceleration to an electrical signal, namely, piezoelectric, piezoresistive, and capacitive change, can be used in the construction of MEMS-based sensors. However, the preferred technology is capacitive sensing MEMS as it offers long-term stability with high sensitivity. For this reason, capacitance-based MEMS are used in some of the most demanding applications. These sensors are available in one-, two-, or three-axis versions. Multiple axis measurements can also be grouped into a single monitor, allowing capturing of movement in multiple planes. Figure 1.5 shows the functions of an MEMS inertial sensors to detect and measure tilt, shock, rotation, vibration, or any other types of motion.

MEMS are silicon-based micromachined sensors, which have on-chip integration for measurements such as acceleration and vibration. The chip includes the sensor and the signal conditioning circuitry and consequently require only a few external components. Some chips also have built-in analog-to-digital converter to convert the analog output of the signal conditioner to a digital format facilitating direct display on an LCD. They include adequate memory to record physical activity over 21-day periods.

**Figure 1.5** Various functions of an MEMS-based sensor.



**Figure 1.6** Layout of various components on an MEMS capacitance change-based accelerometer.

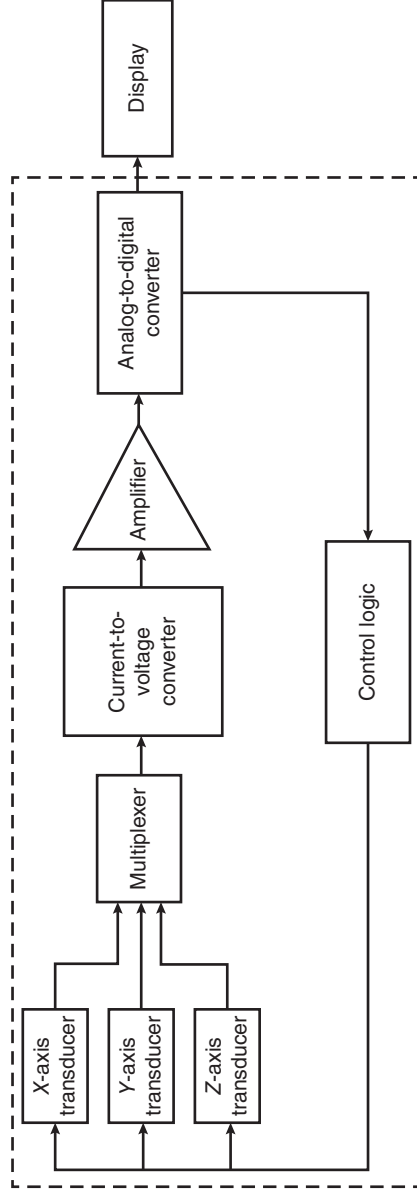


The MEMS chip comprises springs, masses, and motion-sensing components. These sensors are fabricated using the standard IC processing technology commonly employed in wafer fabrication facilities. The sensor with a 3D structure, which allows free movement in all directions, is designed by using layers of oxide and polysilicon, IC photolithography, and selective etching techniques. The sensor is of differential capacitor type in which the plates on the wafer can be driven  $180^\circ$  out of phase. Any movement of the mass on application of force unbalances the capacitor and results in a square wave output whose amplitude is proportional to the acceleration.

Figure 1.6 shows the layout of various components of MEMS capacitance change-based accelerometer on the chip. The digital accelerometers give output in the form of a variable frequency square wave, the method being known as pulse-width modulation (PWM). A pulse width-modulated accelerometer takes readings at a fixed rate, typically, say, at 1000 Hz. The value of the acceleration is proportional to the pulse width or duty cycle of the PWM signal. A demodulator in each axis rectifies the signal and determines the direction of acceleration. This output is given to a modulator that filters the analog signal and converts it to a duty cycle output. A microcontroller can be used to measure acceleration by timing both the duty cycle and the period of each axis. The duty cycle output would be 50% at a 0g acceleration. A typical commercial MEMS-based accelerometer chip is available from M/s Safron Collibrys, Switzerland, which is shown in Figure 1.7.

**Figure 1.7** Typical MEMS-based accelerometer chip.





**Figure 1.8** Block diagram of a three-axis accelerometer circuit including in-built A/D converter of MMA7660FC integrated chip from M/s Freescale.

Three-axis accelerometers can detect motion in three different directions. A three-axis accelerometer MMA7660FC as an integrated chip is available from M/s Freescale. The circuit diagram is shown in Figure 1.8. Although it basically targets handset applications, it can also be used in biomedical applications. It incorporates a range of user-programmable interrupts and sample rates. The chip is packaged in a small footprint ( $3\text{ mm} \times 3\text{ mm} \times 0.9\text{ mm}$ ) DFN package. It communicates 6-bit X-, Y-, and Z-axis information with the processor, eliminating the need for an external A/D converter. The device draws only as little as  $47\text{ }\mu\text{A}$  in active mode and  $2\text{ }\mu\text{A}$  in standby mode.

The accelerometers have been found to be useful for measuring activities such as walking and running, but they do not accurately estimate others such as stationary biking and elliptical trainer. Accelerometers also have limitations in capturing upper extremity movement of the body and related activities. Many accelerometers can separate human movement from movement outside of the human range such as mechanical vibration, which may result from riding in a car, and similar sources of movement.

Accelerometers or devices based on them can be easily attached to a belt, which can be worn around the waist of the user. Some are also suitable to be wrapped around the wrists, thigh, or ankles. Ankle-worn accelerometers can significantly reflect gait-related features during locomotion or walking. In addition, steps, travel distance, velocity, and energy expenditure information can be measured using an ankle-worn accelerometer.

### ***Important Features of Accelerometers***

A typical accelerometer is characterized by several features that include bandwidth, number of axes, and output range.

**Bandwidth:** The bandwidth of an accelerometer is usually expressed in hertz. The human body can create motion only up to the range of 10–12 Hz. For this reason, a bandwidth of 40–60 Hz is considered adequate for sensing tilt or human motion in an accelerometer.

**Number of axes:** Accelerometers can measure in one, two, or three dimensions. Although the most familiar type of accelerometers measure across two axes, the three-axis accelerometers are also becoming increasingly common.

**Output range:** To measure the acceleration of gravity for use as a tilt sensor, an output range of  $\pm 1.5\text{ g}$  is sufficient. For use as an impact sensor, which is one of the most common applications,  $\pm 5\text{ g}$  or more is desirable.

## **Specifications**

*Sensor type:* MEMS

*Range:*  $\pm 8\text{ g}$  or  $\pm 16\text{ g}$

*Resolution:* 12 bit (3.9 mg resolution)

*Logging frequencies:* 10–100 Hz

*Memory:* 0.5 Gb nonvolatile

*Period of recording:* 12 hours

## Applications

Accelerometers are finding increasing application mostly related to fitness and sports activities. Besides the usual applications involving walking and running, accelerometer-based step counters are promoted to encourage people to walk a few thousand steps each day. Accordingly, renowned shoe manufacturing companies are manufacturing and marketing sports watches for runners that include footpods, containing accelerometers to help determine the speed and distance for the runner wearing the unit. Accelerometers have also been employed to calculate gait parameters, such as stance and swing phase.

## 2

### Air Bubble Detector

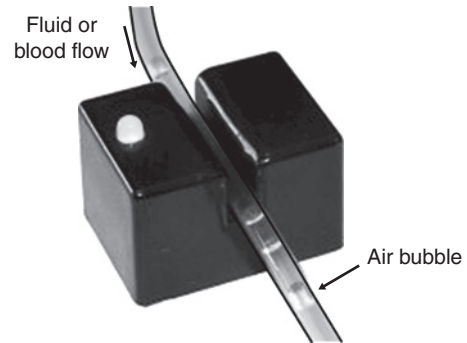
#### Purpose

Air bubble detectors, also called as bubble sensors or air-in-line sensors, are used with patient-connected medical devices to monitor presence of air bubbles in dialysis machines, infusion pumps, transfusion lines, and blood processing systems and thus play a critical safety role in such devices.

#### Principle

Bubble detection is critical to maintain the steady fluid flowing circuit and prevent complications from air embolism. Air bubbles usually originate within the extracorporeal tubing and are carried with the solution flowing into the bloodstream. Such a situation may be present in haemodialysis while priming and preparing the lines for use. Air bubbles may also be formed as a result of turbulent flow of the fluids in the tubing and the vascular access. There is a likelihood of pulmonary microembolization taking place due to these air bubbles during haemodialysis. Thus, while dealing with medical fluid delivery services, it is important to ensure safety of the patient by accurately and reliably detecting small air bubbles flowing through fluid-carrying tubing to prevent air embolism in arteries and veins during medical procedures. Otherwise, treatments requiring fluid delivery can put the patient at risk. Air bubble detectors are usually supplied as original equipment manufacturer (OEM) items so that they may be incorporated in the main equipment such as dialysis machine by their manufacturers. One such sensor is shown in Figure 2.1. The sensors/detectors are usually attached at the designated point of detection to the rigid or flexible plastic tubing of varying diameters. Various techniques that are used to detect air bubbles in flowing fluids are as follows:

**Figure 2.1** Typical air bubble detector module.

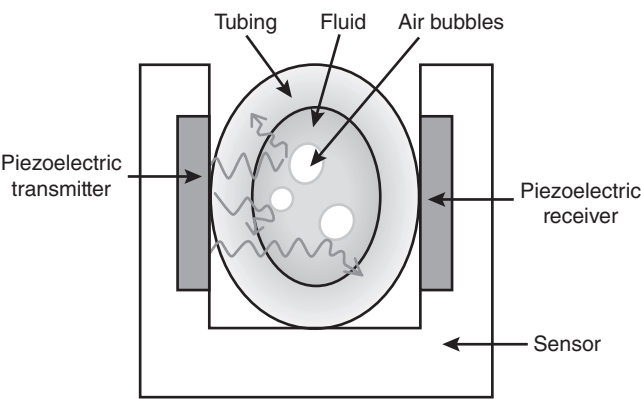


*Photoelectric method:* Different physical principles are employed in air bubbles detection. The simplest method of air bubble detection involves use of a light source and a photodetector mounted opposite to each other across a tube carrying the fluid or blood. The presence of air bubble triggers a signal due to interruption of light if an air bubble is present in the fluid line. These devices were found to be insensitive to fibrin deposits on the inner wall of the bubble trap obstructing the light path. Also, the devices based on this principle are only capable of detecting the presence of macroscopic air emboli of 1 mm diameter or larger. Some researchers have also attempted to detect air bubbles using changes in impedance.

*Capacitance method:* Capacitor-based air bubble detectors have also been developed for detecting micro-air bubbles in the bloodstream in the range from  $620\mu\text{m}$  to  $4.1\text{ mm}$ . The principle of detection is based on detecting the change in capacitance between two plates of the capacitor when air bubbles with different diameters are present in the dielectric solution. Liquids have a higher dielectric constant than gas. So, when an air bubble is in a fluid-filled tube, the capacitance is reduced and the output voltage rises. The size of the bubble is inversely related to the measured capacitance. The main advantages of this device are its reliability, no false reading, and affordability when compared with the other devices.

*Ultrasound method:* A more popular method of bubble detection is by the use of ultrasonic technology. The detection of air bubbles is based on the measurement of the propagation time of alternately transmitted and received ultrasonic pulses in and against the direction of flow. The sensor allows non-contact detection of air and gas bubbles in the liquid through the tube wall and thus allows continuous monitoring of the flowing fluid.

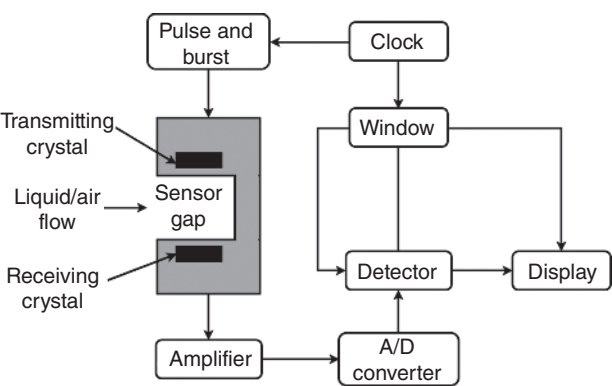
A typical noninvasive ultrasonic bubble sensor utilizes two piezoelectric ultrasonic transducers that work as a transmitter and a receiver. The active piezoelectric element works as a transmitter, which converts electrical energy into ultrasonic energy to generate a high frequency ultrasonic waves. This ultrasonic waves travel through the sensor wall and is coupled to the tubing that is in contact with that wall. The wave then travels through the fluid-filled tubing to the opposite sensor wall and is received by a passive piezoelectric element on the other side as shown in Figure 2.2. The received piezoelectric crystal converts the ultrasonic energy that is transmitted across the gap when liquid is present, back into electrical energy.



**Figure 2.2** Ultrasound-based air bubble detector suitable for use in flowing fluids.

The principle of detection of air present in the flowing fluid is based on the large acoustic impedance difference that exists between the tubing wall or fluid and air. If a bubble comes in the path of the ultrasound beam, it will be partially deflected and the intensity of ultrasound decreases. This large acoustic impedance mismatch between air and fluid creates an acoustic mirror, which reflects the ultrasonic wave back in the direction of the transmitter. Figure 2.3 illustrates a block diagram of the ultrasound-based bubble detector. The controller constantly measures the intensity of the ultrasound and if it becomes lower than a threshold, it detects a bubble. Since energy does not reach the receive side, the sensor will indicate the presence of air.

The ultrasound-based detectors usually employ pulsed ultrasound as transmission signal that consists of short bursts or pulses of ultrasonic energy. Pulse ultrasound is not susceptible to the limitations exhibited by continuous wave ultrasound or by optical detection systems. The return signal, which is received within a specific window of time, which corresponds to the time it takes for the energy to pass through the liquid-filled tubing, is analysed. Only signals received within this time window will indicate fluid, and the signals that are interrupted by the presence of air will not be received within this window. This will generate an appropriate air warning indication to the attending staff.



**Figure 2.3** Block diagram of ultrasound-based air bubble detector.



The ultrasound method is neither able to accurately evaluate the size of individual bubbles nor detect them as individual bubbles when they are close together. Thus, the accuracy of ultrasound measurements becomes poor for small diameter bubbles as it cannot distinguish between micro-air and tiny blood clots. In addition, there could be blind spot areas within the tubing that do not lie in the acoustic path. In such a case, air bubbles that pass through these locations do not attenuate the acoustic signal and will go undetected. This problem is minimized by clamping the tubing into the sensor channel and compressing it to more of a square shape. This maximizes the acoustic window and minimizes the blind spots, which reduces the risk of undetected bubbles.

## Specifications

*Ultrasound frequency:* 1.45 MHz

*Smallest detectable bubble:* 0.5  $\mu$ l

*Tubing outer diameter:* 4 mm

## Applications

The air bubble detectors have application possibilities in the medical, pharmaceutical, and food technology fields. In this way, they ensure bubble-free infusions or bubble-free blood flow in heart–lung machines.

# 3

## Alcohol Analyser

### Purpose

An alcohol analyser is basically a breath analyser, which is a device for estimating blood alcohol content (BAC) from a breath sample of the subject under test. This test is generally employed as a method of assessing alcohol intoxication for legal or medical purposes. BAC is commonly expressed as a percentage of ethanol in the blood in units of mass of alcohol per volume of blood. For example, a BAC of 0.10 implies that there is 0.10 g of alcohol for every decilitre (dl) of blood.

### Principle

When a person drinks alcohol, it is absorbed into the bloodstream where it is neither digested upon absorption nor chemically changed. As the blood moves through the lungs, some of the alcohol moves from the blood across the alveoli into the air. This



**Figure 3.1** Portable alcohol breath analyser. *Source:* Courtesy of M/s Drägerwerk AG & Co. KGaA.

means that the concentration of the alcohol in the alveolar air will be closely related to the concentration of the alcohol in the blood. When a person who has taken alcohol exhales, the presence of alcohol in the alveolar air can be detected by the breath alcohol testing device. The ratio of breath alcohol to blood alcohol has been established as 2100 : 1. This implies that 2100 ml of alveolar air will contain the same amount of alcohol as 1 ml of blood.

Alcohol analysers can be categorized into two types: screening devices and evidentiary machines.

### ***Screening Machines***

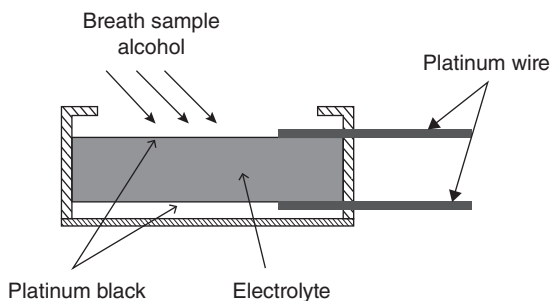
These are usually small, portable, battery-powered devices that have a small LCD display and are usually used for screening purposes. A typical breath alcohol analyser of this type is shown in Figure 3.1. These devices are usually provided to the police personnel working in the field for testing vehicle drivers. When conducting the test, the driver is asked to blow into a disposable mouthpiece. The test results are available in seconds after the subject exhales into the device. Results may be displayed either as numerical value of alcohol in the blood or in qualitative terms such as 'zero', 'pass', 'warn', and 'fail'. If a person fails in the test, he/she is required to undergo an evidential test in a laboratory or at a police station. The screening devices help to test the driver's breath on the spot rather than drawing a driver's blood to test his/her alcohol level.

Modern screening breath alcohol analysers are all electronic devices and mostly operate under the control of a microcontroller. They often use an electrochemical fuel cell or a semiconductor-based sensor to measure the amount of alcohol in the subject's breath.

### ***Fuel Cell Sensor***

In its simplest form, the fuel cell consists of two platinum oxide (called platinum black) electrodes with a porous acid electrolyte material sandwiched between them. A platinum wire is used to provide electrical connections to the platinum black surfaces. The entire assembly is mounted in a case, which has a gas inlet to allow a breath sample to be introduced. The constructional details of a typical fuel cell are shown in Figure 3.2.

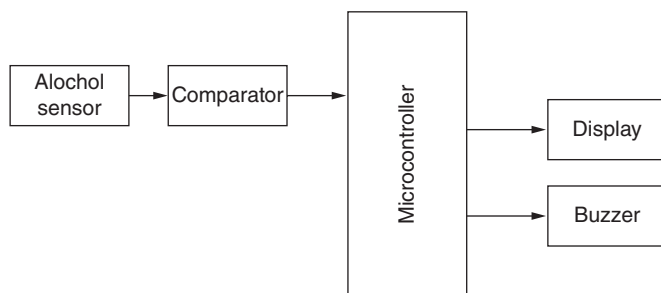
**Figure 3.2** Constructional details of a fuel cell for alcohol content measurement.



When the exhaled air from the subject flows past the fuel cell, the alcohol present in the breath air is oxidized by the platinum black and converts alcohol to produce acetic acid. The process produces electrons as an end product of alcohol oxidation. This reaction takes place at the upper surface of the fuel cell. The reaction also generates  $H^+$  ions, which tend to move from the upper to the lower surface of the fuel cell. There they combine with oxygen from atmospheric air and electrons to form water. In this process, one electron per  $H^+$  ion is consumed. This creates excess of electrons in the upper layer and corresponding deficiency of electrons in the lower layer. In effect, if the two surfaces are electrically connected, a current will flow from the active to the passive electrode in the external circuit. The amount of current flowing in this circuit will give a direct indication of the amount of alcohol consumed by the fuel cell and its presence in the breath air. A microprocessor-based circuit such as shown in Figure 3.3 can measure the electrical current and calculate the BAC. The fuel cell produces a linear relationship between current generated and alcohol concentration in the breath sample. Fuel cell sensor technology is ideal for making screening-oriented breath alcohol analyser.

### **Solid-State Sensor**

Solid-state sensor technology is also used in screening devices for breath analysis. These metal oxide semiconductor-based sensors are mostly called ‘Taguchi’ cells and are manufactured by Figaro, Japan. The Taguchi cell depends for its working on the principle of adsorption of gas molecules on the surface of a semiconductor, causing transfer of electrons due to the differing energy levels of the gas molecules. Figure 3.4 shows a



**Figure 3.3** Simplified block diagram of breath alcohol analyser using fuel cell. Source: Reproduced with permission from Drägerwerk AG & Co. KGaA.

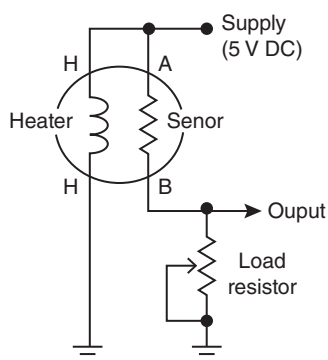


**Figure 3.4** Typical semiconductor alcohol sensor MQ-135.

typical semiconductor-based alcohol sensor. The sensor consists of a tin dioxide sensitive layer inside aluminium oxide microtubes, measuring electrode and a heating element inside a tubular aluminium casing. The front end of the sensor is covered using a stainless steel net and the rear side holds the connection terminals. Ethyl alcohol present in the breath is oxidized into acetic acid passing through the heat element. With the ethyl alcohol cascade on the tin dioxide sensing layer, the resistance decreases. By using the external load resistance, the resistance variation is converted into a suitable voltage variation. The sensing range is from 0.04 to 4 mg/l, which is suitable for breath analysers.

The circuit diagram and the connection arrangement of the alcohol sensor is illustrated in Figure 3.5. The sensing material (tin oxide) has a higher resistance in clean air. When the ethyl alcohol present in the breath passes over the heating element and then falls on the tin dioxide sensing layer, resistance is decreased. This variation in resistance is converted into a corresponding voltage variation using an external load resistor. The voltage output of the alcohol sensor is converted into a digital format using an A/D converter and then given to a microcontroller for processing the signal and display.

Advanced versions of breath analysers have a GPS system to record automatically the exact location of the place where each breath test is conducted. These GPS details along with the actual breath analysis data are stored in the device memory and can then be transferred to a PC for analysis using standard mapping software. This feature enables the authorities to develop a complete picture of the alcohol problem in their area of operation and make a continuous assessment of the measures taken in its detection and control.



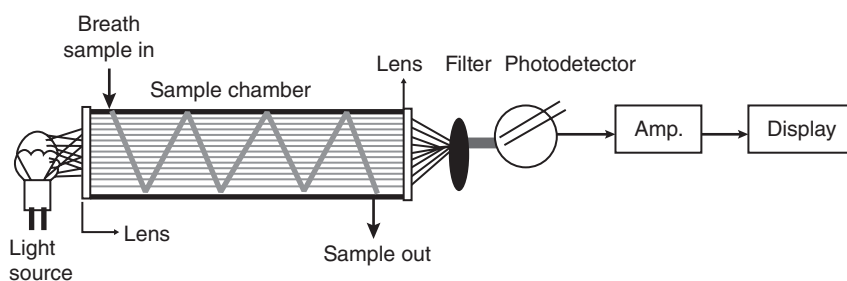
**Figure 3.5** Components and connection diagram of MQ135 semiconductor alcohol sensor.

## Evidentiary Machines

The evidentiary machines are designed to provide measurements of breath alcohol, which are admissible in trial courts due to accuracy. With these machines, the test results can be both displayed and printed at the time of administration of the test. They are usually not portable but can often operate on 12 V police vehicle batteries. In all modern evidentiary breath test machines, the entire operation of the machine is managed by the microprocessor and software, including automating the steps that the machine follows to perform various functions. This autopilot feature attempts to eliminate some of the operator errors, which may affect the final results of the test.

These machines are either based on the use of electrochemical fuel cells or based on the principle of absorption of infrared (IR) energy by the alcohol in the breath sample. While the fuel cell technology is same as that used in screening devices, the IR alcohol analyser is based on the Beer–Lambert law, which is the basis of all spectrophotometric instruments. This law defines the linear relationship between absorbance and concentration of a substance when passed through electromagnetic radiation. When alcohol vapour is introduced into an absorption cell, it will absorb some of the IR radiation transmitted through the cell. The amount of IR absorption will be in direct proportion to the quantity of alcohol present in breath air. However, the absorption of IR radiation by alcohol will be only at a specific wavelength. There are two wavelengths centred at 3.39 and 9.5  $\mu\text{m}$ , which are usually employed. Earlier instruments used 3.4  $\mu\text{m}$  range, but the measurement at this wavelength is prone to interference from some other hydrocarbons and acetone. Modern instruments are based upon IR absorption at 9.5  $\mu\text{m}$  and some even use both the wavelengths of 3.4 and 9.5  $\mu\text{m}$ .

A complete breath alcohol analyser based on IR absorption comprises a source of IR radiation that generates multiple wavelength IR beam as shown in Figure 3.6. The IR beam passes through the sample chamber and is then focused by a lens onto a spinning filter wheel. The filter wheel contains narrow band filters for selecting specific wavelengths suitable for ethanol band. Alcohol molecules absorb a certain amount of IR radiation and if alcohol is present in the sample chamber, a proportion of the light will not reach the sensor. The unabsorbed light after passing through a filter reaches a photodetector placed at the opposite end of the IR source, where it is converted to an electrical signal. The higher the concentration of alcohol, the more IR absorption takes place. The electrical signal is amplified, filtered, and given to an A/D converter from



**Figure 3.6** Block diagram of infrared-based alcohol analyser.



**Figure 3.7** Evidentiary alcohol analyser model 9510. The device uses dual sensor technology.

Source: Courtesy of M/s Drägerwerk AG & Co. KGaA.

where it goes to the microprocessor. The microprocessor processes these digital signals and compares the light received with and without the alcohol sample in order to calculate an alcohol concentration, which is displayed. A typical evidentiary breath alcohol analyser from M/s Drägerwerk AG & Co. is shown in Figure 3.7. This instrument uses dual sensor technology comprising IR and electrochemical sensors. These two common measuring processes for determining breath alcohol concentration levels are based on different principles. While the IR optical sensor measures the absorption of light by ethanol, the signal generated by an electrochemical sensor is produced by the oxidation of molecules on a catalytic layer.

## Specifications

### Screening

*Alcohol sensor:* Fuel cell

*Measuring range:* 0.02–2.50 mg/l

*Response time:* Typically 5 seconds

*Recovery time:* Less than 60 seconds at 1.00 mg/l

*Dimensions:* 195 mm × 80 mm × 42 mm

### Evidentiary machine

*Breath alcohol concentration:* 0–3 mg/l

*Resolution (final result):* 0.01 mg/l

*Blowing time:* >3 seconds

## Applications

The portable alcohol breath analysers are used extensively by law enforcement agencies for screening of drunken drivers, in hospital/clinical test applications, and even for personal use. Although they are an important tool to check roadside drunken cases, their

results are generally not admissible in courts of law. On the other hand, evidentiary breath testers are high standard equipment that produce accurate results that are admissible in courts of law. These have various applications for use by law enforcement agencies, such as post-accident testing and employee suspicion testing.

## 4

# Ambulatory Blood Pressure Monitor

## Purpose

Ambulatory blood pressure monitor is a device that records blood pressures during the normal 24 hour activities, daytime routines, and sleep. These recordings help to study the pattern of blood pressure during different times of the day. Such recordings demonstrate the effects of various factors, such as stress, hypertension, and other influences that contribute to the changes in the blood pressure. This is a more reliable measure of blood pressure than isolated measurements performed in a clinic as it is taken outside the possibly intimidating environment of the physician's office. In fact, the measurement of blood pressure performed in the clinic are useful for screening purposes, whereas ambulatory and home measurements are significantly helpful to the more accurate diagnosis of hypertension and its subsequent care.

## Principle

The objective of ambulatory monitoring is to record one or more physiological variables continuously or repeatedly, without interference on the normal or spontaneous activities of the subject by the restraints of conventional laboratory instrumentation and without influencing the variable being measured. Blood pressure measurements usually done in a clinic use mercury sphygmomanometer, which is still regarded as the gold standard. Besides, self-monitoring blood pressure is also often done at home as and when desired with a portable electronic monitor. But ambulatory monitoring is considered to play an important role in both the diagnosis of hypertensive patients and the evaluation of their response to treatment. The ambulatory monitoring involves measuring blood pressure at regular intervals, usually every 15–30 minutes over a 24 hour period, while patients undergo normal daily activities, including sleep. The monitor is a small, portable, and lightweight device that is carried by the subject by wearing on a belt. The device is connected to a standard cuff wrapped around the upper arm. The principle of operation of the monitor makes use of oscillometric technique for detection of systolic and diastolic pressure, mean blood pressure, and heart rate. After the 24 hour recording is complete, the device is connected to a computer at the doctor's clinic where the report of the 24 hours is prepared showing pressure values and time of the day and night.

The classical method of making blood pressure measurement is adopted even for ambulatory monitoring involving the use of a cuff over the upper part of the patient's arm and applying a transducer over the brachial artery. The compressed air required for inflating the cuff is provided by a pump incorporated in the device. Usually the inflating is done to a preset pressure level, well beyond the systolic value. The inflation rate is approximately 30 mmHg/s. The pressure in the cuff is then decreased at a relatively slow pace at the rate of 3–5 mmHg/s.

The techniques for detection of blood pressure values such as systolic and diastolic include auscultation and cuff oscillometry. The auscultation method is based on detection of appearance and disappearance of Korotkoff sounds using a piezoelectric microphone that is placed over an artery distal to the cuff. The Korotkoff sounds are produced by changes in the flow while arterial blood flows during deflation of the cuff. The sounds first appear when the cuff pressure just falls below the systolic pressure value. The sounds disappear or change in character just below diastolic pressure value when the flow is no longer interrupted. The technique is simple, but it is sensitive to background noise.

Cuff oscillometry is a preferred technique based on detection of cuff pressure oscillations to calculate systolic and diastolic values using an algorithmic approach. When the occluded cuff deflates from a level above the systolic pressure, the artery walls begin to vibrate or oscillate as the blood flows turbulently through the partially occluded artery. These vibrations are sensed by the transducer monitoring the cuff pressure. The systolic pressure corresponds to the cuff pressure at which oscillations first increase, and the diastolic pressure corresponds to the cuff pressure at which oscillations cease to decrease. The values of systolic and diastolic pressures are estimated by analysis of oscillation amplitudes and cuff pressures. Different proprietary algorithms or mathematical criteria are used by different manufacturers, which is likely to result in some variations in the readings among different devices. The technique is though insensitive to background noise, but arm movement may cause erroneous readings.

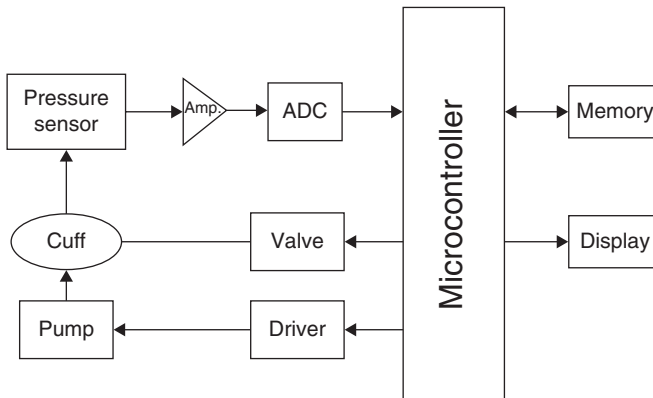
### ***The Monitoring Instrument***

The monitoring device is a small box (Figure 4.1) having an attached cuff. The device contains a pump for inflating and deflating the cuff. It includes a memory device, such



**Figure 4.1** Typical ambulatory blood pressure monitor.





**Figure 4.2** Block diagram of an ambulatory blood pressure monitor.

as tape or digital chip, for storing the blood pressure values. The device is preprogrammed by the physician to take readings and record blood pressure at predetermined time intervals, preferably every 15–30 minutes. The recorded pressures are later retrieved from the tape or memory chip for analysis. The preferred memory device used in the modern ambulatory systems is a small digital chip, which can store much higher data than the tape. In addition, advanced software programs allow analysis to be done automatically to generate a patient's report, which normally includes all blood pressure readings over a 24 hour period, heart rates, mean arterial pressures, and statistic summaries for daytime, night-time, and 24 hour periods.

Figure 4.2 illustrates a simplified circuit diagram of a pressure recording device for ambulatory monitoring. The electrical signal produced by the pressure transducer is proportional to the pressure in the arm cuff. This signal is amplified in the pressure amplifier differentially and converted into single-ended voltage. Some filtering is done in the pressure amplifier to reduce the effect of the pumping action, which adds pulses to the pressure in the cuff. The filters consist of a 2-pole low pass filter and a 2-pole high pass filter. The centre frequency of the pass band is 2 Hz; the 3-dB points are at about 0.9 and 5.5 Hz. The filters narrow down the oscillometric pulse width and generate a pulse with an amplitude that is proportional to the rising edge of the oscillometric input waveform and its original amplitude. The oscillometric pulse is similar to a half-sine wave with an extended trailing edge.

The amplified and filtered voltage is sent to the A/D converter, which in turn gives it to a microcontroller. The 80C51 microcontroller chip contains on board RAM and ROM. Four 8-bit ports provide the data lines, the addressing, and the control and serial bus lines. The on-board ROM provides routines for communications and start-up. The majority of the program is loaded into RAM using the RS-232 port. The RAM is a 32KB×8bit device for storing both patient collected information and programmed information. RAM data is backed up during main battery removal by the 3 V lithium cell. The microcontroller monitoring the sensor drives the motor pump to increase and decrease pressure accordingly. The systolic and diastolic pressures and pulse rate are calculated by the microcontroller and displayed on a four-segment liquid-crystal display (LCD). Information is sent from the microcontroller to the LCD controller by a serial bus.

## Specification

*Method of measurement:* Oscillometer

*Blood pressure range:* 25–280 mmHg

*Heart rate range:* 40–200 bpm

*Accuracy:*  $\pm 3$  mmHg

*Power:* 2 AA alkaline batteries

*Recording duration:* Up to 52 hours, 250 measurements

*Size:* 120 mm  $\times$  80 mm  $\times$  32 mm

*Weight:* 350 g

## Applications

The ambulatory blood pressure monitoring was originally developed as a research tool, but it is now widely applied in clinical practice for diagnosis and management of hypertensive patients. The technique helps to rule out the possibility of white-coat hypertension, to evaluate drug-resistant hypertension, to assess symptomatic hypertension or hypotension, and to assess adequacy of blood pressure control medication in patients at high risk of cardiovascular diseases.

## 5

## Ambulatory Cardiac Monitor

### Purpose

The purpose of ambulatory cardiac monitoring is for diagnosis of cardiac abnormalities by continuously recording ECG over 24–72 hours and to study and evaluate symptoms indicative of cardiac arrhythmias leading to palpitations, dizziness, or syncope. Some ambulatory monitors also have an event monitor feature that is activated when the person notices some symptoms. Ambulatory monitoring of ECG is commonly called ‘Holter cardiography’, after Dr Norman Holter who introduced this concept in 1962.

### Principle

Ambulatory cardiac monitoring is advised when a person has symptoms of abnormal working of the heart, but a resting ECG does not indicate a clear cause. The person is asked to wear the ECG electrodes on the chest, and the electrodes are connected by wires to a small, portable recording device. This can detect certain abnormal heart rhythms that may occur only once a while or they may occur only under certain conditions, such as stress or activity. Currently, there are a number of devices that have been

developed for ambulatory ECG monitoring. They include Holter monitor, event recorders, real-time continuous cardiac monitoring systems, and implantable loop recorders.

Each type of ambulatory monitor has unique features related to the duration of recording time and ability to send the recordings to a central monitoring station. There are two categories of cardiac monitors: external monitors and implantable or insertable monitors.

- *External monitors:* They are designed for short-term use and include traditional heart monitors commonly known as Holter or event monitors for diagnosing heart rhythm problems. They are typically attached to the outside of a patient's body for between 24 hours and 30 days. Another type of external monitor is the patch type of monitor.
- *Implantable or insertable monitors:* They are designed for long-term use to determine causes of infrequent, unexplained arrhythmias. The small device is implanted just under the skin of the chest during an outpatient procedure. The device detects and records abnormal heart rhythms over long periods of time, which could be up to three years.

### **Holter Monitor**

The basic components of a Holter monitor consist of a portable ECG recorder and a Holter analyser or scanner. Both these components have undergone tremendous functional improvements over the last 50 years since the first Holter monitor was developed.

**ECG Recorder** The recorder is a compact, lightweight ECG machine that records the electrical activity of the heart continuously while the subject is not in the hospital or the physician's office. The recording may be done for three or more leads, usually for 24 hours or longer. The ECG electrodes are connected to a small piece of equipment that is attached to the patient's belt or hung around the neck, which keeps a log of the heart's electrical activity throughout the recording period. The patient is asked to maintain a diary to document the time when symptoms are experienced and their description. After the one- to two-day recording period is completed, the patient returns the monitor to the doctor. The data stored is downloaded to a local workstation. The computer-scanned Holter recording is read by a trained person and the physician for final review and interpretation.

Two types of the recorders are available in the market: the cassette tape type or the digital type, which carries a flash memory card. The cassette recorder uses a magnetic tape to record ECG that is required to be sent to the physician's office for study and analysis with an analyser for diagnosis. The disadvantages of this type of recorder are its rather limited memory and its inability to directly transmit ECG information to the monitoring centre for processing of information with a computer software. Therefore, the process is tedious and time-consuming as it normally takes days to produce the analysis report.

The current state of Holter technology uses small recorders (size, 70 mm × 95 mm × 20 mm; weight, about 190 g) using a flashcard to record and store data from several ECG leads attached to the patient's chest as shown in Figure 5.1. The newer digital recorder has higher memory as compared to the cassette tape recorder and it is possible to have the monitoring time much more than 24 hours if required. In addition, the recorded signals are digital, which can be transmitted to the monitoring centre by

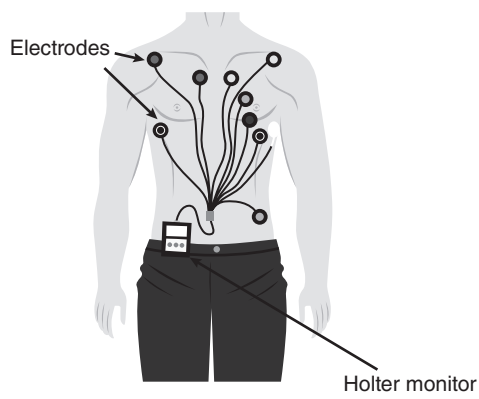


Figure 5.1 A Holter monitor in use.

any of the digital transmission systems via a phone line, e-mail, or wireless technology. The ECG information can be processed quickly with computer software. This facilitates early availability of the patient’s report, allowing treatment to be started without much delay.

Newer Holter monitors are available with up to two weeks of recording capability. The recorders are operated by patient-activated event marker that also specifies the time of the day. The major advantages of Holter monitoring are the ability to continuously record ECG data and that the patient participation is not required in the transmission of data. The recorder is more likely to detect abnormal heart rhythm and can also help evaluate the patient’s ECG during episodes of chest pain due to cardiac ischemia.

Figure 5.2 illustrates the block diagram of a portable ECG recorder. The design shown has fewer patient electrodes with just two leads for acquisition of ECG and one driven lead. The basic analog front end (AFE) allows to acquire ECG signals from multiple channels, which are multiplexed. A typical AFE from analog devices is the ADAS-1000 family, which can be used with three or five electrodes and a driven lead. It also includes

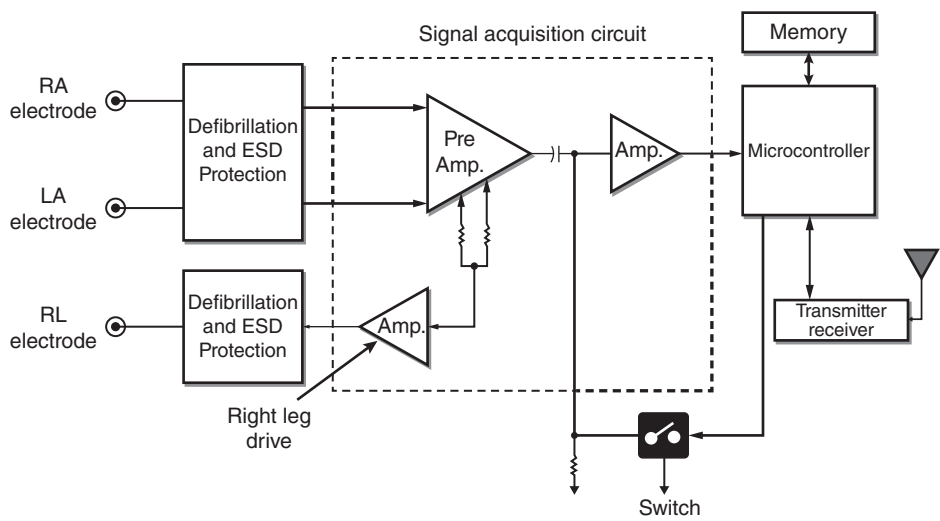


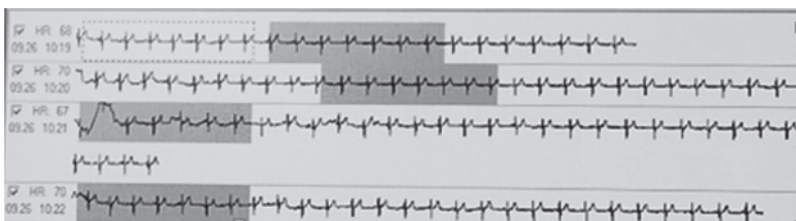
Figure 5.2 Block diagram of a single-lead Holter monitor.

necessary circuitry such as 'lead off' detection and defibrillator protection main filter. It also contains analog signal conditioning circuitry, A/D conversion, power management functions, and digital I/O to interface directly to a suitable microcontroller. The AFE chip can communicate with the microcontroller via a basic SPI interface and consumes only about 20mW of power. The low power consumption is necessary for a portable ECG recorder. The recorder has also a provision for wireless transmission of ECG information over a short range.

### **Holter Analyser (Scanner)**

One major problem, which is inevitably faced when examining long-term recordings, is the huge quantity of data that becomes available in a 24 hour recording easily containing in excess of 100 000 beats. A convenient way of managing enormous ECG data would be to perform real-time rhythm analysis in the recorder itself and discard normal signals instead of recording the total information. Earlier replay and analysis equipment relied on visual inspection of the replayed signals in accelerated time. With manual observer detection, the doctor watches for clues of abnormal beats while playing the tape back at 60–120 times real time. The process is exceedingly tedious and time-consuming and causes high boredom, and consequently fatigue levels can be subject to error. The use of computers for ECG data analysis has revolutionized the process of automatic analysis of the ECG data and offers features such as auto analysis and complete editing capabilities, thus allowing a fast and accurate report. They also display R–R interval histograms and look for essential arrhythmic conditions such as bradycardia, tachycardia, dropped beat, and premature beat. When such abnormalities are recognized, they are written out on a pen recorder for subsequent examination.

Holter analysis systems typically use formal and heuristic feature extraction technique to analyse, for example QRS morphology, QRS width, QRS absolute area, QRS offset, and QRS peak-to-peak amplitude and prematurity. Then, the individual QRS complexes are classified into Normal, Ventricular, Paced, Artifact, or others. The types of analysis generally carried out include mean heart rate, minimum and maximum heart rates, premature ventricular arrhythmias, runs of three or more ventricular ectopics, premature supraventricular ectopic beats, supraventricular tachycardia, and ST segment measurements. Colour-coded beat identification on a computer monitor greatly enhances the ability to discriminate and validate the computer analysis of abnormal beats. Pacemaker analysis is done to analyse the functioning of the pacemaker and the response of the heart. A typical printout of Holter analysis of multichannel data is shown in Figure 5.3.



**Figure 5.3** Typical display of ECG analysis of a Holter monitor. The patched portions indicate abnormal ECG patterns.

### **Event Recorder**

Event or patient-activated recorders are not conventional, continuous Holter recorders, but systems that can provide limited monitoring for a specific type of cardiac event. This device is also worn during normal daily activities, including sleeping, but can be taken off during showers and baths. Small electrodes attached to the chest are connected to a small box about the size of a portable tape player and worn on a belt or shoulder strap. A typical event recorder from M/s Northeast Monitoring, United States, is shown in Figure 5.4. This device has a combination 14 day Holter plus 30 day event recorder integrated into a single unit that is designed for deployment to patients in either 'Holter' or 'Event' mode. In Holter mode, it is available with 3-, 5- or 7-lead patient cables to capture elusive cardiac events – every beat, all the time. When it is deployed as an event monitor, it uses a 2- or 3-lead cable. The data is analysed with proprietary software, which is transmitted via telephone or read directly from the speech discrimination (SD) data card.

When the person feels some abnormal symptoms, he/she presses a button and the recorder is activated. The monitor records the event for the 60 seconds prior to pushing the button and up to 60 seconds after the event. Thus, event recorders document and record abnormal beats but provide no analysis. The recording can be sent immediately or saved and transmitted later, over the phone line. A new form of this device has recently become available that allows automatic transmission of triggered events over the cellular network and there is no requirement for the patient to transmit the data. Event recorders are useful in detecting events such as myocardial ischemia by identifying ST segment changes and measurement of heart rate variability in the assessment of a patient at risk.

Some event recorders are automatically triggered when slow, fast, or irregular heart rates are recognized. Once activated with such an event, data is stored for a programmable fixed amount of time before the activation and a period of time after the activation. These devices are generally referred to as external loop recorders (ELRs).



**Figure 5.4** Typical event recorder from M/s Northeast Monitoring, United States.

**Figure 5.5** Real-time continuous cardiac monitoring system and Heartrak Smart from M/s Mednet Healthcare Technologies, United States.



### ***Real-Time Cardiac Monitoring Systems***

Real-time continuous cardiac monitoring systems combine the benefits and overcome the limitations of Holter monitors and standard ELRs. They are worn continuously and are similar in size to the standard ELR. They automatically record and transmit arrhythmic event data from ambulatory patients to an attending monitoring station. With these devices, cardiac activity is continuously monitored by three chest electrodes that are attached to a pager-sized box. The collected data is then transmitted to a portable monitor that has a built-in cell phone and needs to be in proximity to the patient to receive signals. This monitor analyses the rhythm data continuously and automatically for presence of arrhythmia.

If an arrhythmia is detected, the monitor automatically transmits recorded data by wireless network or landline to a central monitoring station for subsequent analysis. Data can also be recorded through patient-triggered activation. The staff working at a monitoring station analyse live incoming patient data and contact the patient and/or the physician if an urgent intervention is required. This technology is referred to as mobile or real-time cardiac telemetry systems (MCOT).

The Heartrak Smart shown in Figure 5.5 from M/s Mednet Healthcare Technologies is a typical example of such a device that records and transmits real-time ECG data. To record an event, the patient presses the RECORD button and to transmit the event, the patient dials the toll-free Receiving Centre number. The Receiving Centre operates 24 hours a day, 365 days a year. The Heartrak Smart should be placed over the mouth-piece of the phone to transmit the stored ECG for analysis. The device includes 20 minutes of ECG memory and programmable features to meet various monitoring requirements. The patient can wear the monitor on his/her waist, place in his/her shirt pockets, or wear around his/her neck with a cord.

### ***ECG Patch Monitoring***

With the developments in microelectronics and wireless technologies, wearable 'on-body' ECG patch monitoring devices have appeared to meet the needs of ambulatory monitoring. These devices are small, unobtrusive, and easy to use as shown in the Figure 5.6. The ECG patch is a hybrid system in which electronic circuit assembly and textile has been integrated on a flexible polyimide substrate. Such a system is highly



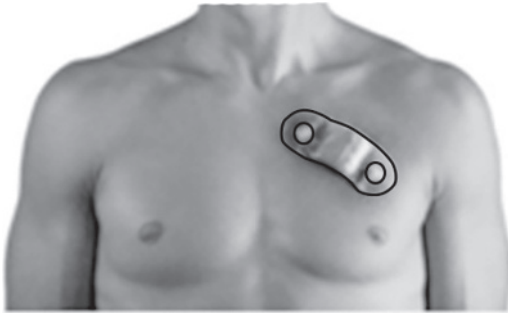


Figure 5.6 ECG patch in use.

flexible and stretchable and can fit body curves without causing any discomfort to the wearer. ECG is acquired by using standard ECG electrodes that are attached to the body. It can therefore be used to monitor cardiac activity when the person is 'on the move' in daily-life conditions. The patch is a single-lead ECG monitor that is applied to the left pectoral region. The patch can be placed on the arm or on the leg for monitoring muscle activity (electromyogram, EMG).

A typical ECG patch monitor consists of a system-on-a chip that converts single channel analog ECG signals to digital format, a low-power Bluetooth low-energy processor (2.4GHz) that transmits the data, and a lithium polymer battery (175mAh). The device has a fork antenna and a snap-on connector for connection to the electrodes. The total size of the flexible core part is  $60 \times 20 \text{ mm}^2$ . The signal from the wireless ECG patch can be sent to a receiver connected to a PC or to a data logger for later download on a computer. With this technology, analysis can be done at any time as the patients are continuously monitored and any cardiac events recorded are instantaneously forwarded directly to the monitoring centre, which is viewed by the physician or clinician who is alerted to the event. This results in immediate diagnosis and faster treatment.

Some patch devices typically include memory storage for medium-term use ranging from days to several weeks, depending on the device. One example of this technology is the Zio Patch (iRhythm Technologies, San Francisco, CA), a waterproof, single-use, continuous ECG monitor that can be worn for up to 14 days and returned for analysis and reporting to the medical consultant. The limitation of this technology is that the patch offers only single lead as opposed to the multiple channels available with conventional Holter monitoring. The patch can be configured for the automatic detection of any combination of the most commonly occurring arrhythmias, plus any patient-activated event. The recordings include 20 seconds pre-event and are configurable for up to seven minutes post-event. Recently, 3-lead ECG continuous long-term patch devices have also become available. These devices are targeted towards medical and research applications such as post cardiac surgery or stroke recovery patients and drug discovery companies.

### ***Ambulatory ECG with Wearable Electrodes***

A further development that overcomes the problem of carrying typically 6 to 10 wires worn around the body throughout the day is by the use of a wearable electrocardiogram (ECG) acquisition system implemented with planar fashionable circuit board (P-FCB)-based shirt. Dry electrodes are screen-printed directly on fabric that allows long-term

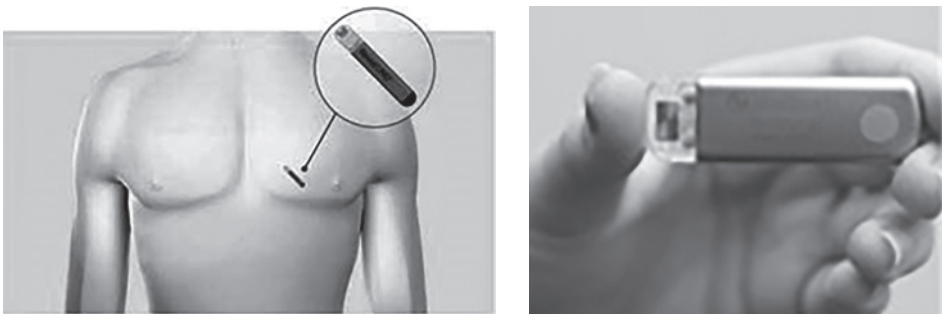


monitoring without skin irritation. The ECG monitoring shirt exploits a monitoring chip with a group of electrodes around the body, and both the electrodes and the inter-connection are implemented using P-FCB to enhance wearability. P-FCB allows the monitoring shirt to bend freely and to closely attach to the body, so a subject will feel comfortable during monitoring in everyday life.

The system is composed of P-FCB electrodes, the ECG monitoring chip, an 8051 microcontroller, an external memory, a debug interface, and a universal serial bus interface. The ECG monitoring chip includes an instrumentation amplifier with a programmable gain amplifier, an analog-to-digital converter (ADC), a compression accelerator, and an encryption block. The ECG monitoring chip is composed of an instrumentation amplifier with a programmable gain amplifier a 10bit ADC and other associated circuitry and P-FCB electrodes. The electrodes are capacitively coupled to the instrumentation amplifier input.

### ***Implantable Loop Recorders***

The patients who experience very infrequent cardiac events would requiring long-term monitoring for detection of such abnormalities. This requirement is met by employing an implantable loop recorder, a thin device inserted just under the patient's skin in the chest area during an outpatient surgical procedure. These leadless devices as shown in Figure 5.7 record a single-lead ECG signal with two electrodes within the device. The device can be triggered automatically or by patient activation via placement of an activator over the device. When symptoms are felt, the patient places a handheld activator over the recorder to activate the storage of cardiac rhythms both retrospectively and prospectively for several minutes. The loop memory enables the device to be activated even after symptoms have resolved, which means that such devices can be used even in the presence of incapacitating symptoms, which normally prevent the activation of ECG monitoring in devices not having this feature. Auto-triggering technology can be adapted to memory loop devices as per predesigned programs. For example, the monitors can be programmed to detect heart rates greater than 175 bpm, less than 35–40 bpm, or an asystole of greater than three seconds. These devices also have provision of remote transmission of data and have a battery life in excess of 36 months. The 'Reveal' from M/s Medtronic USA is a typical example of an implantable loop recorder that is an auto-triggered or patient-activated rhythm recording device. The use of such implantable ambulatory monitors is considered medically necessary only in the small subset of



**Figure 5.7** Implantable loop recorder. *Source:* With Courtesy of M/s Medtronic, USA.

patients who experience symptoms of cardiac problems infrequently that a prior trial of Holter monitor and other external ambulatory event monitors has been unsuccessful.

These devices are equipped with a memory loop and, once activated by the patient at the time of a symptom by means of an external activator, store a one-lead ECG tracing, both retrospectively and prospectively, for several minutes. By implementing dedicated algorithms and sensing parameters similar to those of implanted cardioverter defibrillators (ICDs) and pacemakers, the implantable cardiac monitors are also able to automatically detect any kind of arrhythmic event: from bradycardia to asystole and from atrial fibrillation to ventricular tachycardia.

## Specifications

*ECG input channels:* 3

*Input impedance:*  $>10\text{ M}\Omega$

*Input DC offset:*  $\pm 300\text{ mV}$ , with saturation recovery in 3 seconds max

*CMRR:*  $>60\text{ dB}$  at 10 Hz,  $>80\text{ dB}$  at 50 Hz

*Resolution:*  $2.5\text{ }\mu\text{V}$

*Bandwidth:* 0.05–40 Hz ( $-3\text{ dB}$ )

*Data storage:* 128 Mb nonvolatile internal memory

*Recording length:* 24 or 48 hours

*Dimensions:*  $92\text{ mm} \times 45\text{ mm} \times 15\text{ mm}$

*Weight:* 70 g

*Operating power:* 16 mW typical

## Applications

The ambulatory monitoring is advised to assess heart rhythm of a subject over time, correlate the symptoms with the heart rhythm, and diagnose abnormal heart rhythms. The Holter monitors are generally recommended by cardiology departments of hospitals.

# 6

## Ambulatory Glucose Monitor

### Purpose

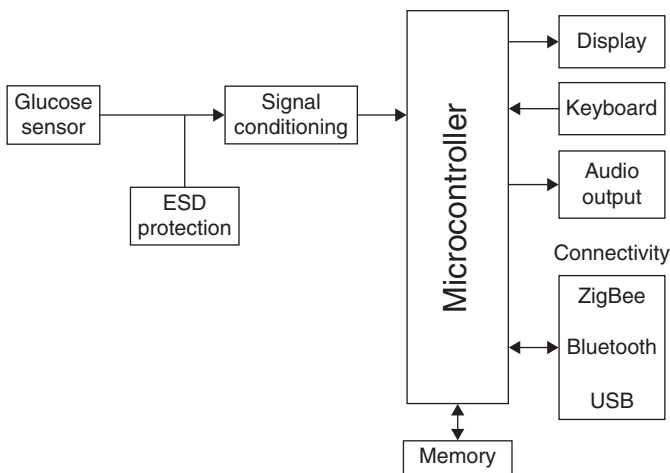
The purpose of an ambulatory glucose monitoring device is to track the level of glucose in the blood throughout 24 hours, day and night, so as to notify the patient of high and low values. This enables the person to take necessary action to correct the abnormality in terms of hypoglycaemia or hyperglycaemia. The technique is known as continuous glucose monitoring (CGM) that helps to make decisions based entirely on the

information provided by the monitor for better management of diabetes by adjusting insulin delivery. CGM values help the doctors to diagnose problematic cases, fine-tune medications, and get tighter control of blood glucose levels for high risk patients. CGM enables patients to evaluate the effects of lifestyle effects on glucose levels and to adopt modifications to certain facets to achieve adequate glucose control. CGM is a major step towards the development of artificial pancreas, which could deliver insulin automatically in response to blood glucose levels, resulting in better quality of life for diabetic patients.

## Principle

Glucose monitoring is an essential part of management of diabetes as it helps clinicians to take necessary action to achieve better glucose control. The most common practice to determine the concentration of glucose in the blood is by utilizing a glucose meter or glucometer. A small drop of blood is drawn by pricking the skin with a lancet and placed on a disposable test strip. The device reads the strip and uses the information to calculate the blood glucose level. The two types of sensors commonly used in the glucometers are based on electrochemical reaction and optical reflection-based method. Glucometers are usually used by individuals for self-monitoring of blood glucose. However, the method is too invasive, time-consuming, and cumbersome to be universally applied with desired frequency. The method is also not compatible with the daily activities of children and even adults. Lack of proper adherence to glucose monitoring can lead to higher risk of complications due to diabetes. Thus, there is a need for continuous and noninvasive technology for glucose monitoring. Real-time information provided by CGM devices form the basis for adjustment of the insulation dose by the patients.

Figure 6.1 illustrates the block diagram of a glucose ambulatory monitoring device, which includes a transcutaneous glucose sensor with a transmitter that can be inserted into the abdomen or arm and a receiver that is typically worn on a belt or can be carried



**Figure 6.1** Block diagram of a continuous glucose monitor.

in a pocket by the patient. Most of the CGM sensors exploit an enzyme-based glucose oxidase needle electrode and are thus mostly invasive, although minimally. When implanted, the sensor becomes exposed to glucose within the interstitial fluid of subcutaneous tissue at the site of insertion. The glucose in the interstitial fluid reacts with the glucose oxidase enzyme and generates an electrical charge that is stored in the memory chip. The concentration of circulating blood glucose is estimated by applying the proprietary algorithm. Readings are then transmitted every few minutes to the receiver, and the data can be downloaded and stored on a PC. The calibration is usually done by finger-prick measurements and entering data into the CGM system.

The data from the memory chips, which record glucose data information, can be later analysed by the clinician. The chips allow easy data transmission via wire or wireless means and convenient analysis with computer software. The glucose data from memory chips can also be uploaded by the patients to web-based data management systems, enabling diabetic patients and their healthcare providers to communicate and analyse glucose information using the Internet.

### ***Glucose Sensors***

The sensor is the most critical component in the CGM device. A number of technologies have been tried over the last two decades with the objective of developing an ideal glucose sensor suitable for ambulatory monitoring. The sensors can be categorized into three types: noninvasive, minimally invasive, and invasive.

#### ***Non-invasive Continuous Glucose Monitoring***

The ideal sensor for ambulatory glucose sensor should be noninvasive so as to minimize discomfort and the potential risk of infection from fluid-withdrawing probes penetrating the skin. The noninvasive sensor will further allow greater tolerability and wearability, facilitating long-term adaptation. The noninvasive devices that have been tried include optical transdermal sensors based on the use of near-infrared light across the stratum corneum to detect glucose concentrations. Multisensor systems are also being studied, which involve biophysical characterization of the multiple physical and chemical properties of the analysed tissue, mainly the skin. Another type of sensor that can continuously monitor blood glucose level in real time without requiring a blood sample follows the impedance spectroscopy technology. It is based on the principle that changes in blood glucose in the blood produce significant changes in the conductivity. The sensor then produces an electrical signal that fluctuates according to the electrical conductivity of the body. A micro antenna in the sensor then detects these changes and correlates them with changes in serum glucose. Despite the advantages of noninvasive approach, there continues to be serious challenges in the development of noninvasive CGM sensors due to various factors such as sensitivity, signal-to-noise ratio, and development of wearable devices for clinical applications.

#### ***Minimally Invasive Glucose Monitoring***

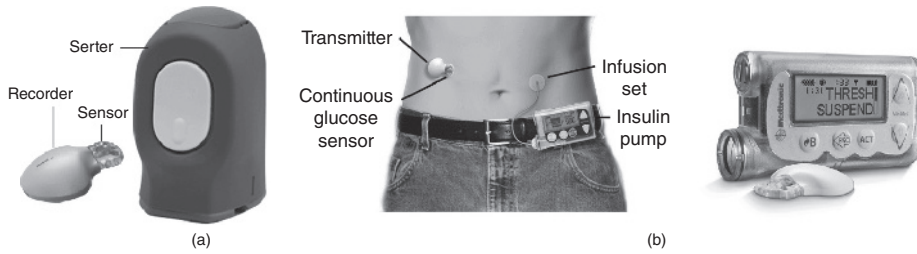
This technology is based on the measurement of glucose concentration avoiding the continuous presence of the sensor or any foreign substance in the body. The

measurement of glucose is done from interstitial fluid or blood obtained from the skin tissue. Here, both the sensor and controller are placed outside the body. They are connected to a fluid-drawing device that is also externally located. The techniques utilized for such monitoring include iontophoresis, sonophoresis, micropore technology, and microneedle technology. Iontophoresis involves application of a low level electrical current across the skin, which induces flow of a tiny amount of interstitial fluid from which glucose can be estimated by an externally located sensor. In sonophoresis, low frequency ultrasound is used to enhance skin permeability that in turn allows extraction of interstitial fluid. Micropore technology is used in creating multiple micropores in the stratum corneum using laser ablation through which interstitial fluid can be collected by application of a small vacuum. In microneedle technology, disposable devices composed of a silicon microneedle are employed that allow to collect a minute blood sample in a pouch. Though the minimally invasive technology appears to be highly appealing, as it avoids transdermal pricking, there are still several issues such as calibration procedure and poor accuracy in their adoption for clinical usage.

### ***Invasive Continuous Glucose Monitoring***

Most current ambulatory glucose monitoring systems use invasive glucose sensors, usually smaller than 5 mm in diameter, inserted into a patient's abdominal subcutaneous tissue. In most cases, the sensor remains in place for three to seven days. The blood glucose levels are derived from the measured interstitial fluid glucose levels. Several devices have been developed based on this approach. They all employ a glucose oxidase-based electrochemical sensor, which is placed subcutaneously. Interstitial glucose measurements are then sent continuously from the sensor to a pager-sized receiver through wireless technology. The sensor sends the information to the receiver to display glucose measurements every five minutes. The data can be transferred to a computer for analysis, which will show the patient's glucose patterns throughout the day. The transmitter is waterproof, lightweight (just 13 g), and quite compact (5.2 cm × 3.1 cm × 1.1 cm) in size. The size of the handheld receiver is just that of a cellphone (6.3 cm × 8.2 cm × 2.2 cm) and weighs only 99 g. In modern devices, the transmitter and the receiver can perform up to a range of 30 m. Catheter-shaped sensors have also been developed, wherein the sensing element is located at the tip of the catheter, while the transmitter is located at its other end, which is located outside the skin. Similarly, a disposable invasive optical fibre has also been introduced that is capable of percutaneous glucose monitoring via spectroscopic measurements.

The devices are equipped with alarms that can be set at specified levels to warn the patient of a hypoglycaemic or hyperglycaemic glucose level. The devices also display the glucose rate of change and trends of blood glucose over specified periods. The device provides the features to enter times of meals, insulin administration, and physical activity and thus gives a complete picture of the potential causes of glucose excursions. There is usually a provision in the devices to present glucose trend graphs over 3 and 24 hours and issue hypoglycaemic and hyperglycaemic alerts. They also have a special feature of indicating predictive alarm to alert the patient based on the rate of change glucose value that can lead to abnormal glucose levels within a specified time period.



**Figure 6.2** Continuous glucose monitor comprising a small sensor, recorder, and inserter with a hidden needle. (a) The instrument takes a reading every five minutes. (b) The device is placed on the abdomen and can record glucose profile up to six days. *Source:* With Courtesy of M/s Medtronic, USA.

There are a number of companies that are manufacturing CGM devices that are clinically used. The prominent among them are Medtronic, United States; DexCom, United States; and Abbott Diabetes Care, United Kingdom. The Medtronic device requires only one device that works as both the insulin pump and the CGM. The device requires two separate insertion sites separated by at least a few centimetres: one for the CGM and one for the insulin pump. Figure 6.2 shows a typical CGM system in use from M/s Medtronic.

The future of CGM would depend upon the technological improvements that are crucial in meeting the challenges of noninvasiveness, wearability, accuracy, improved calibration, cost-effectiveness, comfort, patient safety, and algorithms for processing of data.

## Specifications

*Sensor:* Glucose oxidase-based electrochemical sensor

*Measurement range:* 1.1–27.8 mmol/l

*Sensor life:* Up to 5 days

*Transmitter wireless range:* Up to 3–30 m

*Size:* 32 mm × 31 mm × 11 mm

*Receiver data memory:* 60 days of normal use

*Size:* 96 mm × 61 mm × 16 mm

## Applications

Ambulatory glucose monitoring is an effective method of analysing glucose data of diabetic patients over an extended period of time rather than a single glucose reading. The device is considered to be specifically useful for children as it reduces the often very high number of finger pricks. Patients with poorly controlled diabetes and pregnant women in whom tight glucose control is essential are also potential beneficiaries. Currently, the use of CGM is still not a common practice.

## 7

## Ambulatory Sleep Monitor

### Purpose

Ambulatory sleep monitor is a device to conduct studies to determine the cause of sleep disorders. Sleep apnoea is one of the common sleep disorders wherein breathing stops temporarily during sleep. The sleep study tests mostly done in the home environment are basically aimed at diagnosing patients with obstructive sleep apnoea (OSA). The tests are usually prescribed when the patient has a likelihood of suffering from moderate to severe sleep apnoea. In addition, overnight sleep tests are also done in some cases that include breathing disorders, periodic limb movement disorders, circadian rhythm disorders, hypersomnia, insomnia, and many more.

### Principle

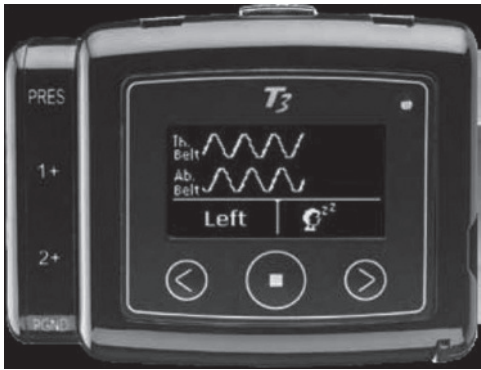
Sleep apnoea is usually a chronic disorder during which breathing appears to stop or become shallow, leading to poor quality sleep. The episodes of apnoea may last for over 10 seconds and likely to recur sometimes more than 5 times/h. Sleep apnoea is usually associated with snoring and increased airway resistance, often accompanied by a loud gasping noise. This results in decrease in oxygen levels, which is sensed by the brain making the individual to wake up to resume breathing. OSA has also been associated with a number of other clinical problems such as adverse cardiovascular and cerebrovascular events. Sleep apnoea usually remains undiagnosed in most patients. Ambulatory sleep monitoring can thus be useful for diagnosis and treatment of OSA.

### *Home Sleep Tester (HST)*

A home sleep tester (HST) is a device used for the diagnosis of OSA. Most HST devices are portable, about the size of a mobile phone, and are battery operated. They are usually designed to measure and record nasal and oral airflow, respiratory effort, and oxygen saturation levels in the blood while sleeping. One such device from M/s Nox Medical, United States, is shown in Figure 7.1.

**Polysomnogram** The gold standard in sleep studies and for the evaluation of OSA is polysomnogram (PSG). This technique comprises study and evaluation of a set of comprehensive measurements and recordings of several body functions during sleep. The parameters for evaluation include brain activity, eye movement, oxygen, and carbon dioxide blood levels, heart rate and rhythm, breathing rate and rhythm, the flow of air through the mouth and nose, snoring, body muscle movements, and chest and belly movement. By studying the sleep quality and the physiological processes, relations





**Figure 7.1** Portable sleep recorder. *Source:* With permission from : M/s Nox medical, USA.

between the two can be established that help to determine the cause for the sleep disorders. To conduct these measurements and monitoring, multiple sensors are applied on the patient's head, face, and body while sleeping. In addition, studies also include recording of EEG, ECG, EMG, and other biologic measurements in a laboratory setting.

The HST sensors include several types of electrodes in the form of small pads or patches that are placed on the head and body with a small amount of adhesive. Soft elastic belts are placed around the chest and abdomen to measure the breathing activity. The blood oxygen levels are checked by a small clip (oximeter) placed either on the tip of the index finger or on the earlobe. The electrodes, elastic belts, and oximeter are so designed that they are comfortable to wear and do not pose a hindrance to sleep. PSG recording equipment and video monitors record the movements and activities automatically while the person is asleep. The technician on duty sits in the adjoining room and continuously checks the recordings. For most PSG studies, the patient is required to spend at least six hours overnight in the sleep laboratory.

If a person suffers from sleep apnoea, he/she is asked to wear a mask that is connected to a continuous positive airway pressure (CPAP) machine. The mask fits over the nose. The purpose of using the CPAP machine is to deliver air or extra oxygen. This increases the air pressure in the throat so that the airway becomes more open when the person breathes in.

Although PSG offers a standard and accurate technique for the diagnosis of OSA and other sleep disorders via objective measurements of several parameters, but the procedure is cumbersome and expensive. This has led to the development of several simpler ambulatory sleep study devices, known as Home sleep testing monitors (HST monitors) that are relatively more user-friendly and serve the same goal of diagnosing OSA with accuracy comparable to that of formal PSG.

**Types of HST Monitors** The portable monitors used in the diagnosis of OSA are categorized into three types:

*Type II monitor:* It has a minimum of seven channels, which include EEG, EOG, EMG, heart rate, airflow, respiratory effort, and oxygen saturation.



*Type III monitor:* This type of monitors has a limited number of channels, which could be four to seven that include respiratory movement and airflow, heart rate, and oxygen saturation.

*Type IV monitor:* These are relatively simpler devices and are designed to measure only one or two parameters, say, oxygen saturation and/or airflow. This type of monitor does not detect sleep stages; instead, it extrapolates the respiratory disturbance index based on the time period over which the recorder was switched on.

### **Monitoring Techniques**

The following techniques are commonly employed for monitoring various apnoea-related parameters:

*Respiratory activity:* Measurement of respiratory activity is crucial to the diagnosis of OSA. The sensor for measurement of airflow is based on sensing pressure changes. It typically employs nasal cannula similar to the ones used to provide nasal oxygen. Alternatively, an oral thermistor sensor can be used to measure mouth breathing, which is preferred for patients with complete or significant nasal obstruction. In addition, chest and abdominal belts can be used to monitor respiratory activity. The movement sensing is typically done with piezoelectric sensors or inductive plethysmography technique.

*Oxygen saturation:* The measurement of peripheral oxygen saturation and pulse is done by using a pulse oximeter attached to either the finger or earlobe. The sensor is based on the measurement of the differential absorption of red and infrared light by oxygenated and deoxygenated haemoglobin. The parameters of interest in sleep monitoring are the number of oxygen desaturation events and the lowest oxygen saturation.

*Heart rate:* Heart rate is derived from the single-lead ECG, using a pair of electrodes attached to the upper part of the chest.

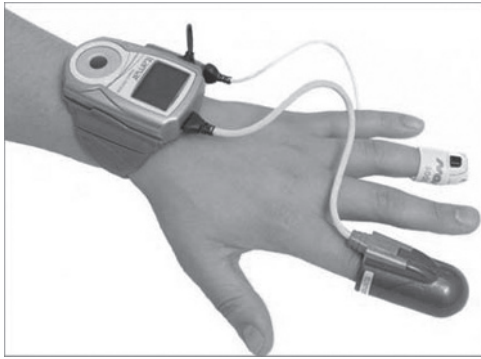
*Snoring evaluation:* Snoring can be audio recorded by placing a microphone on the neck.

*Positioning:* Body position and activity is monitored from an integrated 3D accelerometer.

### **Actigraphy**

If the person is having sleep disorders, which may be due to night-shift duty or any other problem relating to the person's internal clock disturbing the circadian rhythm, the test conducted is called actigraphy. A device is used to measure the person's movement during sleep and when he/she is awake. This information is useful in determining the times during the day the person is active and the times he/she is sleeping. The device used for this purpose looks like a watch worn on the wrist. Sleep studies are usually conducted in a sleep laboratory, but such studies can also be performed with portable equipment that the person can use at home. One such device is the WatchPAT from M/s Itamar Medical, Ltd, shown in Figure 7.2.

The WatchPAT is a wrist-worn ambulatory sleep diagnostic study device to diagnose OSA. It is based on measurement of peripheral arterial tonometry (PAT) along with pulse oximetry and actigraphy to monitor respiratory disturbances. The WatchPAT



**Figure 7.2** Wrist-worn ambulatory sleep diagnostic study device - WatchPAT. Source: Courtesy of M/s Itamar Medical Ltd.

device indirectly detects apnoea and hypopnoea via selectively measuring peripheral arterial volume changes using a finger-mounted plethysmograph. The information is correlated with pulse oximetry in conjunction with heart rate. The software associates waking up with measurement of oxygen desaturation levels and determines respiratory effort-related arousals. The data stored in the WatchPAT is analysed by utilizing proprietary user-friendly software provided on a computer. The algorithm carries out the analysis automatically eliminating the need for subjective scoring of respiratory events. The complete report of the study becomes available within minutes after downloading the data. With the immediate availability of results, treatment can be initiated on the same day and without any delay.

With the proliferation of smartphones, there is a drive for using mobile phone application for everyday sleep monitoring. In one experiment, a smartphone app issues a tone at regular intervals and the person is asked to respond to this tone. If there is no response from the person, then he or she could be sleeping. The smartphone can also be used to give the people useful tips on an active wallpaper. It is believed that by measuring sleep, people can become self-aware and can improve their sleep behaviour themselves.

## Specifications

### NOX-T3

*Storage memory capacity:* 1 GB

*Recording time:* Up to 24 hours

*PC communications:* USB 2.0 hi-speed

*Power source:* One 1.5 V AA lithium battery

*Recorded signals:* Thorax and abdomen RIP nasal pressure/mask pressure snore signal audio channel, 2 bipolar channels, position activity, SpO<sub>2</sub>, pulse, plethysmography, signal quality EtCO<sub>2</sub> (optional)

*Activity/position signals:* Internal 3 axis,  $\pm 2$  g

*Sound signals:* Internal 3.8 kHz bandwidth, 16 bit ADC

*Wireless interface:* Bluetooth V2.0 wireless interface for external devices

## Applications

Sleep apnoea is a disorder characterized by abnormal pauses in breathing or shallow breathing during sleep. Ambulatory sleep monitors are used by the patients for recording various parameters relating to sleep disorders sleeping in the comfort of their own bed rather than spending the night at a sleep laboratory.

## 8

## Amino Acid Analyser

### Purpose

Amino acid analyser is an analytical instrument to analyse the amino acids present in body fluids such as urine, serum, and blood and in food samples. The measurement of amino acids is an essential element of physiological and nutritional studies and thus for monitoring the growth of cells in cultures, as used in the production of biopharmaceuticals. These tests are performed routinely in biochemical, medical, and biological laboratories. They are essential to determine the purity and chemical composition of a protein or peptide. In addition, analysis of amino acids is required in several areas of research and considered as a fundamental tool in product analysis.

### Principle

Most of the nutrients that are necessary for life activities in the human body are proteins. Amino acids are the components of all proteins and as such are essential for the growth and well-being of living organisms. Some are metabolized from the diet by hydrolysis resulting from enzyme activity, while others are synthesized within the organism. Therefore, the presence, distribution or absence of any amino acid in living tissues signifies normality or abnormality in the organism. There are 22 amino acids that combine to form proteins, and they perform important roles in various biological activities, including metabolism, immunity, digestion, central nervous system function, growth and development, biological protection, and locomotion.

### Methods of Analysis

Amino acids are distinguishable from each other only by one or two atoms in their structure. Although the concentration of any free amino acid can be accurately

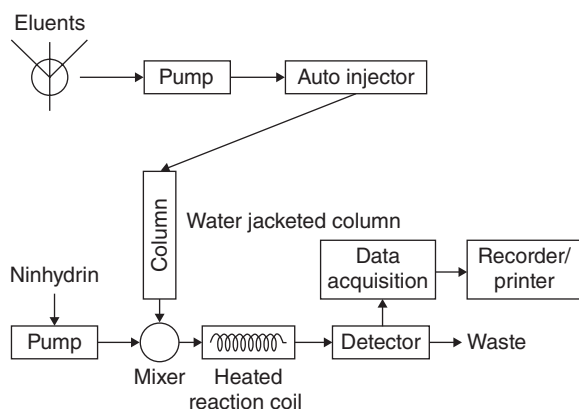
measured colorimetrically, all except two must be measured at the same wavelength. Therefore, they cannot be distinguished from each other by this method, unless they have first been separated in a predictable sequence. The microtechnique of paper electrophoresis, when applied in this application, lacks resolution and reproducibility. Gas chromatography, though potentially fast and simple in operation, loses accuracy during the conversion of amino acids to the gaseous phase and cannot be used for samples containing proteins or polypeptides.

The most widely accepted conventional technique has been ion exchange chromatography column in which the stationary phase support is sulfonated polystyrene resin. The mobile phase of citrate buffer is programmed to form a gradient of increasing pH and ionic strength with time. The amino acids are detected by post-column reaction with ninhydrin, which is continuously added to the column effluent. The mixture is heated and passed through a colorimeter. The resulting blue colour is proportional to the amino acid concentration.

The method gives high accuracy, but the inconvenience of handling many individual samples and the long and laborious process of cleaning of glassware limits the deployment of the technique in routine analysis.

**Automated Amino Acid Analyser** For the separation, identification, and quantization of amino acids and related compounds, automatic instrumentation has been introduced. These instruments permit complete protein or peptide hydrolysate analyses with very small sample amounts and sensitivity of 0.05 mmol or less. The instruments commonly used for amino acid analysis are based on the automated chromatographic instrumentation techniques used for general analytical methodologies. The instrument may be typically a low pressure or high pressure liquid chromatograph capable of generating mobile phase gradients that separate the amino acid analytes on a chromatographic column.

Figure 8.1 shows the schematic diagram of the components and the flow system of a typical amino acid analyser. The system may employ several chromatographic ion exchange columns, having a precision bore having 0.9 cm inner diameter. At the bottom of each of these tubes is a porous Teflon disc, upon which the resin is supported. The sample containing 0.05–2.0 mmol of each amino compound is introduced at the top of



**Figure 8.1** Block diagram of an amino acid analyser based on post-column derivatization.

an ion exchange column. Buffer is supplied to the column from a reservoir by an accurate non-corrosive metering pump at a constant rate of 80.0 ml/h.

Flow pumps are the most important of all the functional elements in the liquid chromatographic system. They should be capable of producing a constant liquid flow to perform quantitative or qualitative analysis. The performance of the pump should not be affected by all adverse effects due to changes in the kind of liquid pumped, its viscosity and back pressure, etc. The pump is double-action and piston driven, in which each stroke performs both the intake and discharge functions simultaneously, and in which a valve is switched in synchronization with the piston movement, so as to achieve a constant liquid flow. The flow rate is varied by the replacement of a set of gears.

Before the buffers enter the pumps, trapped air is eliminated with a bubble-trap type de-aerator to ensure constant volume delivery by the pump and to prevent release of air in the resin bed of the ion exchange column. All columns are enclosed in thermostated water jacket, which can be easily removed for cleaning or replacement and facilitates draining of the resin from the column. The purpose of the water circulating bath is to keep the column temperature at a constant level. The bath is equipped with a 400 W heater, which operates under the control and action of a temperature-sensing electronic circuit. Another heater of 500 W is provided to raise the temperature faster than usual. The circulating water is pumped at a flow rate of about 2 l/min. The bath is equipped with a cooling coil, which is used in case water temperature lower than the room temperature is required.

The complete analysis process is unattended after the sample is applied and initial adjustments are made. As the buffer and sample are pumped through a column, the amino compounds in the mixture separate according to the difference in the affinity that they have for the adsorbent. The resolved amino compounds emerge from the bottom of the column and flow through the capillary tubing to a column selector manifold. Here the column effluent is mixed with a ninhydrin reagent supplied by a pump at a constant rate (typically 40.0 ml/h). The mixture then flows through a reaction coil of Teflon capillary tubing contained in a reaction bath maintained at a temperature of 100°C. The reaction coil is volumetrically calibrated so that the time required for a given portion of solution to pass through the reaction coil is optimum for complete reaction between the amino acids and ninhydrin reagent to produce colours. The stream then passes through a three unit photometer, where the absorbance values at wavelengths 440 and 570 nm are measured for each reaction product. Two of the three photometer units have different absorption path lengths at 570 nm, enabling a wide range of colour concentrations to be measured.

Alternatively, a single photometer is equipped with three interference filters, which are mounted 120° apart, on a revolving wheel. They are switched in cycles by synchronizing signals generated by the recorder. A special wheel is used to turn the filter revolver by 120°, as a servo motor, which drives the cam makes one complete turn. The time required for the motor to make one complete turn is about 0.5 seconds. The absorbance flow cell has a standard thickness of 2 mm. This is a continuous flow type cell and the liquid flows upwards. Photo diodes are used as light source. The photodetector is a photodiode array whose output goes to the PC or a recorder after due amplification. The baseline is established at zero absorbance on the recorder chart, when a blank buffer ninhydrin solution is passed through the photometer. The entire analytical process is automated with the aid of a programming device and a complete

array of electrical controls, which automatically safeguard the operation day and night. Most amino acids do not have characteristic ultraviolet or visible light absorption spectra, and neither are they fluorescent. Therefore, the amino groups are selectively modified to form substances showing fluorescence or visible light absorption and then detected.

**Typical Automated Amino Acid Analyser** All modern amino acid analysis systems are fully automatic in which almost all the functions of the analyser are computer-controlled from sample injection to data processing by the software. They include various analytical standard programs and all the requisite information required to perform the analysis. They mostly adopt classical amino acid analysis methodology based on the basic principle of the continuous flow chromatography procedure. Figure 8.2 shows a typical commercial amino acid analyser from M/s Biochrom, United Kingdom. The system comprises an autosampler, chromatographic unit, photometer, and PC including processing software. The programming features include programming of buffers, flow rates, and temperatures, giving the instrument the ability to run several programs without user intervention.

The analysis is initiated after placing the standard solution, sample solution, and special reagent in the autosampler rack. The *autosampler* aspirates each of these solutions and discharges them into an empty vial for mixing and dilution. The autosampler may have a capacity of loading up to 96 samples. Sample volumes can be programmed from 1 to 5000  $\mu\text{l}$  depending on the loop fitted, with up to nine injections per vial. The sampler provides a wide loading range without any sample wastage. The standard 1.8 ml vials are utilized for most applications, but 300  $\mu\text{l}$  volume vials can be used when only a small volume of the sample is available. As sample numbers increase and sample volumes decrease, it is required to dispense low volumes of liquids rapidly, accurately, and reproducibly. This requirement is met by using microtitre plates and the provision to deliver volumes of liquid as small as 2  $\mu\text{l}$  using a non-contact delivery technique, thus eliminating cross contamination. The sampler is software controlled in which the functions of the autosampler including vial number, sampling method, and injection volume are all specified in the sample list editor.

The analytical column, pump head and fluidics fittings are all made from such materials as to minimize contamination and to ensure long operational life of the instrument. The system employing *ceramic pumps* provides metal-free pumping surfaces,



**Figure 8.2** Amino Acid analyser BioChem 30+. Source: Courtesy of M/s Biochrom, UK.

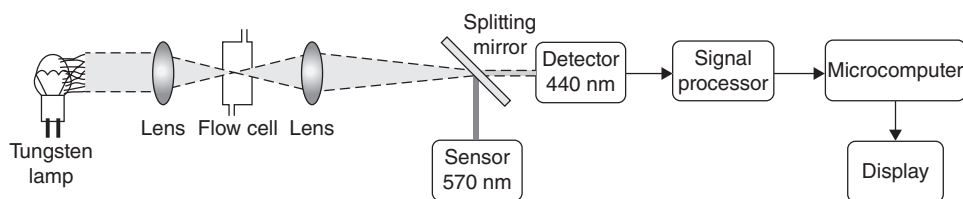
ensures constant flow and low pulsation, and eliminates corrosion. Very little maintenance is required because all the pumps have an automatic piston flush system. Lithium high performance *columns* are used, which allows a full routine analysis of physiological fluids. The system operation is performed through graphic user interface, which shows the operational information of the instrument in real time. It is fully integrated with the data handling software that allows the user to develop methods, design custom-oriented reports, examine calibration curves, acquire and process data, and generate and run batch sequences all from a single window. The system can be network-configured for secure data storage and to maintain data to meet regulatory requirements. A UV/visible spectrophotometer is used to make absorbance and transmission measurements of samples.

The process of analysis in this system starts by loading the sample containing a mixture of amino acids onto a column of cation exchange resin. Buffers of varying pH and ionic strength are then pumped through the column to separate the various amino acids. The temperature of the column (20–100 °C) is tightly controlled by using a Peltier device. The temperature can be set, if required, to achieve the required separation. The column eluent is mixed with the ninhydrin reagent, and the resulting mixture is passed through the reaction coil maintained at high temperature (50–150 °C). The dosing pump for ninhydrin delivery and flushing of the reaction coil after each run provides programmable flow rate from 0.01 to 2.0 ml/min.

The reaction coil is a coiled capillary for the colour reaction of the amino acid–ninhydrin complex. The reaction coil is automatically flushed with a washing solution after each run to prevent the blockage of the capillary. In the reaction coil, ninhydrin reacts with the amino acids present in the elute to form coloured compounds. The amount of coloured compound produced is directly proportional to the quantity of amino acid present in the elute.

From the reaction coil, the eluate/ninhydrin mixture goes to the photometer unit where the amount of each coloured compound is determined by measuring the amount of light absorbed. The light absorption is measured at two wavelengths, as some amino acids develop coloured compounds, which absorb light at a wavelength of 440 nm, whereas other amino acid coloured compounds absorb light at 570 nm. A light splitting mirror as shown in Figure 8.3 is used for the amino acid detection at 440 and 570 nm wavelengths. From the photometer, the output goes to a two channel chart recorder, which plots the amino acid concentrations as a series of peaks. The retention time of the peak on the chart identifies the amino acid and the area under the peak indicates the quantity of amino acid present.

As an amino acid analyser is a comparative instrument, calibration procedure is required to be performed before the analysis process is started. After each sample



**Figure 8.3** Working principle of photometer suitable for analysis of amino acids.



analysis, the column must be regenerated by pumping a strong base through the column that is followed by a buffer, which equilibrates the column prior to the next analysis. A buffer monitoring system reminds the user to top up buffers and reagents before a series of samples are made to run. Some systems, such as from Shimadzu and Ajinomoto Co., use a special-purpose, fast analysis column and a liquid chromatograph–mass spectrometer (LCMS), which allows ultra-fast analysis speeds, and help to achieve the simultaneous analysis of up to 38 amino acid in just nine minutes.

## Specifications

*Reaction module flow rate:* Adjustable from 0.01 to 2.0 ml/min

*Photometer:* Dual filter photometer (440 and 570 nm); optional fluorescence detector

*Column:* Temperature-controlled column oven ( $20\text{--}99^{\circ}\text{C} \pm 1^{\circ}\text{C}$ )

*Derivatization reactor temperature (post-column):* Up to  $180^{\circ}\text{C} \pm 1^{\circ}\text{C}$

*Physiological sample analysis time:* 70–180 minutes.

*Sample compartment:* Temperature controlled ( $5\text{--}70^{\circ}\text{C}$ )

*Solvent delivery flow rate:* 0.01–10.00 ml/min

*Solvent delivery maximum pressure:* Up to 400 bar (6000 psi)

## Applications

The important applications of amino acid analyser are in the fields of life sciences (protein structure), pharmaceuticals (medicine for nutrients), food and beverages, measurement of the essential amino acids found in food, and clinical (diagnosis of amino acid levels and deficiencies) fields. The techniques of amino acid analyses have gained paramount importance in biochemical research during the past couple of decades.

# 9

## Anaesthesia Machine

### Purpose

An anaesthesia machine is a device that is generally used during surgical interventions so that the patient does not feel pain and discomfort. It also helps to provide comfortable and favourable conditions to the surgeon to allow them to carry out the surgical procedure. Anaesthesia is administered to the patient to control the consciousness, analgesia, or both during the intervention. The machine is designed to perform four essential functions: accurately mixing anaesthetic gases and vapours, enabling patient ventilation, providing oxygen, and minimizing anaesthesia-related risks to patients and staff.



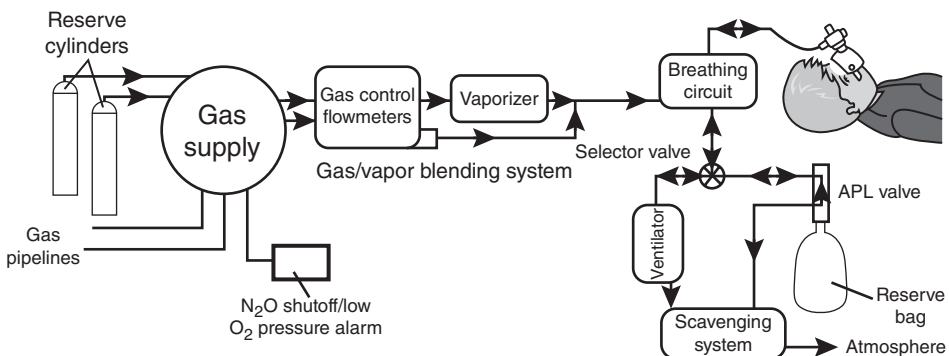
## Principle

The anaesthesia machine delivers a precisely known but variable gas mixture including anaesthetic and life-sustaining gases to the patient's respiratory system. Generally, a variable concentration gas mixture of oxygen, nitrous oxide, and anaesthetic vapour like ether or halothane is obtained from the machine and is made to flow through the breathing circuit to the patient.

When anaesthesia is given, the patient loses consciousness. The usual method is 'inhalation anaesthesia' in which gaseous anaesthetic agents are introduced in the patient's body via the lungs. It is called 'general anaesthesia' in which the anaesthetic agent reaches the brain via the bloodstream. Examples of such agents are diethyl ether, chloroform, halothane, cyclopropane, and nitrous oxide ( $N_2O$ , laughing gas). During anaesthesia, the anaesthetics and oxygen are administered in the required amount and any excess carbon dioxide is eliminated. In the superficial stages of anaesthesia, the patient can breathe independently with spontaneous ventilation. However, at a greater depth of anaesthesia, it may be necessary to support the patient with artificial ventilation known as controlled ventilation.

Figure 9.1 illustrates a block diagram of an anaesthesia machine. The machine performs four essential functions: (i) accurately mixes anaesthetic gases and vapours, (ii) provides oxygen, (iii) enables patient ventilation, and (iv) minimizes anaesthesia-related risks to patient and associated staff. The machine has a set of system function and breathing circuit indicators, which include a number of monitors and alarm systems for indicating levels and variations of different anaesthetic agent concentrations in breathed gas mixtures and status of physiological parameters. Essentially, a modern anaesthetic machine includes the following subsystems:

- (i) Gas supplies: Pipelines and cylinders
- (ii) Gas flow measurement and control (flowmeters)
- (iii) Vapour delivery
- (iv) Humidification
- (v) Patient breathing circuit
- (vi) Ventilators
- (vii) Scavenging
- (viii) Monitoring system



**Figure 9.1** Block diagram of continuous flow anaesthesia system.

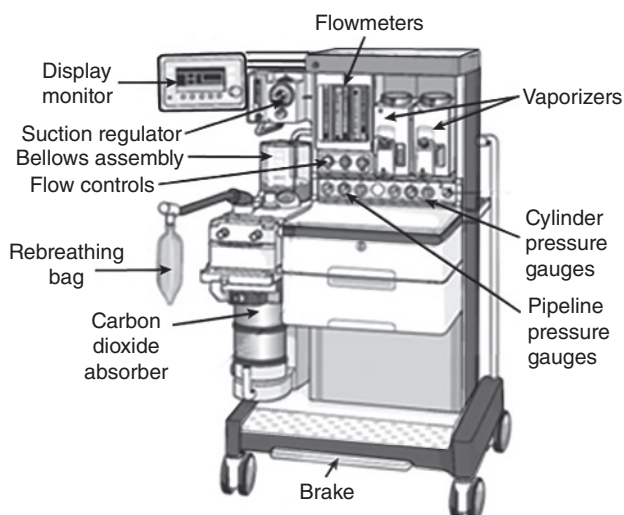
Over the years, the anaesthetic machines have retained the essential elements, technology, and design of the original Boyle's concept of controlled gas delivery. However, safety specifications have enhanced standardization of features between different makes of machines and models. With advancements in technology, computer-controlled anaesthesia systems have become common. The various controls in a modern anaesthesia machine are shown in Figure 9.2. The machine is highly sophisticated and incorporates many built-in safety features and devices, such as a breathing circuit, monitors, a mechanical ventilator, and one or more microprocessors that can enhance, integrate, and monitor all system components. In case monitors are not built in, they can be easily integrated with the basic machine. They usually have modular designs that allow a wide variety of optional configurations and features even within the same product line. The term anaesthesia workstation is therefore often used for modern anaesthesia machines due to their various control and monitoring functions. Use of microprocessors provides features such as sophisticated ventilator modes, automated record-keeping, and networking with local or remote monitors as well as hospital information systems.

The machine is constructed from box-shaped sections of welded steel or aluminium that provide a rigid metal framework. The entire structure is mounted on wheels with antistatic tyres and brakes. Antistatic measures reduce the risk of ignition where flammable vapours are employed. All machines are usually mains powered; however, a rechargeable battery provides up to 60 minutes of backup power. Modern machines even incorporate a ventilator, suction unit, and patient monitoring systems.

### Gas Supply and Control

Gases can be provided to the anaesthesia machine from either a pressurized hospital central supply or small storage cylinders attached to the machine. Since  $O_2$  and  $N_2O$  are used in large quantities, they are usually drawn from the hospital's central gas supplies. *Centralized gas supply* systems consist of main and reserve supply, control equipment

**Figure 9.2** Typical controls on an anaesthesia machine.



such as valves and pressure regulators, a distribution pipeline, and numerous supply outlets. The system is also designed and operated that the necessary supply of gases (oxygen and nitrous oxide) is always available. The gas supplied by the hospital is regulated and maintained at 275–345 kPa (40–50 psi) at the wall outlet.

Another gas supply source is the *gas cylinders* located in yokes attached to the anaesthesia machine. This supply can be utilized as either the main source when a central gas supply does not exist or a reserve when central gas supply is available. The pressure in a full oxygen or air cylinder at 20°C is 137 bar. The pressures in full nitrous oxide and carbon dioxide cylinders are approximately 52 and 58 bar, respectively. Each gas entering the machine from a cylinder flows through a filter, one-way check valve, and primary regulator. Pressure gauges are fitted adjacent to each yoke and pipeline connection. These are calibrated, labelled, and colour-coded for each gas service. The machines usually include 'pin index safety system', which has been standardized to prevent the accidental fitting of a wrong cylinder to the yoke.

### **Gas Flow Measurement and Control**

Modern machines have interlocked oxygen and nitrous oxide flow controls. Most machines include an O<sub>2</sub> supply failure device and an alarm that protect the patient from inadequate O<sub>2</sub> supply. This can be achieved by a mechanical, pneumatic, or electronic mechanism. If the O<sub>2</sub> supply pressure drops below about 25–30 psi, the unit decreases or shuts off the flow of the other gases and activates an alarm. Flow control valves are used to govern the transition from high to low pressure system. They reduce the pressure to 275 kPa (40 psi) before the gas flows through the machine.

Regulations require that there must be safeguards of oxygen–nitrous oxide ratio, which need a minimum continuous low flow of oxygen varying from 200 to 300 ml/min, as indicated by the flowmeter. This is achieved through mechanical devices that prevent the delivery of gas mixtures with an oxygen concentration below a low limit. Oxygen–nitrous oxide ratios vary from 25 : 75 to 30 : 70, depending on the manufacturer. Flowmeters may be mechanical or electronic. Modern machines use microprocessors to control gas flow and the flow is indicated electronically by a numerical display. A paramagnetic oxygen analyser is used to continuously sample the gas mixtures from the flowmeters.

### **Vaporizer**

The various liquids that possess anaesthetic properties are quite strong to be used as pure vapours. They are required to be diluted in a carrier gas such as air and/or oxygen, or nitrous oxide and oxygen. A vaporizer is used to allow vaporization of the liquid anaesthetic agent and its subsequent admixture with a carrier gas for administration to a patient. The vaporizers produce an accurate gaseous concentration from a volatile liquid anaesthetic. There are several types of vaporizers, including variable bypass (conventional), heated blender, and measured flow type. A few anaesthesia units now have a liquid-injector type of vaporizer. This vaporizer is electronically controlled and injects the liquid aesthetic agent directly into the stream of gases.

In the *variable bypass vaporizer*, the carrier gas flow from the flowmeter is split into two streams in a known ratio: one stream known as 'chamber flow stream' flows over

the liquid agent, while the other stream goes through the bypass path and does not enter the vaporizing chamber. The final concentration can be controlled by varying the splitting ratio between the vaporizer gas and the bypass gas using an adjustable valve. The output of vaporizers is linear at the ambient temperature (up to 35°C) due to automatic temperature-compensating devices that increase carrier gas flow as the liquid volatile agent temperature decreases. The variable bypass vaporizers may be mechanically or electronically controlled.

Recent innovations have included injection of volatile agent into the fresh gas stream, at a rate calculated by computer to produce the desired concentration. Integrated electronic fresh gas flow measurement of varying gas mixtures enables the unit to dispense more accurately a dialled concentration, compared with traditional vaporizers. Each is designed and calibrated for a specific anaesthetic vapour. The conventional vaporizers have been replaced with vaporizer cassettes that are more lightweight (2–3 kg) and are virtually service-free.

### ***Humidification***

Dry gases supplied by the anaesthesia machine are likely to cause significant desiccation of mucus, which may result in retention of secretion, stopping of the mucus flow, and consequent fall in the lung compliance. Therefore, air or anaesthetic gases must be humidified. The humidification measures that are commonly employed include heated airway humidifiers, nebulizers, and heat and moisture exchangers. The temperature of the air delivery system is often monitored and controlled to help ensure that the air stream is maintained at the desired level of warmth. The thermistor sensor is coupled to a microcontroller designed to measure air stream temperature and interact with the controller, which controls and regulates the temperature of the air stream.

### ***Patient Breathing System***

The function of a patient breathing circuit is to deliver oxygen and anaesthetic gases to and from the patient and eliminate carbon dioxide. The system describes both the mode of operation and the apparatus by which inhalation agents are delivered to the patient. Carbon dioxide may be eliminated either by washout with adequate fresh gas flow or by soda lime absorption. The breathing system may be as follows:

*Rebreathing type:* This system involves rebreathing of some or all of the previously exhaled gases, including carbon dioxide and water vapour.

*Non-rebreathing type:* In this type, a fresh gas supply is delivered to the patient and rebreathing of previously exhaled gases is prevented. Usually, non-rebreathing type systems are more popular. This system involves the use of an unidirectional non-breathing valve. When fresh gas enters the inspiratory part of the system, it is either sucked in by the patient's inspiratory effort or blown in during controlled ventilation. The design of the non-rebreathing valve ensures that when it is open to admit inspiratory gas, it does not allow the flow from the expiratory part to get through it. During the expiratory phase, when the patient exhales, the reverse happens, as the inspiratory valve is occluded and the expiratory valve is opened to allow expiratory gases to escape.

**Circle patient breathing circuit:** It is the most popular breathing circuit and is a closed loop of large-bore, low pressure tubing divided into an inspiratory and an expiratory limb. The design of this type of breathing circuit is shown in Figure 9.3. Contained within this loop are two unidirectional valves, a CO<sub>2</sub> absorber, circuit gas venting (scavenging), an adjustable pressure-limiting valve, reservoir bag, and airway management equipment including masks and endotracheal tubes. The patient is connected to the absorber by two corrugated hoses, one inspiratory and the other expiratory.

The patient circuit consists of black corrugated antistatic rubber tube, a chrome plated tube fitting (T joint), a two litre rebreathing bag, a Heidbrink valve, and a face mask with an elbow fitting. The face mask is designed to fit the patient's face perfectly without any leaks and yet to exert the minimum of pressure, which might depress the jaws and cause respiratory obstruction. Unidirectional breathing valves are used to allow gases only in one direction. A highly compliant breathing bag helps to accumulate gas during exhalation so that a reservoir is available for the next inspiration. The bag provides a means for visually monitoring the spontaneous breathing pattern of the patient. The CO<sub>2</sub> absorber is soda lime in granule form placed in a container. The granules result in large volume and large surface area for efficient absorption of the CO<sub>2</sub> in the expired gas. The disposable breathing circuits are preferred to protect patients from infection.

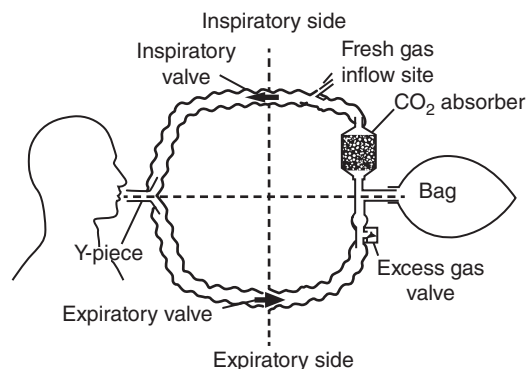
### Scavenging System

A scavenging system captures and exhausts waste gases to minimize the exposure of the operating room staff to harmful anaesthetic agents. Scavenging systems remove gas by a vacuum, a passive exhaust system, or both.

### Ventilation

At a greater depth of anaesthesia, it may be necessary to support the patient with artificial ventilation using a ventilator. The volume of a single breath (tidal volume) and the ventilation rate can be varied, either directly by setting them on the ventilator or indirectly by adjusting parameters such as the duration of inspiration, the inspiratory flow,

**Figure 9.3** Components of a circle breathing circuit.



and the ratio of inspiratory to expiratory time. The ventilatory pattern is adjusted to the varying needs of the patient. They operate either electronically or mechanically with pneumatic or electric power source. The microprocessor-controlled ventilator, with its dedicated breathing system, allows time-controlled, pressure-limited, constant volume ventilation for all patient groups within a tidal volume range of 40–1400 ml to meet the requirements for infants as well as adults.

Traditionally, anaesthetic machine ventilators have a minimal number of controls. However, the newer models are similar to critical care ventilators in their facilities and capabilities. The ventilator is either located within the mainframe of the anaesthesia machine or is usually attached as an accessory unit. The outlet of the ventilator connects directly to the patient breathing circuit of the anaesthetic delivery system at the location and in place of the breathing reservoir bag. The ventilator thus functions as a controller for both ventilation and circuit gas supply by replacing the functions of the reservoir bag and adjustable pressure limiting (APL) valve.

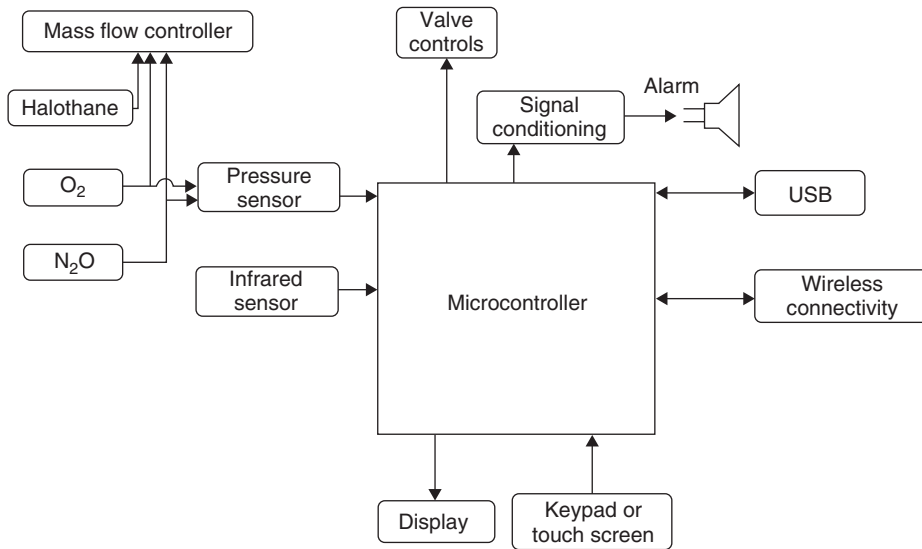
### ***Monitors and Alarms***

Anaesthesia systems must be able to monitor the function of the delivery system itself and the effect of the anaesthesia on the patient. They usually incorporate a set of equipment-related monitors, including those for airway pressure, expiratory volume, and inspired O<sub>2</sub> concentration. They can also include exhaled gas monitors, such as those for CO<sub>2</sub> concentration, N<sub>2</sub>O concentration, and agent concentration, or physiologic monitors such as those for blood O<sub>2</sub> saturation by pulse oximetry, electrocardiogram, invasive and noninvasive blood pressure, and temperature. During the entire procedure, not only is the machine performance monitored and controlled, but its status is also continually assessed and recorded. In order to meet these requirements, the impact of electronics on the design and functioning of the anaesthetic machine has been phenomenal.

The use of microprocessor technology allows us to fully integrate control and safety functions and protects the patient from: gas supply failure, electrical supply failure, hypoxic mixtures, disconnections, vaporizer function, excessive airway pressure exhaled minute volume outside preset limits, oxygen or volatile agents outside the preset limit, end tidal CO<sub>2</sub> outside present limits, and technical failure. All abnormal conditions cause an alarm to appear on the monitor panel, which also displays the nature of the fault. Computer application with appropriate data processing inputs and outputs, automation and integration of machine functions, and record-keeping are increasingly becoming possible.

Figure 9.4 shows essential parameters which are monitored and the electronic circuitry for processing the same in a typical anaesthesia machine. It is composed of different sections. The first is the gas supply and substance delivery system. In this part, the O<sub>2</sub> and the N<sub>2</sub>O are mixed in the desired proportion. The mass flow controller indicates the amount of anaesthetic substance delivered to the patient. The microcontroller (MCU) controls the electromechanical valve that adjusts the flow rate and the volume of the gases (halothane, O<sub>2</sub>, and N<sub>2</sub>O).

The pressures of the O<sub>2</sub> and N<sub>2</sub>O are monitored using pressure sensors. This measurement and the concentration of the substance (halothane) are the variables that control the valves. Further, the MCU measures the concentration of the substances in the blood using appropriate sensors. With these parameters, the MCU determines how



**Figure 9.4** Block diagram of an anaesthesia monitor.

much drug/air/oxygen needs to be delivered to the patient and the required power to apply to the valves.

The mixing process of the halothane, O<sub>2</sub>, and N<sub>2</sub>O takes place in the vaporizer. These substances need to be vaporized so that the patient can breathe them and receive the necessary anaesthesia. Therefore the MCU has to control the rate by adjusting the valves, depending on the pressure of the substances and their concentrations in the patient. Finally, the patient breathes the anaesthesia mixed through the mass flow controller.

The individual responses to a particular dose of anaesthetic vary considerably among the patients. Therefore, it is advisable to measure the effect of the anaesthetic on an individual patient's level of consciousness. A commonly used method to do so is to measure auditory evoked potentials (AEP), which is a neurophysiological indicator of the changes in the level of consciousness of a person during anaesthesia. This is an electrical signal contained within the electroencephalogram (EEG), which is obtained when an auditory stimulus is delivered to the patient's acoustic nerve. Specially designed algorithms have been developed for the fast extraction of the complex AEP signal to obtain the brain's response to the auditory stimulus of the acoustic nerve by mapping the signal and establishing an index, which is developed as a graphic curve and a single number on the monitor screen.

## Specifications

**Gas supply:** Separate indexed (pin index/Diameter Index Safety System, DISS/National Institute of Standards and Technology, NIST) provision for connecting central pipeline gas supply of oxygen, air, and nitrous oxide and mounting capability of two oxygen and two nitrous oxide gas cylinders, all fitted with pressure gauges



*Gas flow management:* O<sub>2</sub> control, 25–100%; fresh flow gas (O<sub>2</sub> and nitrous oxide), 0.25–18 l/min; emergency O<sub>2</sub> flush: >35 l/min

*Anaesthetic agent delivery (fresh gas control):* Content, 35 ml; delivery range, 0–18 kPa

*Ventilator:* Electronically driven and controlled turbine for spontaneous breathing; tidal volume, 20–1500 ml; breathing frequency: 3–80 l/min

*Monitoring:* Touch screen (at least 17 in. colour display) and alarm management facility of all gases and respiratory parameters, complete patient monitoring system

## Applications

Anaesthesia machines find applications for administering inhalation anaesthetic gases and vapours and for controlling ventilation in surgical procedures mostly in operating theatres.

# 10

## Anaesthesia Depth Monitor

### Purpose

Anaesthesia depth monitoring devices are designed to individualize delivered anaesthesia enabling accurate drug administration of anaesthetic agents against the state of consciousness of the patient. The objective is to render the patient unaware so that he/she does not feel pain during the surgery in the operating room or recall the events afterwards. Also, it is to be ensured that the patient does not react to surgical stimuli by movements during the operating procedure. The factors including the avoidance of consciousness or excessive anaesthetic depth are likely to result in better patient outcomes. Therefore, assessment of the depth of anaesthesia is fundamental to anaesthetic practice.

### Principle

Anaesthesia has been in use in medicine for more than a century, though without a clear understanding of the underlying physiological mechanisms that regulate the transition from a conscious state to an anaesthetic-induced unconsciousness. There are subjective and objective methods of assessing the depth of anaesthesia. Subjective methods depend on the interpretation of autonomic responses to noxious stimuli and depend on the experience and expertise of the anaesthetist. Objective methods depend on the use of the monitoring devices. The developments in the field of neurobiology and the digital computer technology have resulted in the availability of a number of devices that have helped to enhance our understanding of fundamental changes during brain activity by general anaesthetics.



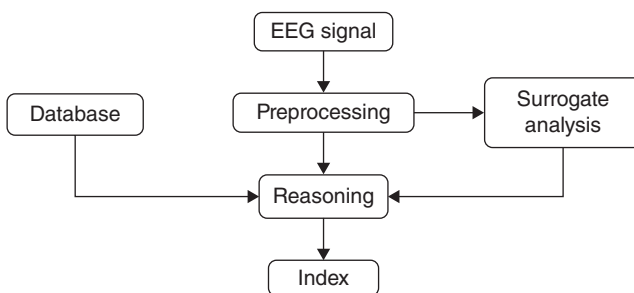
### Basic Design of Anaesthesia Depth Monitors

Most of the recent anaesthesia depth monitoring devices are based on the study of profound changes that occur due to anaesthesia in the brain's spontaneous electrical activity (electroencephalograph or EEG) recorded from electrodes placed on the scalp. The advances in computer hardware and signal processing algorithms have enabled the processing of EEG signals and the development of monitors that can provide estimate of the depth of general anaesthesia on a real-time basis.

From the engineers' perspective, the monitoring of the depth of anaesthesia is essentially a monitoring and control system. A representative block diagram of the monitor is shown in Figure 10.1. A soft sensor is used, consisting of electrodes on the patient's forehead, which are connected to suitable hardware and software. The monitoring is based on analysing the potential fluctuations of EEG signals that are acquired by the electrodes. The EEG signal is in the voltage range of  $1\text{--}500\mu\text{V}$  and comprises  $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\theta$  waves. After amplification and digitization of the analog EEG signal in an analog-to-digital converter, the preprocessing unit determines which part of the signal is required to be analysed.

Various signal processing algorithms are applied to the frequency, amplitude, latency, and/or phase relationship data derived from the raw EEG or auditory evoked potential (AEP), to generate a single number, which is usually referred to as an 'index' and typically scaled between 0 and 100. Then the artefacts arising from eye movement, swallowing, or heart activities are removed by artefact algorithm software. However, these artefacts are sometimes used as surrogate parameters, for example, the facial muscle electromyogram (EMG). The measured signal is then compared against the samples from the database and classified. Consequently, the index is as good as the database against which it was tested. Finally, the calculated index values are post-processed to minimize fluctuations on the output. This is done by averaging over past index values, which stabilizes the index, but may add delay into the index.

Commercially available anaesthesia depth monitors currently are of two types: those that measure and analyse spontaneous cortical electrical activity in the form of electroencephalogram (EEG) and those that measure stimulus-evoked electrical activity in the form of evoked potentials. In practice, the information obtained from EEG is often difficult to interpret instantaneously. So, an extension of these basic techniques is to convert the frontal EEG signal into a user-friendly, dimensionless index of depth of anaesthesia from 0 to 100, where 0 represents no electrical activity and 100 represents



**Figure 10.1** The block diagram for monitoring of depth of anaesthesia.

fully awake and responsive state. This index is known as *bispectral index* (BIS), which represents a measure of the level of a patient's consciousness by algorithmic analysis of their electroencephalogram (EEG) during general anaesthesia.

An awake, unsedated person typically would have a BIS values greater than 95. When drug-induced sedation is progressively administered, BIS numbers start declining. A reading of 40–60 indicates an adequate depth of hypnosis during general anaesthesia. Since the BIS algorithm is constantly updated, the BIS version must be checked when evaluating its performance. In general terms, during anaesthesia, the EEG shifts from a high frequency, low-amplitude signal ( $\sim 10\mu\text{V}$ ) to a more regular, lower frequency, higher amplitude signal.

The BIS monitor is the most studied and documented instrument that uses the spontaneous EEG for deriving depth of anaesthesia. The BIS is a statistically based, empirically derived complex parameter that comprises a combination of time domain, frequency domain, and high-order spectral sub-parameters. It is a proprietary signal processing technique that comprises EEG, EMG, and a previously recorded database of patterns corresponding to the movement of recovery of response to verbal command. The important multiple derived parameters forming BIS include power spectral analysis,  $\beta$ -ratio (calculated as a ratio between empirically determined frequency bands 30–47 Hz and 11–20 Hz), and analysis of phase relationships (bispectral analysis) between the component frequencies of the EEG signal. The undisclosed BIS algorithm quantifies the changes in these EEG features that best correlate with drug-induced changes in clinical state.

The system employs a disposable four-electrode sensor, which is attached on the patient's forehead. This makes the recording procedure easier in clinical situations. Originally, single electrodes were used, but now, three or four electrodes as shown in Figure 10.2 are integrated in one sensor to obtain the electroencephalographic signal from the forehead. The electrodes are same or similar to the self-adhesive pre-gelled standard electrocardiogram (ECG) electrodes. The electrical activity in the brain is picked up, digitized, and processed using a proprietary algorithm to calculate the BIS index. The BIS index is scaled to clinical end points as well as specific EEG features and thus provides a direct measure of the patient's response to anaesthetic drugs. The BIS system is usually integrated into patient monitoring devices. The system is designed to display both raw data from the EEG and a single number between 0 and 100



**Figure 10.2** The location of sensor incorporating four electrodes for monitoring depth of anaesthesia.

**Figure 10.3** Typical bispectral index (BIS)-based anaesthesia depth monitor.  
Source: Image Courtesy: M/s Medtronic USA.



representing BIS. This enables the anaesthesiologist to customize the precise type and amount of anaesthetic or sedative medication that each patient needs. A typical BIS-based commercial instrument is shown in Figure 10.3.

The anaesthesia depth monitors are known by different nomenclatures, such as cerebral state monitor (CSM), cortical injury monitor (CIM), Narcotrend monitor, patient state analyser (PSA), and anaesthesia monitor. The EEG index-based monitors include amplitude-integrated monitor, spectral index monitor, spectral edge frequency monitor, BIS monitor, and entropy- and complexity-based monitor.

The *Narcotrend monitor* (Monitor Technik, Bad Bramstedt, Germany) is another EEG monitor that is designed to measure the depth of anaesthesia. Its algorithm is based on pattern recognition of the raw EEG and classification of the EEG traces into different stages based on dimensionless Narcotrend index. The EEG signal is recorded by standard EEG electrodes for single- and double-channel registration, and automatically analysing the raw EEG data using spectral analysis produces a number of parameters. The information provided by Narcotrend includes the Narcotrend stage and index, the trend, the raw EEG signal and a power spectrum, and several derived EEG parameters.

The PSA based on the patient state index (PSI) involves monitoring four-channel EEG and processing it to generate PSI, which is a proprietary computed EEG variable that is related to the effect of anaesthetic agent. The PSI-based instrument is designed specifically for use in intra-operative or intensive care and clinical research laboratories.

The *Entropy Module* introduced in 2003 by the Datex-Ohmeda Inc. is based on monitoring irregularity in spontaneous brain and facial muscular activity. The concept is that increasing depth of anaesthesia causes increase in regularity of the EEG, which can be used to estimate the depth of anaesthesia. The EEG signals are divided into state entropy (SE) and response entropy (RE) based on the two frequency bands (SE, 0.8–32 Hz; RE, 0.8–47 Hz). Both are dimensionless numbers which may vary between 0–91 (SE) and 0–100 (RE), respectively. SE is based on EEG signal alone, which becomes more regular during anaesthesia, resulting in decreased entropy. RE is based on both EEG and

electromyography. The irregularity of the frontalis EMG diminishes as anaesthesia deepens. So, EMG complements the EEG by providing an indication of analgesic adequacy. During anaesthesia, SE and RE normally have the same values, but if RE diverges by more than 10 points from the SE value, the 'analgesic' component of the anaesthetic may be inadequate. The target range for entropy values is 40–60. However, the interpretation of the results is left entirely to the anaesthetist.

AEP have also been used to monitor the depth of anaesthesia. These potentials are the response of the auditory pathway when the patient is subject to sound stimuli. It is calculated by repeatedly applying an auditory stimulus to the patient and averaging the EEG signals that immediately follow each stimulus. This results in eliminating the non-stimulus-related portion of the EEG, retaining EEG only relating to the specific evoked potentials. These potentials can be classified into several useful segments according to the anatomical area of its origin and the time elapsed after the stimulus was delivered. As the concentration of anaesthetic drugs is progressively increased, it results in a delay in the transmission of the waveforms and a decrease in amplitude. The middle latency AEP, which is generated 40 and 60 ms after stimulation, represents neural activity within the thalamus and primary auditory cortex and is most often used as a measure of the anaesthetic effect. Compared to the raw EEG, AEP are less sensitive to artefacts that are random in time of occurrence since these artefacts tend to be eliminated from the EEG signal by repeated averaging.

For recording AEP, EEG is recorded while the short bilateral clicks of 2 ms duration at 7 Hz are emitted through headphones worn by the patient. The signal is then digitized and the artefacts are removed. The signal is then passed through several bandpass filters to extract various features in different frequency bands. The AEP are detected and analysed in the frequency range 25–65 Hz, while the analysis of the EEG in frequency band between 3 and 47 Hz is performed by a proprietary algorithm. Owing to low signal-to-noise ratio ( $<1 \mu\text{V}$  amplitude), the AEP is calculated by digitally averaging the previous 256 EEG waveforms. This rolling average is continuously updated seven times per second, and software expresses the characteristics of the waveform as an index value, which is monitored simultaneously to ensure optimal sedation of the patient during anaesthesia.

The first commercial instrument was based solely on AEP, whereas later versions also include spectral EEG parameters. All these parameters are monitored simultaneously in order to ensure optimal sedation of the patient during anaesthesia. Unlike other monitors, the instrument derives AEP (autoprogessive) index that can be displayed on two scales: either from 0 to 100 or from 0 to 60. The second scale is usually recommended, and the optimal anaesthesia is achieved if the index values are between 15 and 25.

The CSM from M/s Danmeter A/S, Denmark, is a portable, wireless monitor that uses the time and frequency domain analysis and shows the cerebral state index (CSI) on a 0–100 scale. It is built upon the EEG algorithm of its predecessor AEP monitor and uses the same electrodes.

Despite the development of a number of techniques and availability of several monitoring devices, no single method has been found to measure the depth of anaesthesia reliably for all anaesthetic agents. As the monitors do not measure consciousness, they may not be suitable for every patient undergoing general anaesthesia. However, their use is to some extent justified when there is no other means of measuring anaesthetic agent concentrations in the body.

## Specifications

*Type:* Bispectral index monitor in numbers from 0 to 100

*Computed parameters:* Bispectral index, suppression ratio, EMG signal quality index, and burst count

*User-defined displays:* Trend and real-time EEG waveforms

*Update rate:* Maximum 1 second for BIS number, 10 seconds for trend

*Alarms:* Auditory and visual, user-adjustable limits

*Filters:* On (2–70 Hz with notch) or Off (0.25–100 Hz)

*Input impedance:* 50 M $\Omega$

*Noise:* <0.3 V RMS (2.0 V peak to peak)

*Common mode rejection:* 110 dB at 50/60 Hz

## Applications

Anaesthesia depth monitors are important devices for use mostly in operating rooms because they enable anaesthesiologists to monitor and control the depth of a patient's anaesthesia. They are widely used in operating rooms and during outpatient surgery, intensive care units, and other clinical settings.

# 11

## Anorectal Manometry

### Purpose

Anorectal manometer is a commonly used device intended to study and evaluate patients with constipation or faecal incontinence. This test basically measures the pressures of the anal sphincter muscles, the sensation in the rectum, and the neural reflexes that are required for normal bowel movements. From these tests, useful information can be derived regarding the pathophysiology of disorders that affect defecation, continence, or anorectal pain. Using anorectal manometry, several factors such as anorectal sensory response, anorectal reflexes, and rectal compliance that contribute to faecal continence can be objectively measured. Sensory testing is usually performed along with anorectal manometry and is generally considered its part.

### Principle

The anal and rectal area comprises specialized muscles that are responsible to regulate proper passage of bowel movements. Normally, when stool enters the rectum, the

passage of stool at an inconvenient time is prevented by tightening of the anal sphincter muscle. The anal sphincter is the ring of muscles that control the opening and closing of the anus. Incontinence or leakage of stool is likely to happen in case this muscle is weak or does not contract in a timely way. Normally, when a person would like to have a bowel movement, the relaxation of anal sphincter muscles takes place, resulting in decrease of pressure and consequently facilitating evacuation of stool. In case the sphincter muscles tighten and do not exhibit relaxing tendency while pushing, it can lead to constipation.

Anal manometry provides valuable information as to how strong the sphincter muscles are and whether they can relax as they should when passing a stool. This information can be useful to the physician for treating patients with faecal incontinence or severe constipation. Anal manometry is essentially a pressure profile of the anal canal that provides information on the functional status of the internal and external anal sphincters. It is an objective method for assessing anal musculature tone, rectal compliance, and anorectal sensation and verifying the integrity of the anorectal inhibitory reflex. The advanced computer-based, multichannel manometry equipment provide graphic cross-sectional analysis of the anal canal, which is helpful to detect the presence of segmental sphincter defects.

Anorectal manometry is performed by placing a specially designed catheter with balloon into the lower rectum and anal canal. This pressure-sensitive device is connected to a transducer, which converts pressure into electronic signals. These signals are then recorded and displayed on a computer monitor. The average pressure measured at rest in the anal canal is termed as the *resting pressure*, while the highest pressure recorded along the anal canal is the maximum resting pressure. The increase in pressure over the resting canal pressure due to voluntary contraction of the anal sphincter is called the *squeeze pressure*, while the highest such increase is the maximum squeeze pressure. The resting pressure is largely indicative of the internal anal sphincter function, whereas the squeeze pressure indicates the strength of the external anal sphincter voluntary contraction. 'Normal' range for maximum resting pressure is 40–80 cm H<sub>2</sub>O and for maximum squeeze pressure is 100–200 cm H<sub>2</sub>O. In general, incontinent patients have lower pressures. The parameters evaluated during anal manometry include internal and external anal sphincter pressures; anal and rectal pressure response during straining; anal sphincter length; rectal sensation, capacity, and compliance; and anal sphincter muscle reflexes.

There are many different methods for performing anorectal manometry.

### **Water-Perfused Catheter**

In this technique, fluid-filled catheter assemblies are used to measure pressures from side openings. To perform the test, a catheter with a balloon is inserted into the anus. The catheter has radial side ports spaced 1, 2, 3, 4, 5, and 8 cm from the '0' reference point and is connected to strain gauge pressure transducers. This catheter has multiple canals through which water is perfused slowly using a pneumohydraulic pump. A balloon is tied to one end of the catheter having a capacity of 400 ml. The balloon is gradually inflated causing the nerves and muscles in the rectum and anus to begin to squeeze. The catheter is located inside the anorectum, but the closely spaced pressure transducers are placed outside the body and across the flow of water.

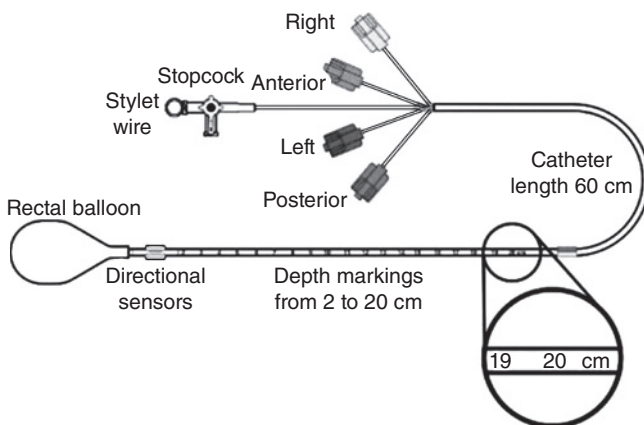
The pressure signals produced by the transducer are amplified and recorded by a microcontroller-based circuit. The recording device measures and records the rectal and anal canal pressures during rest and during voluntary contraction of the anal sphincter. The computerized system facilitates analysis of data and provide convenient means of storage for future retrieval of data or for generating a database. The maintenance of the water perfused system requires that there should be no air bubbles in the water tubing as they can affect the pressure recordings. The reliability of the system depends upon several factors, including compliance of the perfusion system, the size (diameter) of the catheter, rate of perfusion of water, and size of the side ports.

The catheter should be small and flexible as it would be more comfortable for the patient, but may get twisted in the anal canal. The outside diameter preferably should not exceed more than 8 mm in order to minimize perfusion artefacts. The catheters are made from different materials, but most of them are made of soft plastic. Most of the commonly used catheters are open-ended or side-open type. They usually have two to eight lumina, which can provide pressure measurement at different sections of the sphincter muscle during rest, squeeze, or push at a specific height; however four channels are usually adequate. The catheters are normally graduated at 1 cm intervals for vertical orientation. For recording longitudinal pressures in the anal canal, radial catheters are mostly used.

Water-perfused system usually have four radial ports (Figure 11.1) for routine evaluation and eight ports for scientific research studies. For measurement of rectal pressures, an open-end catheter is preferred. The investigation of the anorectal inhibitory reflex is done by spiral catheters. This catheter has eight ports that are set at 45° intervals, 5–8 mm apart on the longitudinal axis. A balloon at the very end of the catheter is used for rapid inflation to elicit the reflex.

### ***Solid State Pressure Sensor***

Solid state pressure transducers are microchips that are mounted on the microtip catheters for pressure measurement. This arrangement does not need any water perfusion setup and are therefore much easier to use and provide more reliable and accurate



**Figure 11.1** Directional anorectal manometry catheter for water-perfused system.



results. This is because the pressure sensors are placed directly at the source of pressure activity. The transducers are basically strain gauge elements, consisting of a pressure sensitive diaphragm with semiconductor strain gauges mounted on its inner surface. This type of measurement system is the most accurate catheter system for performing anorectal manometry. The system is user-friendly and does not suffer from limitations encountered in the perfused system. The catheters are available in a variety of configurations and come with attached probe adapters. The advantage of using this system is that it allows instantaneous and direct measurement of pressure and eliminates potential artefacts of perfusion.

Modern instruments are PC based, which can display three-dimensional physiological map of the anal sphincter along with the pressure data. This enables the physician to assess function and visualize symmetry with a single placement of a probe. Such an arrangement provides a better understanding of the anorectal anatomy with improved diagnostic outcome.

### ***High Resolution Anorectal Manometry (HRAM)***

High resolution anorectal manometry (HRAM) is a new approach of measuring anorectal pressures that offers more information than conventional manometry. These systems use catheters that have closely spaced water-perfused or solid state circumferentially oriented pressure sensors. Such an arrangement of sensors provides much better spatio-temporal pressurization than non-high resolution catheters. While non-high resolution catheters may have three or six unidirectional sensors, HRAM uses several closely spaced circumferential sensor elements along the longitudinal axis. Different systems use varying number of pressure-sensing elements and comprise 16 or 36 circumferential sensors. HRAM catheters provide a continuous and dynamic spatio-temporal mapping of anorectal pressures, allowing easier and more detailed data interpretation.

A special software helps to review all manometry data efficiently and provides fast and accurate determination of diagnostic parameters. The data can also be displayed in a three-dimensional plot. This enables rapid data interpretation via contour plots which can provide more diagnostic information. The display also allows to recognize sphincter damage or defects. HRAM significantly reduces the examination time because this technique does not require a pull-through procedure, and the topographic display enables rapid positioning of the probe. Although HRAM can be conducted with water-perfused or solid state catheters, solid state systems are preferred as they have better dynamic performance and accuracy. A typical high resolution anorectal catheter is shown in Figure 11.2.

### ***High Definition Anorectal Manometry (HD-ARM)***

High definition anorectal manometry (HD-ARM) provides a topographic and three-dimensional profile of anorectal pressure. The HD-ARM probe from M/s Given Imaging is 6.4 cm in length and has an outer diameter of 10.75 mm. The sensing segment comprises 256 sensing elements that are arranged in 16 rows, each of which has 16 circumferentially oriented sensor elements. The spacing between the sensors is 4 mm axially and 2 mm radially. The system displays data from all the 256 sensors individually. The





**Figure 11.2** Catheter for high resolution anorectal manometry. *Source:* Courtesy of M/s Laborie, USA.

balloon is composed of a non-latex, clear, thermoplastic elastomer and is 3.3 cm long, with a maximum capacity of 400 ml. The manometry and topographic images are displayed on a computer monitor using a proprietary software. The system operates at a frequency response of  $>20$  Hz, a scan rate of 10 Hz, and an output resolution of 0.1 mmHg. The HD-ARM requires thermal compensation to correct for the pressure drift with time. HD-ARM studies can be analysed in two dimensions (2D) or in 3D maps.

Figure 11.3 shows a typical high resolution solid state anorectal manometry system Solar GI, from M/s Laborie, that employs QuickView analysis program, 360° HRAM, 3D anorectal pressure topography, and new catheter technology. These systems provide information on several parameters including resting pressure, squeeze pressure, endurance squeeze, push-defecation test, sensation compliance, cough, external stimulus using toothpick, balloon expulsion, etc.

**Figure 11.3** Typical anorectal manometry system based on solid state pressure sensors. *Source:* Courtesy of M/s Laborie, USA.



## Specifications

*Equipment type:* HRAM

*Channels:* Up to 36 pressure channels

*Catheter type:* Fluid-filled and solid state catheters

*Pressure range:* 0–350 mmHg

*Pressure accuracy:* 1% or 2 mmHg

## Applications

Anorectal manometry is applied to patients with disorders of continence and defecation, including those with intractable constipation and faecal incontinence.

# 12

## Antibiotic Susceptibility Analyser

### Purpose

An antibiotic susceptibility analyser is an instrument used for testing the susceptibility or sensitivity of a bacterial strain (microorganisms) to a specific antibiotic or a panel of antibiotics. The test results are helpful to the clinician as a guide for the selection of the most appropriate treatment for the infection and the individual patient. The purpose of antimicrobial susceptibility testing is to predict the *in vivo* success or failure of antibiotic therapy. The tests to measure the growth response of an isolated organism to a particular drug or drugs are done *in vitro*. Antibiotic susceptibility testing (AST) can also be used to detect bacterial resistance to antibiotics.

### Principle

Antibiotic susceptibility is determined by measuring the effect of antimicrobial drug on multiplication of test organisms or on the metabolic products of organism growth. The microorganism is placed in contact with the antibiotic(s) and the test indicates if the microorganism will grow or not in the presence of the antibiotic(s). This measurement is reported to the physician in terms of the minimum inhibitory concentration (MIC), which reflects a microorganism's susceptibility or resistance to an antibiotic.

The most important requirement of any AST is the rapid and reliable prediction of antimicrobial success in the treatment of infection. Currently, AST is typically performed using either classical manual methods or growth-dependent automated systems. The automated instrumentation comes with various degrees of automation,

ranging from simple mechanization of traditional methods to fully automated systems. The automated systems that provide rapid antimicrobial susceptibility data in 3–10 hours are now available.

### ***Disc Diffusion Method***

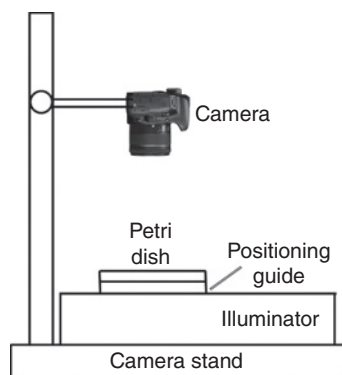
Disc diffusion or the Kirby-Bauer test is one of the classic techniques and is still very commonly used in clinical laboratories. This test provides the greatest flexibility and cost-effectiveness; however, the test takes a long time and there are limitations in its accuracy. The Kirby-Bauer method consists in placing small wafers containing antibiotics onto a plate upon which bacteria are growing. The plates are then incubated at 35–37°C for a period of 24 hours. If the bacteria are sensitive to the antibiotic, a clearing, or circular zone of inhibition, will be seen around the wafer indicating poor growth and susceptibility to that antimicrobial. Using reference tables, the size of zone can be related to the MIC and results recorded as whether the organism is susceptible (S), intermediately susceptible (I), or resistant (R) to that antibiotic. Modern instruments display an enlarged plate image with antibiotic discs and zone diameter reading with the option to adjust on screen by the user. The instruments automate disc position, drug code recognition, zone diameter reading and S–I–R interpretation.

More recently, there has been a growing interest in the use of improved instrumentation for reading disc diffusion tests. The systems use a camera or scanner to capture an image of the plate and then use an image analysis software to measure zone sizes. The automated zone readers minimize operator variability in reading plates and sometimes error in transcription of results. They also provide automatic interpretation of zone diameters using so-called ‘expert’ software that provide better quality of interpretation by the filtering of results according to a set of rules. High definition colour images taken with a 1.4 megapixel scientific-grade CCD camera ensure that zone measurements are fast, accurate, and reproducible. The zones (inhibition and AST) can be measured accurately to 0.5 mm with a theoretical detection limit of 0.1 mm. The system uses LED lighting system configured for illumination of samples.

Test results and high resolution images are saved automatically and may be printed or sent to the lab’s laboratory information system/laboratory information management system. This would enable efficient data handling, as well as the storage and retrieval of epidemiological information that could be utilized for local, regional, or national resistance surveillance.

### ***Agar Dilution Method***

Agar dilution susceptibility testing is regarded as the golden standard for all other susceptibility testing methods. The test is used to determine the minimum concentration of antimicrobial agent required to inhibit or kill microorganisms. The antibiotic to be tested is added to agar, which is then placed in dilution plates with serial dilution with varying levels of water. This is followed by the addition of the pathogen to be tested plus a reference plate that does not receive any antibiotics. The dilution plates are then incubated at 37°C for 16–18 hours. The incubation time may vary for bacteria populations that divide quickly. After incubation, the plates are examined to determine if bacterial expansion has occurred. The lowest concentration of antibiotics that stopped the spread



**Figure 12.1** Schematic of an imaging station using a digital camera for use with agar dilution method. The camera is positioned so that the plate barely fills the view field. A positioning guide enables fast placement of plates.

of the bacteria is considered to be the MIC of that bacteria. The earlier devices were simply mechanical, but most of the systems used today are motorized.

The images of agar plates can be acquired by two methods. In the first method, a digital camera mounted on top of the sample is used to acquire images. The arrangement is shown in Figure 12.1. The distance from the camera to the sample is kept approximately 15 cm for 24-spot plates. Images are acquired at the maximum resolution of the camera with no zoom. Alternatively, a scanner can also be used. In this case, plates are placed on a scanner, covered by soft gloss paper. The scanning is done at 1200 dpi, resulting in 8 bit greyscale images of the plates.

### **Broth Dilution System**

In this method, tests are performed with antibiotics in liquid media that is inoculated with isolated colonies from the patient specimen. Double dilutions of antibiotics are normally done and the lowest concentration of drug, which prevents visible growth after incubation, is determined. The tests can be performed by the macrodilution method using test tubes. However, it is preferable and convenient to use the microdilution method involving plastic trays (microtitre plates) having an array of test wells for serial dilutions of the selected antibiotics. A typical tray has 96 separate wells in 12 columns and 8 rows. The plate is just 130 mm long, 100 mm wide, and 13 mm deep. Microtitre plates or ready-to-use strips are commercially available.

### **Automated Systems**

In manually operated systems, visual readings are taken and results are manually encoded in the computer. The computer programs are simply used as an aid in recording, storage, and analysis of data and in the generation of hard copy reports. The automated systems incorporate microprocessor-controlled robotics for the manipulation of test cultures during incubation and instrument-based growth detection by turbidimetric or fluorometric methods before data handling and reporting.

Several automated susceptibility testing systems have been developed during the last three decades; however, only a few have become popular. One of them is the VITEK 2 from M/s bioMérieux shown in Figure 12.2. The instrument uses bar coding and a coded computer chip for specimen and test identification and employs robotics for card

**Figure 12.2** Automated antibiotic susceptibility testing system. *Source:* Image courtesy of BioMérieux, France.



filling and incubation. Instead of using standard size microtitre tray, a thin plastic card, comprising 64 wells or microcuvettes, is employed. The wells are linked by capillaries through which a bacterial test suspension passes to inoculate wells and rehydrate reagents in the wells. The cards are available as a variety of configurations of antimicrobials and identification media.

This system automates sample processing, including initial inoculum preparation, density verification, card filling, and card sealing. It automatically transfers cards to the reader/incubator and ejects them into a disposal bin at the end of testing. The system allows the testing of up to 20 antimicrobials, depending upon the species tested.

A 64-well card is read by an automated photometer, which takes kinetic turbidimetric readings every 15 minutes during the incubation and analysis period. Detection of growth in the inoculated plates is robotically automated and the data is managed using computer-based algorithms. Growth is determined up to 15 hours. LEDs are used as light sources at wavelengths of 660, 568, and 428 nm. The computer-based analysis of growth readings is used to determine the MICs of the antimicrobial agents included in various test cards.

## Specifications

*Cassette capacity:* 4 cassettes

*Maximum capacity:* 15 cards per cassette

*Dispenser capacity:* 1000 ml

*Dispensing volume:* 2.33–2.63 ml

*Pipettor dispensing volume:* 60–300  $\mu$ l  $\pm$ 5% or  $\pm$ 5  $\mu$ l

*Incubator temperature:* 35.5  $\pm$  1  $^{\circ}$ C

## Application

Antibiotic susceptibility analysers are used for microbial identification (bacteria and yeast), AST, and resistance mechanism detection and epidemiologic trending and

reporting. The accurate and efficient methods of rapid AST is extremely important for public health as these enable the clinicians to choose appropriate antibiotics to combat a particular infection in a patient, thus reducing the use of broad-spectrum antibiotics, which target many types of bacteria.

## 13

# Aortic Balloon Pump

### Purpose

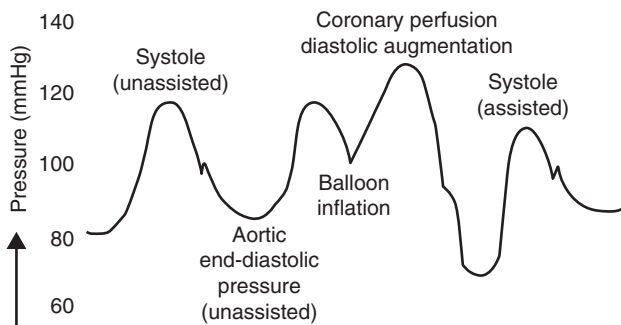
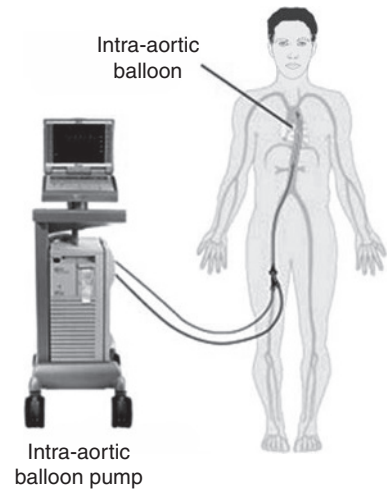
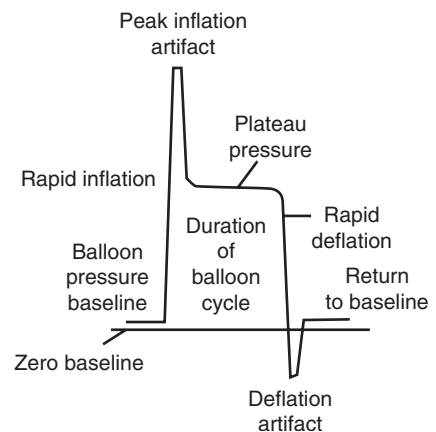
Intra-aortic balloon pump (IABP) is a device that provides temporary mechanical circulatory support to patients with certain heart conditions by assisting the heart to do its work. It achieves this by increasing the amount of oxygen to the heart while decreasing its workload with respect to systolic unloading and diastolic augmentation. This results in increase of cardiac output, ejection fraction, and coronary perfusion. An IABP is normally used to stabilize a person who is in the hospital for acute mitral valve regurgitation or severe heart failure. The device is only used for a short period of time, varying from few hours to some days.

### Principle

When the heart of a person does not receive enough oxygen due to blocked coronary arteries or other cardiac malfunction, it has to work harder to provide adequate level of oxygen to the body. IABP therapy helps restore the balance between supply and demand for oxygen that is required for the heart and other organs to function properly. The IABP therapy involves of two main components: one is a thin catheter with a balloon on the end of it and the other is the pump system as shown in Figure 13.1. The balloon is positioned in the aorta – the largest artery that takes blood from the heart to the rest of the body – after being introduced through an artery in the leg. The pump continually inflates and deflates the balloon with the rhythm of the heart. This helps the heart pump blood to the body and thus reduces the workload on the heart.

IABP assists the heart during both its rest phase and work phase. In the rest phase, after the left ventricle has finished contracting, the balloon inflates. This inflation pushes more oxygen-rich blood to the heart and the rest of the body. In the work phase, when the left ventricle is about to pump out blood, the balloon deflates. This deflation decreases the blood pressure in the aorta, which makes it easier for the heart to pump out more blood. This decreases the workload on the heart allowing it to function more efficiently. A typical aortic waveform when supported by IABP therapy is shown in Figure 13.2.

Figure 13.3 shows the normal shape of the balloon waveform. In a normal state, the balloon resting pressure is 0 to  $\pm 2.5$  mmHg. On inflation, there is a rapid upstroke of the

**Figure 13.1** Intra-aortic balloon pumping system.**Figure 13.2** Typical arterial waveform when supported by intra-aortic balloon pump (IABP) therapy.**Figure 13.3** Normal shape of the balloon waveform.

waveform. At the highest level of the inflation, an overshoot is seen due to the artefact caused by gas pressure in the pneumatic line. The waveform then settles to a plateau. This is followed by deflation that is seen as a rapid descent on the waveform. The descent also exhibits undershoot of the balloon pressure waveform, the reason for



which is the same as that of overshoot, except that the flow of the gas is in the reverse direction. The balloon pressure then returns to the baseline pressure.

### ***Instrumentation***

The IABP catheter is of double lumen having a long sausage-shaped inflatable balloon at the distal end. This is called an intra-aortic balloon (IAB). The computer console contains a pump that regulates inflation and deflation of the balloon. One lumen of the balloon catheter is connected to a pressure transducer that continuously monitors the arterial aortic pressure of the patient. The second lumen with a 10–15 cm balloon is connected to a helium gas reservoir. The console has a helium gas tank, which supplies gas for inflation for appropriate time. The console has a monitor that displays electrocardiogram (ECG) and arterial waveforms, which are helpful in properly controlling inflation and deflation timings. The IABP balloon is made of biocompatible polyurethane and is available in a wide range of sizes from 25 to 50 cc that will fit patients of any age and size. The catheter is usually 7.5 F and it may be sheathed or sheathless. The newer catheters have fibre optics-based pressure sensors for waveform detection and timing purposes.

The balloon is inserted percutaneously from the femoral artery, which acts as the entry point, and the proximal descending aorta as its destination. It is guided into the descending aorta, approximately 2 cm from the left subclavian artery. Once the balloon catheter is placed in the right position, its placement is confirmed by fluoroscopy or chest X-ray as the catheter tip is radio opaque. The IABP is designed to inflate and deflate contrary to the cardiac cycle. At the start of diastole, the balloon inflates, augmenting coronary perfusion. The balloon deflates at the beginning of systole ejecting the blood from the left ventricle, increasing the cardiac output by as much as 40%. When the inflation and deflation is correlated with ECG waveform, the balloon begins to inflate in the middle of the T-wave and to deflate before the end of the QRS complex. The technique is known as counterpulsation. There is a perforation at the balloon–catheter connection, which allows pressurized gas to move in and out of the balloon, causing inflation and deflation to take place. The IAB is designed to occlude 85–90% of the aortic lumen during inflation. Total occlusion of the aortic lumen is to be avoided as it may result in aortic wall trauma and damage to red blood cells and platelets. Inflation of the balloon can be triggered according to the patient's ECG, their blood pressure, a pacemaker if they have one, or a preset internal rate.

The balloon is mostly inflated with helium, which is an inert gas and is easily absorbed into the bloodstream in case of leakage or rupture. Moreover, its viscosity is extremely low compared with other gases, allowing significant volumes to be moved in and out of the balloon in short periods through a manageable diameter of tube. Also, helium diffuses rapidly and would therefore be removed from bubbles in the circulation faster than some gases minimizing chances of gas embolism in the event of a rupture of the balloon.

### ***The Console***

The IABP is driven by the balloon pump control console that determines when the balloon will inflate or deflate. The fibre optic arterial pressure (AP) signal coming from the transducer is converted to an aortic flow signal by an algorithm within the pump.

The aortic flow waveform is then utilized to set inflation of the balloon in synchronization with aortic valve closure on a beat to beat basis. This technique allows intra-beat timing of inflation to maintain consistent and appropriate timing.

It is desirable that the IABP has a consistent signal in order to perform trigger and timing functions. For this purpose, it requires a clear and clean signal from the patient. Both the ECG and the AP waveforms are the signals, which are normally utilized for this purpose and are therefore continuously monitored. If for some reason, like electrode falling off, the ECG trace is lost, the pump will automatically use the pressure signal for triggering of the inflation and deflation cycle. The IABP therapy may be timed to 1 : 1, 1 : 2, or 1 : 3. This implies that the balloon inflates and deflates according to each cardiac cycle, every second cardiac cycle or every third cardiac cycle, respectively. The operating controls are mostly of touch pad type in modern instruments. The on-board battery provides power for up to two hours.

### ***Fibre Optic Pressure Transducer***

Aortic pressure can be remotely measured by means of fluidic pressure transduction through the catheter and an external pressure electrical transducer. However, this system has a limited dynamic response due to fluid mass inertia and elasticity of the catheter conveying the fluid. Also, it may give unreliable and inconsistent aortic waveform. Alternatively, a miniature ( $\varnothing$  550  $\mu$ m) fibre optic-based pressure transducer is placed at the very tip of the IAB catheter where the aortic pressure waveform has to be measured. It allows in situ pressure measurement avoiding all fluidic transduction problems and related measurement uncertainties and provide accurate and fast, high quality measurements. This allows the hardware and algorithm to measure and identify key markers on the arterial waveform and optimize the left ventricular support. It also provides the potential for automatic in vivo calibration, further increasing the accuracy and quality of the IAB support.

The transducer is based on the principle of Fabry–Pérot white light interferometry. The sensor consists of a micromachined silicon diaphragm membrane that acts as the pressure sensing element that is bonded on a cup-shaped glass base. This forms a Fabry–Pérot cavity, whose optical length changes with the pressure variation. The sensor is connected to a multimode optical fibre that transmits the light between the sensor and the signal conditioner. White light from a lamp is directed towards the Fabry–Pérot cavity, which modulates the optical signal. The optical signal that is wavelength modulated, is then reflected back towards the signal conditioner where the cavity length/pressure-related information is extracted using cross-correlation technology. The fibre optic-based sensor is not disturbed by incident radio frequency (RF), electromagnetic (EM), or microwave (MW) fields that are often encountered in clinical environment. The quick response and high sensitivity of these sensors are useful factors in applications requiring detection of fast and subtle physiological signals, such as those available in IABP therapy.

## **Specifications**

*Pressure measurement:* Fibre optic pressure transducer

*Display:* At least 3 waveforms as ECG, invasive pressure and balloon

Pressure waveform: Indication for helium level in the cylinder and battery level

*Trigger:* Automatic trigger, i.e. ECG or pressure with 7 mmHg of pulse pressure

*Compressor:* Dual head diaphragm pump with brushless DC motor

*Gas:* Medical-grade helium ( $\text{He}^+$ ) – 0.5l (2900psi) or 0.69l (2200psi)

*Blood leak:* Detection for blood coming into the balloon lumen due to IABP leak

## Applications

IABP therapy is used temporarily to help patients recover from critical heart diseases or cardiac surgery or to wait until a transplant is performed. It is specifically employed in cases of cardiogenic shock, heart failure, acute heart attack, and support during high-risk percutaneous transluminal such as coronary (balloon) angioplasty and coronary stent placement.

# 14

## Apnoea Monitor

### Purpose

Apnoea monitor is a device used to detect the cessation of breathing (apnoea) in infants and even adults who are at risk of respiratory failure and to alert the parent or attendant about the condition. However, it is most commonly employed for monitoring neonates and infants. These monitors can be used in the hospital or in the patient's home.

### Principle

Apnoea may occur in premature babies during the first few weeks of life because of their immature nervous system. Apnoea may also precede the arrest of the heart and circulation in several clinical situations such as drug overdose, anaesthetic complications, and obstructive respiratory diseases. In case apnoea persists for a prolonged period, it is likely to severely damage the brain function. Therefore, apnoeic patients are required to be closely and constantly observed and monitored of their respiratory activity. Apnoea can be monitored both by contactless and contact-type methods. The various types of sensors used in the apnoea monitor include mattress motion sensor, pneumatic abdominal sensors, thermistors, proximal airway pressure sensors, and carbon dioxide ( $\text{CO}_2$ ) sensors. The other techniques for apnoea monitoring are using chest impedance electrodes, ultrasonic motion detectors, and pressure-sensitive air-filled mattresses.

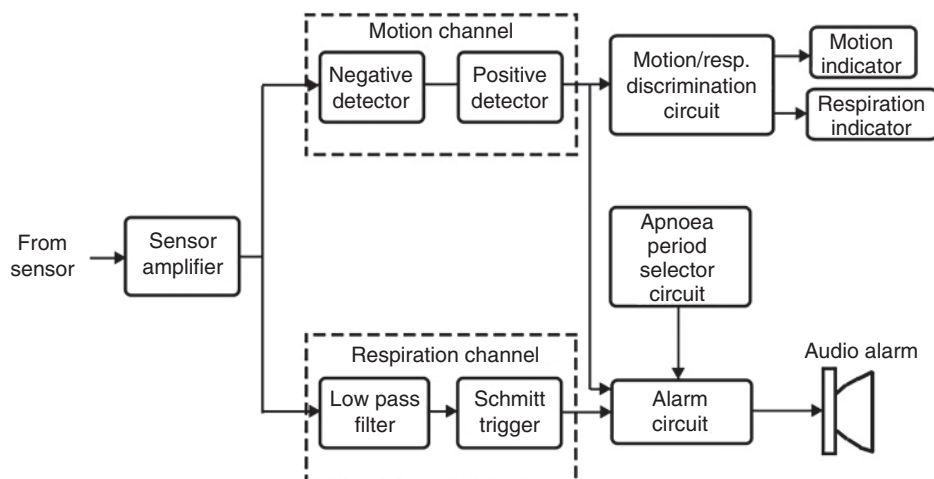


Figure 14.1 Block diagram of an apnoea monitor.

### Contactless Motion Sensors

These sensors detect breathing movements of the infant without direct patient contact. There are two types of such sensors: one uses devices that are placed under the infant, while the other uses a remotely located sensor to sense the movement of the infant. The latter type of sensors is mostly used outside of the hospital, such as in the home. One popular device involves the use of motion sensing pad on which the infant is simply placed. The device responds to periodic compression variations caused by movements of infant due to breathing activity that can be sensed using motion detector sensors. These sensors include piezoelectric polymer film and polyvinylidene fluoride, which has its surfaces metalized to form electrical contact. The major limitation of the motion sensing pad is its sensitivity to movements other than those related to respiratory efforts of the infant.

As apnoea monitors are basically motion detectors and are thus subject to other motion artefacts, which could result in giving false readings, there are instruments that usually provide means of elimination of these error sources. Figure 14.1 shows a block diagram of an apnoea monitor. It basically consists of an input amplifier circuit, followed by motion and respiration channels, a motion/respiration discrimination circuit, and an alarm circuit. The input circuit consists of a high input impedance amplifier, which couples the input signal from the sensor pad to the logic circuits. The sensor is generally a strain gauge transducer embedded in the mattress. The amplified signal goes to motion and respiration channels that are connected in parallel. The motion channel discriminates between motion and respiration as a function of frequency. In the case of motion signals, high level signals above a fixed threshold are detected by the sensor. In the respiration channel, a low pass filter is incorporated. Low frequency signals below 1.5 Hz (respiration) cause the output of the Schmitt trigger circuit to pulse at the respiration rate. Higher frequency signals, above 1.5 Hz (motion), cause the output of the trigger to go positive. Absence of the signal (apnoea) causes the output of the Schmitt trigger to go negative.



**Figure 14.2** Apnoea monitor from M/s SIMS Graseby Ltd, United Kingdom, which consists of an encapsulated foam pad connected to a plastic tube. Expansion of the baby's abdomen with each breath produces changes in pressure, which are detected using a pressure transducer.

The outputs of the motion and the respiration signals are combined in a comparator circuit, which compares the polarities of the motion and respiration channel signals to indicate respiration. The output of the discrimination detector also goes to an apnoea period selector circuit, a low frequency alarm oscillator and driver, a tone oscillator, and audio amplifier connected to a speaker. Audible alarm is given at a frequency of 800–1000 Hz, which is pulsed at 2 Hz. A typical portable apnoea monitor is shown in Figure 14.2.

### ***Mattress Monitor***

Many other *contactless methods* have been developed for monitoring the respiration of infants. The most successful apnoea monitors to date have been the mattress monitors. These instruments depend for their operation on the fact that the process of breathing redistributes an infant's weight, which can be detected by some form of a pressure sensitive pad or mattress on which the infant is nursed. The mattress, in its simplest form, is a multicompartment airbed, and in this case the weight redistribution forces air to flow from one compartment to another. The air flow is detected by the cooling effect it produces on a heated thermistor bead. Though the technique is simple, the main disadvantage with the air mattress is the short-term sensitivity variation and the double peaking effect when inspiration or expiration produces separate cooling of the thermistor.

### ***Capacitance-based Sensor***

Alternatively, a capacitance-type pressure sensor in the form of a thin square pad is usually placed under or slightly above the infant's head. Respiratory movements produce regular pressure changes on the pad, and these alter the capacitance between the electrode plates incorporated in the pad. This capacitance change is measured by applying a 200 kHz signal across the electrodes and by detecting the current flow with a phase-sensitive amplifier. Two types of electrodes can be used: (i) 70 mm plates, 350 mm apart in a plastic tube placed alongside the body, and (ii) 250 mm long, 60 mm diameter

cylinders placed one on either side of the body. This system is much too sensitive to people moving nearby and thus an electrically screened incubator is essential for the infant.

### **Inductive Sensor**

Another method of detecting apnoea is based on electromagnetic induction. It consists in passing a high frequency alternating current through a transmitting coil and creating an alternating magnetic field. The transmitting coil is placed at some distance from the infant. The receiving coil is applied on to the abdomen of the infant. The alternating magnetic field induces an emf in the receiving coil. The movement of the abdominal wall with the infant's respiration results in inducing an amplitude-modulated signal in the receiving coil. If this amplitude-modulated signal is demodulated, the modulation frequency corresponding to the respiration frequency can be recovered.

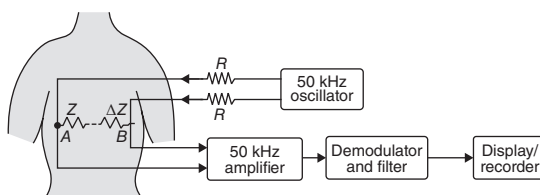
### **Radiation Reflection**

Another contactless method for monitoring the breathing activity of premature babies is using electromagnetic radiation in the microwave range. It operates by directing low intensity microwave energy (10 GHz) at the infant to be monitored and detecting this energy, after its reflection from the moving chest or abdominal surface of the infant. The difference between the transmitted and received microwave frequencies (Doppler shift) provides a signal voltage, which can be amplified and used as an indicator of the continuance of respiratory activity. Other radiation reflection-based sensors are ultra-sonic Doppler (sonar) or infrared radiation. The problem with these methods is that the movement of any surface that reflects the radiation will be detected. The instruments based on this principle have therefore not met with commercial success.

### **Impedance Method**

This is an indirect technique for detection of apnoea involving the detection of respiratory activity through small changes in electrical impedance as air enters and leaves the lungs and as the blood volume changes in the thoracic cavity. Using externally applied electrodes on the thorax, the impedance pneumograph measures rate through the relationship between respiratory depth and thoracic impedance change. The method consists in passing a high frequency current through the appropriately placed electrodes on the surface of the body, injecting high frequency current and detecting the modulated signal due to respiratory cycle. This is shown in Figure 14.3. To avoid the stimulation of sensory receptors, nerves and muscle, currents higher in frequency than 5 kHz must be used for the measurement by impedance method. The frequencies usually employed lie

**Figure 14.3** Principle of impedance pneumography by two electrode method.



in the range of 20–100 kHz. The electrode used for impedance pneumograph are of the self-adhesive type. The electrodes, when the skin is properly prepared, offer an impedance of 150–200  $\Omega$ . The change in impedance corresponding to each respiratory cycle is of the order of 1% of the base impedance. The instruments are usually microcontroller based with built-in memory for storage of readings.

Apnoea monitors are generally designed to give audiovisual signals under apnoeic conditions when no respiration occurs within a selectable period of 10, 20, or 30 seconds. Most of the apnoea monitors have two types of alarms: patient and system. Patient alarms are for apnoea, low breath rate, low/high heart rate, and low/high  $\text{SpO}_2$ . The system-related alarms are for conditions such as loose lead, loose probe, low battery, full memory, or accidental power off.

Traditionally, home apnoea monitoring devices have been designed to monitor respiration only, to detect sudden apnoea. This form of monitoring, however, is no longer considered sufficient, as even the best respiration detection technology used in infant apnoea monitors can fail to detect certain life-threatening event, such as the obstruction of air passages. Consequently, simultaneous monitoring of a second physiological parameter, such as heart rate and/or blood oxygen saturation, is recommended in order to detect the consequences of apnoea. Normally, an apnoea monitor measures both ECG and heart rate in a standard manner and respiration activity by means of impedance plethysmography. Monitoring the heart rate and respiration thus gives an extra measure of security.

Oxygen saturation is monitored through the integration of a commercially available pulse oximeter module. Central apnoea can be detected quickly since it results in the absence of respiratory movements. Obstructive apnoea can be detected when the level of oxygen has declined in the blood and/or results in slowing of the heart rate. The disadvantage of impedance pneumography technique is that the placement of the electrodes is very critical and is subject to cardiovascular artefact. This results from the detection of movement between the electrodes because of the cardiovascular system, rather than due to respiration.

## Specifications

*Respiration rate:* 4–150 breaths/min

*Apnoea alarm:* Delay settings of 10, 15, 20, 25, 30, and 40 seconds

*ECG range:* 10–275 bpm

*Alarms for heart rate:* Bradycardia, tachycardia

*System alarm:* Loose connection, low battery warning, full memory

*Memory capacity:* 2 MB, 1000 patient event listings, 100 ECG QRS, HR trend

## Applications

Apnoea monitors find applications both in the hospitals as well as in patient's home. In-hospital monitors are used to typically measure respiratory movements, heart rate, and pulse oximetry. Home apnoea monitors most frequently measure only respiratory movements and/or heart rate. They are generally used with premature infants who are otherwise ready for discharge from the medical facility.



## 15

# Argon Plasma Coagulator

### Purpose

Argon plasma coagulator (APC) is a special non-contact form of medical endoscopic procedure used for the management of bleeding and the devitalization of tissue abnormalities. APC has proven to be a safe, effective, and yet cost-efficient technique as compared to traditional laser treatment. This has become possible with the development of flexible probes, which are placed at some distance from the bleeding lesion for coagulation.

### Principle

Argon plasma coagulating technique has become the most commonly used endoscopic coagulation technique that involves the use of a jet of ionized argon gas (plasma) that is directed through a probe passed through the endoscope. The probe is placed at some distance from the bleeding lesion, and argon gas is ionized by a high voltage discharge. High frequency (HF) electric current is then conducted through the jet of gas, resulting in coagulation of the bleeding lesion on the other end of the jet. The procedure has been found to give few complications creating effective haemostasis and a homogeneous surface coagulation with a limited penetration depth. Since transmission of the electro-surgical current is by a non-contact technique as the instruments do not come into direct contact with tissue, the instruments almost never stick to the tissue. The APC produces a homogeneous current and its effects are more uniform and precise with less tissue carbonization and smoke than with laser or electric current, allowing better visualization of the operative field.

APC is basically a monopolar electrosurgical procedure in which electrical energy is transferred to the target tissue using ionized and, thus, conductive argon gas. Argon gas is chosen because it is biochemically inert, has a low breakdown voltage, and is relatively inexpensive. Also, it is a colourless, odourless, and tasteless noble gas, which is chemically inert and, therefore, non-toxic. The technique employs HF current to the targeted tissue in a non-contact mode in which the usual electrical current is substituted by the argon gas. The entire system includes an argon source, an HF current source, and the appropriate catheter that contains an electrode. Like any electrical system, the current requires a closed circuit to propagate. A second neutral electrode patch is placed at the hip of the patient that acts as a return path for the current. For the transfer of energy, it is important to ensure the greatest possible concentration of gas between the tip of the probe and the target tissue.

When the HF voltage is applied between the first electrode and the tissue, argon gas flows out of the catheter and gets ionized in the high voltage (6kV) electric field that has been created resulting in formation of plasma. Heat energy produced by this process causes the tissue coagulation or haemostasis. The heat evaporates intra- and extracellular water and denatures protein, producing the coagulative and destructive effects on tissue.

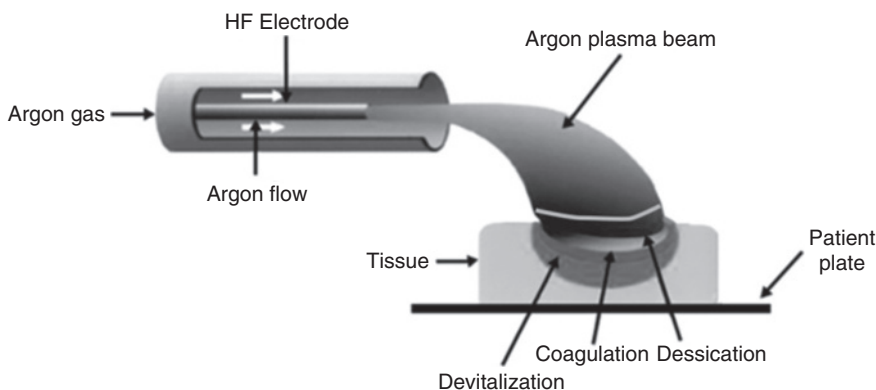
A desiccated tissue loses electric conductivity because of its higher electrical resistance. The APC beam then moves to the next viable area. In this way, the whole area is uniformly desiccated and, most importantly, at the same depth. The depth is generally limited to 3 mm at most, depending upon the application time. Thus, APC can hardly remove bulky tumour masses. Clinically, it is desired to keep carbonization or charring to a minimum. For that, argon gas is quite suitable as during the procedure, and it displaces oxygen, thereby minimizing carbonization and preventing an oxidation reaction.

When the probe is properly oriented, the current spreads out uniformly over a wide surface area as shown in Figure 15.1. The depth and tissue volume covered by the procedure depend on the voltage (power) applied to the gas and the application time. At power settings from 40 to 120 W and application times of  $\leq 2$  seconds, the depth of penetration is  $< 5$  mm. In APC, the probe can be up to a centimetre from the tissue surface and still generate current. If that distance is exceeded, the probe is too far away from the tissue surface, the circuit remains open, and no current is produced.

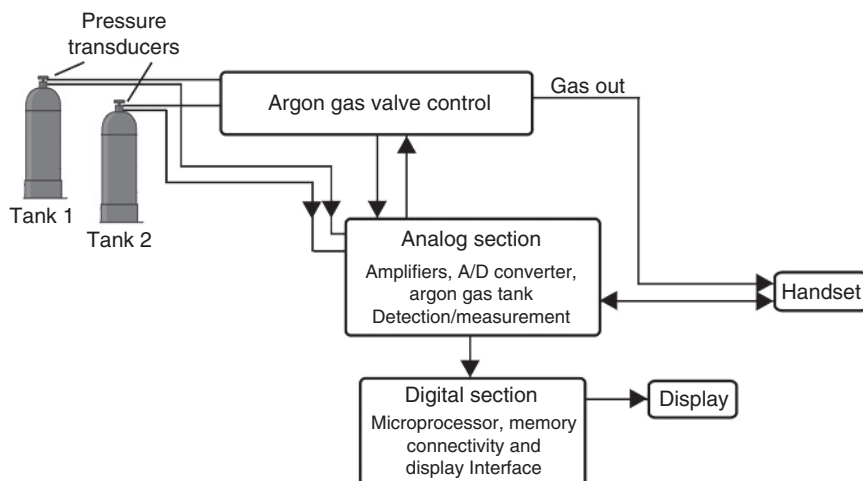
The argon plasma follows the path of least electrical resistance, regardless of whether the tissue lies directly in front of the electrode or lateral to it and regardless of the direction of the flow of the argon gas. The catheter probes for delivering the argon plasma are accordingly of two types depending upon the direction of the beam, i.e. beam parallel or perpendicular to the catheter axis. The current can be applied axially, laterally, or radially, depending on the indication. These catheters are covered with Teflon material and are disposable. There are two sizes available: 2.3 and 3.2 mm in diameter and 2.2 m in length each. The argon flow rates vary from 0.1 to 9 l/min.

### Block Diagram

The circuit diagram of a typical argon laser plasma coagulator is shown in Figure 15.2. The argon gas delivery is controlled by a single chip microprocessor. The unit can be connected to a computer with RS 232 interface for troubleshooting purposes. The supply of the argon gas is provided by one or two cylinders of compressed gas pressurized to a maximum of 2000 psig. The gas control system has a high pressure transducer and regulator, High Efficiency Particulate Air (HEPA) filter, control valve with dual inlet tank



**Figure 15.1** A typical argon plasma coagulator probe in which plasma is generated by ionized argon gas. Transfer of energy from the argon plasma coagulator (APC) probe to the tissue takes place through argon plasma.



**Figure 15.2** Block diagram of argon laser plasma coagulator.

selector valve, and a delivery pressure relief valve. The control system also comprises five fixed orifices capable of delivering flows of 0.5, 1, 2, 4, and 8 l/min. Argon passes from the gas tanks to the regulators, through the pressure transducers and leaves the regulators at 60 psig. Based on the selected flow rate, appropriate fixed rate orifices are opened and the rate is displayed in litre/min. The control circuit checks for any dosage error and sounds an alarm in such a case. The panel also displays the gas remaining in each tank.

The two pressure transducers measure the pressure at the argon gas inlet chamber and the argon gas outlet chamber. The third pressure transducer monitors the pressure the peritoneal cavity pressure. The electrical signals from each of these transducers are amplified and filtered. An A/D converter converts these analog signals to digital values. The A/D converters also convert analog signals from overvoltage monitors and tank measurement circuits to digital formats. The flow and pressure readings are displayed by digital display, while a bar graph shows the percentage of gas remaining in the tank. The Cut and Coag modes can be selected by handset or foot switch.

**Plasma Generation** The plasma is generated due to high voltage discharges taking place between active electrode and the tissue under treatment. The active electrode is a tungsten wire with a diameter of a few millimetres. It could also be a needle- or spatula-shaped tip made of stainless steel. The flow of argon takes place through a tube that surrounds the electrode. The discharge is ignited by an AC voltage with an amplitude of typically 4–6 kV and a frequency of typically 350 kHz. After breakdown, a current with a peak value of typically 2–5 A starts flowing, which induces the heating effect in the tissue. The oscillation then gets damped due to the discharging of the oscillating circuit within the generator. The plasma is maintained as long as the oscillating circuit is able to deliver enough current.

**APC Probe** The APC probe is a flexible device that is typically used in endoscopic interventional procedures. In principle, the probes differ according to their diameter, length, and circumferential tip design. The length of the endoscope and the size of a working channel dictate the diameter of the APC probe to be employed. The distal tip

design determines the direction of the argon gas flow and, for the most part, the plasma direction, which will create various plasma and tissue effects.

A wide range of applicators and probes are available for APC procedures in open surgery, endoscopy, and laparoscopy. Specialized range of instruments are available for the medical specialties of gastroenterology, ENT, bronchoscopy, laparoscopy, open surgery, etc., to meet the needs of different applications and anatomical sites. Different APC modes are suitable for different applications, depending on the location of the target tissue requiring treatment, and the intended desired clinical outcome. The APC modes are basically current waveforms used for coagulation in monopolar applications with more controllable thermal effects. They have different coagulation properties that are more suitable for specific clinical requirements. For example, pulses 1 time/s are used for focused coagulation, while pulses 16 times/s are used for widespread coagulation. A constant beam is often employed for devitalization of tissue.

Black rings are generally provided at intervals of 10 mm at the distal tip of the probe. In order to prevent the beam from damaging the end of the endoscope, the distal tip of the APC probe should be extended at least 10 mm outside the endoscope. The black marking rings are also helpful as a scale to estimate distance and the size of lesions.

The conventional electrosurgical units also include APCs to provide a controlled flow of argon over the active electrode. A variety of handsets provide argon-enhanced



**Figure 15.3** Electrosurgical unit VIO<sup>®</sup> ESU/APC System that includes argon plasma coagulator to provide a controlled flow of argon over the active electrode. *Source:* Courtesy of M/s ERBE, USA.

electrosurgery as well as standard electrosurgery. This provision allows improved visibility of the target tissue, a more finely directed coagulation effect, and enhanced control at higher power settings. The argon-enhanced coagulation permits the coagulation of certain tissue in a more controlled manner than with standard electrosurgical coagulation. One such commercial instrument from M/s ERBE, United States, is shown in Figure 15.3.

The increasing popularity of APC is due to its various advantages: effective and safe coagulation, non-contact mode of action, marked desiccation, no destruction of metal stents, little smoke or vapour, easily handled device, lower cost compared to laser, and, finally, no extended safety precautions.

## Specifications

*Type of gas (argon):* 4.8 (99.998% pure)

*Initial pressure:*  $5 \pm 2$  bar,  $72.5 \pm 29$  psi

*Max. final pressure:*  $2 \pm 0.4$  bar,  $29 \pm 5.8$  psi

*Adjustable gas flow:* 0.1–8 l/min

*Flushing duration:* 3 seconds

## Applications

APC finds applications in nearly every surgical specialist area, such as general and visceral surgery, urology, gynaecology, gastroenterological and bronchological endoscopy, and ENT. The major application fields are haemostasis and tissue devitalization, with a focus on endoscopic applications. APC is finding a remarkable spectrum of clinical applications, raising questions as to whether it should replace laser in clinical practice.

# 16

## Arrhythmia Monitor

### Purpose

Automated arrhythmia monitor is a device that is intended to identify an abnormality or disturbance in the rate and rhythm of a person's heartbeat. Although ECG has well served the purpose for the detection and diagnosis of such conditions for over a century, its interpretation is largely based on the expertise of the clinician. This is especially problematic in such situations, where the availability of medical experts is low or may not be readily available. Such a need is fulfilled, to some extent, by automatic arrhythmia monitoring systems that constantly scan ECG rhythm patterns and issues alarms to events that may be premonitory or life threatening.

## Principle

Any disturbance in the heart's normal rhythmic function is called an arrhythmia. It is a commonly encountered medical condition relating to a broad range of heart-related pathologies, some of which may point out to the development of impending serious heart diseases. It is possible to treat and reverse many of these dangerous episodes if they could be detected early and an advance alert of their onset could be made available. The need for early detection of the arrhythmias led to the establishment of coronary care units in hospitals in the early 1960s for the intensive monitoring and treatment of such patients. The continuous monitoring and timely detection of arrhythmias provided opportunities to effectively carry out resuscitation techniques such as cardiac massage and transthoracic defibrillation and save valuable lives. During the last three decades, however, attention has been focused on early detection and treatment of arrhythmias and the emphasis of treatment switched from resuscitation to aggressive prophylactic therapy.

An atrial arrhythmia can originate in any one of the upper chambers of the heart, left or right atrium. Similarly, ventricular arrhythmias occur in the ventricles, the lower chambers of the heart, which is likely to severely affect the blood pumping action of the heart. Examples of ventricular arrhythmias include ventricular fibrillation and ventricular tachycardia, whereas atrial arrhythmias include atrial fibrillation, atrial flutter, and supraventricular tachycardia. Ventricular tachycardia and ventricular fibrillation have rates of 120–240 and >240 bpm, respectively.

Detailed and extensive examination of ECG records have shown that abnormalities in the functioning of the heart invariably manifest themselves in ECG waveform, and, therefore, the arrhythmias can be monitored by recording and interpreting ECG. Usually, ECG testing is performed under three conditions: resting ECG, ECG stress test, and ambulatory ECG. In ambulatory monitoring, arrhythmia analysis is done in an offline fashion, whereas in implantable cardioverter defibrillator (ICD), implantable atrial defibrillators and automatic defibrillators (AEDs), the arrhythmia detection has to be done on real-time basis. All arrhythmia analysis algorithms in ICDs have heart rate as a fundamental component for detection of arrhythmias.

Diagnostic statements as observed from the ECG records are classified into two classes: (i) morphological statements, primarily based on ECG wave shapes that attempt to describe the state of the working muscle masses, and (ii) rhythm statements, concerned with the site and rate of the intrinsic cardiac pacemaker and the propagation of impulses through the conduction system. Arrhythmia monitors are available in various degrees of sophistication, but are mostly ventricular oriented, detecting most of the significant ventricular arrhythmias including ventricular premature beats, which comprise the majority of such events.

### ***Morphology Characterization***

Morphology refers to characteristics of the electrocardiogram (ECG) waveform, which are easily identifiable and measurable. Such features generally include peak-to-peak amplitude, slew rate of waveform, sequence of slope patterns, sequence of amplitude threshold crossings, statistical pattern recognition of total waveform shape by correlation coefficient measures, and others. This is based on analysing the shape of the QRS complexes and

separating beats into groups or clusters of similar morphology. Most algorithms for real-time arrhythmia analysis maintain no more than 10–20 clusters at a time, in order to limit the amount of computation needed to assign a QRS complex to a cluster.

*Timing classification:* It involves categorization of the QRS complexes based on the time interval between two of them, i.e. premature or late. The observed R-R interval is compared to an estimate of the expected R-R interval. If the R-R interval is less than 85% of the predicted interval, it is declared as premature. Similarly, if an R-R interval is greater than 110% of the predicted value, it is considered as long.

*Beat labelling:* Here, each QRS complex is assigned a physiologic label. For example, the possible beat labels that can be attached by a beat classification module may include the following types: normal, supraventricular premature beat, premature ventricular contraction (PVC), etc. This is the most complex form of the algorithm and is rarely disclosed by the manufacturers.

*Rhythm labelling:* This is the final stage in arrhythmia analysis. It is based on defined sequences of QRS complexes. Special detectors are employed to identify rhythms such as atrial fibrillation or ventricular fibrillation. The analysis systems are heavily oriented towards detecting ventricular arrhythmias, particularly single PVCs.

*Atrial fibrillation detection:* It is based on detecting abnormal rhythms from the timing sequence of QRS complexes.

*Ventricular fibrillation:* This is usually detected by frequency domain analysis. The system is characterized as a narrow band, low frequency signal with energy concentrated in a band around 5–6 Hz. It can be distinguished from noise (16–18 Hz) by appropriately designing bandpass filters.

The results of morphology characterization of the cardiac rhythm over long time periods may be presented in the form of a table or graphically. Trend plots of heart rate and abnormal beats are particularly helpful to the clinician for diagnosis purposes. Alarms are incorporated in these instruments to alert the nursing staff on the serious arrhythmias suffered by the patient with appropriate audiovisual signals.

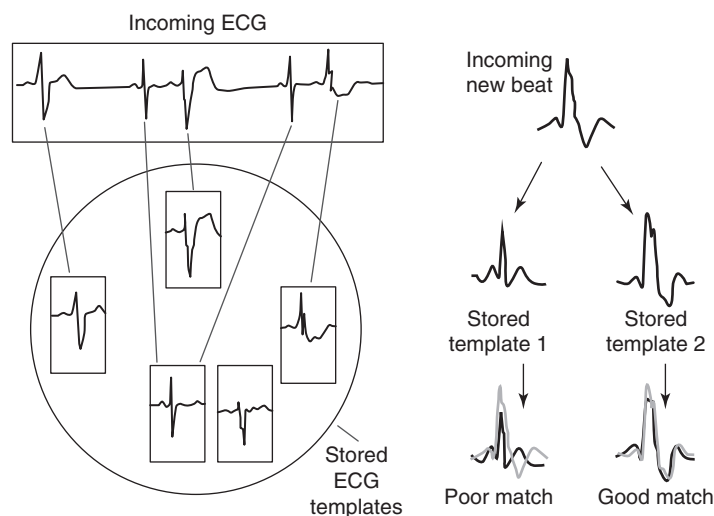
Advanced software techniques and sophisticated algorithms are constantly being developed for the automated analysis of arrhythmias. Recent efforts are focusing on the possible application of artificial intelligence methodology into the design of such systems particularly to ensure optimal alarm strategies.

### **QRS Detection Techniques**

There are several methods and computer programs in existence for the automatic detection of QRS complexes. These include the use of digital filters, non-linear transformations, decision processors and template matching. Generally, two or more of these techniques are used in combination in a QRS detector algorithm.

**Template Matching** A popular approach in the detection of arrhythmias is based on template matching. A model of the normal QRS complex, called a template, is derived from the ECG complex of a patient under normal circumstances. This template is stored and compared with the subsequent incoming real-time ECG to look for a possible match, using a mathematical criterion. Template matching is the generic algorithm in pattern





**Figure 16.1** Template matching technique for detection of arrhythmias. *Source:* Hewlett Packard 1999: ST/AR Arrhythmia Algorithm, Application Note.

recognition, which is used to determine the similarity between two entities, which may be points, curves, or other features of specified type. The effort is to recognize indications of diseases, by comparing the test ECG with a template with respect to the metrics and similarity. A close enough match to the template represents a detected QRS complex. If a waveform does not match the available template but is a suspected abnormal QRS complex, it is treated as a separate template, and future suspected QRS complexes are compared with it. Obviously, the system requires considerable memory for storing the templates. Alternatively, algorithms have been developed based on digital filters to separate out normal and abnormal QRS complexes.

Figure 16.1 illustrates the technique of template matching, which is based on the use of template families to represent recurring morphologies. For each patient, up to 16 different active template families can be created for each individual lead. To keep the template family information current, they are dynamically created and replaced as the patient's beat shape changes. When a beat is detected, it is matched against the stored waveform templates for that patient. This process involves overlaying the beat on the template and using a mathematical procedure to measure the differences between the two shapes as illustrated in the diagram.

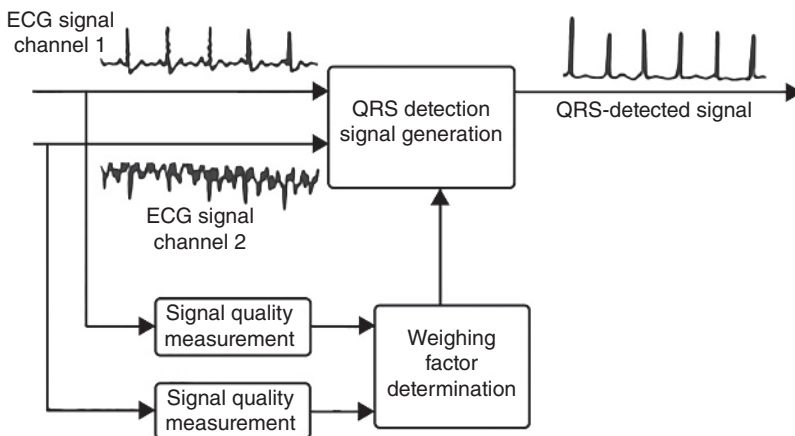
**ST/AR (Arrhythmia) Algorithm** The ST/AR (ST and arrhythmia) algorithm, which was introduced by Hewlett Packard is a multi-lead ECG algorithm designed for both arrhythmias and ST segment monitoring on surface ECG. Through a sophisticated computer algorithm, QRS complexes are detected, labelled, and classified. The algorithm processes the ECG signals for both paced and non-paced patients and performs several processes on the incoming ECG waveform, including filtering the signal, detecting and classifying the QRS, generating heart rate, identifying ectopic events and rhythms, and generating alarms, when necessary.

The first step in the arrhythmia detection process is to check the quality of the ECG to detect noisy signals and other inoperative (detached electrodes or broken wires) or technical problems to take corrective action. This is followed by sampling the patient's ECG at 8000 samples/s. This high rate of sampling is essential to preserve the narrow pacemaker pulses for accurate pacemaker analysis. However, within the arrhythmia monitoring analysis algorithm, a sampling rate of 250 samples/s is employed for QRS detection and QRS classification and detection of ventricular fibrillation, where high sampling rates are not required. This is followed by filtering of the digitized ECG signal where low frequency noise, baseline wander, and muscle artefacts are minimized and QRS features are preserved.

In order to reliably detect the QRS, the detection threshold is kept as 0.15 mV to prevent the detection of T waves or baseline noise as QRS complexes during a complete heart block or asystole. For optimal performance and to prevent false alarms, the lead selected for monitoring should have adequate amplitude. Figure 16.2 represents the arrangement for generating the QRS detection signal using multiple leads. The contribution from each ECG lead to the QRS detection signal is proportional to its measured quality based on the waveform amplitude and the amount of muscle and baseline noise. The weighting factors are updated at least every 200 ms to allow for quick adaptation to signal quality changes.

The QRS detector checks the QRS detection signal for the presence of the peak of an R wave. Search begins after an absolute refractory period from the previously identified QRS complex. The value used for the refractory period is 192 ms. This helps to prevent a T wave from being identified as an R wave.

After detection of the QRS, a number of features that represent beat characteristics and can be used to discriminate between different types of beats are measured. The features measured are height, width, area, and timing (R-R interval). Once the QRS is detected and measured, the beat is labelled. Labelling means that the algorithm assigns the complex one of the following labels: normal (N), supraventricular premature (S), ventricular ectopic (V), paced (P), questionable (?), and learning (L). If the signal quality is not good, the algorithm assigns the label 'inoperative (I)' and 'artefact (A)'.



**Figure 16.2** Method for generating QRS detection signal in ST/AR HP system. Source: Obtained from Hewlett Packard 1999 : ST/AR Arrhythmia Algorithm, Application Note.

A separate detector continuously examines the ECG signal for ventricular fibrillation. If a flutter or sinusoidal waveform persists for more than four seconds in any ECG channel, then the monitor alarms for ventricular fibrillation. Normally, the heart rate is computed by averaging the most recent 12 R-R intervals. This average gives a stable estimate of the heart rate even when the rhythm is irregular. Alarms are activated by the alarm generator wherein higher priority alarms such as asystole take precedence and supersede lower priority alarms, such as low heart rate.

Any computerized arrhythmia algorithm would not make 100% accurate analysis of all patients. Databases are available for the testing of arrhythmia detection algorithms. These databases consist of records of patient ECG waveform, together with a set of annotation files in which each beat has been labelled by an expert cardiologist.

### ***Instrumentation***

An arrhythmia monitor is basically a sophisticated alarm system as it continuously scans ECG rhythm patterns and issues alarms to events that may be premonitory or life threatening. The monitor uses the user-selected ECG leads for single lead or multi-lead arrhythmia analysis. The arrhythmia monitor is designed to detect premature QRS complexes, widened QRS complexes and runs of widened complexes. It measures signal features such as R-wave height, width, and timing, creates beat templates, classifies and labels beats to aid in rhythm analysis and alarm detection, and examines the ECG signal for ventricular fibrillation, asystole, and noise. All these are achieved in automated arrhythmia analysis systems through a computer.

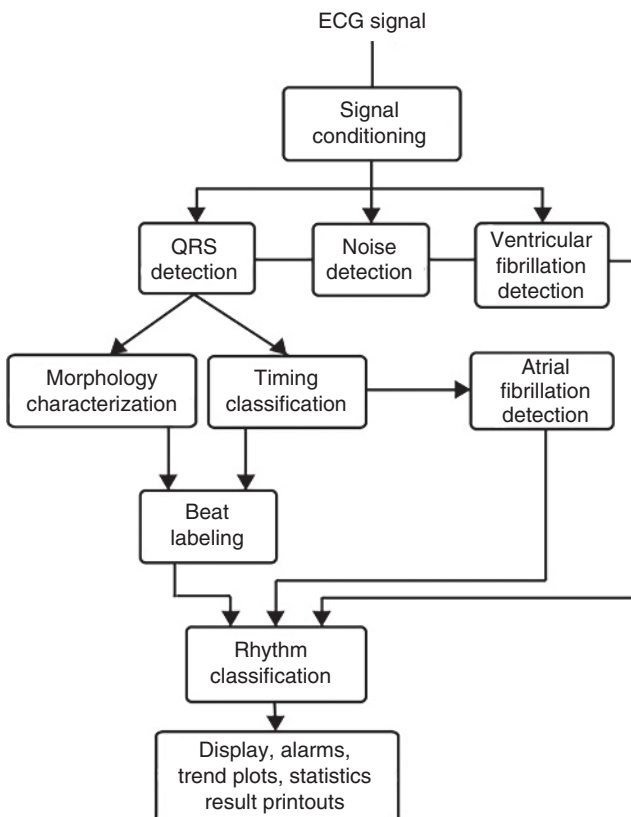
Because each patient's ECG may differ, the instruments generally base their determination of abnormal or ectopic beats upon a reference obtained from the patient. Therefore, the basis for any arrhythmia monitoring instrument for operation is in the following sequence:

- Digitizing each recorded ECG channel by using an analog–digital converter and a special data acquisition software or a digital signal processing (DSP) chip. The resulting digital signal is processed by a series of specialized algorithms, which start by suitable conditioning and removing noise, base level variation, etc.
- Subjecting to mathematical analysis of all channels in order to identify and measure essential features important for interpretation and diagnosis. These features include the peak amplitude, area under the curve, displacement in relation to baseline, etc., of the P, Q, R, S and T waves, the time delay between these peaks and valleys, heart rate frequency (instantaneous and average), and many others. Some types of secondary processing involving Fourier analysis and wavelet analysis may also be performed with a view to provide input to pattern recognition-based programs.
- Applying logically processing and pattern recognition techniques using rule-based expert systems, fuzzy logics algorithms, artificial neural networks techniques to derive conclusions, interpretation, and diagnosis.
- Initiating an alarm automatically, when ectopic beats are detected – either the ventricular prematured or widened varieties – and giving alarm light signals whenever the prematured or widened ectopic beats at a rate of 6 or 12 min<sup>-1</sup>.
- Detecting and triggering alarm when artefacts are present at the source, e.g. muscle tremor due to patient movement, baseline shift and improperly connected electrodes.

Figure 16.3 shows the major signal processing tasks performed by most automated arrhythmia monitoring and analysis systems. The function of each of these blocks is as follows:

*Signal conditioning:* Single or multiple ECG leads may be used for arrhythmia monitoring. Although the first-generation arrhythmia systems were used on a single lead, the present-day systems analyse two or more leads simultaneously. The ECG signal picked up by the surface electrodes is amplified, filtered (0.05–100 Hz for diagnostic purposes, 1–40 Hz for monitoring purposes), and digitized using an 8 or 12 bit analog-to-digital converter with a typical sampling rate of 250 Hz.

*Noise detection:* Digital filtering is performed on the ECG signal to remove unwanted noise and artefact such as baseline wander, motion artefact, and muscle noise that overlap the ECG signal spectrum. The ECG waveform is processed by two digital filters: a detection filter and a classification filter. The *detection filter* removes low frequency noise (baseline wander) and muscle artefact. This filter helps avoid an erroneous detection of tall T waves as beats. Even though the shape of the QRS is distorted, the output from the detection filter is used only for



**Figure 16.3** Block diagram of basic arrhythmia monitoring system flow diagram. Source: Adapted from Hathaway, JC 1988 : Automated Arrhythmia Analysis, In *Encyclopedia of Medical Devices and Instruments*, (ed. J.G.Webster), p. 120. John Wiley & Sons.

beat detection. The *classification filter* removes signal irregularities and preserves the important features of the QRS. So, the resulting ECG output can be used for feature measurements and beat classification. Electrode motion artefact is the most troublesome for arrhythmia analyzer as motion of the electrode with respect to the skin causes changes in the contact impedance generating electrical artefact. The impedance signal can thus provide an independent measure of electrode motion, which can be helpful to prevent false alarm.

**QRS detection:** Arrhythmia monitors require reliable R wave detectors as a prerequisite for subsequent analysis. The steep, large amplitude variation of the QRS complex is the obvious characteristic to use and this is the function of the R wave detector. Any subsequent analysis is entirely dependent upon the output from the R wave detector, and, therefore, it is important that this unit should function reliably. QRS detection is now almost universally performed digitally in a two-step process. The ECG is first preprocessed to enhance the QRS complex while suppressing noise, artefact, and non-QRS portions of the ECG. The output of the preprocessor stage is subjected to a decision rule that confirms detection of QRS if the processor output exceeds a threshold. The threshold may be fixed or adaptive.

Modern bedside monitors have built-in arrhythmia monitoring systems using 32 bit architecture processor. The software employs waveform templates and real-time feature extraction to measure such features as the R-R interval and QRS complex width and template correlation, in which incoming waveforms are compared point by point with already classified waveforms. The bedside monitor has adequate memory to retain ECG tracing record for later review of the information by the clinician. Arrhythmia monitors are also employed for remote monitoring of ambulatory patients.

An example of an automated arrhythmia analysis system for use with ambulatory systems is from M/s GE Healthcare, United States, that helps to identify patients at higher risk. This is shown in Figure 16.4. The instrument performs rapid analysis of both morphology and rhythm on patient's two to three ECG leads. The acquisition



**Figure 16.4** Arrhythmia monitoring system SEER 1000 comprising ambulatory recorder and monitoring station for ambulatory patients. *Source:* Courtesy of M/s GE Health Care.

module captures, amplifies, digitizes, and stores every heartbeat of the patient and is connected to the system. The system also stores and transmits these analyses and waveforms to central processors via telephone, cellular phone, or satellite. It then provides a computerized ECG analysis. The system detects atrial fibrillation, QT interval, R-R interval, ST segment measurement (deviation and slope), heart rate variability, and pacemaker spike detection.

## Specifications

*ECG sensitivity:* 2.5, 5, 10, and 20 mm/mV

*Frequency response:* 0.01–100 Hz

*Input impedance:* 100 M $\Omega$ , defibrillator protected

*Common mode rejection:* 130 dB

*Analysis programs:* Heart rate, atrial fibrillation detection, QT interval measurement, ST segment measurement, heart rate variability, pacemaker detection

## Applications

Automated arrhythmia analysis instruments find applications in hospitals, home, or ambulatory settings. Bedside monitors usually have built-in single channel arrhythmia detection facility. A similar application is incorporation into AEDs and portable ECG machines used in telemedicine. These machines are used to send ECG recordings via a telecommunications link, such as telephone and cellular phones. Most conventional ECG machines also include basic features of arrhythmia detection built in them.

# 17

## Arthroscope

### Purpose

Arthroscope is a device that is intended for use in diagnosis and therapy of orthopaedic disorders. Although the term ‘arthroscopy’ is a broader term covering all joints, its major emphasis is on the knee joint. Basically, knee arthroscopy is a surgical procedure that allows doctors to view the knee joint when making a small incision through the skin and other soft tissues rather than the larger incision needed for open surgery. This results in less pain for patients and often reduces the time to recover and return to normal activities. The therapeutic aspect of arthroscopy includes removal of intra-articular debris, joint debridement, lyses of adhesions, and torn tissues.

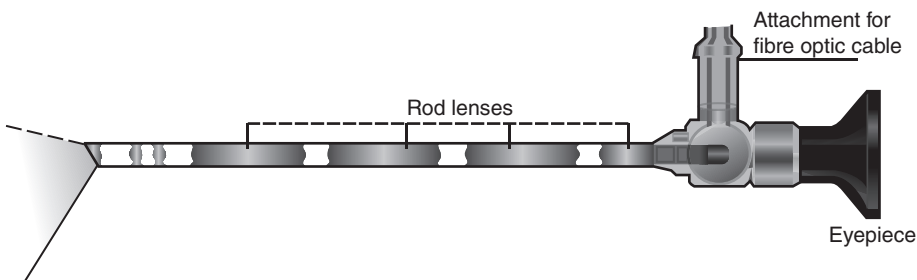
## Principle

The word arthroscope is coined using the word 'arthro' meaning 'joint' and the 'scope' meaning 'looking', so arthroscope is an instrument for looking into the joint. In earlier instruments, the joint used to be viewed by looking from the positioned eyepiece across the joint, but in modern instruments, the image is captured by a camera and relayed onto a large video monitor screen. As a procedure, an arthroscope is inserted through an incision in the skin near a joint under investigation. The arthroscope is available in a variety of diameters and lengths and with a choice of viewing angle, which could be forward, oblique right angle, etc. Illumination is usually by a fibre optic light source.

The heart of the arthroscopic system is the telescope (arthroscope) that comprises an eyepiece, light cable attachment, and a series of lenses and optical fibre cable for transmitting light. Achromatic lenses were used in the older arthroscopes, but they provided only a relatively small viewing field. Modern instruments use Hopkins rod lens system, which have a comparatively smaller overall diameter, but allows larger field of view, better contrast, higher definition, and brighter image. The basic components of an arthroscope are shown in Figure 17.1.

There are several factors that are important for understanding the functioning of the arthroscope. These include viewing angle, barrel length, diameter, etc. Arthroscopes are available with various viewing angles such as  $0^\circ$ ,  $30^\circ$ , and  $70^\circ$ . In  $0^\circ$ , the visual field is directly in line with the barrel length. In the  $30^\circ$  and  $70^\circ$  arthroscopes, the viewing angle is  $30^\circ$  or  $70^\circ$  with respect to the barrel length or optical axis and provides a wide angle field of view. The advantage of this angulation is that by rotating the scope, a much wider field of vision can be seen without moving the telescope from side to side. The barrel length of the arthroscope may vary from manufacturer to manufacturer. However, arthroscopes of 18 cm are usually recommended for knee applications. An arthroscope with shorter barrel length makes it difficult to examine and work on posterior areas of the knee. The diameter of the arthroscope barrel varies between 1.7 and 4 mm, depending upon the joint to be examined. For knee applications, the standard size used is 4 mm.

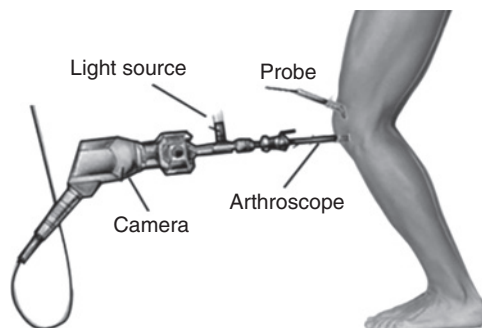
For illumination of the joint, light from a light source is transmitted to the site through a light cable integrated into the arthroscope. The source of light may be cold light source (150 W) or xenon source, which can give a higher light intensity. The light cable may be either fibre optic or fluid type. The fibre optic cables are flexible and easily sterilizable. Their length varies between 150 and 180 cm. The fluid cable is made of plastic tube



**Figure 17.1** Basic components of an arthroscope that uses rod lenses.



**Figure 17.2** An arthroscope in use.



filled with a special fluid. Although they are more efficient than fibre optic cables, they are used only for special applications due to the difficulty in their handling.

The video system comprises a video camera, the camera cable, the monitor, and the control unit. The cameras are based on the use of a semiconductor chip and may use only one chip, in which case the colour images are produced by covering the light sensors with appropriate colour filters. In the three chip camera, each primary colour is separately detected and processed. Obviously, a three chip camera gives much better image quality. A single chip camera provides 450 lines of resolution, whereas a three chip camera has 759 lines. Since these cameras operate on digital technology, which makes it possible to adopt image processing techniques for better image quality, these cameras are also equipped with automatic exposure control and zoom facility. The entire video system works under the control of a control unit, which after processing the digital images transmits them to the video monitor.

The arthroscopic examination is performed by the orthopaedic surgeon who makes a small incision in the patient's skin and then inserts pencil-sized instruments (arthroscope) that contain a small lens and lighting system to magnify and illuminate the structures inside the joint. Light is transmitted through fibre optics to the end of the arthroscope that is inserted into the joint. The surgeon can see the interior of the joint on a monitor through this very small incision. The use of the arthroscope is shown in Figure 17.2.

If the end of the arthroscope is too close to any structure within the knee, it is difficult for the surgeon to visualize it correctly. Two methods can be adopted by the surgeon in this respect. Firstly, the knee can be fully distended with saline to allow enough space. For this, the surgeon introduces the arthroscope and turns on the irrigation to inflate the knee with saline, looks at the screen, and orient the camera correctly. Alternatively, the scope can be pulled back within the available space to clearly visualize the object.

## Specifications

*Field of view:* 30° and 70°

*Diameter:* 4 mm

*Length:* 16–18 cm

*Sheath:* Rotatable, diameter 5.5–6 mm, working length 12 cm

*Light source:* Xenon lamp of 300 W, colour temperature of approximately 6000 K

*Light transmission:* Fibre optic cable of 3.5 mm in diameter and 230 cm in length

*Camera system:* Image sensor of 3 chip CCD

*Pixels:* 1920 (H)  $\times$  1080 (V) pixels per chip

*Lens:* Integrated zoom lens  $f = 15\text{--}31$  mm (2x optical zoom)

*Fluid pump:* Flow rate 1–2 l/min

## Applications

Arthroscope finds applications in examination and sometimes treatment of a damaged joint through minimally invasive surgical procedure. They are mostly used in orthopaedic departments of hospitals.

# 18

## Atomic Absorption Spectrometer

### Purpose

Atomic absorption spectroscopy (AAS) is a spectro-analytical procedure for the quantitative determination of chemical elements using the absorption of optical radiation (light) by free atoms in the gaseous state. The technique is used in analytical chemistry for determining the concentration of a particular element in a sample and has been employed to determine over 70 different elements in samples in the fields of pharmacology, biophysics, and toxicology research where it offers great specificity, sensitivity, precision, and adaptability. Atomic absorption is so sensitive that it can measure down to parts per billion of a gram in a sample.

### Principle

AAS consists in analysing the concentration of elements by measuring the amount of light absorbed at the resonant wavelength as the light passes through atoms in the gaseous state. As the number of atoms in the light path increases, the amount of light absorbed increases in a predictable way. By measuring the amount of light absorbed, a quantitative determination of the amount of analyte element present in the liquid sample can be made. The use of special light source and careful selection of wavelength allow the specific quantitative determination of individual elements in a sample in the presence of other elements.

The sample, normally in liquid solution for fine suspension, is sprayed into a flame. The flame vaporizes the sample and puts the atoms in a condition where they can absorb energy. Monochromatic light is obtained by isolating a single spectral line emitted from a hollow cathode lamp using an interference filter. A photodetector measures the light passing

through the flame, both before and after introduction of the sample into the flame. The results can be displayed by a meter, digital display, or captured by a computer. The amount of light absorbed by the atoms in the flame is proportional to the concentration of the element in the sample solution. The unknown concentration of the element in the sample may be determined by comparing the absorbance reading based on the relationship of absorbance versus the concentration made from data of known concentrations of the element.

In atomic absorption spectrophotometry, the absorption lines are very narrow, approximately 0.002 nm wide. This is because, being atomic bands, they do not have broadening due to rotational or vibrational structure, as is the case in molecular absorption bands. The narrow absorption band of the atoms necessitates the use of a very narrow source line, and, therefore, a continuous radiation source, like tungsten or hydrogen lamp, cannot be used in atomic absorption spectrophotometers. Usually, a hollow cathode lamp or an electrodeless discharge lamp is used for each element to be determined.

### Instrumentation

The components of an atomic absorption spectrometer are illustrated in Figure 18.1 and consist of a nebulizer, premix burner (atomizer), light or radiation source, modulation system or beam chopper, and flame. The spectrometer part comprises a monochromator to isolate the specific wavelength of light to be measured, a detector to measure the light accurately, electronics to process the data signal, and a data display or reporting system to show the results.

**Hollow Cathode Lamps** The hollow cathode lamp is the most commonly used source of radiation for AAS. It is a discharge lamp which emits the characteristic light of the element to be analysed. The lamp consists of a cylindrical thick-walled Pyrex body, which has an end window made of quartz as shown in Figure 18.2. It contains one anode and a cup-shaped cathode, which are both connected to tungsten wires, for taking out the electrical connections. The cathode is a hollow metal cylinder 10–20 mm in diameter. It is constructed of the metal having the desired emission spectrum or it may simply serve as a support for depositing a layer of the element. The lamp is emptied and filled with a highly pure inert gas at low pressures of 1 or 2 mm. The gases generally used are helium, neon, or argon. Mica sheets are placed inside the lamp to limit the radiation to within the cathode. Lamps generally operate at currents below 30 mA and voltages up to 400 V.

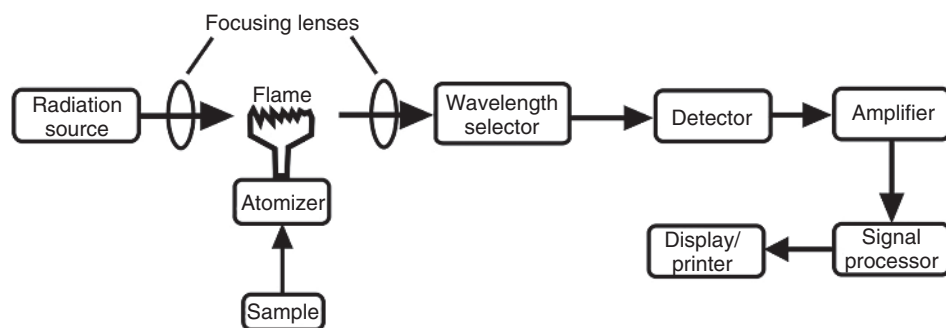
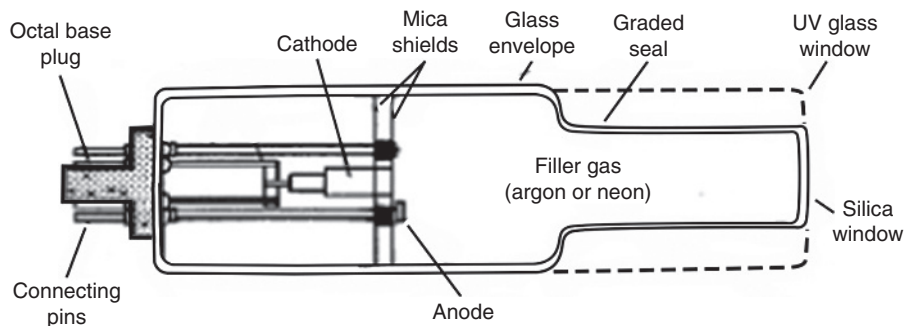


Figure 18.1 Block diagram of an atomic absorption spectrometer.



**Figure 18.2** Various components of a hollow cathode lamp.

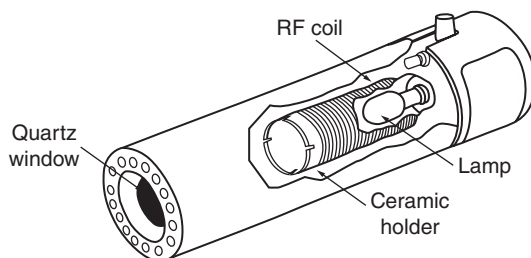
When the voltage is applied, discharge takes place between the two electrodes, resulting in ionization of the inert gas atoms. The ions are accelerated towards the cathode surface by the electrical potential existing between the two electrodes. When the positively charged ions collide with the negatively charged cathode surface, the metal atoms are ejected from the cathode. These metal atoms absorb energy by colliding with the filler gas ions, elevate to excited electronic states, and subsequently return to the ground state by emitting radiation characteristic of the metallic surface.

Choice of the window material of the lamp depends upon the wavelengths of the resonance lines of the element concerned. For wavelength shorter than 250 nm, a silica window is chosen, whereas for wavelengths longer than 250 nm, either silica or ultraviolet, glass is employed. Hollow cathode lamps have been constructed for almost every naturally available element.

A limitation of hollow cathode lamp is the need for a different lamp for each element to be analysed. Some instruments make use of a turret, which can hold up to six lamps. These lamps are kept at their operating currents, thereby avoiding delay, which is encountered while changing from one element to another, due to the warm-up time for the hollow cathode lamps. The rotation of the turret is computer controlled, which brings the lamp in the desired source position. Another approach is to combine certain elements in the same hollow cathode in such a way to provide very nearly equal performance to single element lamps. These lamps are called multi-element lamps. The instruments are provided with a switching system, which puts each lamp into its approximate current range. Multi-element lamps emit very complex spectra. Therefore, only dual or triple element lamps, especially for related elements such as calcium–magnesium, sodium–potassium, and copper–nickel–cobalt, are generally constructed.

**Electrodeless Discharge Lamp** The electrodeless discharge lamp (EDL) is a useful source of atomic line spectra. Its design is shown in Figure 18.3. A small amount of the element or salt of the element for which the source is to be used is sealed inside a quartz bulb containing a few torr of an inert gas such as argon. The lamp contains no electrodes but is energized through a coiled antenna from a radio frequency (RF) or microwave generator operating at 2450 MHz and 200 W power output. When an RF field of sufficient power is applied, the coupled energy will vaporize and excite the atoms inside the bulb into emitting their characteristic spectrum.

**Figure 18.3** Constructional details of an electrodeless discharge lamp.



EDLs are available commercially for more than 15 elements. They are typically much more intense and, in a few cases, more sensitive than comparable hollow cathode lamps. They therefore offer the analytical advantages of better precision and lower detection limits. In addition to providing superior performance, the useful lifetime of an EDL will exceed that of a hollow cathode lamp for the same element. The EDLs, however, offer definite performance and lifetime benefits for instruments that are optically compatible with the EDL source.

**Atomizers** The atomizers most commonly used nowadays are flames and electrothermal graphite tube. There are other atomizers, such as glow discharge atomization, hydride atomization, or cold vapour atomization, which are used only for special purposes. The most commonly used atomizers in AAS are flames, principally the air–acetylene flame with a temperature of about 2300°C and the nitrous oxide system ( $\text{N}_2\text{O}$ )–acetylene flame with a temperature of about 2700°C. Usually, a slot burner is used in atomic absorption spectrometry that provides very thin flames over a long path. The slot dimensions are dependent upon the fuel and oxidant gases. Usually, a 10 cm slot is used for air–acetylene flame and a 5 cm slot for a nitrous oxide–acetylene flame. The port is usually 0.4–0.6 mm in width. The slot dimensions are dependent upon the fuel and oxidant gases. The radiation beam passes through this flame at its longest axis, and the flame gas flow rates may be adjusted to produce the highest concentration of free atoms.

Many elements emit strongly in the flame at the same wavelength at which they absorb. This creates a serious error in measurement of the absorption. This error can be eliminated by modulating the light from the lamp, either by using an A/C discharge or by using a mechanical or electronic chopper between the lamp and the flame. The detector circuit is designed that only the modulated light is recorded and the unmodulated flame emission gets eliminated.

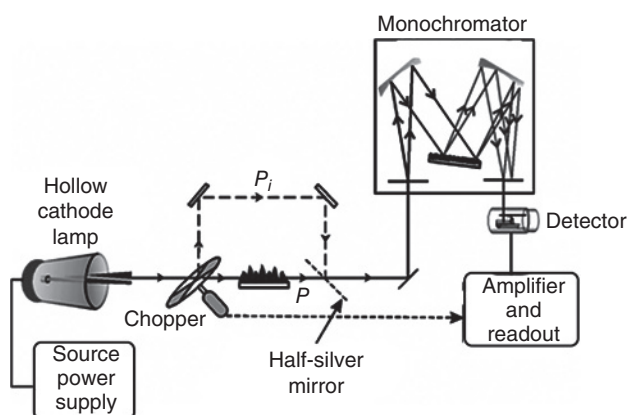
There has also been an increasing interest in the use of non-flame techniques, like electrothermal and cold vapour atom formation devices. One such device is the *graphite furnace* that consists of graphite tubes, which are heated due to their ohmic resistance using a low voltage, high current power supply. The tube dimensions are typically 20–25 mm in length and 5–6 mm inner in diameter. With this technique, liquid, dissolved solid, and gaseous samples may be analysed directly into a graphite tube, which is then heated in a programmed series of steps to remove the solvent and major matrix components and to atomize the remaining sample. A measured volume, typically 10–50  $\mu\text{l}$ , or a weighed mass, typically around 1 mg, of a solid sample is adequate. Its sensitivity and detection limits are significantly higher than AAS flame and is considered as a preferred technique for the determination of trace elements in complex matrices.

**Sampling System** Liquid or dissolved samples are typically used with flame atomizers. A sampling system is used to supply a constant feed rate of a sample into the burner. The sample introduction system consists of three components: (i) a nebulizer that breaks up the liquid into small droplets; (ii) a device that removes large droplets from the stream, allowing only drops smaller than a defined size; and (iii) the flame or atomizer that converts the analyte into free atoms. The sample solution is aspirated by a nebulizer, transformed into an aerosol, which is introduced into a spray chamber, where it is mixed with the flame gases and conditioned in a way that only the finest aerosol droplets ( $<10\mu\text{m}$ ) enter the flame. The design of nebulizers and spray chambers have been optimized to provide the best aerosol drop size in the flame for interference-free analyte vaporization. Mostly, pneumatic nebulization approach is used in the vast majority of atomic spectroscopy determinations in case of liquid samples. Normally, sample uptake rate of the system is 3–4 ml/min. The sampling system may be coupled to an automatic sample changer, which may have a number of sample holding polythene cups. Each cup passes the sampling point in turn, and contents are sampled by an automatic head.

Most atomic absorption spectrophotometers use pneumatic nebulizers in which the sample solution is introduced through an orifice into a high velocity gas jet. Liquid is drawn through the sample capillary with the pressure differential produced by the high velocity gas stream and passing over the sample orifice. This forms a cloud of droplets in the spray chamber. The major limitation of air pneumatic nebulizers of conventional design is that they produce aerosols with a wide drop range. Much finer aerosol can be generated by using an *ultrasonic* nebulizer, which offers up to 30% efficient production of droplets in the size range from 1.5 to  $2.5\mu\text{m}$  at a 0.3 ml/min solution flow rate. As the nebulizers and spray chambers operate interactively, they must be optimized as a unit rather than individually.

**Spectrometer** The optical system uses a double beam configuration. In this design, the beam from the hollow cathode lamp is split through a mirrored chopper, one half passing by the atomizer and the other half around it, as schematically displayed in Figure 18.4. The two beams are then recombined through a half-silvered mirror and passed through the double monochromator for high resolution. The ratio among the

**Figure 18.4** Block diagram of a double beam optical configuration in an atomic absorption spectrophotometer.





**Figure 18.5** Typical atomic absorption spectrophotometer model Pinnacle 900. *Source:* Reproduced with permission of M/s Agilent Technologies, Inc., USA.

reference and sample signal is then amplified and fed to the readout device and recorder. These instruments correct the fluctuations within the intensity of radiation coming from the radiation source and for changes within the sensitivity of the detector. Most instruments are equipped with a device for background correction.

The *electronic system* of AAS is computer controlled, which uses a multi-lamp turret controlled by the same computer, which tunes the desired wavelength. The computer also controls the flame composition and burner height. The instruments are self-optimizing with the gases controlled via a binary flow system with feedback of absorbance signal to automatically set the optimum fuel flow. The photomultiplier tube is the most commonly used detector for AAS. However, solid state detectors are now replacing conventional vacuum-type photomultipliers. The integrated electronic circuits amplify, filter, and process the electrical signal, using a series of chips and microprocessors, transmitting the result to an internal or external computer, which manages all data handling and display. One instrument uses a linear charge coupled device (CCD) array with 200 pixels as the detector. Figure 18.5 is a typical modern commercial AAS instrument from M/s PerkinElmer, United States.

## Specifications

*Automatic lamp:* 8-lamp holder for hollow cathode and electrodeless discharge

*Selection:* Lamps

*Wavelength range:* 190–900 nm

*Monochromator:* Littrow design with motorized drive for automatic wavelength selection and peaking

*Diffraction grating:* 1800 lines/mm

*Spectral bandwidths:* 0.2, 0.7, and 2.0 nm

*Detector:* Solid state detector



*Burner flame system:* 10 cm, single-slot burner head

*Temperature:* Ambient up to 3000 °C in steps of 10 °C

*Sampler table:* Sample tray with 88 and 146 sampling positions

*Sample and reagent volume:* 1–99 µl, selectable in increments of 1 µl

## Applications

AAS has many uses in different areas in biomedical field including clinical analysis for analysing metals in biological fluids and tissues such as whole blood, plasma, urine, saliva, brain tissue, liver, muscle tissue, and semen. It also finds applications in pharmaceutical manufacturing processes to detect minute quantities of a catalyst that remain in the final drug product and for water analysis for its metal content.

# 19

## Atomic Emission Spectrometer, Flame

### Purpose

Atomic emission spectroscopy (AES) is another analysis technique that employs the intensity of light emitted from a flame at a particular wavelength to determine the quantity of an element in a sample. The wavelength of the atomic spectral line reveals the identity of the element, while the intensity of the emitted light is proportional to the number of atoms of the element and thus the concentration of the analyte. Flame emission photometric methods are performed to determine the concentration of trace elements or heavy metals in biological specimens and for the regulation of alkali metals in the pharmaceutical processes. The other energy source that can be used in place of flame is an electrical arc or, more recently, a plasma.

### Principle

Flame AES is based on the principle that every element has a specific number of electrons associated with its nucleus. The normal orbital configuration of an atom is known as the 'ground state', which is the most stable state. If energy is applied to an atom in a particular form, the energy will be absorbed resulting in the outer electron raised to a less stable configuration termed as the 'excited state'. When the excited atoms return to the ground state from this unstable state, they release energy and emit radiation in the UV–visible light range. The emitted radiation is detected and used to determine which element is present in the sample and its concentration.

There are some situations where the use of flame emission technique is preferred. It can be used when wavelength specific lamp is not available and the number of samples

does not justify obtaining one. Flame emission has better detection limits than atomic absorption for several elements including the alkali metals. AES is ideally suited for multi-elemental analysis because all analytes in a sample are excited simultaneously. If the instrument includes a scanning monochromator, it can be programmed to move rapidly to an analyte's desired wavelength, pause to record its emission intensity, and then move to the next analyte's wavelength. This sequential analysis allows for a sampling rate of 3–4 analytes/min. Another approach to a multi-elemental analysis is to use multiple detectors that can be positioned in a semicircular array around the monochromator at positions corresponding to the specific wavelengths for the analytes.

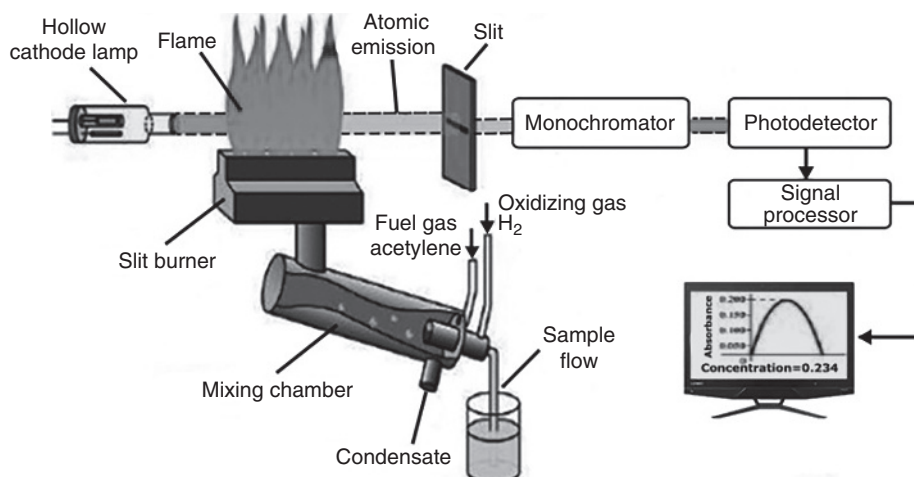
### **Instrumentation**

An flame atomic emission spectrometer is similar in design to the instrumentation for atomic absorption spectrometer (AAS). However, there is a basic difference in the principles between atomic emission and atomic absorption spectroscopy. In atomic emission, the flame serves a dual purpose of converting the sample aerosol into an atomic vapour and then thermally elevating the atoms to an excited state, whereas in atomic absorption, the only function of the flame is to convert the sample aerosol into atomic vapour, which can then absorb light from the light source.

Due to similarity in design between AAS and AES, it is easy to adapt most flame atomic absorption spectrometers for atomic emission spectrometer by turning off the hollow cathode lamp and monitoring the difference in the emission intensity when aspirating the sample and when aspirating a blank. A typical flame atomic emission/absorption spectrometer from M/s PerkinElmer is shown in Figure 19.1. Many atomic emission spectrometers, however, are dedicated instruments designed to take advantage of features unique to atomic emission. They use plasmas, arcs, sparks, and lasers as atomization and excitation sources and have an enhanced capability for multi-elemental analysis.



**Figure 19.1** Atomic emission/absorption spectrophotometer. *Source:* Reproduced with permission from M/s Perkin Elmer Inc., USA.



**Figure 19.2** Block diagram of flame atomic emission/absorption spectrophotometer.

The essential components of an AES are illustrated schematically in Figure 19.2. It consists of a nebulizer within a spray chamber, a premix burner, flame, monochromator, detector, and readout system. The monochromator, detector, and readout systems are similar to those used in a conventional spectrophotometer. All these components perform the following functions: (i) deliver the analyte to the flame, (ii) induce the emission spectral transitions for the determination of the analyte, (iii) isolate the relevant spectral lines necessary for the analysis, (iv) detect the intensity of radiation at the isolated lines, and (v) record the intensity data to calculate the concentration of the analyte.

**Pretreatment of Sample** AES requires that the analyte be dissolved in a solution in order to undergo nebulization to provide a steady flow of aerosol into a flame. Solid samples may be analysed by dissolving in a solvent. It should be ensured that the reagents used to dissolve samples do not contain substances that lead to interference problems. For atomization of the liquid sample, three components are used: (i) a nebulizer that breaks up the liquid into small droplets; (ii) an aerosol modifier that removes large droplets from the stream, allowing only droplets smaller than a certain size to pass; and (iii) the flame or atomizer that converts the analyte into free atoms. An autosampler is generally used with AES to allow reproducible sample injection and injection of up to 50 samples as well as automate preparation of standards.

**Nebulization** Most atomic spectroscopy determinations use pneumatic nebulizer in which the sample solution is introduced through an orifice into a high velocity gas jet. The sample stream may intersect the gas stream in either a parallel or perpendicular manner. Liquid is drawn through the sample capillary by the pressure differential generated by the high velocity gas stream passing over the sample orifice, forming a cloud of droplets in the spray chamber. In the spray chamber, the larger droplets are removed from the sample stream by breaking them into smaller droplets by impact beads or wall surfaces. The final fine mist aerosol is combined with the oxidizer/fuel mixture and carried into the burner. Droplets larger than about 20  $\mu\text{m}$  are trapped in the

spray chamber and flow to waste. Atomization and excitation in flame atomic emission is accomplished using the same nebulization and spray chamber assembly used in atomic absorption.

**Flame Atomizer** The atomizer converts the analyte atoms and molecules within the aerosol from the ground state to the excited state via thermal collisions. A satisfactory flame source must provide the temperature and fuel/oxidant ratio required for a given analysis. The maximum operating temperature of the flame is determined by the identities of the fuel and oxidant, whereas the exact flame temperature is fixed by the fuel/oxidant ratio. The burner head consists of single or multiple slots, or a Meker-style burner. Older atomic emission instruments often used a total consumption burner in which the sample is drawn through a capillary tube and injected directly into the flame. Various combinations of combustible gases and oxidants can be used to create flames with different temperatures (e.g. acetylene, propane, natural gas, oxygen, compressed air).

**Optical System** Upon their return to a lower or ground electronic state, the excited atoms and molecules emit radiation characteristic of the sample components. The emitted radiation passes through a monochromator that isolates the specific wavelength for the desired analysis. The monochromatic light is obtained by filters with narrow bandpass to eliminate background light emitted from the flame. Diffraction gratings are used as monochromators in most sophisticated instruments with a slit to limit the bandwidth of light being detected. A photodetector measures the radiant power of the selected radiation, which is then amplified and sent to a readout device, meter, recorder, or microcomputer system.

The emission lines in the spectra are generally narrow due to the distinct atomic energy levels during transitions. If there are multi-elements in a sample, the spectra can be very congested. This would require a spectrometer of high resolution for spectral separation of nearby atomic transitions. Also, as all the atoms in a sample are excited simultaneously, it is possible to detect them simultaneously. This is a major advantage of AES as compared to AAS. Array detectors interfaced to a microcomputer system permit simultaneous analyses of several elements in a single sample.

While it is possible to perform AES using a flame as an excitation source, the flame is not an ideal excitation source for atomic emission. This is because the typical temperatures for an acetylene flame used in AES are 2000–3000 K. The lower end of the temperature range corresponds to air–acetylene flames, whereas the upper end to nitrous oxide–acetylene flames. In the last decade, instruments using a high temperature gas plasma emission have become commonplace. They include the inductively coupled argon plasma (ICP) and the microwave plasma (MP), both of which provide significantly hotter sources. These are considered as excellent excitation sources for AES.

Atomic emission spectrometer is an electrical equipment that operates using compressed gases, flames, and hazardous materials including corrosive fluids and flammable liquids. Use and operation of this instrument by unskilled, untrained, or careless workers can create explosion hazards, fire hazards, or other hazards that can cause fatal accidents, serious injury to personnel, or severe damage to equipment and property. Information on safety practices is usually provided by the manufacturers in their user manual, which must be thoroughly read and followed before using the instrument.

## Specifications

The broad specifications of AES are the same as that of AAS.

*Wavelength:* 185–900 nm

*Optical configuration:* Double beam

*Vaporization:* Flame atomization

*Safety features:* Automatic gas control/flame safety system

## Applications

Most applications of flame AES have been the determination of trace metals, especially in liquid samples. They find wide applications in environmental and clinical analysis. Flame emission detectors are also used in gas chromatography.

# 20

## Atomic Emission Spectroscopy: Microwave Plasma

### Purpose

Microwave plasma atomic emission spectroscopy (MPAES) is used for simultaneous multi-analyte determination of elements. The technique offers two important advantages in terms of its low running cost and laboratory safety as it does not require the use of expensive or flammable gases. The technique further provides better linear dynamic range, detection limits, and analysis speed as compared to conventional flame atomic absorption spectrometers (AAS). It is thus a suitable and efficient alternative to flame atomic emission spectrometer and flame AAS for many important applications.

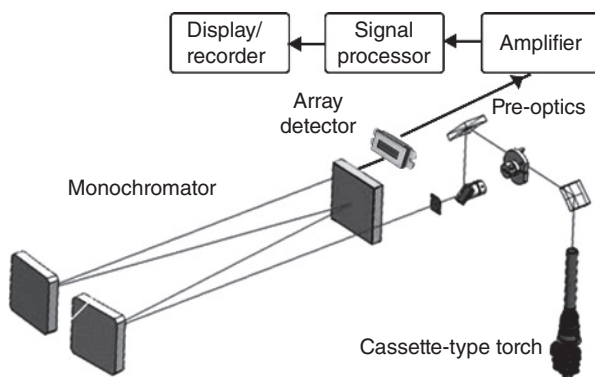
### Principle

Just like flame atomic emission technique, MPAES is also an atomic emission technique. The basic principle is that once an atom of a specific element is excited by providing it an external energy, it emits radiation (light) in a characteristic pattern of wavelengths forming an emission spectrum, as it returns to the ground state. In MPAES, the source for atomic emission is the microwave plasma.

### Instrumentation

A schematic diagram of MPAES is shown in Figure 20.1. The heart of the system is a plasma generating source. It is a high temperature source in which the nitrogen-fuelled microwave plasma can attain temperatures nearing 6000 °C with up to 1 kW of power.

**Figure 20.1** Block diagram of microwave plasma atomic emission spectrometer. *Source:* Reproduced with permission, courtesy of Janet Shih Hajek of M/s Agilent Technologies Inc., USA.



The microwave excitation assembly comprises a solid state, high voltage power supply and an industrial-grade, air-cooled magnetron that operates at 2450 MHz. The system does not require any cooling water supply, because the plasma generator is air cooled. The plasma is ignited by using a computer-controlled momentary flow of auxiliary argon with a purity of 99.0% and with a flow rate of 1.5 l/min at 210 kPa (30 psi). Once the plasma is operational and stabilized, it automatically switches to nitrogen for routine operation.

The nitrogen gas required for generating a plasma discharge can be supplied from a gas cylinder or a liquid nitrogen source or extracted from ambient air using a nitrogen generator. The nitrogen gas should have minimum purity of 99.5% with a flow rate of up to 25 l/min at 500 kPa (72.5 psi). In the Agilent 4200 MPAES (Figure 20.2), the *nitrogen generator* employs 'pressure swing adsorption' technology to produce high quality nitrogen from a supply of dry, oil-free, and dust-free compressed air. The process depends upon the differential adsorption of oxygen and nitrogen under high pressure conditions. The nitrogen supply is used for plasma generation, sample nebulization, and transport.

Using a magnetic field rather than an electric one for excitation can generate a very powerful plasma that is capable of handling a wide range of sample types. An optimized microwave waveguide is used to produce electromagnetic field at the plasma torch. Magnetic excitation gives a toroidal plasma and effective central zone for sample

**Figure 20.2** A typical commercial microwave plasma atomic emission spectrometer. *Source:* Reproduced with permission of M/s Agilent Technologies, Inc., USA.



injection. The axial magnetic field and the radial electrical field result in focusing the microwave energy to produce a robust plasma and high intensity atomization emission lines.

The plasma torch is standard one-piece quartz torch optimized for high precision and sensitivity with the recommended power and gas flow settings. The torch has a polymer base that automatically makes gas connections and aligns the torch when inserted using the torch loader. The torch can be mounted for vertically oriented plasma for improved matrix handling, axial viewing for optimum sensitivity, and best detection limits. A pre-optics protection gas flow of compressed air (25 l/min) is used to divert heat from the plasma away from the pre-optics.

When working with MPAES, care has to be taken for eye protection due to high intensity of the plasma light. Exposure to microwave radiation can also result in causing subsurface skin burns. Therefore, the microwave excitation assembly is designed that it contains microwave radiation and generates the plasma while still allowing easy installation of the plasma torch and viewing of the plasma. In addition, the MPAES system has an interlock arrangement that is designed to extinguish the plasma if either the pre-optics window holder is opened or the torch is unloaded. The interlock system should never be bypassed. Besides, noxious or corrosive fumes are exhausted by the instrument. So, the instrument chimney must be connected to an exhaust system.

The *sample introduction system* includes a multipurpose sample introduction system to create aerosol and consists of a nebulizer, a spray chamber, and pump tubing. A peristaltic pump operates under the control of PC and provides a variable speed of 0–80 rpm. It has three channels for sample, drain, and internal standard/ionization buffer. Five channel pumps are also available. From here, the aerosol is introduced into the centre of the hot plasma. The aerosol dries, decomposes, and is then atomized.

The control of gases is achieved through computer-controlled solenoid valves that automatically enable and regulate the flow. The plasma gas is fixed at 20 l/min and the auxiliary gas is fixed at 1.5 l/min. Nebulizer gas flow is also computer controlled to provide accurate flow in the range 0.3–1.0 l/min.

The *optical system* consists of a fast-scanning, high resolution system using Czerny-Turner design monochromator with 600 mm focal length and fixed entrance slit for ease of operation. Holographic diffraction grating with 2400 lines/mm is blazed at 250 nm for optimum UV performance. The system operates in the wavelength range of 180–780 nm. The optical system is purged with air or nitrogen for protection in dusty or corrosive environments.

The *detector* is a hermetically sealed solid state charge coupled device (CCD) detector with  $532 \times 128$  pixels. It is designed especially for low light level detection with quantum efficiency greater than 90% at peak sensitivity. The detector is directly cooled to 0°C using a thermoelectric Peltier device for low dark current and reduced baseline noise. The array detector collects the analyte spectra and the background spectra, allowing simultaneous background correction for better stability and precision. Using a scanning monochromator and a solid state detector combination, the MPAES eliminates the need for individual lamps and offers faster multi-element analysis. The concentration of an element in a sample is worked out automatically by comparing its emission to that of known concentrations of the element, plotted on a calibration curve.



## Specifications

*Magnetron frequency:* 2450 MHz

*Wavelength range:* 180–780 nm

*Resolution:* <0.050 nm

*Nebulizer flow rate:* 0.75 l/min

*Gas source:* Nitrogen generator

*Sample input:* Autosampler

*Detection limits:* 3 sigma detection limits ( $\mu\text{g/l}$ )

## Applications

The major applications of MPAES are mostly in the field of food and beverages and more prominently in the field of environment for analysis of elements.

# 21

## Audiometer: Diagnostic

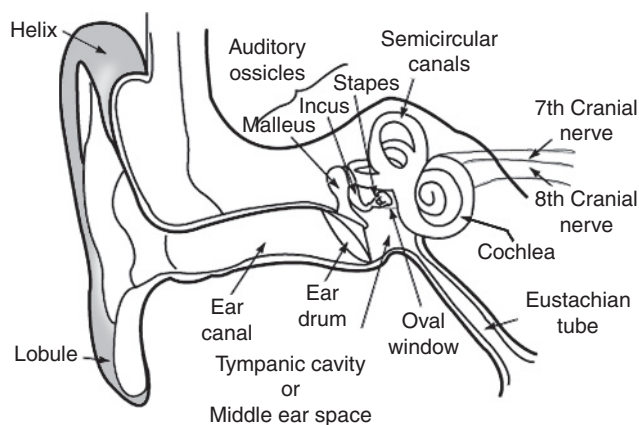
### Purpose

Diagnostic audiometer is an instrument used for evaluating hearing impairment and the probable anatomic site/sites of dysfunction within the auditory system. Audiometers are basic equipment in audiology centres because evaluation of hearing ability of a person is an essential first step in the management of such patient. With the audiology equipment, it is possible to assess the functions of the peripheral and central auditory parts of the human body.

### Principle

#### *Mechanism of Hearing*

Sound waves are longitudinal waves in which the motion of each particle of the medium, in which the wave is travelling, moves backward and forward along a line in the direction in which the wave is propagated. The human aural system responds to these oscillating pressure changes and transmits them to the brain through a series of steps. Figure 21.1 shows the anatomy of the human ear. The function of the external or outer ear is to funnel sound into the auditory canal or external auditory meatus to the ear drum. The sound vibrations then go through the middle ear by means of the ossicles (the malleus, the incus, and the stapes) to the inner ear. The external auditory meatus is a convoluted tube, about  $1\text{ cm}^3$  in volume, and has at its inner end in the tympanic membrane. The distance the tympanic membrane moves during a wave of compression



**Figure 21.1** Anatomy of the ear.

is a function of the force and velocity with which the air molecules strike it and is, therefore, related to the loudness of sound.

The tympanic membrane stretches across the ear canal and separates it from the middle ear cavity. The middle ear is exposed to atmospheric pressure, contains air, and is connected to the nose through a valved tube called the Eustachian tube, which is responsible for keeping the pressure equal on the two sides of the ear drum. The sound energy from the tympanic membrane is transmitted to the labyrinth, which is filled with fluid. The fluid conducts the sound to the cochlea where the receptor cells are located, which convert the acoustic signal to nerve impulses, are located. The nerve impulses thus generated are propagated along the acoustic nerve fibres to the brain with a speed of 100 m/s. The pattern of nerve impulses arriving in the brain is associated with the subjectively experienced sound, which has attributes of loudness, pitch, and timbre (quality).

The cochlea is a fluid-filled coiled tube about 1 cm long, which is a wound, snail-like, and round cone of bone (called modiolus), which run the nerve fibres that form the auditory nerve. The cochlea is a very complex structure but essentially it consists of a fluid-filled tube with a sensitive (basilar) membrane dividing it. The membrane has different resonating properties along its length, responding to high frequencies at the stapes' end and to low frequencies at its upper end. The actual sensitive elements are hair-like structures, which respond to vibrations at different frequencies by setting up patterns of nerve impulses that travel along the auditory nerve to the brain.

The sounds reaching the ear are characterized by *loudness (intensity)*, which depends upon the amplitude of the waves; by *pitch*, which depends upon their frequency; and by *quality*, which results from the combination and interaction of the waves. The human ear responds to vibrations ranging from 20 to 20 000 Hz.

Hearing capability gets affected by anything that interferes with the conduction of sound waves to the cochlea, such as a perforated tympanic membrane (ear drum), disease of the middle ear or disease of the cochlea itself, or its connection in the central nervous system. Normally, the disorders of hearing can be classified as follows:

*External ear:* The hearing capacity of the ear is reduced whenever the acoustic pathway is blocked due to swelling or deposit of foreign bodies.

*Middle ear:* Middle ear hearing problems are due to perforation of ear drum or diseased cochlea.

*Inner ear:* Hearing ability may be affected in case the sound signal is not transmitted properly to the brain due to injury or prolonged exposure to excessive noise.

### ***Air and Bone Conduction***

Air conduction, by definition, is the transmission of sound through the external and middle ear to the internal ear (cochlea). Bone conduction, on the other hand, refers to transmission of sound directly to the internal ear by mechanical vibration of the cranial bones and soft tissues. Hearing loss is usually classified into two types: conductive and sensorineural. Conductive hearing loss is due to a condition of the outer or middle ear that prevents sound from being conducted to the cochlea in the inner ear. Sensorineural hearing loss is due to a problem with either the sensory transducer cells in the cochlea or, sometimes, the neural pathway to the brain. In some cases, conductive and sensorineural hearing loss can occur simultaneously, resulting in so-called mixed hearing loss.

Air and bone conduction hearing loss can be determined by measuring hearing sensitivity using two different types of earphones. For air conduction testing, a pure tone is presented via an earphone or a loudspeaker to the outer ear, whereas in bone conduction testing, an electromechanical earphone is placed on the skull. This causes direct stimulation of the cochlea via mechanical vibration of the skull with almost no stimulation of the outer and middle ear.

### ***Threshold of Hearing***

The human ear has an extremely wide dynamic range as regards its hearing capability. The lower limit of hearing, where sound is just detectable, is referred to as the threshold of hearing. In other words, it is minimal stimulus intensity that is just barely adequate to elicit a response. The upper limit of hearing, where sound begins to become uncomfortable for hearing, is referred to as the threshold of discomfort. The objective of conducting audiological examination is the determination of the hearing threshold.

Studies involving measurement of the minimum audible level of hearing have been made with stimuli presented to each ear separately or both ears together. A complete audiogram thus obtained shows both air and bone conduction thresholds bilaterally. It is a graphic representation of the dB loss at different frequency levels for both air and bone conduction and also indicates the type and location of the hearing impairment. Thus, on the basis of the audiograms, the conduction and sensorineural hearing deficiencies can be easily separated from each other. The results from the two methods show human hearing to be generally most sensitive between 500 and 10 000 Hz. In audiometers, the hearing loss is measured in terms of decibels usually from 10 to 100 dB for the audible range of frequencies.

### Diagnostic Audiogram

The diagnostic audiogram employs sounds of specific frequencies and intensity levels for determining what the person can hear in each ear. The sounds are delivered to the person through headphones and he/she is asked to identify each time a sound is heard in which ear. The intensity of sound is progressively reduced to determine the level at which a patient can barely hear, which defines the hearing threshold. The hearing threshold levels are determined by both air conduction and bone conduction audiometry. In air conduction audiometry, the test signal is delivered to the patient by earphones. In bone conduction audiometry, the test signal is provided by a bone vibrator placed on the mastoid of the patient. The purpose of masking is to apply a signal (noise) to the non-test ear to keep it from responding instead of the ear being tested. A narrow band noise centred on the pure tone test frequency or a wide band white noise is used for this purpose. *White noise* is a noise containing all frequencies in the audible spectrum at approximately equal intensities.

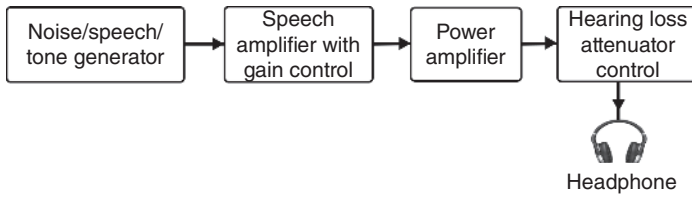
### Instrumentation

An audiometer is used to identify hearing loss in individuals for quantitative determination of the degree and nature of such a loss. It is essentially an oscillator driving a pair of headphones and is calibrated in terms of frequency and acoustic intensity. Both frequency and intensity are adjustable over the audio range. The instrument is also provided with a calibrated noise source and bone conductor vibrator.

Audiometers may be divided into different types on the basis of the type of stimulus they provide to elicit auditory response. A *pure tone audiometer* is primarily a diagnostic instrument to obtain air conduction and bone conduction thresholds of hearing. *Speech audiometers* are normally used to determine speech reception thresholds for diagnostic purposes and to assess and evaluate the performance of hearing aids. *Screening audiometers* are used to separate two groups of people: one that can hear equal to or better than a particular standard and the other that cannot hear so well. *Diagnostic audiometers* include all routine tests for tone and speech audiometry as well as different special tests. It offers pure tone audiometry via earphones or bone conduction, masking and speech audiometry with speech recognition threshold (SRT), and speech discrimination (SD). Additional features include hearing loss simulator (HLS) and master hearing aid (MHA). These dual channel instruments support speech audiometry from live or recorded sources.

Most audiometers are microcontroller-based instruments. Such equipment offers greater convenience in calibration, test signal presentation, and versatility. Automated data collection and storage are essential features included in such equipment. They generate signals in a frequency range from approximately 100 to 10000 Hz. The frequency in this range is adjustable in discrete octave or semi-octave steps, while others provide for continuously variable frequency over their designed range. The frequency must remain accurate at a value within 1–3% of the indicated value. The test frequencies should be of sufficient purity of sine wave signal with the total harmonic distortion not more than 3%.

The intensity range of most audiometers starts from approximately 15 dB above normal to 95 dB below normal over a frequency range from approximately 500 to 4000 Hz. The intensity range is somewhat less for frequencies below 500 Hz and above 4000 Hz.



**Figure 21.2** Block diagram of a diagnostic audiometer.

This is partly because of certain instrumental limitations imposed by the earphone or vibrator and partly due to the desire to avoid the threshold of feeling from stimulation at the lower frequency levels. The threshold of feeling is the sensation of pain or tickle in the ear, which results from sound pressures and limits the maximal sound intensity that can be tolerated by the ear. The intensity level at which the threshold of feeling is stimulated varies with frequency.

Figure 21.2 shows a block diagram of a diagnostic audiometer. It consists of two generators, namely, pure tone generator and noise generator, and each channel having an attenuator, equalization circuit, and power amplifier. The pure tone generator is a single frequency sound wave. It has an oscillator that generates signal with controllable frequency in the range from 250 Hz to 8 kHz. The signal intensity can be varied from 10 to 100 dB using an attenuator. An equalization circuit is required to provide frequency dependent attenuation in order to calibrate the output sound levels in dB HL and also to provide different amount of attenuation for different output devices used (headphone, loudspeaker, and vibrator). The attenuator, known as the hearing or tone level control, should be capable of controlling the output sound level over a desired range in steps of 5 dB. The output sound level should be within 3 dB of the indicated value. A power amplifier is required to amplify the signal. The signals are given to the ear through an earphone or headphone.

For the masking purpose, the noise generator provides wide band noise, which has energy spectrum equally distributed over the test frequency range, i.e. up to 8 kHz. There is a facility for narrow band noise, whose output should be distributed around the test frequency. The output power available from the power amplifier determines the maximum sound pressure level available from the headphones and the bone vibrator. The amplifier must have low distortion and a good S/N ratio to meet the standard requirements. The audiometer can be connected to a PC for data processing.

For conducting the speech test, spoken voices are used. A CD player is used when the test is to be conducted with the recorded speech. Live voice facility is incorporated in the microphone amplifiers for the purpose of communication.

### **Audiometric Booth**

Although by using the noise protected headphones, audiometric tests can be conducted in a low level of environmental noise, it is preferable that the tests are essentially conducted in especially designed small cabins that provide the noise-free environment. Since most of the time the environmental noise is difficult to control, the noise-free conditions are achieved by using a sound isolating enclosure that is capable of attenuating all frequencies within the sensory range below the threshold of hearing of normal

ears. By using double-wall construction and appropriate sound absorbing material, it is common to achieve 25 dB attenuation at 125 Hz and 60 dB attenuation at frequencies between 1000 and 8000 Hz. Standard features of such booths or enclosures include lighting, carpeting, vibration isolators, universal jack panel, forced air ventilation, and an audiometer shelf.

## Specifications

*Tests:* Pure tone audiometry, speech audiometry

*Frequency range:* 125–8000 Hz

*Masking:* Narrow band/wide band noise, speech-masking noise

*Transducer:* Earphones, bone vibrator, insert free-field loudspeaker via extension amplifier

*Test modes:* Air conduction, bone conduction, free-field

*Speech test input:* Microphone or CD player

## Applications

Diagnostic audiometer is intended to be used by an audiologist or hearing healthcare professional to detect hearing loss in a patient.

# 22

## Audiometer: Evoked Response

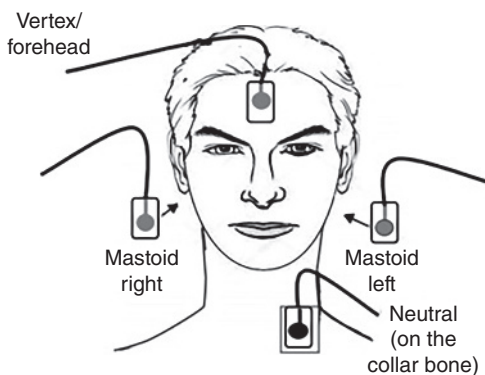
### Purpose

An evoked response audiometer is a diagnostic device that is used in the place of conventional audiometers especially for the purpose of diagnosing possible defects in the vestibulocochlear nerve and brainstem auditory pathways, infant hearing screening and evaluation, auditory assessment of non-cooperative patients such as children and adults, and determination of hearing loss type and degree. The ability to make such tests and evaluation helps in early detection and rehabilitation of hearing impairment in newborns, young children, and people who have neurological problems.

### Principle

Evoked response audiometry is an objective electrophysiological test that measures the electrical activity in the cochlea and auditory pathways from the auditory nerve to the brainstem in response to auditory stimulus such as clicks or tone pip from an

**Figure 22.1** The electrode positions generally used in evoked response audiometry.



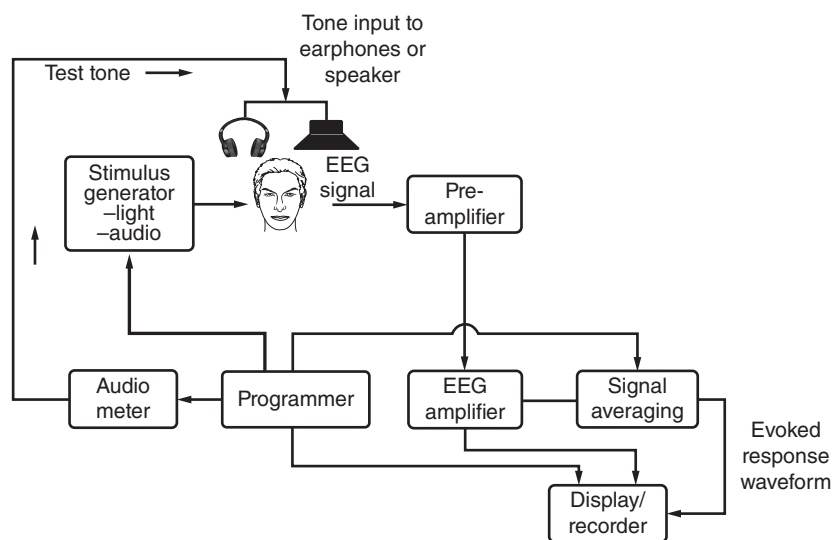
acoustic transducer such as an insert earphone or headphone that generates a response from the brainstem. The evoked potential recorded via electrodes placed on the scalp is a short latency potential, since it occurs within the first 10 ms after presentation of the sound stimulus. The surface electrodes are typically placed at positions behind the ears, or on the forehead, and a neutral electrode at a somewhat arbitrary position on the cheeks, or on the collarbone. The position of the electrodes usually used is shown in Figure 22.1.

Potential differences measured from the skull are amplified and then transferred to and displayed on a PC. The evoked potentials have an amplitude of the order of a few hundred nanovolts ( $10^{-9}$  V), up to some microvolts ( $\mu$ V) at maximum. The amplitude of the response signal is averaged and plotted against the time (millisecond), in a similar way as that of an EEG. When auditory evoked potentials are present, a typical wave pattern emerges and certain waves can be identified. The labelling of the waveform peaks has been standardized as I–VII. The recording gives information about the capability of the cochlea (inner ear) and brain pathways for hearing of a person with signs, symptoms, or complaints regarding the type of hearing loss in the brain or a brain pathway. In automated systems, this response is recorded and analysed by a computer, and based on the computer algorithm, the subject either passes or fails the screening. The results from non-automated screening machines require interpretation by an expert audiologist.

### **Instrumentation**

Auditory evoked response systems for recording evoked potentials are commercially available. All of them have similar subsystems that typically include a stimulus generator capable of generating a variety of audio stimuli in the form of clicks; tone bursts; tones; transducers for stimulus presentation such as insert earphones, standard earphones, and bone oscillator; pre-gelled EEG surface electrodes; and electronic circuits including a differential main amplifier, filters, analog-to-digital converter, and a signal averaging computer, data storage, display monitor, and printer. Figure 22.2 illustrates a simplified schematic diagram of a typical instrument. The major subsystems are described as follows:





**Figure 22.2** Block diagram of an evoked response audiometer.

*The stimulus generator:* It is a wide range pure tone audiometer whose frequency output can be selected in the range from 250 to 8000 Hz. The output power levels are adjustable from  $-5$  to  $+110$  dB in 5 dB steps. In addition to the pure tones, internally generated broadband noise can be used as the stimulus. There is a provision for external input for other types of stimulus, which may include narrow band noise, speech, high frequency auditory signal for animal research, or photic or tactile stimulator. The rise/decay times can be selected from 1 to 100 ms. Outputs are provided for the left ear, right ear, or both. A variable intensity masking noise source is included in the generator. A power amplifier is incorporated to drive a speaker or tactile transducer. Total harmonic distortion should not exceed 2%. Stimuli from 12 to 16 kHz are included to facilitate investigation into high frequency hearing loss and ototoxic drug effects.

Modern evoked response audiometers are built around microcomputers. In these instruments, the stimulator, preamplifier and amplifiers, and filters are all digitally controlled via the central processing unit. They do not carry any push button or dials as the parameters can be varied by means of the keyboard or touchscreen operation. The parameters can be varied over a very wide range, which would not be otherwise possible with conventional knobs and switches.

*The programmer:* The programmer operates under the control of a computer, which ensures the system operation is in correct time sequence. It helps to achieve a selectable rate of stimulus presentation, stores the number of pulses that the operator chooses to constitute a run, starts the recorder at the beginning of the run, and turns the audiometer tone generator on and off to provide the auditory stimuli at the proper time. It also speeds up the chart drive for the detailed signal samples. Some test parameters are pre-programmed and stored in non-volatile memory. These parameters are retained when the power supply is cut off but can be reprogrammed or upgraded from a personal computer by an authorized personnel as necessary.

*Signal averaging computer:* The function of the signal averaging circuit is to separate evoked responses from the normal EEG activity by ignoring those components, which are not synchronized with stimuli. Because the waveform of the evoked potential will be essentially the same every time in response to the tone presentation and the other electrical activity will vary randomly, the evoked response accumulates in the computer memory and the noise component tends to average to zero with repeated presentations. It may be provided with about 100 averaging points depending upon the degree of resolution required. The integrating time can be selected from 5 to 500 seconds and sweep duration or analysis time from 0.1 to 5 seconds. A delay circuit is included to select a delay time from 0, 0.2, 0.5, and 1 seconds, between the onset of the stimulus and the start of analysis by the signal averager. The amplitude of the evoked response may be normalized to that of the on-going EEG monitoring signal using a gain control. The computer output can be displayed either on an liquid-crystal display (LCD) screen or on an X-Y plotter.

*Chart recorder:* In the two-channel recorder, one channel is used to display the averaged response after it has been processed by the computer and the other displays unprocessed EEG. There are two event markers, one of which is activated by each gating pulse from the programmer to show the beginning and duration of each stimulus and the other is available for registering any mark at the desired instant. The chart can be driven at four different speeds (1, 5, 25, 125 mm/s), which are automatically switched by the programmer.

It may be noted that the electrode placement, stimulus rate and polarity, signal repetition rate, filter characteristics, stimulus characteristics, and sampling rate during analog-to-digital conversion all affect the recording and so must be controlled by the clinician.

## Specifications

*Biosignal input*

*Number of channels:* 2

*Gain:* 114.5 dB

*Resolution voltage:* 0.63 nV

*Amplitude range:* 0.63 nV–63  $\mu$ Vpp

*Common mode rejection ratio (CCMR):* 110 dB

*High pass filter:* 160 Hz, adjustable

*Low pass filter:* 4 kHz

*Input impedance:* 30 M $\Omega$

*Impedance test of electrodes:* Software controlled

*Stimuli*

*Click:* 150  $\mu$ s

*Burst:* 320 ms (0.5, 1, 2, 3, 4 kHz)

*Amplitude-modulated sine wave:* Carrier: 0.5, 1, 2, 4 kHz; modulation: 80–90 Hz

**Outputs/transducers**

*Stimulus:* 0–100 dB HL adjustable in 10 dB steps

*Stimulation rate:* 8, 16, 20, 24, 32 Hz; default: 20 Hz

*Time window (measurement time):* Up to 15 ms, adjustable

*Masking white noise maximum:* 70 dB HL

## Applications

Evoked response audiometry has a wide range of clinical applications. The equipment is used by audiologists, audiological assistants, and medical doctors working in the field of audiology.

## 23

### Audiometer: Impedance (Tympanometry)

#### Purpose

An impedance audiometer is a device designed to test the functional status of the middle ear and mobility of the tympanic membrane (eardrum) and the conduction bones. The technique is also known as *tympanometry*. The test enables the audiologist to measure how well the eardrum is vibrating when sound strikes it and how well the tiny bones of the ears are functioning to transmit those vibrations. The other purpose of the test is to assess acoustic reflex pathways including the auditory brainstem and the cranial nerves. This test, however, does not evaluate auditory sensitivity directly. Tympanometry is an important part of the audiometric evaluation as abnormal finding on this test may suggest a conductive loss.

#### Principle

Impedance audiometry, or most commonly referred as tympanometry, is based on producing variations of air pressure in the ear canal by means of a probe measuring the middle ear's acoustic resistance. Acoustic impedance is considered to be a response to acoustic admittance, which involves the measurement of air pressure or energy flow in the eardrum and associated structures. The reciprocal of acoustic admittance is acoustic impedance. As these measurements are performed in terms of impedance rather than admittance, the technique is often known as impedance audiometry. As admittance implies how energy is transmitted through the middle ear, the instrument is designed to measure the reflected sound that is expressed as an admittance or compliance. The results are plotted on a chart known as a *tympanogram*, which is a graphic representation of the relationship of external auditory canal air pressure to impedance.

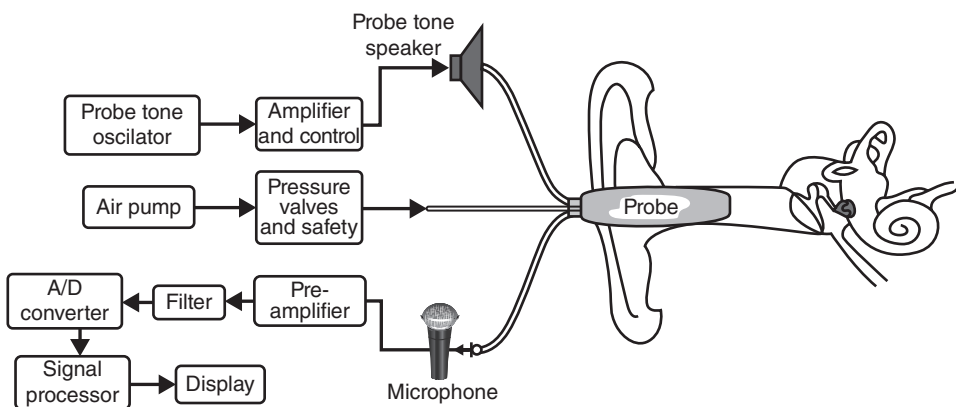
### Acoustic Reflex Measurement

Acoustic reflex threshold of the middle ear (contraction of stapedius muscle) is a response to loud noise presented to the auditory pathway. When the stapedius muscle contracts in response to a loud sound, there is a change in the middle ear admittance due to this contraction. This change in admittance is reflected as a deflection in the recording. The test is performed by presenting stimulus tones of varying intensities at 500, 1000, 2000, and 4000 Hz at short bursts. Reflex measurements are normally carried out with air pressure in the outer ear canal set for maximum compliance. Usually this test is conducted after performing routine tympanometry. The reflex measurements along the impedance curve measurement forms the basis for study of the integrity of the complete middle ear system, which is of great diagnostic value.

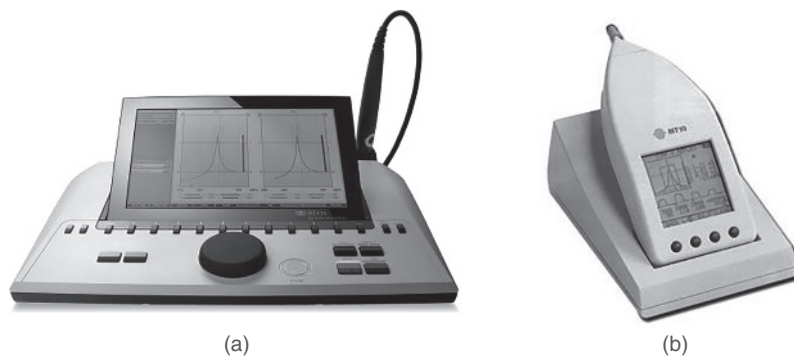
### Multiple Frequency Tympanometry

In addition to the standard 226 Hz probe tone tympanogram, a higher frequency probe tone can also be employed for tympanometry. However, there are different screening protocols for different frequencies of the high probe tone. A tympanogram recorded using high probe tones is generally considered better suited for screening of neonates than tympanograms recorded using the conventional 226 Hz probe tone. In high frequency test, measurements are made through a series of frequencies ranging from 250 to 2000 Hz.

Figure 23.1 illustrates the block diagram of acoustic impedance audiometer. A hand-held probe with a flexible and soft tip is inserted into the ear canal to obtain an airtight seal. The inside of the handheld probe contains three tubes. These tubes contain a loud speaker to deliver pure tone signal and a microphone to receive reflected sound and another one for air delivery from an air pressure pump. A pure tone is sent to the tympanic membrane, and the response of the tone sent back from the eardrum is recorded through the tube connected to the microphone. The air pump generates air pressure in the external ear canal that can be varied from  $-400$  to  $+400$  mm H<sub>2</sub>O. The air pressure pump assembly consists of a DC step motor. The pressure is measured using a strain gauge type transducer whose output goes to an A/D converter, processor, and display



**Figure 23.1** Block diagram of an acoustic impedance audiometer.



**Figure 23.2** Typical models of impedance audiometers: (a) table model and (b) handheld tympanometer. *Source:* Reproduced with permission from Interacoustics, Denmark.

screen. In this way, the impedance of the eardrum can be calculated. Any disease process in the middle ear can result in either increase or decrease in the flexibility of the eardrum and may be an indication of hearing loss. A tympanometer typically has a signal generator and transducers that can be used to deliver high intensity tones at various frequencies for the purpose of acoustic reflex testing.

A tone of 226 Hz is generated by the tympanometer and delivered into the ear canal, where the sound strikes the tympanic membrane, causing the vibration of the middle ear. This in turn results in the conscious perception of hearing. Some of this sound is reflected back and picked up by the microphone. From the middle ear, the acoustic transmission is maximum when the air pressure in the ear canal and middle ear is equal. This implies that the lowest impedance will be observed when the air pressure will be equal on both sides of the tympanic membrane. This would be indicated by the highest compliance to the sound waves and is also referred to as a compliance peak. Mobility of the tympanic membrane is indicated by the height of the compliance peak on the tympanogram. Low compliance is indicated by stiffness of the middle ear and tympanic membrane.

Tympanometry is an objective test of middle ear function and is not a hearing evaluation, but is rather a measure of energy transmission through the middle ear. The results of the test should always be viewed in conjunction with pure tone audiometry. Commercial instruments for tympanometry are available both as desktop and as handheld portable type. The two examples are shown in Figure 23.2. The instruments provide a versatile combination of testing capability for tympanometry alone, tympanometry combined with screening acoustic reflex measurements, and screening audiometry. They also allow storing of data by printing or by transferring data to a computer.

## Specifications

**Tympanometry:** Probe tone: frequency: 226 Hz for all functions; 678, 800, 1000 Hz for traditional curve tympanometry; level: 85 dB sound pressure level (SPL); air pressure:

–400 to +400 mm H<sub>2</sub>O; function: automatic, where pump speed start and stop pressure can be user-programmed

*Acoustic reflex functions:* Automatic testing with four stimuli to each ear; stimulus duration 1.0 second; intensity (maximum): 110 dB HL

*Audiometer:* Screening audiometry; intensity: 10–50 dB HL; frequency: 0.5, 1, 2, 3, and 4 kHz

## Applications

Impedance audiometry tests are mostly performed in good hospitals.

## 24

## Audiometer: Pure Tone

### Purpose

Pure tone audiometer is a device that is generally used to perform the key hearing test to assess the nature, degree, and configuration of hearing loss. Thus, the test provides the basis for diagnosis and plans the most appropriate interventions for management of the problem. The test is, no doubt, subjective because for determining the hearing threshold, the clinician has to rely on the patient's response to pure tone stimuli. The test is suitable for adults and children old enough to cooperate and respond to the test procedure.

### Principle

Pure tone audiometry involves assessing the hearing response of an individual to the pure tones. A pure tone is a tone that has a single specific frequency. The frequency of the tone is determined by the rate or speed at which the sound source vibrates. Intensity of sound is defined as the amount of energy transmitted per second over an area of 1 m<sup>2</sup>. For the purpose of audiometry, the loudness of the tone can be considered as the intensity of the pure tone. Sound intensity is expressed in decibels (dB). In audiometry, different dB scales are used for different applications that include the dB hearing level (HL) scale, the dB sound pressure level (SPL) scale, and the dB sensation level (SL) scale. However, the most common dB scale used in audiology is the dB HL scale.

Pure tone audiometry employs both air and bone conduction techniques to assess the hearing loss. An air-conducted signal travels through the air and reaches the ear in the same way as we normally hear on daily basis. Thus, air conduction audiometric threshold measurements are indicative of a person's hearing for air-conducted sounds as much as the same manner by which humans typically hear most sounds. Bone conduction, on the

other hand, stimulates the cochlea directly with pure tone signal, bypassing the outer and middle ear. This type of testing helps to evaluate whether a hearing loss measured via air conduction reflects a cochlear/neural deficit or an outer or middle ear dysfunction.

The results of pure tone audiometric testing representing an individual's hearing status are plotted on a graph commonly called as the audiogram. Frequency, measured in hertz (Hz), is plotted on the horizontal axis, generally from 250 up to 8000 Hz, whereas the intensity level of the sound in dB HL is represented on the vertical axis of the audiogram. Audiograms generally represent lower intensities at the top and higher intensities at the bottom, increasing in 5 dB steps.

### **Instrumentation**

Pure tone audiometers vary from simple, inexpensive screening devices used in public health programs to more sophisticated and expensive diagnostic audiometers used in hospitals and clinics. However, some components are common to all audiometers, which include the following:

*Oscillator:* An audio oscillator is required in all pure tone audiometers to generate pure tones of different frequencies. The frequency variation may be of continuous type, but it is usually in discrete steps of 125, 250, 500, 750, 1000, 2000, 3000, 4000, 6000, and 8000 Hz.

*Amplifier:* The output power available from the power amplifier determines the maximum SPL available from the headphones and the bone vibrator. The amplifier amplifies the oscillations to a fixed intensity level, e.g. 110 dB HL. The amplifier must have low distortion and a good signal-to-noise ratio to meet the standard requirements.

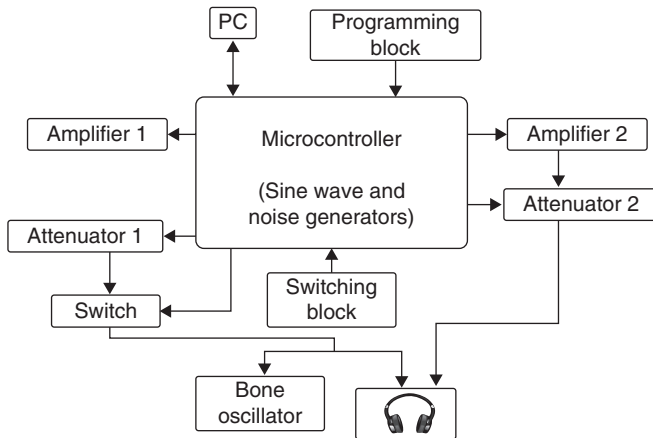
*Attenuator:* The attenuator is used to control the intensity of the amplified oscillations with a view to vary the energy reaching the ear. The range of variation is from 0 to 110 dB HL in 5 dB HL steps. The audiometers generally display the maximum intensity that is allowed at each frequency.

*Earphones:* Earphones are transducers that convert electrical energy into acoustic energy that is presented to the ear. Rubber cushions are usually fitted to the earphones or insert earphones may be used, which are inserted into the ears. For bone conduction studies, the sound is sent directly to the inner ear via the skull.

*Masking:* Most audiometers have facilities to generate a masking noise, which is especially required when the hearing thresholds differ significantly between the ears. For the masking purpose, the noise generator should provide wide band noise, which has energy spectrum equally distributed over the test frequency range, i.e. up to 8 kHz. There is a facility for narrow band noise whose output should be distributed around the test frequency.

Modern instruments are mostly microprocessor based in which the software controls the hardware, stores the data, and prints a standard audiogram report. Figure 24.1 shows a block diagram of an audiometer. It consists of two channels, namely, pure tone generator and noise generator, each channel having an attenuator, equalization circuit, and power amplifier. The tone generator or oscillator has a controllable frequency range from 250 Hz to 8 kHz. The equalization circuit is required to provide





**Figure 24.1** Block diagram of a pure tone audiometer.

frequency-dependent attenuation in order to calibrate the output sound levels in dBHL and also to provide different amounts of attenuation for different output devices used (headphone, loudspeaker, and vibrator). The attenuator, known as the hearing or tone level control, should be capable of controlling the output sound level over a desired range in steps of 5 dB. The output sound level should be within 3 dB of the indicated value. Some audiometers have an automatic sequencing mode, in which a special audiometric test sequence is presented automatically by the audiometer. As with most clinical tests, calibration of the test environment, the audiometer, and the stimuli to ISO standards is needed before proceeding for the test.

### **Procedure**

During the test, the person is asked to sit in a soundproof room to prevent any background noise interfering with the test results. For air conduction audiometry, the person is asked to wear a pair of headphones. Pure tones generated by an audiometer are presented to the patient via a transducer. The audiologist selects the frequency of the tones, the intensity of the tones, and the transducer through which the stimuli are presented to the patient. The person is asked to signal whenever the sound is heard by the person, usually by pressing a button or raising the hand. Different types of transducers that include supra-aural air conduction earphones, circumaural air conduction earphones, insert air conduction earphones, bone conduction headphone, and loudspeakers (sound field) are available.

For bone conduction test, a bone conductor vibrator is attached to the head at the centre forehead position to see whether the hearing threshold improves. If it does, then the disorder is most likely wholly or partly conductive in origin. To avoid stimulation of the ear not under test with the vibrator, it can be temporarily made deaf by introducing a suitable masking noise in the non-test ear via an earphone. A narrow band noise centred on the pure tone test frequency or a wide band white noise is used for this purpose.

## Specifications

*Frequency range:* 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz

*Frequency range accuracy:* Better than  $\pm 3\%$

*Hearing threshold range:* 0–90 dB, 5 dB steps

*Hearing threshold range accuracy:* Better than  $\pm 2$  dB

*Harmonic distortion:*  $<3\%$

## Applications

Pure tone audiometric test reflects a key indication of an individual's ability to hear and respond to sounds. The pure tone audiogram is widely accepted as the gold standard assessment of peripheral auditory function. Depending upon its sophistication level, it is used mostly in clinics and hospitals.

# 25

## Audiometer: Screening

### Purpose

Screening audiometer is a device for rapid measurement of the hearing capability of an individual or a group against a predetermined limit of normality. It consists in testing and evaluating auditory responses to different frequencies at a constant intensity level. These instruments are of simpler design than those instruments used for in-depth diagnostic evaluation for medical purposes.

### Principle

A screening audiometer is designed to give calibrated signals of variable intensity, at different frequencies ranging between 250 Hz and 8 kHz, into the headphones or earphones used for testing hearing capability of an individual. The test is conducted under suitably soundproof setting. The screening audiometer can be manual or automatic. The operation of the *manual audiometer* is controlled by the operator throughout the test. The test time is quicker in manual instruments as the operator can make quick changes in the intensity of the sound based on the response of the subject, whereas the computer controlled test provides only gradually increasing signals, thus may be taking longer time.

### Automatic Screening Audiometry

Most of the screening audiometers in use are of automatic type. These instruments once started will complete the test consisting of various steps involving presentation of

**Figure 25.1** Screening audiometer.  
 Source: Reproduced with permission  
 from Interacoustics, Denmark.



pure tones in a computer-controlled manner, evaluating each response, and deciding whether a hearing threshold response has been achieved. Hearing threshold refers to the smallest tone heard when the signal volume is being continuously increased. The machine is programmed to deliver a different set of frequencies or present a different signal type (pulsed or continuous tone). The frequency change is done in a sequence given to one ear, and then the same sequence in other ear. Most audiometers used for workplace screening are supplied with audio cups or some type of cushions, which exclude more noise than standard headphones. A typical screening audiometer from M/s Interacoustic Denmark is shown in Figure 25.1.

The neonates do not respond well to the conventional testing or screening methods. However, various test possibilities allow the tester of having at least some evaluative result. It has been found that complex signals like white noise (WN) provide better responsiveness on neonates and up to the age of approximately seven months than, e.g. pure tones and narrow band noise. These tests are based on various reflexes aroused as result of the sound stimuli reactions.

The screening test is primarily a 'preventive audiometric testing' to perform 'hearing checks' on all employees who are constantly exposed to noise in the workplace. The purpose of these tests is to identify the possible early noise-induced hearing loss (NIHL). This is to take precautionary measures to prevent further progression of NIHL by reducing the level of noise exposure, ear protection, or on some occasions removing a particular person from the workplace. Thus the purpose of any screening program is to identify individuals at risk. They can also be subject to further examination at the earliest age possible. Screening of children for hearing deficiency is extremely important as in children, this deficiency can interfere with normal speech and language development, communication, and the ability to learn, which may put them at a disadvantage educationally, emotionally, and socially. Similar screening tests are also usually required to be performed in schools.

## Specifications

*Frequency range:* 125–8000 Hz

*Frequency accuracy:* <1%

*Distortion:* <2%

*Output level range (AC):* -10 to 100 dB HL

*Output level accuracy:* Within 3 dB

*Output level step size:* 5 dB

*Tone present:* Single, pulsed, warble, or continuous

## Applications

Screening audiometers are ideal equipment for schools, industry, and primary medical practices or wherever quick hearing screening evaluations are performed. This is because large numbers of persons of many ages are readily accessible in such establishments and the tests can be accomplished in a short period of time with relative ease.

## 26

### Audiometer: Speech

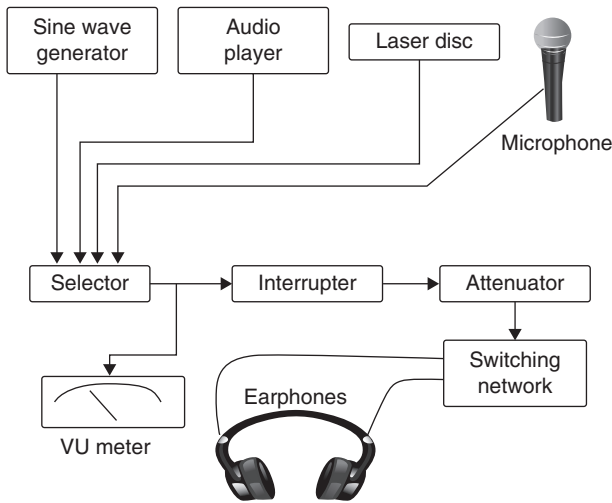
#### Purpose

A speech audiometer is a device that utilizes speech signals to determine the ability of the patient to understand everyday communication. The technique consists in examining the processing ability of the patient in relation to their degree and type of hearing loss. However, the patient's pure tone threshold and speech threshold do have a predictable relationship. Therefore, speech audiometry can be considered as a crosscheck of the pure tone audiogram, because the results with speech audiometry can vary greatly between patients with the same hearing loss configuration. Speech audiometry also provides information regarding discomfort or tolerance to speech stimuli and on word recognition abilities.

#### Principle

Besides tonal audiometry, it is often necessary to carry out tests with spoken voices. These tests are particularly important before prescribing hearing aids and in determining the deterioration of speech understanding of patients. Specially designed speech audiometers are used for this purpose. However, most of the diagnostic audiometers incorporate facilities for both tonal and speech audiometries. Figure 26.1 is a block diagram of an audiometer that provides both tonal and speech testing arrangements.

Speech audiometer input devices include microphones for live voice testing, tape recorders, and CDs for recorded testing. The audiometer has a provision for connecting for microphone for live voice or tape recorder or CD player, from which



**Figure 26.1** Block diagram of a speech and tonal audiometer.

word lists for threshold and discrimination determination can be played back. An auxiliary CD/tape channel may be used for playing recorded masking signals. Same types of transducers such as earphones, ear inserts, bone conduction vibrators, and loudspeakers as those used for pure tone audiometry are used to present speech stimuli to the ear.

Speech audiometry can be conducted using a number of tests. The most common test is to determine speech reception threshold (SRT) that refers to the level at which the patient can correctly respond to 50% of the presented two-syllable words (spondees). Spondees are words of two syllables having equal stress, e.g. shotgun, aeroplane, workshop, etc. The test is performed by using threshold word lists. Each ear is tested separately and the patient is asked to repeat the word he hears one at a time. This test may be performed using either live voice or recorded speech. Another test is referred to as speech discrimination scores (SDS) that reflect the number of words correctly expressed as a percentage.

*Live voice* presentation is recommended for both its effectiveness and flexibility allowing the clinician to perform the test to the particular needs of a patient. The test with live voice should only be done when the audiometer is used in a sound cabin, so that the patient cannot hear the audiologist's voice directly. If the audiologist and the patient are in the same room, false results would be obtained particularly when the person is having normal or almost normal hearing. In the two room arrangements, the audiologist works from the audiometric equipment room containing the speech audiometer while patients undergo testing in the evaluation room.

The CD player has a capacity for recording a limitless variety of test materials and a consistency of speech input, which cannot be obtained for live voice audiometry in relation to test–retest repeatability. The use of pre-recorded word lists gives the advantage of always presenting the same program for the patient in repeat tests presenting the same test words and sentences to cater for the widely differing needs of age, intelligence, dialect, and language. This is not the case with live voice as there is the risk

that the same operator may not be there each time and this can alter the results. However, the disadvantage of using standardized recorded tests is the lack of flexibility of live voice testing corresponding to the individual needs of the patient. The audiometer is usually equipped with an interface for directly controlling an external CD player. When a word is selected on the display, that word can be transmitted from the CD player to the patient's earphone at a given intensity and his reply scored in percent on the speech matrix.

*Masking* is also very essential in speech audiometry to minimize the risk of response from the ear not being tested. Speech noise is generally recommended as the masking noise of choice, but white noise is also preferred by many audiologists. Speech noise is actually white noise filtered to a low and middle frequency spectrum. For speech audiometry, the audiometer allows masking to be employed together with air, bone, and free-field outputs. Any type of pre-recorded masking may be used via the CD/tape input.

*Free-field speech audiometry* test is performed employing built-in power amplifier and a pair of external loudspeakers. Different types of amplifiers are used depending on the maximum intensity level required in the free field. These intensities can vary from 80 to 100 dB above threshold, which corresponds to the 100–120 dB sound pressure level. The two crucial factors affecting the results of free-field testing are the distance from the loudspeaker to the patient and the degree of absorption of the sound room. Free-field testing is often used in speech audiometry when testing children because many children dislike wearing headphones.

Modern speech audiometers using microprocessor based technology have several advanced benefits including software with embedded speech tests for word recognition score and speech in noise. This provides quick and accurate diagnostic and pragmatic speech testing features. Digital speech files for children and adults in different languages can be embedded into portable and larger audiometers, thereby replacing internal and external tape recorders, CD players.

## Specifications

*Tests:* Tone tests and speech tests

*Masking signals:* Narrowband noise and speech noise

### ***Air conduction***

*Frequency range:* 125–8000 Hz

*Level range:* –10 to 120 dB HL depending on headset and frequency

### ***Bone conduction***

*Frequency range:* 250–8000 Hz

*Level range:* –10 to 80 dB HL depending on headset and frequency

### ***Free field***

*Frequency range:* 125–8000 Hz

*Level range:* –10 to 90 dB HL

## Applications

The applications of speech audiometry include speech understanding, evaluating auditory communication impairment, assessing effectiveness of a hearing aid fitting, facilitating a comparison between hearing aids, assessing degree and type of hearing loss, and detecting possible central auditory processing disorder. Speech audiometry also helps in audiological rehabilitation management.

## 27

## Audiometric Calibrator

### Purpose

The audiometric calibrator is an important instrument used by the audiologists to regularly test and calibrate an audiometer in order to maintain its measurement accuracy. Accurate and reliable measurements with audiometers are fundamental to characterize and quantify hearing loss of a person at different frequencies and selecting the most appropriate hearing aid. Incorrect measurements can lead to wrong diagnosis resulting in prescribing an incorrect hearing aid.

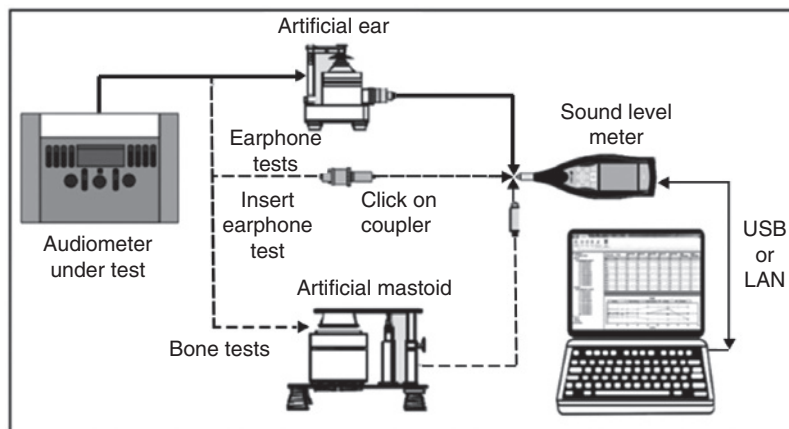
### Principle

The purpose of any calibrator is to check and verify that the measurement equipment is giving correct measurements. In this context, regular testing and calibration of an audiometer is considered necessary to maintain maximum measurement accuracy. Properly carried out calibration procedure on audiometers ensures that if a person's hearing is tested anywhere in the world, the threshold obtained will be consistent, irrespective of the place of their testing. This is achieved by calibrating the equipment against established standards and specifications. The current audiometer specifications are ANSI S3.6-2010 developed by the American National Standards Institute (ANSI).

For proper calibration of an audiometer, it is important that the calibrating technician has knowledge about each audiometer model and more importantly, the knowledge of the correct applicable ANSI standard. These calibration activities are usually conducted at the manufacturing facility or an outside laboratory, but it is essential that they are carried out on site at least annually. For example, calibration of speakers in a sound field is generally conducted on site because the unique acoustic characteristics of a specific field cannot normally be reproduced in a remote calibration facility.

Figure 27.1 illustrates the schematic diagram for calibration of the audiometer covering calibration of the audiometer itself, of ear phones, and of bone vibrators. The system is built around a sound level meter and analyser. The audiometers are calibrated using an ear simulator and a calibrated microphone with an associated





**Figure 27.1** A complete portable audiometer calibration system i714 including sound level meter, artificial ear (mastoid), and laptop computer with necessary software. *Source:* With permission from M/s Bruel & Kjaer.

coupling volume open on one side allowing application of headphones when testing. While the system comprises of an artificial ear for testing air conduction hearing mechanisms, the bone conduction hearing mechanisms is tested utilizing an artificial mastoid. This device uses a series of rubber layers to couple the bone vibrator to a force transducer.

### Sound Level Meter

A sound level meter is a device designed to respond to sound in the same way as the human ear and to provide objective, reproducible measurements of sound pressure level (SPL). In fact, they measure the pressure of the sound waves travelling through the air from a source of noise. That's why they are often referred to as SPL meters. The measurement of sound intensity by these devices is usually expressed in units called decibels.

There are many different sound measuring systems available. Although they may differ in detail, each system has some basic components such as a microphone, a processing section, and a read-out unit. An octave filter set is used to the sound level meter to limit the instrument to measuring sound levels in a certain frequency range, rather than the overall sound level. The microphone is mounted at the top as a pointy stick, which samples and measures the sound. This arrangement gives more accurate measurements as the microphone keeps away from the body of the instrument, thereby cutting out reflections. The sound detected by the microphone is measured by electronic circuits where it is amplified and filtered in various ways before displaying it on digital liquid-crystal display (LCD) display.

Before the sound level meter is used to make any measurement, it is calibrated with a known signal to verify that the meter is reading accurately. Self-contained calibrators are available (QC-20 from M/s Raeko, USA), which generate stable acoustic signals at a controlled frequency and amplitude to provide quick, precise calibration to

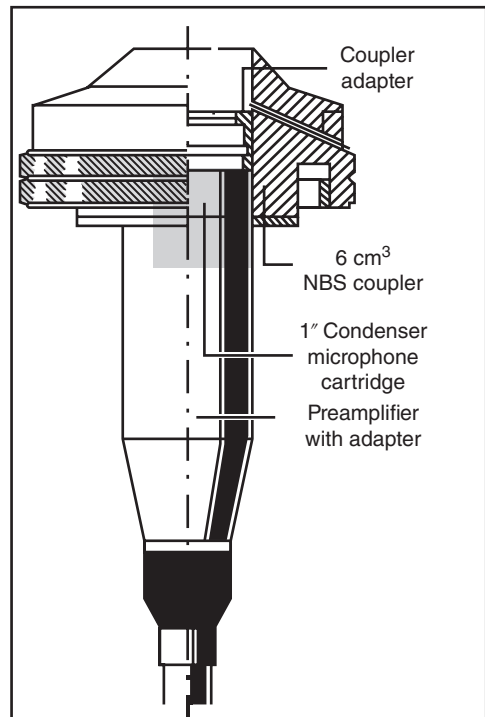
verify the accuracy of the sound level meter in the field. It is a dual-frequency, dual-amplitude device and generates four selectable reference tones: frequencies of 250 and 1000 Hz, each at levels of 94 and 114 dB, respectively.

### **Artificial Ear/Ear Simulator/Coupler**

The ear simulator is a device that has an acoustic impedance closely resembling that of an average human ear. When the device is coupled to a sound source, the impedance will load the sound source similar to the loading caused by the human ear. It is primarily intended for measurement of output sound pressure of an earphone under well-defined loading conditions in a specified frequency range. The measurements are made on insert earphones, e.g. used in hearing aids, operator headsets, etc., for parameters such as frequency response, sensitivity, and distortion measurements. The simulator consists of a principal cavity of specified volume, an acoustic load network, and a calibrated microphone. They are designed to meet the requirements of IEC 60711 and ANSI S3.25 (ASA39/1979) standards for an ear simulator for measurements using insert earphones.

The artificial ear comes complete with a coupler, preamplifier, microphone, adapter to 1 in. and  $\frac{1}{2}$  in. microphones, and a base plate with a mechanism for clamping the object being tested as shown in Figure 27.2. The clamping mechanism is spring loaded and provides a force that is adjustable from 2 N (approx. 0.2 kg) to 10 N (approx. 1 kg) as per recommendations of the relevant ANSI standard. The effect of vibration is minimized during the measurements, by isolating the artificial ear from shock and vibration by means of three soft rubber feet.

**Figure 27.2** Schematic diagram of an ear simulator Model 4152. The coupler is mounted directly on a microphone. *Source:* With permission from M/s Bruel & Kjaer.

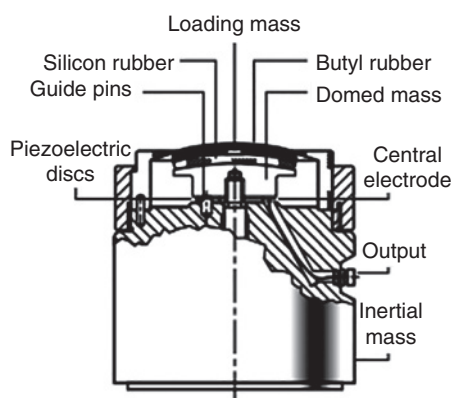


The ear canal volume is of a similar shape and volume to that of the actual human ear. A 1/2 in. microphone is mounted in the housing of the ear simulator, terminating the main ear canal volume. The couplers are available in the sizes of 2.5, 6, and 7.5 cm<sup>3</sup>. The 2 cm<sup>3</sup> coupler may be used directly on the microphone with preamplifier without use of the main housing. This gives an artificial ear, which is very small and useful for special measurements on, e.g. spectacle type hearing aids. The 6 cm<sup>3</sup> couplers may also be mounted directly on the microphone with the aid of a stop collar. It is important to ensure that the earphone is well coupled to the sound level meter and that there are no leaks that would cause inaccurate SPL readings.

### Artificial Mastoid

Bone conduction audiometry is an important part of the audiologic evaluation as it provides useful diagnostic information about the site of lesion of an auditory impairment. Since the stimuli given for conducting this test are vibratory signals delivered to the head, they are calibrated differently from the acoustic signals used for air conduction audiometry. The standard technique for the calibration of audiometric bone vibrators involves the use of an artificial mastoid, which is a coupling device that converts the vibratory signal to an electrical analog signal. The signal can then be given to a measuring device for display. The mechanical input impedance of the device is designed to represent the average mechanical impedance of the human head. International standards such as ANSI S13.1-1987, IEC 60318-6-2007 specify the mechanical impedance that should be designed into the artificial mastoid. The artificial mastoid is used for calibration of bone conduction hearing aids and bone vibrators used in audiometry.

The artificial mastoid consists of a mechanical simulation of the human head, incorporating a built-in force transducer to monitor the output of the device to be calibrated. As shown in Figure 27.3, it contains an inertial mass, simulating the human head that is mounted on a base plate by resilient plastic spacers that surround the securing bolts. The base plate is carried on a suspension composed of three conical springs filled with foam rubber to provide damping. The natural frequencies of this suspension, which isolates the whole apparatus from external disturbances, are all below 5 Hz, which is much below the low frequency limit of the working range. The base plate also carries a loading arm that maintains the device to be calibrated reliably in position, pressing against the calibration surface of the artificial mastoid with a static force that can be adjusted between 2 and 8 N.



**Figure 27.3** Cross-sectional view of key components of an artificial mastoid Model 4930.  
Source: With permission from M/s Bruel & Kjaer.

### Microphone

The 1 in. microphone is a pressure field based microphone that has a flat pressure frequency response over a wide frequency range due to optimum design of the damping of the diaphragm. It does not require any correction to the pressure response below 8 kHz. Its use is recommended where measurement of the local pressure is of interest, for example, for coupler measurements. The device is stable and has low inherent noise and high sensitivity, which are necessary parameters for coupler measurements and other laboratory measurements.

The ½ in. microphone is again a pressure field based microphone that is designed for high precision coupler measurements. The microphone is externally polarized and may be used at higher temperatures without severe changes in sensitivity. Both the microphones have sensitivity of 50 mV/Pa, frequency of 2.6 Hz to 8 kHz, and dynamic range of 10–146 dB.

### Bio-acoustic Simulator

The bio-acoustic simulator is a measuring device that is a kind of ‘dummy’ ear that is used to check the calibration of the manual or automatic audiometers using either pulsed or continuous tones on a daily basis. With this device, daily audiometer checks can be performed without the need for a human test subject. It is used to check the audiometer earphones in the 45–75 dB HL range. The simulator is generally programmed with 60 dB HL thresholds at each test frequency. The tests should be performed in a noise-free environment within an audiometric room for best results.

Figure 27.4 shows a block diagram of the bio-acoustic simulator. It uses two independent electret microphones to convert earphone signals into corresponding electrical signals. These signals are then amplified and sent to rectifiers for conversion to DC voltage, which further enters its respective detector. When sufficient signal is present at the earphone coupler, the appropriate indicator light (right or left) will light and the response relay will activate. Once this occurs, the earphone signal must be decreased by at least 10 dB (hysteresis) to deactivate the indicator light and the response relay. The filter and detector circuits select and detect various frequency components within the room noise spectrum. If the room noise is intense enough within a given octave band, it will activate the respective indicator light. Various resistor dividers can be used to allow different levels to be detected.

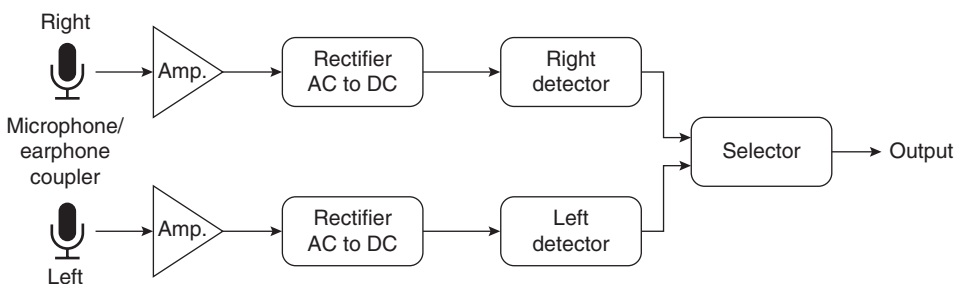


Figure 27.4 Simplified block diagram of bio-acoustic simulator.

The calibration procedures can be applied only to hardware audiometers, which are mostly available in hospitals, clinics, and research institutes. The PC-based audiometers using software techniques cannot be calibrated but they are available in several pre-determined configurations. Although the accuracy of these devices is usually not very high as compared with hardware audiometers, they are so simple that their operation is user-friendly.

## Specifications

*Sound level meter:* Sound measurements, tone assessment, loudness, and noise rating measurements; time history analysis parameters and spectra  
Artificial ear or ear simulator

1 in. and ½ in. pressure field microphones  
2 cm<sup>3</sup> click-on coupler, ear plug simulator  
6 cm<sup>3</sup> coupler

*Resonant frequency:* 13.5 ± 1.5 kHz

*Pressure:* 101.3 ± 3 kPa (1013 ± 30 mbar)

*Artificial mastoid:* Should have facility for the calibration of bone conduction; input adapter, ½ in. microphone and vibrators, frequency range: 50 Hz to 10 kHz, adjustable static force: 2–8 N, calibration surface area: 1260 mm<sup>2</sup>, inertial mass: 3.5 kg

## Applications

Audiometers are required to be calibrated regularly as they play a vital role for testing of hearing capabilities of persons in the hospitals. Calibration assists in ensuring accurate and reliable results that in turn would help doctors determine the extent of hearing loss the patient is suffering from. audiometric calibrators are mostly used in clinics and hospitals.

# 28

## Autotransfusion Unit, Blood

### Purpose

Autotransfusion units are designed to collect and process blood lost by a patient to extract red blood cells (RBCs) for subsequent transfusion into the same patient. They are particularly intended for use in surgeries that involve substantial volume blood loss. In this case, blood may be used during post-operative recovery and in emergency conditions or intensive care units after trauma. The system functions as a critical tool in helping to avoid unnecessary allergenic transfusions.

## Principle

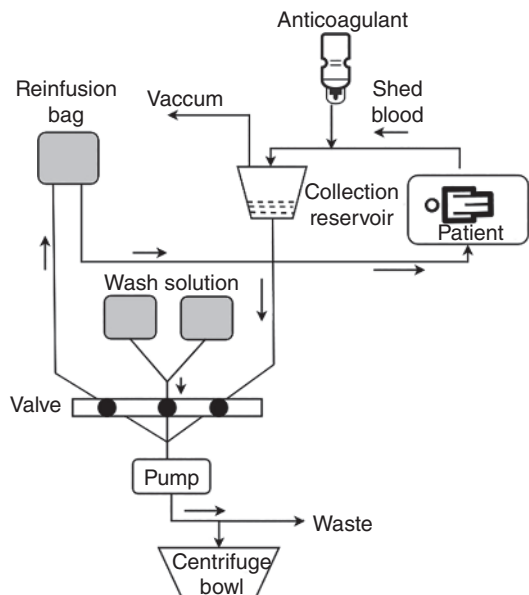
Autotransfusion is used in many commonly encountered situations characterized by the loss of blood. It is especially advantageous in cases involving rare blood groups, risk of transmission of infectious disease, non-availability or limited homologous blood supply, or other medical conditions for which the transfusion of homologous blood is contraindicated. A typical autotransfusion system typically comprises a disposable suction system to collect blood from the surgical site and a reservoir to store the blood. In addition, there is a centrifugation device to separate waste and wash the RBCs in saline. This is followed by microfilters that are employed to remove particulate matter. The RBCs suspended in saline are stored in the reinfusion bag.

The principle of autotransfusion is shown as block diagram in Figure 28.1. It consists of a special double lumen suction tubing through which fluid is aspirated from the operative field and is mixed with an anticoagulant solution. The fluid so collected is filtered in a sterile reservoir that has a capacity of between two and three litres of fluid. After sufficient volume of fluid is collected, processing phase begins. The processing phase involves the following steps:

### Prime Phase

In this phase, centrifuging action takes place. The speed of the centrifuge rotation can be selected from the control panel. The typical speed of rotation is 5600 rpm. Simultaneously, a pump starts operating, allowing the transfer of the contents of the reservoir to the wash bowl. The centrifuging action separates the components of the fluid according to their weight. The filling of the wash bowl continues until its level reaches the preset level of the

**Figure 28.1** Principle of autotransfusion system.



wash bowl. In automatic autotransfusion devices, a level sensor is used, which is designed to detect a full bowl and takes the process to the wash phase automatically.

### ***Wash Phase***

The wash phase starts when the wash bowl is appropriately filled with red cells. During this phase, all undesirable components are removed. Thereafter, the waste fluid moves out of the wash bowl into a waste reservoir bag. Washing continues till the end of the program and is terminated when 1–2l of wash solution has been transferred.

### ***Empty Phase***

When this phase is initiated, it allows the transfer of the wash bowl contents to the reinfusion bag. When the bowl has been completely emptied, the cycle is ended and a new cycle can begin. The reinfusion bag may contain a significant amount of air, which must be carefully monitored to avoid the risk of air embolism. Some machines use a separate blood bag attached to the reinfusion bag to reduce the chances of an air embolism. This second bag can be disconnected, air purged from it, and then tied off before giving for reinfusion.

Several commercial devices that perform autotransfusion are available. There are some commercial systems that collect blood from the surgical area post-operatively, and then wash or filter that blood for reinfusion. The term 'cell-saver' is used by M/s Haemonetics, USA, designated as Cell Saver Elite system. This device uses proprietary SmartSuction® technology integrated into the system. This technology provides the patients with a greater number of viable RBCs. The system also provides improved data collection and transfer with an integrated bar code reader, a USB port for quick download of up to 100 stored procedures, and a facility for data storage and reporting.

## **Specifications**

*Pump speed:* 0–1000 ml/min (adjustable)

*Centrifuge speed:* 5650 rpm

*Suction:* Automatic or manual suction up to –250 mmHg

## **Applications**

The applications of autotransfusion systems are in the field of surgeries during which substantial amount of blood loss occurs. It is thus a critical tool in the effort to avoid unnecessary allergenic transfusions.



## 29

## Balance, Electronic

### Purpose

Electronic balances are designed to measure precisely very small weights. They can give resolutions of a thousandth of a gram or better. Electronic balances are among the most vital pieces of equipment in a laboratory. These devices are available in a variety of sizes, variable resolutions, and multiple weight capacities. The more precision the balance offers, the smaller the unit of measurement resolution, each varying by additional decimal points. They are used by academic, pharmaceutical, drug discovery, genomics, and proteomics laboratories. The balances are sophisticated and sensitive electromechanical devices that demand special care and knowledge in their operation and maintenance.

### Principle

To understand the principle of various types of electronic balances, it would be advantageous to understand some of the commonly terms used in their operation. These terms are as follows:

*Mass:* Mass is a constant unit of the amount of matter possessed by an object. The unit of mass is kilogram. It remains the same irrespective of the location of measurement.

*Weight:* Weight is the product of mass and the earth's relative gravity at a particular place. Therefore, its value is not fixed, but depends upon the location. The weight is commonly expressed in the unit newton (N).

*Accuracy:* The ability of a scale to provide a result that is as close as possible to the actual value is known as accuracy.

*Calibration:* Calibration is the process of comparison between the output of a balance and a standard value.

*Capacity:* Capacity represents the heaviest load that can be measured on the instrument.

*Precision:* Precision indicates the amount of agreement between repeated measurements of the same quantity. It is also known as repeatability. For example, a balance can be extremely precise, but not necessarily accurate and vice versa.

*Readability:* Readability represents the number of places after the decimal point that the scale can be read. In other words, it is the smallest division at which the scale can be read. It can vary as much as 0.1–0.000 000 1 g.

*Tare:* The action of the balance to subtract a known weight of an object, usually the weighing container, to zero a scale, so that the final reading will be the real weight of the material to be weighed. Most balances allow taring to 100% of capacity.

In laboratories, two types of electronic balances are commonly used. These are the analytical balance and the precision balance. The difference between them is the degree of accuracy. Analytical balances are more precise and thus more expensive. More accurate balances are known as semi-microbalance, microbalance, or ultramicrobalance. The accuracies of different types of electronic balances are as follows:

- Precision balance (0.001 g)
- Analytical balance (0.0001 g)
- Microbalance (0.000 000 1 g)
- Ultramicrobalance (0.000 000 1 g)

Electronic balances can provide weights in different units that include grams, kilograms, pounds, newtons, grains, and ounces. They have several application modes that can be selected for statistics, formulation, differential weighing, density determination, pipette calibration, parts counting, percent weighing, filling, gross-net-tare weighing, and animal weighing. It is thus important to choose a balance that can provide the information specified by the laboratory protocols and quality control requirements. Besides, when choosing an electronic balance, care should be taken to consider the capacity, resolution, weight, containers, and size of their samples, as well as the speed at which the results are presented.

### ***Analytical Balance***

An analytical balance (often called a 'lab balance') is a class of balances designed to meet the highest accuracy requirements of analytical weighing processes, especially in the sub-milligram range. The measuring pan of an analytical balance is kept inside a transparent enclosure with doors so that it eliminates interfering ambient effects such as collection of dust on the pan and any air current in the room affecting the performance of the balance as shown in Figure 29.1. Thus, the enclosure acts as a draft shield. Also,



**Figure 29.1** Typical analytical balance.

the temperature of the sample should be at room temperature so that air currents due to convection do not enter inside the enclosure, which may cause an error in reading. These balances incorporate automatic internal calibration mechanism to keep the balance calibrated at all times, thus ensuring optimum weighing accuracy. They feature all digital design with digital readouts with provision for interfacing to a PC, a laboratory robot, and digital printer. Some models are equipped with Bluetooth technology, for wireless communication. Also analytical balances offer piece counting, recipe weighing, percentage weighing, change of weighing units, and a data interface with a PC.

### **Precision Balance**

Precision balances are used to measure mass with a precision of up to 1 mg. They are widely used in the laboratories because their accuracy is high enough for the common measurements. Precision balances are microprocessor controlled that makes their usage easy and brings more functionality to the balance. Besides normal and tare weighing, additional features in such type of balances also include piece counting, recipe weighing, percentage weighing, change of weighing units, and connection with other equipment or with a computer via data interface. A typical precision balance is shown in Figure 29.2.

**Microbalance** Greater accuracy is possible with a microbalance, which is capable of making precise measurements of weight of objects of the order of a million parts of a gram. In comparison, the standard analytical balance is 100 times less sensitive and is limited in precision to 0.1 mg. These balances are generally used in a laboratory as standalone instruments but are also incorporated into other instruments, such as for thermogravimetry and surface property instruments. Its accuracy falls into the gap between analytical balance and mass spectrometer.

**Instrumentation** Various principles are utilized for measuring the weight of objects with a balance. However, the electronic control units of analytical and precision balances

**Figure 29.2** Typical precision balance.



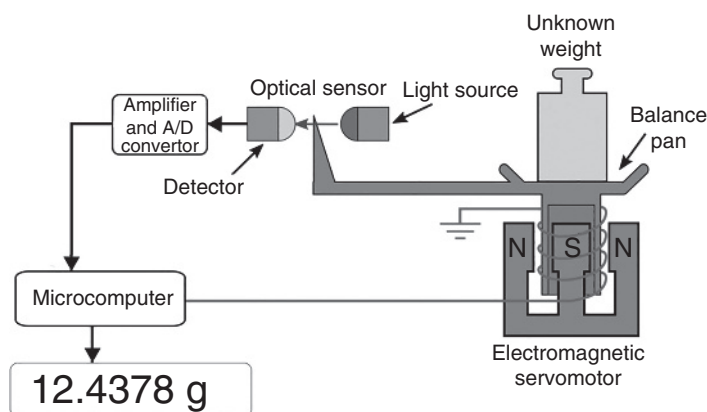
are in general identical so that the application possibilities are also similar. The main difference is the additional feature of automated calibration function in analytical balances, requiring no external calibration weights to calibrate the balance before the measurement. There are two basic types of designs utilized in electronic balances. These are the following:

- Electromagnetic type
- Load cell type

Both these methods are completely different. However, the only commonality between them is that neither of these directly measure mass, but measure the force that acts downward on the pan. The reference standards for mass are weights, which when placed on a pan results in a force that is equivalent to a given number of grams. The force is converted into an electrical signal and displayed on a digital display. For measuring force, the electromagnetic balance method employs the electromagnetic force generated from a magnet and coil, whereas the load cell method is based on the change in resistance value of a strain gauge attached to a piece of metal that bends in response to a force.

### ***Electromagnetic Type Balance***

Most of the modern electronic laboratory balances operate on the principle of magnetic force restoration. In this system, the force exerted by the object being weighed is lifted by an electromagnet. The current required to oppose the downward motion of the weight in the magnetic field is measured by a detector. Figure 29.3 illustrates the principle of the electromagnetic type of electronic balance. In this arrangement, the force of the load weight is measured directly by creating a counteracting force that works against the weight. This force is measured when the weighing pan is in balance. The weighing pan with the unknown weight is attached to a coil that is suspended in a magnetic field generated by current from an amplifier. An optical sensor detects the position of the coil and provides a feedback signal to the amplifier.



**Figure 29.3** Principle of electromagnetic type electronic balance. Balancing is achieved by applying electromagnetic force instead of placing weights.

The position of the coil is controlled to an accuracy better than a thousandth of a millimetre. The current is automatically adjusted by the amplifier to maintain the position of the coil at a reference position or the 'null' point. The amount of force exerted by the coil is directly proportional to the amount of current flowing in it. So, by measuring that current, the force can be calculated. The amplifier is designed to deliver always the correct amount of current to keep the lever in balance, regardless of the weight on the pan. The current flows through a precision resistor across which a measurement voltage is generated. An A/D converter transforms the analog voltage into a digital signal. The digitized signal is then given to a microprocessor with an appropriate software that delivers the measurement result finally shown on the display. A temperature sensor is used for compensating the effect of temperature on the amplifier and ensuring the accuracy of the balance.

### Load Cell Type Balance

Load cells are strain gauge transducers consisting of an elastically deformable body on which they are mounted and change their resistance on deformation. Figure 29.4 shows load cell type electronic balance. The strain gauge is mounted on an aluminium beam, which is milled out in the centre. The weighing pan is attached to one end and the other end is mounted to the base of the balance. A load on the pan creates force and the aluminium beam gets deformed. Since at the thinnest part of the beam strain gauges are embedded, these length-sensitive resistors also get deformed and so change their resistance. Their resistance change is proportional to the deforming force acting on it. The change in resistance can be correlated to the magnitude of the strain induced by the weight. The strain gauge is placed as Wheatstone bridge, and the mass is then obtained from the amount of balancing current required due to the force.

Precision balances are microprocessor controlled that makes their usage easy and brings more functionality. In principle, all balances run on low voltage or battery, which is important for laboratories with unreliable power supply. Most of the precision balances have no internal calibration weights for which certified calibration weights must be used. Precision balances come in different capacities. They have spill-resistant housing and are available in different model options as per requirement of the application.

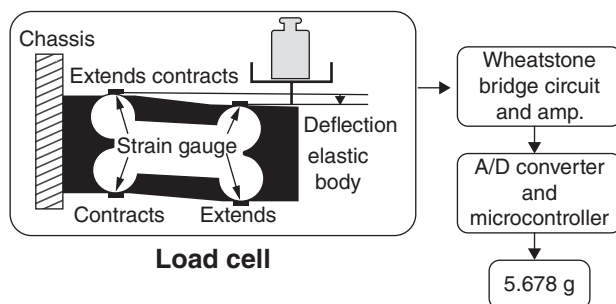


Figure 29.4 Block diagram of a load cell type electronic balance.

**Quartz Crystal Microbalance**

The microbalance is based on the use of piezoelectric properties of the quartz crystal. This technique uses the changes in resonance frequency of the crystal to measure the mass on the surface because the resonance frequency is highly dependent on any changes of the crystal mass. With some simplifying assumptions, this frequency change can be quantified and correlated precisely to the mass change. Common equipment allows resolution down to 1 Hz on crystals with a fundamental resonant frequency in the 4–6 MHz range. A typical setup for the quartz crystal microbalance contains frequency sensing equipment through a microdot feedthrough, an oscillation source, water cooling tubes, and a measurement and recording device. A quartz crystal microbalance is capable of measuring mass deposition down to 0.1 ng.

**Specifications**

| <i>Parameter</i> | <i>Analytical balance</i> | <i>Precision balance</i> |
|------------------|---------------------------|--------------------------|
| Readability      | 0.01 g                    | 0.1 mg                   |
| Capacity         | 3200 g                    | 220 g/300 g/600 g        |
| Repeatability    | 0.01 g                    | ±0.1 mg                  |
| Pan size         | 170 mm × 190 mm           | 90 mm                    |
| Calibration      | Internal                  | Internal                 |

**Applications**

Electronic balances find applications in hospital laboratories, pharmaceutical industry, research institutions, and schools. They are used in laboratories for the manufacture of pharmaceutical products, analysis, quality assurance, or final checking requiring precision performance. They are specifically used for piece counting by setting the weight of the single piece of the item in advance and then displaying the number of pieces in the sample. Percentage weighing refers to measuring the weights as a percentage of reference weight and formulation when mixing a number of different samples together according to a pre-programmed formula.

**30**

**Ballistocardiograph**

**Purpose**

A ballistocardiograph (BCG) is a machine for producing a graphical representation of the movement imparted to the body with each beat in the heart cycle. These movements occur during the ventricular contraction of the heart muscle when the blood is

ejected from the heart with sufficient force. The machine provides an immediate, sensitive, and specific test of the contractility of the heart in which each individual heartbeat captured during the measurement period by the machine can be identified and analysed independently. BCG is also employed in preventive medicine, particularly in the early detection of coronary heart disease.

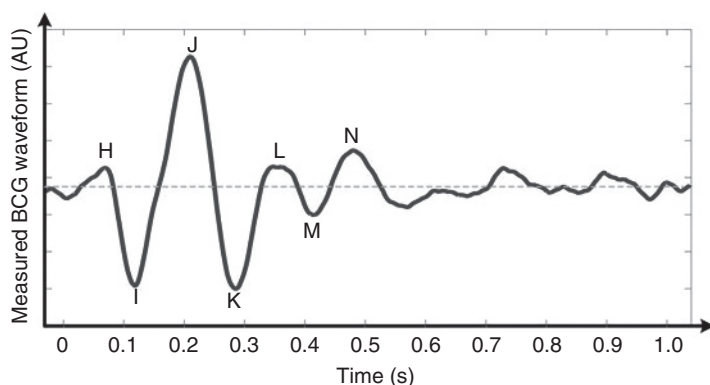
## Principle

A BCG measures the mechanical force generated by ballistic forces on the heart by measuring the recoil of the body as blood is pumped from the ventricles. It has been established that the body recoils each time the blood is ejected by the heart into the arteries. These cardiac-related body movements can be recorded noninvasively from the surface of the body that represents a vital sign in the 1–20 Hz frequency range. By observing and analysing the BCG signal, the effect of major heart malfunctions can be identified.

### BCG Waveform

In the early days, BCG was recorded as a measure of the displacement BCG and sometimes even velocity BCG, its first derivative. Modern equipment is designed to measure the acceleration BCG, which is the second derivative of displacement BCG. This is because the sensors used in them measure force, which is mass times acceleration. Figure 30.1 illustrates an example of a typical BCG waveform for one heartbeat. There are several waves designated as the 'I', 'J', and 'K' waves, which are typical of BCG recordings. Trained clinicians can detect the signs of certain pathologies by simply examining the BCG recordings visually as they produce visually distinguishable patterns. In the measurement process, filters with a passband of 0.3–50 Hz are generally used.

BCG waveform is analysed quantitatively by measuring the amplitudes, time intervals, slopes, etc. The most important parameter is the I–J amplitude. The other amplitudes are much smaller and are more subject to background and other variations. The time intervals of the waveforms are often studied taking R-spike of the ECG as a reference.



**Figure 30.1** BCG (ballistocardiograph) waveform for one heart beat and its components. The peaks of the BCG waveform are denoted with letters H, I, J, K, L, M, and N.



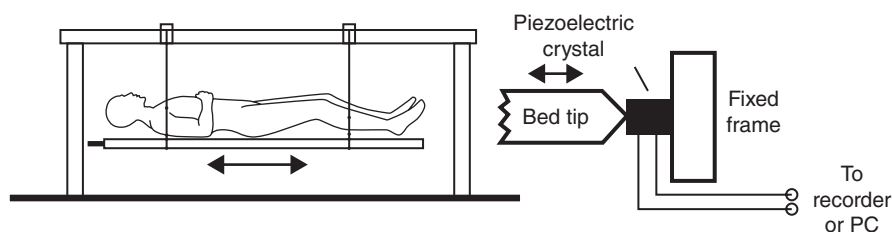
## Instrumentation

A BCG, in its simplest form, is a rigid, rectangular, metallic framework with the help of a horizontal table that is suspended with the support of four nylon cords as shown in Figure 30.2. The table is perfectly balanced in the horizontal plane with the help of four adjustable screws. There is no need to connect any electrode to the subject to record the BCG. The body movements transmitted to the table can be evaluated by measuring the displacement, force, or acceleration by using appropriate transducers connected to the table. This graph represents displacement (mm) or force (dyn) in the vertical axis versus time (s) in the horizontal axis.

The body oscillations can be sensed by using a piezoelectric crystal and displayed on a PC monitor. The record is quantified in terms of the wave amplitude or the area under the curve after recording the BCG waveform continuously over 5–20 heart beats. Usually, a two-channel recorder for BCG and ECG channels is used to demonstrate the time relation between both the signals. Along with BCG signal, there could be artefacts due to the respiratory and body movement-related motion. Suitable filters are required to be used to minimize their interference in the BCG record.

M/s Heart Force Medical Inc. (HFM), a Canada-based company, has developed a digital BCG designated as dBG (Figure 30.3). The device consists of three major components: the sensor, the digitizing transceiver unit, and the proprietary software for device control and data analysis. The device captures, processes, analyzes, and records the motion of the lower sternum imparted by the movement of the heart during each cardiac cycle. The movement in terms of acceleration or force is sensed by a triaxial accelerometer aligned to the three principal axes. Modern BCG machines use micro-electromechanical system (MEMS)-based accelerometers. The signal is processed digitally and displayed with the acceleration amplitudes as the vertical axis and time as the horizontal axis. Measurement of acceleration is expressed in milli-gravity (mG) units and time is recorded in milliseconds (ms). The device captures three waveforms, one for each axis that forms the essence of the BCG.

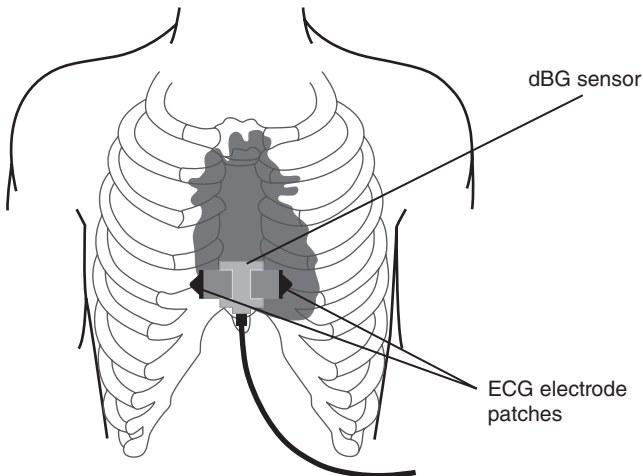
A single channel ECG is sensed, recorded, and displayed simultaneously with the BCG. The integrated sensors are placed on the chest of the subject under test as shown in Figure 30.4. The two waveforms are displayed on a computer screen, which carries out analysis of the waveforms using a proprietary software. The transceiver unit carries out digitization of the captured data and transmits it via a secure Bluetooth connection to a PC.



**Figure 30.2** Schematic of a ballistocardiographic system based on a suspension table in which piezoelectric crystal is used as a force transducer and connected to a recorder or PC monitor.



**Figure 30.3** The digital ballistocardiograph, sensor, and transceiver. *Source:* Courtesy of Heart Force Medical Inc. Canada.



**Figure 30.4** Digital ballistocardiograph sensor placed on sternum. *Source:* Courtesy of M/s, Heart Force Medical Inc. Canada.

## Specifications

Information on specifications about BCG is not available from the company (M/s Heart Force Medical Inc., Canada) at the moment.

## Applications

BCG has so far been used mostly for research purpose only. It is rarely used in routine clinical applications. With the advancements in technology, BCG is likely to complement already available cardiac diagnostic equipment. It is expected that BCG will eventually be used to assess the capability and the relative efficiency of the heart to pump blood.

## 31

# Bilirubinometer

## Purpose

Bilirubinometer is a device designed to determine the concentration of bilirubin in the blood or other clinical specimen. The purpose is to make easy and quick assessment of hyperbilirubinemia (high level of bilirubin) in neonates. Hyperbilirubinemia, a condition that is commonly known as jaundice, appears when bilirubin levels rise above 5 mg/dl and manifests itself in the form of a yellowish discolouration of the skin, eyes, and mucous membranes. Bilirubin is a product of haemoglobin breakdown, which remains in the body until the liver can convert it into a form that can be excreted. Early monitoring of bilirubin concentration is thus very important in children and in adults where elevated levels may indicate some metabolic disorder.

## Principle

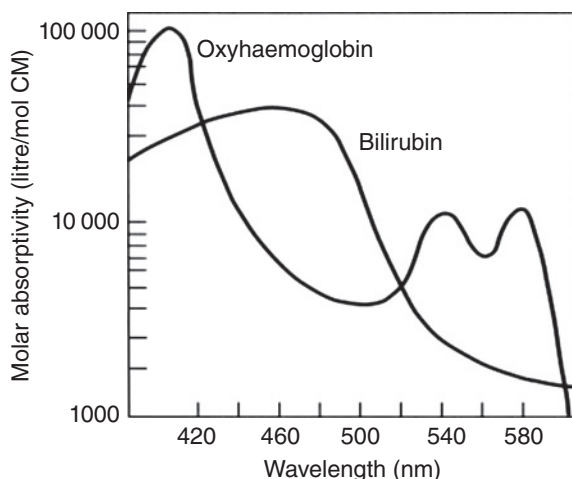
Jaundice can be easily diagnosed by a visual inspection as the signs are clearly evident in the form of a yellowish colour acquired by the skin and the whites of the eyes. This colouration is caused by elevated bilirubin levels in the blood. Still, a bilirubinometer is generally employed to confirm this diagnosis and assess the risk level of bilirubin.

Bilirubinometers are available in a variety of physical configurations. The portable handheld instruments are relatively small and simple to operate. They are often placed in the neonatal intensive care units to facilitate rapid on-site bilirubin measurement. The bench-type bilirubinometers are larger in size and are located mostly in the clinical laboratories.

Bilirubin concentrations can be determined either by whole blood or serum analysis using spectrophotometric technique or by skin-reflectance measurements. Portable instruments are mostly of reflection type. They work by directing white light on to the skin of the newborn and measuring the intensity of the specific wavelengths of the reflected light that is returned. If the spectral properties of the components within the skin are known, the concentration of bilirubin can be determined by subtracting out the interfering components.

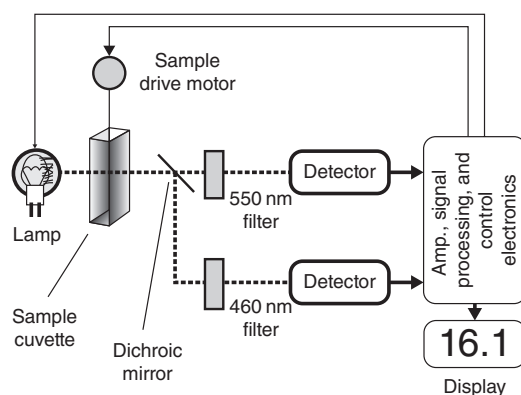
## Laboratory Model

The laboratory models depend upon direct spectrophotometric method that measures total bilirubin in serum samples. The absorption spectra of bilirubin and oxyhaemoglobin are shown in Figure 31.1. The peak absorption of bilirubin occurs at 460 nm, which is in the blue part of the spectrum. This is the reason that blue light is mostly used for phototherapy of hyperbilirubinemia cases. Figure 31.2 shows a block diagram of the optical and measuring system of the system. A beam of white light from a xenon lamp



**Figure 31.1** Graph showing absorption of bilirubin and oxyhaemoglobin.

**Figure 31.2** Optical diagram of a bilirubinometer.



is made to pass through the sample cuvette. The beam is split by a dichroic mirror and directed towards the 460 and 550 nm filters. Two photodetectors are used to measure the transmittance of the light exiting the filters. The total bilirubin is calculated by control electronics from the output of the photodetectors. Since peak absorbance is shared by bilirubin and oxyhaemoglobin at 460 nm, it is necessary to correct the presence of oxyhaemoglobin. This is done by measuring oxyhaemoglobin at 550 nm and finding the difference in the readings at 460 and 550 nm, which will represent the total bilirubin value. These devices require periodic calibration at least at six months interval. They must be recalibrated after all service procedures, including bulb changes.

### Portable Instruments

These new noninvasive transcutaneous instruments are usually based on the principle of reflection photometry. The process consists in directing white light from a xenon tube into the skin of the patient. The light is capable of passing through the skin into subcutaneous tissues. The light is reflected back from the skin to an integrated spectrophotometer.



**Figure 31.3** Portable Jaundice Meter – bilirubinometer. *Source:* Courtesy of M/s Drägerwerk AG & Co. KGaA.

Depending upon the design, a number of wavelengths are used in different transcutaneous bilirubinometers. The optical spectrum signal reflected from the patient's subcutaneous tissues is converted to electrical signal by a photodetector. These electrical signals are processed by a microprocessor to generate a true serum bilirubin value. The instrument emits intense light. Therefore, the light should not be allowed to fall directly on the eyes. The measurement should be taken on the forehead or sternum of the patient.

There are four major skin components, which contribute to the spectral reflectance from the skin. These are the (i) melanin, (ii) dermal maturity, (iii) haemoglobin, and (iv) bilirubin. The earlier transcutaneous bilirubinometers used mostly two wavelengths for bilirubin and oxyhaemoglobin, ignoring the likely interference from the impact of dermal maturity and melanin content. This required separate analysis for each patient population especially for different ages and races. The bilirubin value was derived by referring to different conversion tables for each category of population.

Modern instruments, such Jaundice Meter from M/s Drägerwerk AG & Co, perform a spectral analysis at more than 100 different wavelengths. By subtracting the spectral contribution of the known components, the bilirubin absorbance is quantified. Figure 31.3 is a typical example of an instrument of this category. The intensity of reflected light is converted into absorbance units, the optical density (OD) for analysis. The total OD is the sum of ODs contributed by various components. By using known spectral characteristics of various components, the contribution of interfering components is sequentially subtracted from the total OD. The remaining value will correspond to the bilirubin value that is calculated by a proprietary algorithm. Bilichex displays the results in clinically appropriate units: mg/dl or  $\mu\text{mol/l}$ . The commonly used measurement sites are the forehead and the upper end of the sternum.

## Specifications

*Sample size:* 20  $\mu\text{l}$

*Measuring range:* 0–40 mg/dl (0–684  $\mu\text{mol/l}$ )

*Results displayed:* 5 seconds.

*Turnaround time:* 15 seconds.

*Accuracy:*  $\pm 5\%$  (0–30 mg/dl/0–513  $\mu\text{mol/l}$ )

## Applications

The major application of bilirubinometers is in the neonatal and paediatric departments of hospitals and clinics to diagnose or assess the risk of hyperbilirubinemia. Transcutaneous portable bilirubinometers can serve as screening tools, especially where services of a neonatologist are not easily available.

## 32

## Biosafety Cabinet

### Purpose

A biological safety cabinet is a piece of equipment designed to protect the operator, the laboratory environment, and the work materials from exposure to biohazards and cross-contamination emanating from infectious aerosols and splashes that may be generated during routine procedures involving manipulation of substances containing infectious agents, such as viruses, bacteria, and primary tissue cultures.

### Principle

Biosafety may be defined as the application of combinations of laboratory practices and procedures, laboratory facilities, and safety equipment when working with potentially infectious microorganisms. A biosafety cabinet (BSC) serves as a means to protect the laboratory worker and the surrounding environment from various types of biohazards so as to ensure adequate level of biosafety. In construction, a BSC is an enclosed, ventilated laboratory workspace for safely working with materials that may be contaminated with pathogens. Different situations require different levels of biosafety, which have been duly defined at international level. Accordingly, several different types of BSCs are available to meet the varied requirements of the degree of biocontainment.

### *Classes of Biosafety Cabinets*

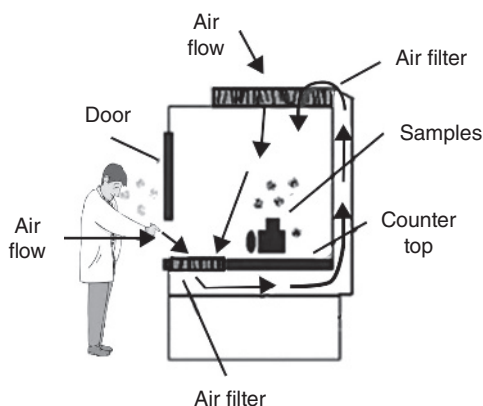
The BSCs have been classified into three classes. These three classes and the types of BSCs within them are categorized on the basis of the level of protection provided to the personnel, the environment, and the product.

*Class I:* This class of cabinets provides personnel and environmental protection but no product protection.

*Class II:* They provide both kinds of protection: of the samples and of the environment.

*Class III:* They are generally used in the case of high-risk biological agents and are meant to provide maximum protection.

**Figure 32.1** Principle of working of a biological safety cabinet, Class II, Type B2.



The most commonly used cabinets in the clinical and research laboratories are Class II cabinets. The principle of working of this type of cabinet is illustrated in Figure 32.1. The cabinet involves the use of a fan mounted on the top of the cabinet, which serves as a curtain of sterile air over the products that are being handled. The air is then drawn underneath the work surface and back up to the top of the cabinet where it passes through the high efficiency particulate air (HEPA) filter. The HEPA filter removes the harmful bacteria and viruses. The air that is exhausted is the air being drawn into the front of the cabinet underneath the work surface. The air acts as a barrier to potentially contaminated air coming back out to the operator.

Biological safety cabinets should not be confused with fume hoods and clean benches. Laminar flow clean benches can protect research products from contamination, but do not afford protection to the user. The clean bench blows unfiltered exhaust air towards the user and is not safe for work with pathogenic agents. Similarly, a fume hood is used to protect personnel from exposure to chemical hazards, but cannot provide the environmental protection that HEPA filtration can do in a BSC. Fume hoods are thus not suitable for work involving biohazards.

Based on the amount of air that is recirculated within the cabinet, Class II cabinets have been put under different types, namely, Type A2 (recirculate 70%), Type B1 (recirculate less than 50%), and Type B2 (recirculate 0%). Type B2 cabinet is mainly used in toxicology laboratories, where it is required to safely use hazardous chemicals. Due to the potential risk of contaminated air flow into the laboratory in case of exhaust system failure of a Type B1 or B2 cabinet, cabinets of these types are generally designed to monitor the exhaust flow, shutting off the supply blower and sounding an alarm if the exhaust flow is insufficient. All these monitoring and control functions are performed by a microprocessor-based electronic system.

### Equipment

All BSCs operate based on the following principles:

- **Filtration:** Filtration and retention of particulates by HEPA filter(s).
- **Laminar airflow:** Laminar airflow is the movement of a body of air in a single direction, with a uniform velocity. In practice, the laminar down flow of air in the cabinet captures any aerosol generated in the work area of the cabinet and directs it to the HEPA filters.



- *Directional airflow:* Air is drawn into the front of the cabinet at the front grille. This 'curtain' of air makes it more difficult for aerosols to escape out of the work area of the cabinet and into the outside environment.

These functions are achieved in the BSC by using the HEPA filter(s) or optional ultra-low penetration air (ULPA) filters, the motor/blower to force air through the cabinet, cabinet air intakes (grilles), ductwork, and air balance control.

### **HEPA Filter**

Control of airborne particulate materials has become possible with the development of filters, which can efficiently remove microscopic contaminants from the air. The most popular filter is the HEPA filter that is disposable and whose filter material is typically made of borosilicate microfibers formed into a thin sheet. This sheet is folded or pleated to increase its surface area. The pleats are held in place by corrugated aluminium separators. The separators prevent the pleats from collapsing in the air stream and provide a path for airflow. The pack is then set into a frame and sealed. These filters can remove particles of  $0.3\mu\text{m}$  with an efficiency of at least 99.97%. Particles both larger and smaller than this size are removed with a high efficiency. These filters can efficiently remove bacteria, spores, and viruses from the air. In reality, the HEPA filter is the heart of the biological safety cabinet.

ULPA filters are used in place of the standard HEPA filters in the high purity BSCs. They offer at least 99.999% efficiency in removing particles of the size  $0.1\text{--}0.2$  or  $0.2\text{--}0.3\mu\text{m}$ . These filters capture all infectious agents and ensure that only microbe-free air is exhausted from the cabinet or directed to the work surface.

The HEPA filters, over a period of time, will gradually accumulate airborne particulate matter from the environment and from work performed in the cabinet. The rate of accumulation will depend upon the level of cleanliness of the room air, the operating time, and the nature of work being done in the cabinet. A filter gauge is usually provided to accurately display the balance life of the filter and indicate the requirement for its replacement.

### **Motor/Blower**

The function of the motor/blower assembly is to pull room air into the cabinet from the front and recirculate it internally. During its recirculation, the air is split into two separate streams. One path leads through the exhaust HEPA filter and out of the unit. The second path flows through the supply HEPA filter, which then flows down through the work area. The motor is a brushless DC motor whose operation is monitored and controlled by a microprocessor. The motor is pre-programmed so as to deliver a consistent volume of air, even when there may be load variations on the HEPA filter over time.

### **Ultraviolet (UV) Lamp**

Shortwave ultraviolet (UV) is considered as germicidal and virucidal resulting in cellular death or viral inactivation. Therefore, a UV lamp is often provided in the BSC. The UV lamp generates a primary wavelength of light of 254 nm. The cabinet usually records the number of hours of operation of the UV light and can give a replacement message as programmed.

### Electronic Control System

The electronic control system is designed to meet the control requirements of the BSC. The control safety system consists of the following modules for performing various functions:

*Touch screen control panel:* It consists of LCD touch screen that controls and displays all system functions including on/off functions for blower motor, interior outlets, fluorescent light, and UV light, timers, and a menu icon. There are several timer functions such as outlet timer, UV timer, auto-run timer, night setback timer, set-purge timer, or weekend turn-off.

*Basic controls:* They include a Minihelic pressure gauge to measure HEPA filter loading, motor voltage regulator, power switches for both interior outlet and blower/motor, and circuit breakers for both main and outlet power.

*Airflow monitor:* Whenever the air velocity falls below the set point, the air fail alarm will be triggered. Also, if the ambient temperature exceeds 18–30°C (cabinet working temperature), the airflow monitor is automatically disabled. Thermal anemometer is used to measure the flow rate of the air flowing through the surface of exhaust filter at multipoints.

*Alarms:* There is an alarm that warns users if the airflow in the cabinet gets compromised. The alarm usually is an indicator of ineffective user and environmental protection or when the filters do not allow air to pass through them anymore. Do not work in the BSC if the alarm sounds continuously, since it indicates a problem with the BSC.

### Specifications

*Air flow:* 0% of air recirculation and 100% exhaust through ULPA/HEPA filter

*Filters:* HEPA filters with an efficacy of 99.999% for particles size of 0.3 μm

*Dimensions:* (i) Length: 100–130 cm, (ii) width: 40–60 cm, and (iii) height: 50–80 cm

*Constructional material:* Stainless steel

*Lamps:* Fluorescent lamp for illumination and programmable UV light system

*Display:* LCD graphical display for (i) inflow and down flow air velocity, (ii) exhaust and recirculated airflow volumes, and (iii) time and date

*Alarms:* Low inflow velocity, low down flow air velocity, and HEPA filter life

*Noise:* <65 dB

### Applications

Biological safety cabinets are the primary means of containment of infectious microorganisms and are designed to provide personnel, environmental, and product protection in the laboratories when appropriate practices and procedures are followed.

## 33

# Bioelectrodes: ECG Electrodes

## Purpose

A bioelectrode is a conductor that is designed to serve as an interface between biological structures and electronic systems. Its function is to either sense and measure (passive) the electrical activity within the biological structure or stimulate (active) it by inducing external electrical potential. Various biological structures generate electrical currents that give rise to potential differences. These potentials can be measured using bioelectrodes that can give an insight in the functioning of the biological structure. Conversely, when current has to be applied to the biological structure, it is done through the bioelectrodes to obtain the necessary effect on the target. Depending upon the purpose, the same electrode may perform either the passive or active function. electrocardiograph (ECG) electrodes are one type of bioelectrodes that are used to pick up electrical potentials generated by the pumping action of the heart from the surface of the skin.

## Principle

Bioelectrodes have been developed in various sizes, forms, and shapes to suite the requirements of a particular application. The size of bioelectrodes generally ranges from microscopic intracellular research electrodes (microelectrodes) to large (8–12 cm) defibrillation paddles. In this chapter, ECG electrodes are described, which are used for recording the ECG. ECG electrodes are available in different shapes and sizes and are made up of different materials depending upon the different clinical applications such as routine ECG recording, ambulatory ECG, intensive care units (ICUs), etc.

Electrocardiography is the process of recording the electrical activity of the heart over a period of time using metallic electrodes placed on a patient's body. The electrical activity generated by the heart within the body is conducted to the surface of the body through the body tissues, reaches the electrodes through the skin electrode transition, and is then conducted by direct wire connection to the input circuit of the recording machine. Electrodes make a transfer from the ionic conduction in the tissue to the electronic conduction, which is necessary for making measurements. Therefore, a bioelectrode is generally considered as a transducer that converts ionic current into electronic current or vice versa.

## Contact Impedance

The surface electrodes pick up the potential difference from the tissue surface when placed over it without damaging the live tissue. The impedance at the electrode–skin junction comes in the overall circuitry of the recording machine and, therefore, has

significant effect on the final record. Skin electrode impedance is known as the *contact impedance* and is of a value much greater than the electrical impedance of the body tissue as measured beneath the skin. The outer horny layer of the skin is responsible for the bulk of the skin contact impedance and, therefore, a careful skin preparation is essential in order to obtain best results when using ECG electrodes. Electrodes play an important part in the satisfactory recording of bioelectric signals, and their choice requires careful consideration. They should be comfortable for the patients to wear over long periods and should not produce any artefacts. Another desirable factor is the convenience of application of the electrodes.

### **Types of ECG Electrodes**

The most commonly used electrodes in patient monitoring and routine recording of ECG are surface electrodes. The surface electrodes are available both as *reusable* and *disposable* electrodes. One of the important desirable characteristics of the electrodes designed to pick up signals from biological objects is that they should not polarize. This means that the electrode potential must not vary considerably even when current is passed through them. Electrodes made of silver/silver chloride have been found to yield acceptable standards of performance. By properly preparing and selecting the electrodes, pairs have been produced with potential differences between them of only fractions of a millivolt. In addition, there is an uneven distribution of cations and anions at the electrodes, which gives rise to a small voltage called *half-cell potential* associated with the current. The difference between the half-cell potential and the zero potential is known as the DC offset, which is an undesirable characteristic. Silver/silver chloride electrode is preferred due to its low half-cell potential of approximately 220 mV.

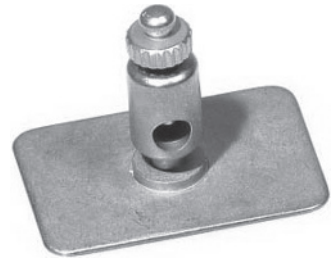
Silver/silver chloride electrodes are fabricated by coating a thin layer of silver on plastic substrates and the outer layer of silver is converted to silver chloride. Silver/silver chloride electrodes are also nontoxic and are preferred over other electrodes, like zinc–zinc sulfate, which also produce low offset potential characteristics, but are highly toxic to exposed tissues. Silver/silver chloride electrodes meet the demands of medical practice with their highly reproducible parameters and superior properties with regard to long-term stability.

In order to avoid movement artefacts and to obtain a clearly established contact (low contact impedance), an electrolyte gel or electrode paste is usually employed as an interface between the electrode and the surface of the source of the event. The gel contains free chloride ions such that the charge can be carried through the electrolyte. Therefore, the electrolyte can be considered as conductive for ion current like the human tissues, thus facilitating current to pass from the human tissues to the electrode.

### **Reusable ECG Electrodes**

Reusable ECG electrodes allow their use over several years and can be used multiple times, and therefore, they are highly economical. They are generally made of German silver, an alloy of zinc, copper, and nickel. Other materials used are nickel silver and nickel-plated steel. When used to obtain diagnostic ECG record, it takes about 5–10 minutes and may require use of up to 10 electrodes. The reusable electrodes come in several shapes. The common ones are described as follows:

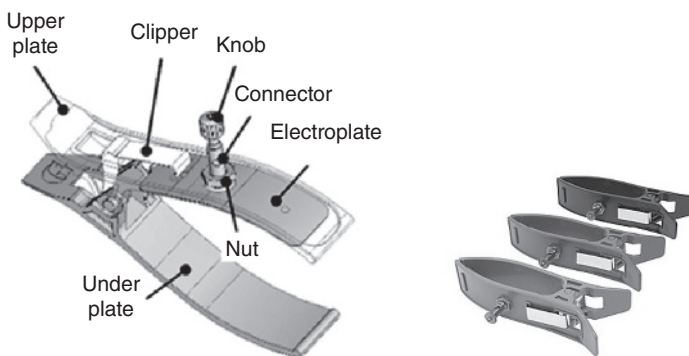
**Figure 33.1** Limb or plate electrodes for recording ECG.



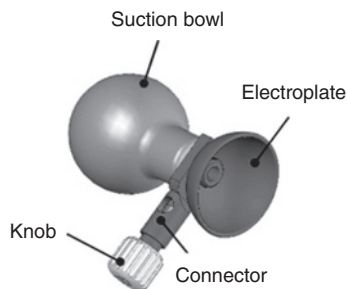
*Plate electrodes:* The most common type of electrodes routinely used for recording ECG is rectangular or circular surface plate or limb electrodes as shown in Figure 33.1. The plate electrodes are intended to be applied to the four limbs. An elastic rubber strap is used to hold the electrode in position. Before these electrodes are attached, a conductive paste or electrode gel is applied on the skin to reduce artefacts arising from variations due to electrode skin impedance, which can otherwise result in wandering of the ECG trace baseline. The typical value of the contact impedance of these electrodes is nearly  $2\text{--}5\text{ k}\Omega$  when measured at  $10\text{ Hz}$ . They are also called limb electrodes as they are most suitable for application on the four limbs of the body. The size of the limb electrodes is usually  $3 \times 5\text{ cm}$ .

Limb electrodes are generally preferred for use during surgery because the patient's limbs are relatively immobile. Moreover, chest electrodes cannot be used as they would interfere with the surgery. Limb electrodes are not suitable for use in long-term patient monitoring because the long flowing leads are inconvenient to the patient. Also, the electromyographic voltages generated by the activity of the limb muscles make them unsuitable for use when monitoring conscious and semi-conscious patients.

*Clamp electrodes:* They are designed to secure ease of attaching the electrodes on the limbs such as the wrists and ankles. They are in a way modern versions of the limb plate electrodes and have a convenient spring clip mechanism, which dispenses with the need for the rubber strap. A typical ECG clamp electrode is shown in Figure 33.2. The electrode is  $3\text{ cm} \times 8\text{ cm}$  in dimension providing a  $24\text{ cm}^2$  area to maximize contact. The electrodes can be connected to any bioamplifier with snap-connect lead wires. They also require to be used with the electrode gel.



**Figure 33.2** Clamp electrodes.



**Figure 33.3** Various parts of a suction cup electrode.

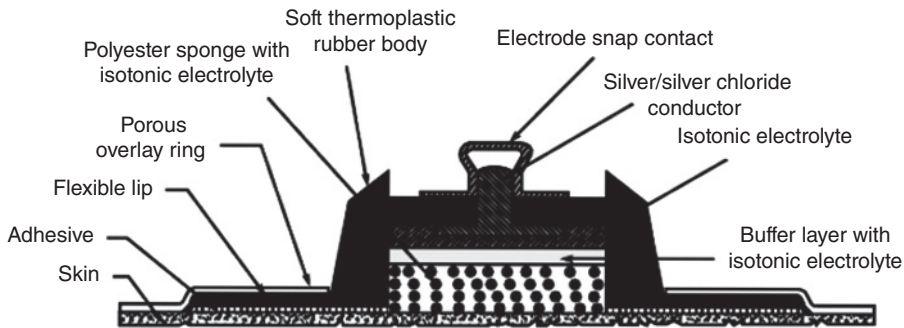
*Welsh electrode:* Welsh cup electrode or suction electrode shown in Figure 33.3 is a cup-shaped electrode that is used for recording ECG from various positions on the chest. It is commonly used to record the unipolar chest leads. The electrode is often called the Welsh or suction cup or bulb electrode and consists of a hollow, metallic, cylindrical electrode that makes contact with the skin at its base. This type of electrode is made of silver/silver chloride or nickel silver. A rubber suction bulb fits over the other end of the cylinder. The suction bulb is squeezed while the electrode was held against the skin. Upon releasing the bulb, the electrode is held in place. Electrode jelly forms the vacuum seal. It has a high contact impedance as only the rim of the electrode is in contact with the skin. The suction electrode can be used anywhere on the chest and can even be used on hairy subjects. A single electrode can, if necessary, be used to take a measurement at a given location and then moved to another site.

The cup electrode has been popular for its practicality, being easily attachable to fleshy parts of the body. However, the weight and bulk of the electrode generally rules out its use on upright, ambulatory, or clothed subjects. They are, therefore, now being gradually replaced with disposal electrodes, as they are liable to infection due to inadequate cleaning procedures.

### **Disposable ECG Electrodes**

Electrodes, which are employed in stress testing or long-term monitoring, present additional problems because of the severe stresses, perspiration, and major body movement encountered in such studies. This necessitates both design considerations and application techniques of electrodes to prevent random noise on the baseline and baseline wandering on the ECG record. To overcome problems due to prolonged application, special disposable electrodes have been developed. The disposable electrodes are designed to be flexible in structure and more comfortable to wear. They are very handy because of integrated gel and adhere very well to the contours of the skin. They are generally known as pre-gelled electrodes. However, they can be used only once and have to be disposed after a single use.

In construction, the electrode has a small retaining ring or plastic cup that is held in place by means of a surrounding disk of adhesive foam as shown in Figure 33.4. The plastic cup holds the gel-impregnated sponge in place and stops the gel from spreading beyond the defined boundary during storage or use on the patient. They have Ag-/AgCl-plated plastic eyelets, and the leads are connected to the electrodes via snap fastener studs. The plastic

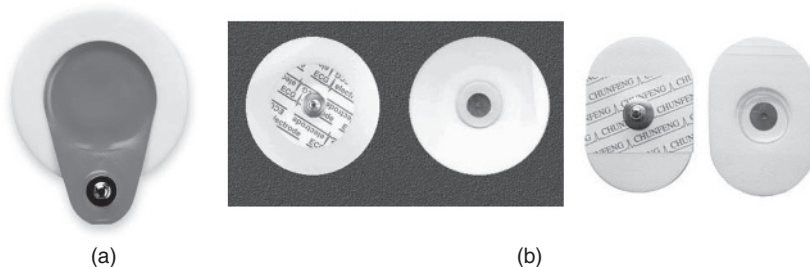


**Figure 33.4** Constructional details of a pre-gelled ECG electrode.

eyelet has a diameter of 0.5–1.5 cm and is electroplated with silver up to a thickness of 10 mm. The surface of the Ag layer is partially converted to AgCl. The rigid retaining ring is, however, uncomfortable as it does not allow the electrode to conform optimally to body contours. The rigid ring is now removed in many modern disposable electrodes and replaced with a recess formed by a hole in the adhesive foam layer. The backing label serves to hold the snap and eyelet in place as well as to present the company's logo.

The main design feature of these electrodes, which helps in reducing the possibility of artefacts, drift, and baseline wandering is the provision of a high-absorbency buffer layer with isotonic electrolyte. This layer absorbs the effects of movement of the electrode in relationship to the skin and attempts to maintain the polarization associated with the half-cell potential constant. Since perspiration is the most common cause of electrode displacement, the use of an additional porous overlay disc resists perspiration and ensures secure placement of the electrode on the skin even under stress conditions. Figure 33.5 shows some examples of typical pre-gelled electrodes. The electrode diameters range from 4 to 6 cm. There are some advantages of these electrodes as compared with plate and Welsh bulb electrodes. As there is no risk of infection, which is possible with reusable electrodes, their smaller size makes them less prone to detachment and also less time is required per ECG procedure.

The growing monitoring market has led to the development of even lower-cost disposable electrodes. Solid conductive adhesive or hydrogel electrodes have been developed, which reduce the number of electrode parts required and thus dispense with the need of a gel-impregnated sponge or a surrounding disk of adhesive tape. This results in



**Figure 33.5** Various types of shapes of disposable ECG electrodes (a) ECG electrode with off centre connecting stud and (b) ECG electrode with stud in the centre.



smaller area, low-profile electrodes suitable for neonatal monitoring, especially when coupled with integrated leads. Their advantage includes their small size, no risk of infection, less prone to detachment, and much less time required for recording ECG.

## Specifications

### *Reusable electrodes*

*Plate electrodes:*  $3\text{ cm} \times 5\text{ cm} = 15\text{ cm}^2$ .

*Clamp electrodes:*  $3\text{ cm} \times 8\text{ cm} = 24\text{ cm}^2$ .

*Welsh electrodes:* Cup diameter 15 mm

### *Pre-gelled electrodes*

*Electrode size ( $L \times W$  or diameter in mm):*  $57 \times 48$

*Sensor material:* Silver/silver chloride (Ag/AgCl)

*AC impedance typical:*  $500\ \Omega$

*DC offset voltage typical:* 0.2 mV

*Connector (stud):* Nickel-plated brass

## Applications

Reusable electrodes are mostly used to record ECG for routine diagnostic purposes. Plate and clamp electrodes are usually used on the limbs, whereas the Welsh electrode is used to make measurements on the chest. Disposable pre-gelled ECG electrodes are mostly employed for patient monitoring over a long period of time, which could be in the intensive care or post-operative units. They are almost exclusively used in ICU critical care units (CCUs), and operating rooms during surgery and in monitoring ECG for ambulatory ECG recording and for exercise stress tests.

# 34

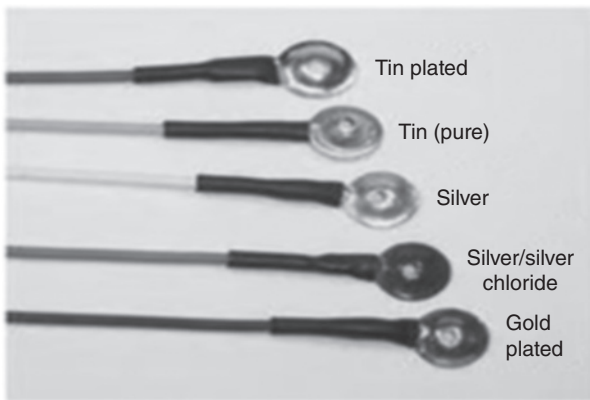
## Bioelectrodes: EEG Electrodes

### Purpose

EEG electrodes are used to record the electrical activity of the brain, the recorded graph commonly known as electroencephalograph.

### Principle

The EEG signal can be picked up with electrodes either from the scalp or directly from the cerebral cortex. There is a great variety of electrodes that can be used for recording EEG from the scalp. The majority of them are small discs of stainless steel, tin, gold, or silver



**Figure 34.1** Typical EEG electrodes made of different materials.

covered with a silver chloride coating as illustrated in Figure 34.1. They normally have a lead attached to them for connection to the recording instrument. Some of the general types of EEG electrodes include reusable discs, EEG caps with discs, adhesive gel electrodes, subdermal needles, etc. However, the most commonly used electrodes for use on the surface of scalp are small metal discs usually made of silver covered with a silver chloride coating. The peak-to-peak amplitude of the waves that can be picked up from the scalp is normally  $100\mu\text{V}$  or less, while that on the exposed brain is about  $1\text{mV}$ . The frequency varies greatly with different behavioural states. The normal EEG frequency content ranges from  $0.5$  to  $50\text{Hz}$ . The nature of the EEG wave varies over the different parts of the scalp.

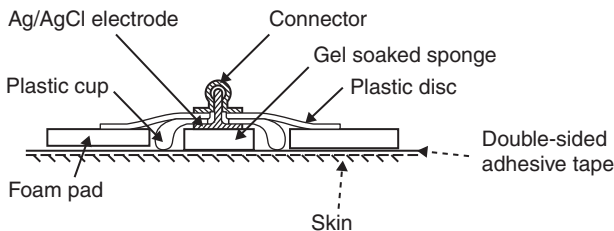
The EEG electrodes must exhibit minimum contact impedance between electrode and the skin surface and ensure a stable and reliable contact by creating an effective interface between an ionic solution (the subject) and a metallic conductor (the electrode). These demands are met by silver/silver chloride electrodes when used with a special conductive gel, applied in the hair between electrodes and the scalp. Since an EEG usually requires some dozens of electrodes, all electrodes have to be applied to the represented cap carefully one by one for recording EEG.

They are placed on the scalp in special positions. These positions are specified using the International 10/20 system. Each electrode site is labelled with a letter and a number. The letter refers to the area of brain underlying the electrode, e.g. F – frontal lobe and T – temporal lobe. Even numbers denote the right side of the head and odd numbers the left side of the head. Figure 34.2 shows EEG cables with disc electrodes to which electrode gel is applied to maximize skin contact and allow for a low resistance recording of EEG from the subject's scalp.

A typical reusable EEG electrode is made of sintered silver/silver chloride electrodes made with  $1\text{mm}$  thick Ag-/AgCl-sintered sensor mounted in an epoxy ring housing. The electrode is in the shape of a domed disc around  $7\text{mm}$  in diameter with a hole in the centre and has a  $1\text{mm}$  lead wire soldered to it. All parts are encapsulated with epoxy, resulting in a tough, durable waterproof assembly. The EEG electrodes provide enough space to contain electrode gel. In these electrodes, the skin never touches the electrode material directly. The electrode–tissue interface has impedance depending on several factors. Some of these factors are the interface layer (such as skin preparation, fat mass, hair, etc.), area of electrode's surface, and temperature of the electrolyte.



**Figure 34.2** Disc electrode for recording EEG.

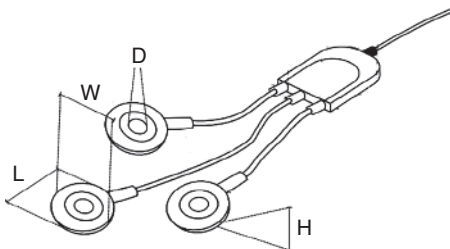


**Figure 34.3** Constructional details of an EEG electrode that can be applied to the skin by an adhesive tape.

Another type of EEG electrode is the chlorided silver disc having approximately 6–8 mm diameter as shown in Figure 34.3. Contact with the scalp is made via an electrolytic paste through a washer of soft felt. It acts as a malleable extension of the electrode, so that the movement of the electrodes cables is less likely to produce artefacts. The gel maximizes skin contact and allows for a low-resistance recording through the skin. They have AC resistance varying from 3 to 20 k $\Omega$ .

Besides, small needle electrodes are sometimes used for carrying out special EEG studies when they are inserted subcutaneously. Needles are available with permanently attached wire leads, so the whole assembly must be discarded after use. They are made of stainless steel or platinum. Implanted EEG electrodes can also be used to stimulate the brain and map cortical and subcortical neurological functions. Silver ball or pellet electrodes covered with a small cloth pad are useful when electrical activity is to be recorded from the exposed cortex, but they have high DC resistances.

## Specifications



*Dimensions:  $W \times L \times H$ : 1.5 cm  $\times$  2.3 cm  $\times$  0.4 cm*

*Diameter: 0.4 cm*

*Material: Silver/silver chloride*

## Applications

EEG electrodes are used for recording the EEG and evoked potentials.

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## Bioelectrodes: EMG Electrodes

### Purpose

EMG electrodes are used to record the bioelectrical activity inside the muscle of a human body, the recorded graph being known as electromyograph (EMG). EMG electrodes are also used when applying a stimulus or recording a signal during nerve conduction, somatosensory, or muscle twitch recording with human subjects.

### Principle

There are several types of EMG electrodes, which have been developed on the basis of their intended application, e.g. surface EMG or intramuscular EMG. Accordingly, the electrodes can be broadly categorized into two classes: (i) surface or skin electrodes for surface EMG studies and (ii) inserted electrodes for intramuscular EMG studies. Inserted electrodes are of further two types: (i) needle and (ii) fine wire electrodes.

#### *Surface EMG Electrodes*

Surface EMG electrodes offer a noninvasive method for detection and measurement of EMG signal. Their principle of working is the same as that of electrocardiogram (ECG) electrodes that form an interface between the electrode surface and the skin of the body through electrolytic conduction, so that current can flow into the electrode. They are simple and very easy to apply. A pair of electrodes or a more complex array of multiple electrodes is generally employed. Surface EMG recording requires more than one electrode because EMG recordings display the potential difference between two separate electrodes. Surface electrodes can be simple platinum or silver disc electrodes, pre-gelled Ag/AgCl electrodes, or wet-gel electrodes. The disc electrodes are reusable, while the gel electrodes are for single use.

Surface electrodes are usually pre-gelled electrodes that use an electrolytic gel as a chemical interface between the skin and the metallic part of the electrode. Silver/silver



**Figure 35.1** Reusable EMG electrodes.

chloride (Ag/AgCl) is the most common composite for the metallic part of pre-gelled electrode like other bioelectrodes. Gelled electrodes are available as either disposable or reusable. Disposable electrodes are more common since they are very light and easy to apply. They come in different shapes, sizes, patch materials, and the conductive gel. A set of reusable EMG electrodes is shown in Figure 35.1. The advantage of disposable electrodes, when properly applied, is that they minimize the risk of electrode displacement even during rapid movements and are thus most commonly used.

*Active EMG electrodes* shown in Figure 35.2 that contain a preamplifier attached to surface electrodes to minimize noise interference in the low level EMG signals due to long connecting wires between the electrode and the instrument and partly due to the high electrode–skin impedance associated with dry electrodes have been introduced. The inbuilt high impedance amplifier provides preamplification at the electrode site and transfers the preamplified signal to the rest of the circuitry. Dry electrodes are mostly used in applications where geometry or size of electrodes does not allow use of gel. The examples of dry electrodes are bar electrodes and array electrodes. In general, dry electrodes are considerably heavier than gelled electrodes, thus increasing the difficulty in maintaining electrode fixation, as compared with gelled electrodes. Figure 35.3 shows a typical dry bar electrode, while Figure 35.4 illustrates its application on a subject.

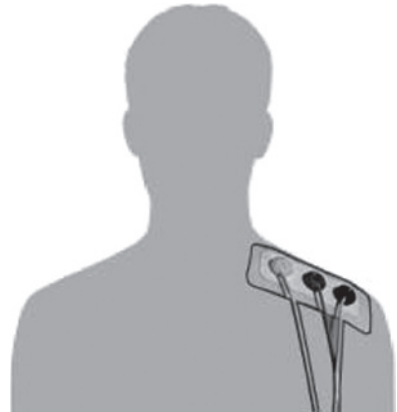


**Figure 35.2** Active EMG electrode.

**Figure 35.3** Typical bar dry type electrode for EMG.



**Figure 35.4** A reusable bar electrode applied to the subject – an example of dry EMG electrode.

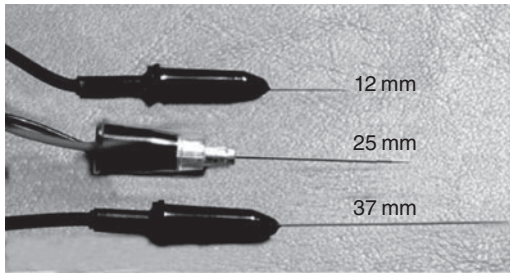


Surface EMG electrodes are mostly used in motor behaviour studies, neuromuscular recordings, sports medical evaluations and those subjects who are averse to needle insertions like children. Besides, surface EMG is utilized to detect muscle activity to control prosthesis for physically disabled and amputated population. However, there are certain limitations of surface electrodes. Since these electrodes are applied on the skin, recordings are restricted to superficial muscles only and are easily influenced by the depth of the subcutaneous tissue at the site of the recording, which can be highly variable. Crosstalk from other muscles is a major problem. Their position must be kept stable with the skin; otherwise, the signal will get distorted.

### ***Intramuscular EMG Electrodes***

Electrodes for intramuscular electromyographic work are usually of the needle type. From the point of view of construction, needle electrodes are the simplest. The material of the diagnostic needle electrode is typically stiff (generally stainless steel) enough to penetrate the skin and insulated with only the tip exposed. A surface electrode is used for reference. In spite of the fact that stainless steel is unfavourable electrode material from the point of view of noise, it is preferred in EMG work due to its mechanical solidity and low price.

**Needle Electrodes** Figure 35.5 shows different types of intramuscular needle electrodes. The choice of the type of electrode that can best measure the physiological function of interest depends upon the specific features associated with each electrode type, their limitations, cost, availability, and potential risk.

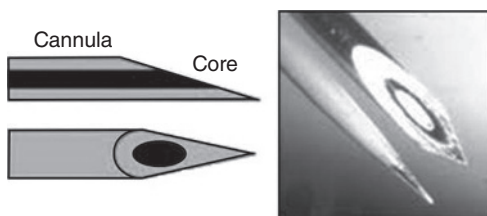


**Figure 35.5** Various sizes of needle electrodes from M/s Biopac Systems Inc., USA.

Needle electrodes come in various forms. The monopolar needle electrode is made up of a Teflon-coated insulated solid needle except at the most distal  $300\ \mu\text{m}$  at the tip, referenced to a surface electrode. Thus, the tip of the needle electrode is used as a detection surface. It is found that after the needle has been used a number of times, the Teflon coating will recede, increasing the tip area. The needle must be discarded when this occurs. Bipolar (double coaxial) needle electrodes contain two insulated wires within a metal cannula. The two wires are bared at the tip and provide the contacts to the patient. The cannula acts as the ground. Bipolar electrodes are electrically symmetrical and have no polarity sense.

A concentric (coaxial) core needle electrode contains both the active and reference electrode within the same structure. It consists of an insulated wire contained within a hypodermic needle. The inner wire is exposed at the tip and this forms one electrode. The concentric needle is very convenient to use and has very stable electrical characteristics. Concentric needle electrodes are made by moulding a fine platinum wire into a hypodermic needle having an outside diameter less than  $0.6\ \text{mm}$ . One end of the needle is bevelled to expose the end of the wire and to provide easy penetration when the needle is inserted. The surface area of the exposed tip of the wire may be less than  $0.0005\ \text{mm}^2$ . The commonly used concentric needle electrode (Figure 35.6) has a single insulated wire inside the cannula of a hypodermic needle, fixed in place by epoxy glue and cut flush with the needle tip. This recording wire has a recording surface of  $150$  by  $600\ \mu\text{m}$  at the tip.

Multi-element needle electrodes are used to pick up the signals from individual fibres of muscle tissue. Special needles are available using  $25\text{-}\mu\text{m}$  diameter electrode surfaces and having up to 14 pickup surfaces down the side of one needle. However, edging of the needle point to the suitable angle, providing a proper plastic coating, making them resistant against thermal and chemical stresses, and ensuring histological suitability, is a difficult manufacturing process.



**Figure 35.6** Concentric needle EMG electrodes for intramuscular studies.



For the measurement of potentials from a specific part of the brain, longer needles are actually inserted into the brain. The needles are precisely located by means of a map or atlas of the brain. Generally, a special instrument called a stereotaxic instrument is used to hold the subject's head and guide the placement of electrodes. Often, these electrodes are implanted to permit repeated measurements over an extended period of time. Single fibre EMG needle electrodes are designed to have very tiny recording areas and allow for the discharges of individual muscle fibres to be discriminated.

Needle electrodes have two major advantages. One is that due to its relatively small pickup area, it is possible to detect individual muscle action potentials. Secondly, the electrodes after insertion may be conveniently repositioned within the muscle so that new tissue territories may be studied. Needle electrodes are designed to be fully autoclavable and in any case they should be thoroughly sterilized before use.

### **Ground Electrode**

The ground or reference electrode for EMG studies usually consists of a conducting strip, which is inserted into a saline soaked strap and wrapped around the patient's limb. The ground electrode is usually positioned over bony structures rather than large muscle masses, in the vicinity of the recording and stimulating electrodes and, where possible, equidistant from them. Surface electrodes usually consist of square or circular metal (chlorided silver) plates with lead wires attached. They are held in place by rubber straps or adhesive tapes or Velcro band. To reduce electrical resistance between the skin and the electrode, the use of saline soaked felt pads or a small amount of electrode gel between the electrode surface and the skin is recommended. Disposable, adhesive type electrodes are also used for EMG work. A typical EMG ground electrode should be large at least  $2\text{ cm} \times 2\text{ cm}$ . The ground electrode should be placed over a bony prominence rather than over large muscle masses, in the vicinity of stimulating and recording electrodes.

**Fine Wire Electrodes** When intramuscular EMG is required to assess the electrical activity of deeper or overlaid muscles, thin and flexible fine wire electrodes are used. The fine wire electrode is inserted into the muscle site of interest. The needle or steel cannula is removed, and the electrode wires are connected to the steel spring adapters to minimize movement of artefacts. Fine wire electrodes are of small diameter, highly non-oxidizing, stiff wire with insulation. Alloys of platinum, silver, nickel, and chromium are typically used. Wire electrodes are extremely fine; they are easily implanted and withdrawn from skeletal muscles. Because of small size, they are generally less painful than needle electrodes whose cannula remains inserted in the muscle throughout the duration of the test. A typical fine wire electrode is shown in Figure 35.7.

**Figure 35.7** Fine wire electrodes for recording EMG signals.



## Specifications

### *Needle electrodes*

*Needle:* 28 gauge stainless steel needles, Teflon coated

*Unipolar:* 2.5 cm (long)  $\times$  300  $\mu$ m (dia); 61 cm lead

*Bipolar:* 3.0 cm (long)  $\times$  460  $\mu$ m (dia); 91 cm lead

### *Active electrode*

*Gain:* 330 (nominal)

*Input impedance:* 100 M $\Omega$

*CMRR:* 95 dB (nominal)

*3 dB bandwidth:* 12–500 Hz

*Noise voltage:* 2  $\mu$ V RMS (bandwidth of 12–500 Hz)

*Stainless steel disk diameter:* 11.4 mm

*Dimensions:* 17.4 mm wide  $\times$  51 mm long  $\times$  6.4 mm thick

### *Disposable pre-gelled electrodes*

*Material:* Ag/AgCl electrode conductor: 11 mm diameter, 95 mm<sup>2</sup> conductive contact area mounted on 35 mm diameter, moisture resistant, vinyl backing tape (0.12 mm thick) with adhesive

## Applications

Pre-gelled surface electrodes are most suitable for general-purpose, short-term recordings. The small diameter permits relatively closely spaced biopotential measurements. Active electrodes are designed for multiple-channel surface EMG measurements. Bar electrodes are employed for use when applying a stimulus, or recording a signal, during nerve conduction, somatosensory, or muscle twitch recordings. Needle electrodes are used in clinical electromyography, neurography, and other electrophysiological investigations of the muscle tissues underneath the skin and in the deeper tissues. They are widely used in clinical procedures in neuromuscular evaluations and stimulation.

## 36

## Biofeedback Instrumentation

### Purpose

Biofeedback instruments are designed to be used in physical therapy, occupational therapy, chiropractic therapy, and in other healthcare or athletic settings. These devices are employed to increase the ability of a person to control voluntarily physiological activities by providing information about those activities. The biofeedback technique

allows an individual to manipulate at will the physiological activity so as to assist the person in improving health and performance. For example, biofeedback therapy can be used to restore functioning of the muscles damaged by injury. This therapy has also proved useful in athletic training to enhance performance by improving muscle activity.

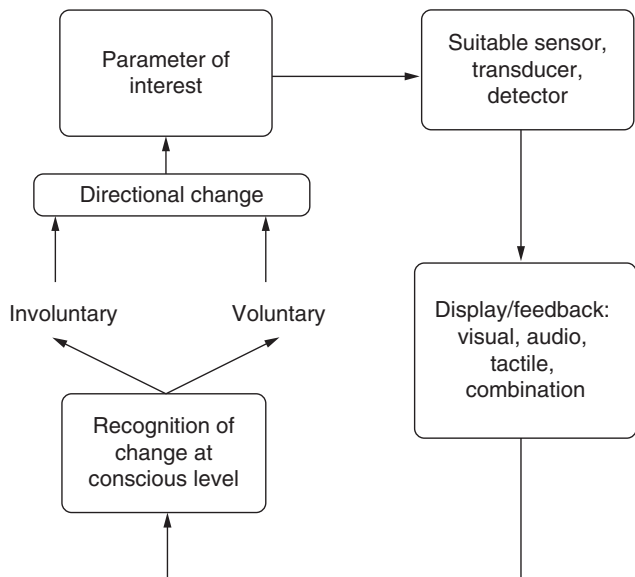
## Principle

Feedback is a common engineering term that refers to its function of controlling a process. The human body uses feedback systems to control certain functions. A feedback system uses one of the products of a pathway, usually the end product, to control the activity of the pathway and to regulate the amount of that product. When the feedback concept is applied to biological processes within the body, it is termed as biofeedback. Biofeedback provides a means for gaining control of the body processes to create a specially required psychological state so as to increase relaxation, relieve pain, and develop healthier and more comfortable life patterns.

The biofeedback therapy has been used to help prevent or treat conditions, including migraine headaches, chronic pain, incontinence, and high blood pressure. As the technique is noninvasive and does not involve drugs, the potential for risk or undesirable side effects is reduced, which could make it suitable for those who wish to avoid medications or those who cannot use them due to some physiological reasons. In principle, the technique involves the measurement of a variable produced by the body process and compares it with a reference value. Based on the difference between the measured and reference value, action is taken to bring the variable to the reference value. Biofeedback instruments can be applied for research, clinical, and trainer use.

Figure 36.1 illustrates the basic principle of biofeedback, which shows its essential functional aspects – detection of information and providing it to the patient in an

**Figure 36.1** Principle of biofeedback instrumentation.



understandable way. The patient can then, at their own initiation, use the information to achieve a measure of control over the same process. The clinical biofeedback instruments are usually computer-based systems that can monitor the patient's bodily responses such as surface muscle potentials or surface skin temperature. Information regarding the patient's physiological responses are then fed back to the patient. The feedback may be in the form of auditory or visual signals. Through this physiological feedback, the patient can learn to control the bodily responses through mental adjustment.

It may be noted that biofeedback is not a treatment. Rather, biofeedback training is an educational process for learning specialized mind/body skills. Through practice, one learns to recognize physiological responses and to control them rather than having them control us. The person thus learns to gain self-regulatory skills through biofeedback training, which helps to adjust the activity in various systems to optimal levels. Many different physiological processes have been evaluated for possible control by biofeedback methods. However, the following four neural functions are commonly employed:

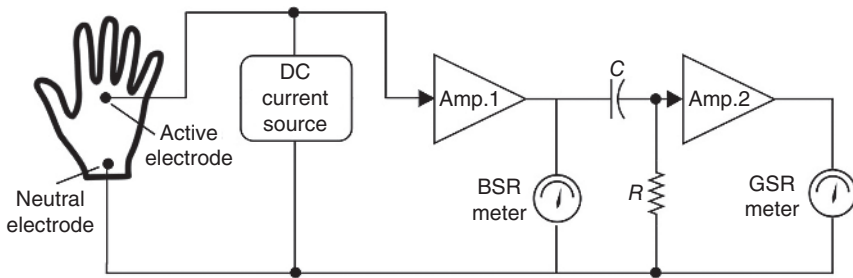
- *Electrodermal activity* (galvanic skin response [GSR] measurement)
- EMG (electromyograph measurements)
- EEG (electroencephalograph measurement)
- *Temperature pattern* (thermistor readings)
- *Pulse* (heart rate monitoring)

Biofeedback instrumentation for the measurement of galvanic skin resistance, EMG, temperature, and pulse/heart rate is similar to conventional instruments used for the measurement of physiological variables. They employ transducers and amplifiers to sense and measure the variable that is to be controlled by the feedback process. The feedback may be in different forms. It may be visual, for example, needle movements on a meter or varying light intensity, auditory in terms of change in pitch of a continuous tone or in click rate, or combinations of various modalities. The magnitude of the measured variable or changes in the magnitude are transformed into a corresponding auditory or visual stimulus that is presented to the subject. As a response to the stimulus, the subject is trained to control the abnormal conditions. Computer-based biofeedback instrumentation has been developed to provide guidance programs in the privacy of one's home.

### ***Electrodermal Biofeedback Instrumentation***

Electrodermal biofeedback therapy is used for treating problems such as anxiety, excessive sweating, and stress. Electrodermal measurements have been a part of the polygraph test, commonly known as lie detector, as they rapidly and accurately reflect changes in emotional activity or anxiety. Besides, the technique is used as an adjunct to psychotherapy as a result of increasing patient's awareness of their emotions.

The electrodermal activity reflects the level of functioning of sweat glands that are linked to the dynamic processes of the central and peripheral nervous systems. It essentially measures palmar sweat gland activity of the fingers or hands. It is observed that due to increased sweat gland activity, the electrical conductivity of the skin increases in response to unexpected stimuli, arousal, and worry. The feedback device reflects those changes. Specifically, when the conductivity increases the pitch of the feedback sound



**Figure 36.2** Block diagram for measurement of basal skin resistance (BSR) and galvanic skin response (GSR).

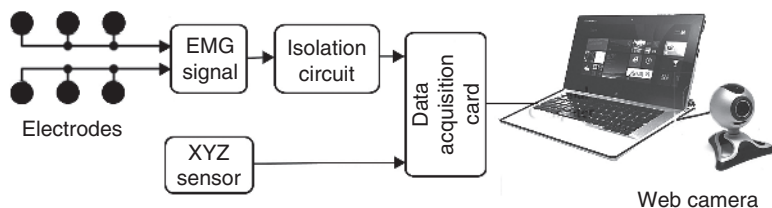
increases; when the conductivity decreases the pitch of the sound decreases. So, electrodermal biofeedback is a process in which sensors monitor and feedback skin conductance in order to treat anxiety disorders, chronic pain, and stress. Skin conductance is measured in microsiemens.

Electrodermal activity is generally measured either as resistance, called skin resistance activity (SRA) or its reciprocal skin conductance activity (SCA). Usually, SRA is measured in two ways: basal skin response (BSR) and GSR. BSR is a measure of the average activity of the sweat glands, whereas GSR is a measure of the phasic activity (the high and low points) of these glands. BSR gives the baseline value of the skin resistance, whereas GSR is due to the activity of the sweat glands. A GSR works by measuring changes in the skin's resistance as the anxiety levels of the person wearing it changes due to increased sweat gland activity. The GSR is measured most conveniently at the palms of the hand, where the body has the highest concentration of sweat glands. The measurement is made using a direct current (DC) current source. Eight millimetre silver/silver electrodes are used to measure and record the BSR and GSR. Figure 36.2 shows the arrangement for measuring these parameters. The BSR output is connected to an RC network with a time constant of three to five seconds, which enables the measurement of GSR as a change of the skin resistance.

### **EMG Biofeedback Instrumentation**

EMG biofeedback is the process of measuring and transforming the physiological information from the muscle into visual and audio signals. The technique can help create awareness of and develop confidence in the patient in voluntary control of the muscular activity. Biofeedback therapists have used EMG biofeedback in treating numerous problems such as anxiety and worry, chronic pain, headache, low back pain, physical rehabilitation, and so on.

The EMG signals for clinical biofeedback are acquired using surface electrodes that are applied over or in the vicinity of muscle(s) to be studied. The signals are the summation of muscle cell action potentials generated by the underlying muscles monitored at the skin surface. Although needle or wire subcutaneous electrodes can provide better EMG signals, they are not preferred because of their complexity and invasive nature. Today, most EMG biofeedback studies are conducted using disposable electrodes often composed of an  $\text{Ag}^+/\text{AgCl}$  disk and an adhesive attached to the skin.



**Figure 36.3** Block diagram of an EMG biofeedback system.

As a first step, the signals from the electrodes are amplified and conditioned by low noise, high performance differential amplifiers. Some amplifiers are small enough for mounting directly on the electrode structure. The amplifiers have a high input impedance of the order of more than  $100\text{ M}\Omega$  and common mode rejection ratio of greater than  $100\text{ dB}$ . The signal amplitude is in the range of  $0.1\text{--}2000\text{ mV}$  and bandwidth of interest lies in the range  $5\text{--}200\text{ Hz}$ . Following amplification, the EMG signal is processed in three ways: rectification, filtering, and integration. The rectification is done in a precision operational amplifier to produce the time-variant average or root-mean-square average that is required for quantification and display. The amplified signal is then processed to a form suitable for display to the subject. Most modern instruments are microcomputer based and implement filtering, rectification, averaging, and display through software algorithms. Some stand-alone instruments have data storage, statistical reporting, and downloading capabilities.

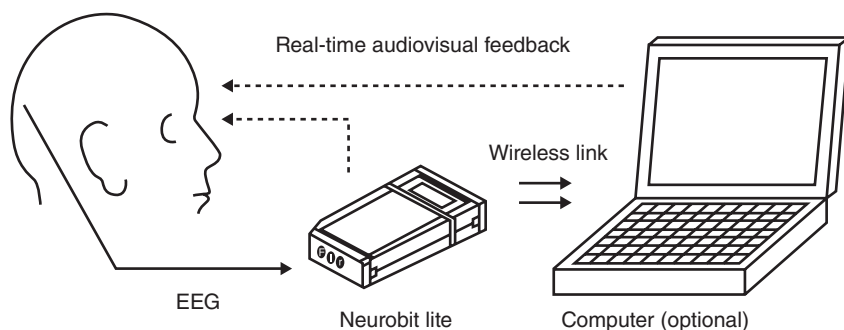
PC-based systems are available in which the signal acquisition and conditioning hardware are interfaced to PC having suitable processing software. A block diagram of a typical EMG biofeedback system is shown in Figure 36.3.

A typical PC-based EMG biofeedback instrument provides for measuring two channels of surface electromyography and two channels of electrical stimulation in a wide variety of configurations and modalities. The instrument can be connected to a PC via a USB cable.

### EEG Biofeedback Instrumentation

EEG biofeedback or neurofeedback is a kind of therapy that is being used or researched to treat many psychophysiological disorders. EEG biofeedback involving real-time monitoring and altering of brain activity has been found to effectively treat problems such as epilepsy, mood disorders, addictions, hyperactivity, and attention deficiency. Neurofeedback instruments display the kind of brainwaves a person is producing, making it possible for the individual to learn to change them to improve attention. The mechanism is essentially self-regulated training. EEG biofeedback is being used by clinicians and scientists to help with a variety of conditions such as attention, learning, better concentration, creativity, and behaviour problems.

Biofeedback EEG therapy involves placing one or more electrodes (sensors) on the scalp and one to each ear. The electrodes are then connected to a computerized device that records the natural activity of the brain, analyses it electronically, and displays the same graphically. Brain activity is evaluated by examining the graphical recording. The brainwaves are classified as either  $\alpha$ ,  $\beta$ ,  $\theta$ , or  $\delta$ . The  $\alpha$  waves ( $8\text{--}15\text{ Hz}$ ) indicate a calm and relaxed state of mind,  $\beta$  waves ( $15\text{--}40\text{ Hz}$ ) reflect an alert and awake state such as



**Figure 36.4** Schematic of an EEG biofeedback system. *Source:* Courtesy of M/s Neurobit Lite.

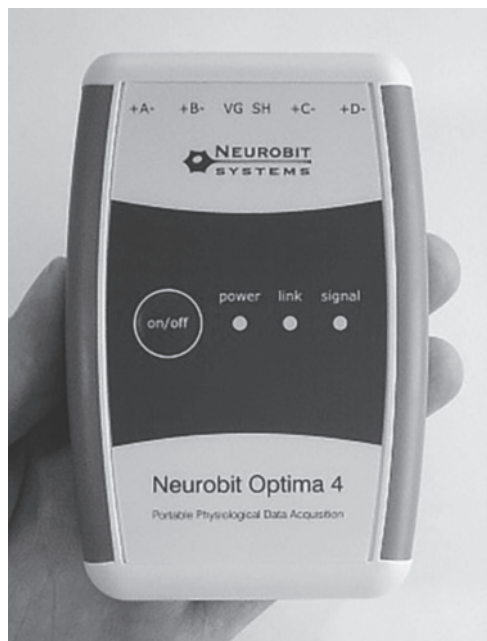
when a person is solving a problem, and lastly,  $\delta$  waves (0.5–4 Hz) and  $\theta$  waves (4–8 Hz) are indicative of meditation or drowsy state. By examining the brainwaves, the functioning of the brain can be evaluated and a therapy plan worked out if some abnormality is present. Feedback regarding brain activity is presented to the patient in the form of auditory and visual indicators, which indicate how well the brain is successful in maintaining the particular wave state it has been asked to achieve. Usually, the person is asked to play a video game on the computer's monitor screen. The person is rewarded by the computer for good concentration and thus, the session becomes quite enjoyable. With frequent use, EEG feedback has shown to improve a variety of brain-related ailments.

The EEG biofeedback instrumentation, in general, is similar to EMG biofeedback instrumentation. Figure 36.4 shows a block diagram of an EEG biofeedback system. The EEG signal is acquired on the scalp using pre-gelled disposable surface electrodes. A high performance differential amplifier amplifies and conditions the signals. The typical EEG signal amplitude is 2–200  $\mu\text{V}$  and frequency range of 0.1–50 Hz. Modern EEG biofeedback instruments have digital filtering on the amplified and conditioned EEG signal to obtain the frequency band of interest or full spectrum of interest by performing fast Fourier transform (FFT). The feedback display is a computer-generated graphic animation sequence such as video games and/or audio feedback comprising several types of files and songs. Auditory feedback is useful for closed eyes training and special situations. Electronic circuitry and software of commercial instruments vary widely in terms of amplifier bandwidth, filter cut-offs, rectifiers, and integrators, making it difficult to generalize their performance parameters. M/s Neurobit Systems have introduced two models of EEG biofeedback devices. Neurobit Lite has a wireless link with PC, whereas Neurobit Optima (Figure 36.5) is a versatile device that provides neurobiofeed, EMG, heart rate variability (HRV), GSR, temperature, and other types of biofeedback.

### **Biofeedback Instrumentation for Other Physiological Parameters**

Biofeedback has been a subject of interest for studying many other physiological parameters. However, most of them still remain subjects of research and only a few of them have found clinical applications. One such parameter is *temperature* biofeedback, which is primarily used to improve poor peripheral blood flow.





**Figure 36.5** EEG biofeedback system model Neurobit Optima 4. *Source:* Courtesy of M/s Neurobit Lite.

The sensors used in temperature biofeedback instrumentation are thermistors, having negative coefficient of change of their resistance. The thermistors have a linear negative change in resistance over the limited temperature range of 20–38°C. A small DC voltage when applied across the thermistor results in increased current flow because of increased heat due to increased blood flow from the subject.

Another area of interest in biofeedback is the study of *cardiovascular system*, with a focus on hypertension and cardiac arrhythmias. Researchers have also been active in the field of biofeedback relating to gastrointestinal responses and pH and sexual dysfunction.

**Wearable devices** have also been developed for biofeedback therapy. One such wearable device involves wearing a sensor on the waist that monitors the breathing and tracks the breathing patterns using a downloadable app. The app can alert you if you're experiencing prolonged tension, and it offers guided breathing activities to help restore your calm. Another device, which is a microcontroller with advanced power management, firmware, and an easy-to-use Android app for GSR reference design, integrates digital-to-analog (DAC) and analog-to-digital (ADC) converters.

## Specifications

### *EMG amplifier*

*Input impedance:* >100 MΩ

*Low internal noise:* <0.5 μV, p–p

*Bandwidth (3 dB) for biofeedback:* 20–500 Hz  
*Common mode rejection ratio:* CMRR >107 dB  
*Gain stability:*  $\pm 1\%$

### *Stimulator*

*Stimulation intensity:* 0–100 mA  
*Stimulation pulse rate:* 2–100 Hz  
*Pulse width:* 50–400  $\mu$ s

## Applications

The biofeedback technique is adopted to enhance performance and possible health improvement and to bring about physiological changes often occurring in conjunction with changes to thoughts, emotions, and behaviour. Eventually, these changes can be maintained without the use of any extra equipment. Biofeedback helps in relaxation of muscle spasms, prevention or retardation of disuse atrophy, maintaining or increasing range of motion and treatment of stress, etc.

## 37

## Biotelemetry: ECG (Single Channel)

### Purpose

Biotelemetry systems permit evaluation of the physiological data of a man or an animal under normal environment and in natural surroundings without discomfort or obstruction to the person or animal under investigation. This allows recognition and evaluation of factors influencing healthy and sick persons during the performance of their daily tasks. Wireless biotelemetry has made a possible study on active subjects under conditions that so far inhibited measurements. Biotelemetry is, therefore, an indispensable technique in situations where no cable connexion is feasible. It can be used to obtain physiological signals from swimmers, riders, athletes, pilots, or manual labourers. Telemetric monitoring is also of great value during transportation within the hospital area and for the continuous monitoring of patients sent to other wards or clinics for check-up or therapy. Of course, the most common application of biotelemetry is telemetering ECG, employed mostly for monitoring heart rate and arrhythmias.

### Principle

The establishment of heavily instrumented intensive/coronary care units has resulted in substantial reduction in the mortality rates of hospitalized patients. When a patient's condition has stabilized within a few days, it is necessary that he is monitored during

the early stages of increased activity and exertion to determine if his heart has sufficiently recovered. This can be conveniently done by the use of telemetry, which provides a sort of intermediate stage of care that smoothenes the patient's transition back to a normal life without the unnatural constraints of confining the patient to bed.

Biotelemetry monitoring usually refers to a special way of monitoring a hospital patient's heart activity, although it serves the same purpose as a conventional heart monitor. However, the difference between the two is that the patient is asked to wear a transmitter that relays the data to the central monitoring station in the hospital. The central station displays the ECG waveforms of the patients on telemetry, analyzes it, and issues alarms to alert staff about clinically significant events. Each transmitter sends its data out on a different frequency so that the transmitters do not interfere with each other. This way, it allows monitoring of the patient to get up and move around, at least within the device's transmitting range. This is highly advantageous as the patient need not be confined to a bed when his heart's activity can be observed.

Typically, a basic biotelemetry system comprises two main components, the transmitter and the receiver. The *transmitter* has several subsystems including one or several transducers to capture the physiological signals, signal processing capability with amplifiers and filters, and communication arrangement through an radiofrequency interface. The transmitter carries an on-board power supply, usually a battery or receives power from outside using inductive coupling. The devices are packaged so that they are least obtrusive to the patient. The *receiver* is designed to receive the signal from the transmitter, perform the desired analysis, and display the results. Since telemetry systems use radio-wave transmission, cables are not required to connect the patient and transmitter to the display monitor, thereby allowing greater patient mobility.

### Modulation Systems

The physiological signal alone cannot be transmitted with reasonable efficiency as a radio wave because of its low frequency. Therefore, a high frequency carrier wave is usually used as a transmitting vehicle. The signal information is forced upon the carrier by modulation, that is, by a signal-dependent, and thus time-variant, characteristic parameter such as amplitude, frequency, or phase.

For transmission of biological signals, two types of modulating systems are commonly used. A comparatively lower frequency subcarrier is employed in addition to the very high frequency (VHF) carrier, which finally transmits the signal from the transmitter. The use of double modulation gives better interference-free performance in transmission and reception of low frequency biological signals. The sub-modulator can be a frequency modulation (FM) system or a pulse width modulation (PWM) system, whereas the final modulator is practically always an FM system.

*Amplitude modulation* (AM) is a simple method of signal transmission; its application, however, is rather limited. AM signals are more adversely affected by sources of interference that additively superimpose the carrier than the signals modulated by other procedures.

In *FM*, information is transmitted by varying the instantaneous frequency in accordance with the signal to be modulated on the wave, while keeping the amplitude of the carrier wave constant. The rate at which the instantaneous frequency varies is the modulating frequency of the biosignal.

The PWM is another modulation technique used in most communication systems for encoding the amplitude of a signal. Here, only discrete samples representing the signal are used to modulate the carrier. The parameter of a pulse waveform that may be varied includes the amplitude (pulse amplitude modulation [PAM]), PWM, or pulse position modulation (PPM) of the pulse. The major advantage of PWM is that the signal remains digital all the way, minimizing the noise effects and distortion.

### **Carrier Frequency**

The choice of *radio carrier frequency* is another factor that plays an important role in biotelemetry. In every country there are regulations restricting frequency and bandwidth to be used for medical telemetry purposes. Therefore, the permission to operate a particular telemetry system needs to be obtained from the concerned department of the country concerned. The radio frequencies normally used for medical telemetry purposes are of the order of 37, 102, 153, 159, 220, and 450 MHz. Transmitter is typically of 50 mW at 50  $\Omega$ , which can give a transmission range of about 1.5 km in the open flat country. The range will be much lesser in built-up areas. In the United States, two frequency bands 174–216 MHz and 450–470 MHz have been designated for short-range medical telemetry work by the Federal Communications Commission (FCC). The output is limited to a maximum of 150  $\mu$ V/m at a distance of 30 m in the lower frequency band and much higher in the upper frequency band. So, such infrastructure was built around regulatory domain-controlled technologies, such as Wireless Medical Telemetry Service (WMTS) in the United States.

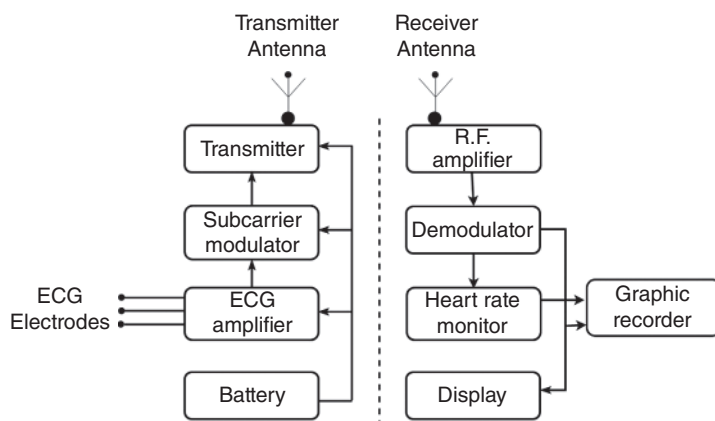
Although the term biotelemetry usually refers to wireless data transfer mechanisms using radio, ultrasonic, or infrared systems, it also today includes data transferred over other media such as a telephone or computer network, optical link, or other wired communications like power line carriers. Many modern telemetry systems take advantage of the low cost and ubiquity of GSM networks by using SMS to receive and transmit telemetry data.

### **Single Channel ECG Telemetry System**

In a majority of the situations requiring monitoring of the patients by wireless telemetry, the parameter that is most commonly studied is the electrocardiogram. It is known that the display of the ECG and cardiac rate gives sufficient information on the loading of the cardiovascular system of the active subjects. Most ECG telemetry systems operate in the 450–470 MHz band, which is well-suited for transmission within a hospital and has the added advantage of having a large number of channels available. Figure 37.1 shows a simplified block diagram of a typical single channel analog type telemetry system suitable for transmission of electrocardiogram. The following are the two main parts:

- *Telemetry transmitter:* This consists of ECG amplifier, subcarrier oscillator, and ultra-high frequency (UHF) transmitter along with cell batteries.
- *Telemetry receiver:* This consists of a high frequency unit and a demodulator, to which an electrocardiograph can be connected to record, display, and store ECG. A heart rate meter with an alarm facility can be provided to monitor continuously beat-to-beat heart rate of the subject.

For distortion-free transmission of ECG, the patient should be able to carry on with his normal activities while carrying the instruments without the slightest discomfort.



**Figure 37.1** Block diagram of single channel analog telemetry system.

The person should be able to forget their presence after some minutes of application. Also, the battery life should be long enough so that a complete experimental procedure can be carried out.

While monitoring paced patients for ECG through telemetry, it is necessary to reduce pacemaker pulses. The amplitude of pacemaker pulses can be as large as 80 mV compared with 1–2 mV, typical of the ECG. The ECG amplifiers in the transmitter are slew rate limited so that the relatively narrow pacemaker pulses are reduced in amplitude substantially.

In the legacy systems, the transmission of physiological signals was unidirectional. This means that the signal could only be sent from a transmitter (patient) to the central station, but there was no way for the central station to communicate back to the patient. For example, if there was a signal loss because of some reason during transmission from the patient to the central station, there was no way for the central station to communicate this back to the patient and request for resending of the lost data. Use of digital wireless technologies now offers the advantage of two-way or bidirectional communication.

### ***Use of Digital Technologies***

The explosion of digital and wireless technologies has allowed the emergence of several wireless standards, especially in the industrial, scientific, and medical (ISM) band, which can be exploited for telemetry purposes. The ISM band (2.4 GHz) frequency spectrum can be used by anyone without a license. Bluetooth and wireless local area network (WLAN) are two popular technologies that provide wireless networking capabilities, but they have different focus and areas of applications. Bluetooth aims mainly at solutions that result in minimizing the requirement of cables over a short range as required in telemetry.

The WLAN enables networking capabilities just like a wired LAN. As compared with Bluetooth, it offers higher bandwidth and longer range of operation. The range of operation of a WLAN may cover several rooms, floors, or possibly the entire hospital building. This enables monitoring of a patient and sending his/her data to the central monitoring station, even when the patient is moved from one room to another or to some other part of a building. WLAN and Bluetooth share the same 2.4 GHz ISM frequency band and complement each other.

Bluetooth is a wireless technology standard for exchanging data over short distances using radio waves in the ISM band of 2.4–2.485 GHz from fixed and mobile devices. It is a standardized secure protocol for sending and receiving data. It is ideal for short-range, low power, low-cost wireless transmissions between electronic devices. Bluetooth technology allows direct wireless communication to cellular phones, laptops, and other Bluetooth enabled devices such as sports and fitness watches and other personal monitoring devices. All mobile phones today, even entry-level phones, have Bluetooth connectivity. Bluetooth supports data throughput up to 2Mbps and is mostly used in point-to-point topology.

ISM band in biotelemetry systems usually uses Wi-Fi, Bluetooth, or ZigBee networks when there is mobility. However, such networks have narrow range. WiMAX that has larger range of operation is therefore more popular. ISM band is not specific to its use in medical telemetry only. Many different devices such as laptops and portable phones use the ISM band for wireless related functions, so the hospital has to coordinate interoperability between its telemetry systems and other wireless systems such as the WLAN. Over the past decade, many medical device manufacturers have incorporated WLAN in their devices in a number of devices, resulting in the next generation of smart infusion pumps, portable patient monitoring, and, within the past five years, telemetry systems.

The introduction of Wi-Fi has enabled to increase networking speed, quality of service, and security in telemetry applications. The technology has developed a level of performance capability whereby it is now displacing the wired Ethernet network. A typical telemetry device Infinity TeleSmart system (Figure 37.2) from M/s Drägerwerk

**Figure 37.2** Typical patient-worn telemetry monitor, Model Infinity TeleSmart. Source: Courtesy of M/s Drägerwerk AG & Co. KGaA.



AG & Co. features a compact device capable of monitoring ECG and SpO<sub>2</sub>. The device runs on an industry-standard Wi-Fi network. The system provides the performance of a full-size patient monitor, packaged in the size of a patient-worn telemetry device for adult and paediatric patients.

The device allows continuous standalone monitoring and allows two-way communication between the device and the central station for wireless data exchange and signal integrity within the hospital's wireless network coverage area. The colour display shows the patient's ECG for all monitored leads, heart rate, SpO<sub>2</sub>, and electrode status. The device also displays patient demographics to help confirm the patient's identification before giving medications, taking blood samples, or providing treatment. It includes arrhythmia classification and pacer detection algorithms to enhance ECG processing and reduce false alarms. The device has a built-in battery that can be recharged via a bedside charger while the patient wears the device, or at a patented multi-device charger at the central monitoring station. Built-in alarm facility provides alarm alerts while the clinician is at the patient's side or at the central monitoring station. From the colour display, it is convenient for the clinician to assess the alarms and respond accordingly.

Two-way communication supports the latest generation of patient-worn monitoring devices. These devices send patient vital signs data to the central monitoring station for display and alarming, as did yesterday's telemetry transmitters, but they also display and alarm locally. So if the patient accidentally walks outside of the Wi-Fi network coverage area, the patient will continue to be monitored locally. The caregiver is therefore able to monitor the patient without compromising the mobility of ambulatory patients.

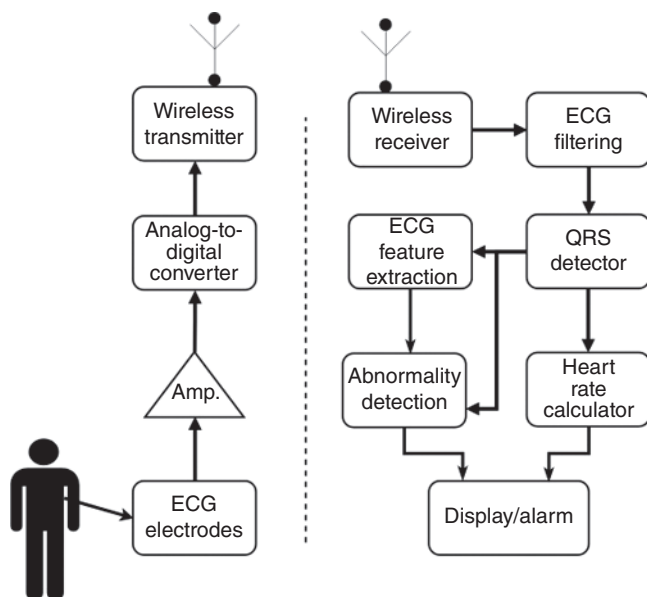
### ***Bluetooth-based Telemetry System***

A block diagram of an ECG telemetry system is shown in Figure 37.3. The design is based on the use of Bluetooth as a method of transmission. On the transmitter side, the ECG signal is acquired with the help of disposable pre-gelled electrodes, which are placed in a triangle formation around the heart, forming Einthoven's triangle. The next step is to amplify the ECG to a level at which an analog-to-digital converter (ADC) can sample the data with a high resolution. The first stage in any amplification circuit is the instrumentation amplifier followed by simple amplifiers to provide the necessary amplification. The instrumentation amplifier has a high common mode rejection ratio to minimize common mode signals.

Filters are the other essential components in the signal conditioning circuitry. In almost all ECG circuits, high pass and low pass circuits are used to allow only the limited band necessary for the ECG signal. Besides, a band-stop or notch filter is used to remove the noise that is produced from the common AC mains supply. The ADC is built in the microcontroller unit. The wireless transmission typically performed using Bluetooth connection employs 2.4 GHz band and provides a working range of 30 m. It has a transfer rate of approximately 1–3 Mbps.

On the receiver's side, the first stage is the Bluetooth transceiver, which is followed by ECG signal processing techniques used for detecting heart abnormalities. Typical stages in signal processing are preprocessing of ECG, wave amplitude and duration detection, heart rate calculation, ECG feature extraction algorithms, and finally identification of





**Figure 37.3** Block diagram of biomedical signal transceiver for real-time acquisition, processing, and monitoring system for assessing heart condition. The right portion of the system can be implemented in smartphone or PDA for smart health monitoring.

abnormalities. Prior to applying different signal processing techniques for extraction of different ECG features of clinical interest, the data requires to be filtered to reduce noise and artefacts.

Detection of QRS complex is the most important step in ECG signal processing. QRS detection provides temporal information of each beat and QRS morphology information that form the basis of the other algorithms. Many methods for detection of QRS complex have been described in the literature. Most of them are based on filtering, non-linear transformation, or use of template matching method. However, wavelet transform based algorithms are now becoming popular. Once the QRS is detected, average heart rate can be computed by counting the number of heart beats over one minute time period. Instantaneous heart rate can be derived by measuring the time interval between two R–R peaks and calculating the rate from the formula: Heart rate = 60/RR interval in seconds.

ECG telemetry systems have the provision for arrhythmia detection. They incorporate ECG feature extraction and diagnostic capabilities such as tracking of the heart rate, ST segment changes, number of episodes, and duration of atrial fibrillation, bradycardia, tachycardia, and pause episodes.

For satisfactory operation of a radiotelemetry system, it is important to have proper orientation between transmitting and receiving antennas. There can be orientations in which none of the signals radiated from the transmitting antenna are picked up by the receiving antenna. It is, therefore, important to have a means of indicating when signal interference or signal dropout is occurring. Such a signal makes it possible to take steps to rectify this problem and informs the clinical staff that the information being received is noise and should be disregarded.

### Special Features

Some telemetry transmitters are provided with special indicators like low transmitter battery and nurse call facility. In both these situations, a fixed frequency signal is generated, which causes a deviation of subcarrier and when received at the receiver, actuate appropriate circuitry for visual indications. Also, some telemetry systems include out of range indication facility. This condition is caused by a patient lying on the leads or the patient getting out of range from the receiver capability. For this, the RF carrier signal from the transmitter is continuously monitored. When this signal level falls below the limit set, the alarm will turn on.

### Specifications

#### ECG

*Input configuration:* 3, 5, or 6 electrodes

*QRS detection range:* 0.5–5 mV

*Frequency response:* Up to 40 Hz

*Lead fail detection:* Indicates failed lead wire

*Input impedance:*  $>5\text{ M}\Omega$

*Common mode rejection:* 100 dB minimum

*Defibrillator protection:*  $\pm 5000\text{ VDC}$ , 360 J into  $100\ \Omega$

*Defibrillator recovery time:* Within 5 seconds

*Pacemaker detection:*  $\pm 2$  to  $\pm 700\text{ mV}$  (RTI);  $100\ \mu\text{s}$ –2 ms;

#### Transmission

*Network:* IEEE 802.11b/g/n (2.4 GHz)

*Wireless encryption:* WPA2 – Personal Mode

*Radio power output (2.4 GHz):* 25 mW maximum

### Applications

ECG telemetry is highly valuable for cardiac patients going through a physical rehabilitation process wherein the recovery of the patient depends on his movements while he is still being monitored by the healthcare team. A built-in warning system included in the system can inform the patient as well as central monitoring facility about any abrupt abnormality in the heart.

## 38

### Biotelemetry: Multichannel

#### Purpose

Multichannel biotelemetry systems are designed to monitor several physiological parameters simultaneously from subjects through wireless transmission. Such systems are particularly useful in athletic training programs and monitoring patients recovering

in the hospitals. With appropriate electrodes/transducers, the multichannel systems permit the transmission of parameters such as ECG and heart rate, respiration rate, temperature, intravascular, and intracardiac blood pressure. Then there are multi-patient single parameter telemetry systems that are used on patients making satisfactory recovery in ICU/CCU wards who can vacate the hard wired instrument beds but remain under monitoring, which provides a positive psychological effect on their recovery.

## Principle

In multichannel telemetry, one can monitor either a number of patients for the same parameter or a number of parameters of the same patient. Thus telemetry is a tremendously useful tool in hospitals, as it allows hospital personnel to monitor the required physiological parameters of a patient at a remote location like a nursing station.

In design, the multichannel telemetry systems use the same subsystems as those present in the single channel systems. However, the number of subcarriers required is the same as the number of signals to be transmitted. Each channel therefore has its own modulator. The radiofrequency (RF) is same for all channels. This unit converts the mixed frequencies into the transmission band. Similarly, the receiver unit contains single RF unit but individual demodulator for each channel.

Pulse width modulation is preferred for multichannel biotelemetry systems. Such systems are insensitive to carrier frequency shifts and have high noise immunity. FM-FM systems for similar use may have low power consumption and high baseline stability, but they are more complex and turn out to be more expensive. In such systems, there can be interference between different channels. Techniques for separation usually require expensive and complex filters, and even with these, crosstalk can still be a problem. Similarly, pulse-position amplitude modulation easily gets into synchronization difficulties caused by noise and thus results in a loss of the information transmitted. On the other hand, advantages of pulse-width modulation include lower sensitivity to temperature and battery voltage changes and its adaptability to miniaturization due to their availability in the specific integrated circuits.

For multichannel radiotelemetry, various channels of information are combined into a single signal using multiplexing technique. There are two basic methods of multiplexing. These are the following:

- *Frequency-division multiplexing:* The method makes use of continuous-wave subcarrier frequencies. The signals frequency modulate multiple subcarrier oscillators, each being at such a frequency that its modulated signal does not overlap the frequency spectra of the other modulated signals. The frequency modulated signals from all channels are added together through a summing amplifier to give a composite signal in which none of the parts overlap in frequency. This signal then modulates the RF carrier of the transmitter and is broadcast.
- *Time-division multiplexing:* In this technique, multiple signals are applied to a commutator circuit. This circuit is an electronic switch that rapidly scans the signals from different channels. An oscillator drives the commutator circuit so that it samples each signal for an instant of time, thereby giving a pulse train sequence corresponding to

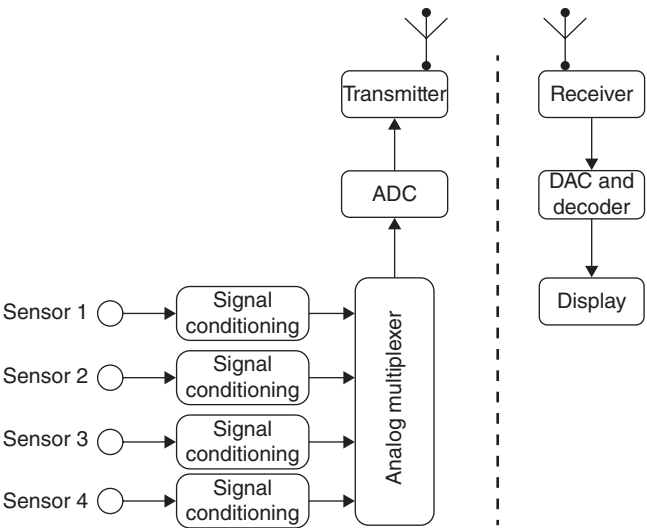
input signals. A frame reference signal is also provided as an additional channel to make it easy to recognize the sequence and value of the input channels.

### Instrumentation

A block diagram of a typical multichannel telemetry system is shown in Figure 38.1. Depending upon the parameters to be monitored, various types of sensors (electrodes/transducers) are used for capturing the signal of interest. Each sensor has its corresponding signal conditioning circuit that consists of buffering amplifier, and filtering circuits. This is followed by an analog multiplexer. Some systems tend to digitize each channel prior to multiplexing, but such systems usually require more power, which is not a desirable feature in battery operated telemetry systems. The multiplexed signal is then given to an A/D converter for digitization followed by an RF transmitter and antenna. On the receiver side, the received signal is demodulated and different channels are separated. Although many modulation techniques are available, most commonly used scheme is the pulse-code modulation. Application-specific integrated circuits constructed with low power RF circuit design have become available for use in telemetry systems.

Just as in single channel systems, mobile phones, PDAs, and Wi-Fi systems have helped in the design of a new range of biotelemetry systems. Commercially available wireless chips have led to the development of standard platform for a variety of applications. The use of the Bluetooth system in WLAN systems is particularly attractive for biotelemetry systems. Bluetooth, operating at 2.4 GHz carrier frequency, data rate at 1–3 Mbps, and range of 30 m, has lower power consumption than Wi-Fi system.

Multichannel systems can be divided into two types based on the source of power. One type is operated with a battery and the other type that is powered from outside using an inductive link. Battery-operated biotelemetry systems use different communication schemes than the inductively powered schemes.



**Figure 38.1** Block diagram of a multichannel biotelemetry system.

### **Multi-patient Single Parameter Telemetry**

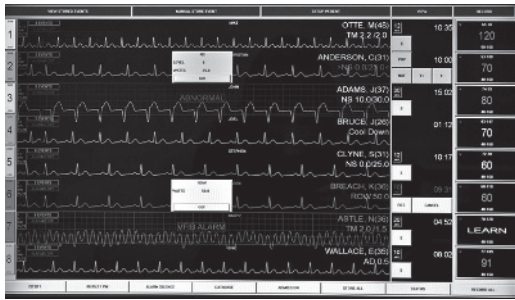
The main advantage of a multi-patient single parameter telemetry system is that patients making satisfactory recovery in a hospital can vacate the hard wired instrument beds in the ICU/CCU units, which provides a positive psychological effect to the patient. The patients regain mobility after an extended period of confinement, thereby improving their muscle tone and circulation. Transmitters as small as 8 cm × 6.25 cm × 2.25 cm in size and weighing less than 115 g including battery are commercially available. Data from different patients is received at the nurses' central station. The station may have the facility of continuous non-fade display of received waveforms, an ECG recorder that gets activated when the patient goes into alarm, loose lead/loss of signal alarm. The heart rate of each patient is derived and displayed simultaneously with a digital display. Multi-patient telemetry is usually done using crystal-controlled circuits, which provide frequency stability to within  $\pm 0.0015\%$ . Codes are necessarily provided on both the transmitter and the receiver units to indicate their calibrated frequencies.

The multi-patient telemetry systems, having utility mostly with cardiac patients, should have transmitters provided with defibrillator protection to 5000 V, 400 W s. ECG waveforms should not be seriously affected in the presence of pacemaker pulses of 2.5 ms in width and at rates up to 150 bpm. Telemetry transmitters that consist of an array of sensors embedded into the fabric of the wearer to continuously monitor the physiological parameters and transmit by wireless means to a remote monitoring station are available.

Using telemetry, a single nurse can monitor all of the patients in the unit from the nursing station. Nurses can also monitor patients at their bedsides, looking at the telemetry readouts on bedside monitors while assessing patients. The central station has arrhythmia and alarm detection facilities that allow to choose the parameters per patient, including measurement in ST changes. It also incorporates HL7 interface that allows to integrate database information with the hospital information system (HIS). Sixteen patients can be monitored on a single central workstation. There is sufficient memory in the central monitor to provide 96 hours of stored data for later study. A paging system is usually integrated with the system to alert clinicians when patients have an alarm event. The CARESCAPE Telemetry T14 transmitter from M/s GE Healthcare shown in Figure 38.2



**Figure 38.2** Multichannel patient telemetry transmitter. *Source:* Courtesy of M/s GE Health Care.



**Figure 38.3** Typical display of data in eight patient telemetry receiver.

is a typical example of multi-patient telemetry system, which allows to monitor up to 640 patients across the coverage area. The physiological parameters monitored by this device include ECG, noninvasive blood pressure (NIBP), and  $\text{SpO}_2$ . The system uses a bidirectional, frequency-hopping, spread-spectrum infrastructure, allowing it to ‘hop around’ the frequency spectrum to help prevent interference. This allows protection of life-critical patient data transmissions from interference, dropout, and downtime.

The central monitor has a provision of displaying several parameters that include 5-lead ECG, NIBP,  $\text{SpO}_2$ , respiration, and dual temperature. It has automatic arrhythmia detection and ST analysis with 72 hours of graphical and tabular trending data. A large LCD display provides ability for large numeric display of patient vitals and up to 8/16 waveforms. A typical central station display is shown in Figure 38.3.

Modern biotelemetry systems comprising of physiological sensors make use of miniaturized electronics to condition, process, and digitize wireless transmission circuit integrated into a single module. These sensors are strategically placed at various locations on the wearer’s vest. A number of sensors integrated into the fabric form a network (personal area network) and interact with the human system to acquire and transmit the physiological data to a wearable data acquisition system. The wearable data acquisition hardware collects the data from various sensors and transmits the processed data to the remote monitoring station. A number of wearable physiological monitoring systems have been developed to monitor the health status of the individual wearer.

## Specifications

### *Transmitter*

*Transmitter parameters:* ECG (single channel), respiration,  $\text{SpO}_2$ , NIBP

*Transmission frequency:* 608–614 MHz

*Battery type:* 1.5 V AA alkaline

*Battery life:* 24 hours

### *Central monitoring station*

ECG

*ECG leads:* I, II, III, MCL (multichannel), ECG 1, or ECG 2 (single channel)

*Sweep speed:* 25 or 50 mm/s (normal), 6.25 mm/s (compressed),

Numerical data display

Heart rate or pulse rate, VPC (ventricular premature complexes) rate, ST level, SpO<sub>2</sub>, NIBP, respiration ECG

*Alarms:* For tachycardia, bradycardia, asystole, VF (ventricular fibrillation), VT (ventricular tachycardia), VPC

Respiration monitoring

*Measuring range:* 0–150 breaths/min

SpO<sub>2</sub> monitoring

*Measuring range:* 50–100%

NIBP monitoring

*Pressure display range:* 0–300 mmHg

Thermal array recorder

*Number of channels:* 3

## Application

Multichannel biotelemetry enables a patient to leave the hospital or clinic but still have their health monitored remotely for various physiological parameters. In many cases, it is advantageous to be able to remotely monitor patients while they are active, particularly when they are undergoing physical rehabilitation. The physicians can monitor their patients while they are away from their medical centres in real time remotely from their office or home computer.

## 39

# Bladder Volume Measuring System: Ultrasonic

## Purpose

Ultrasonic bladder volume measuring system, popularly known as ultrasound bladder scanner, is used to noninvasively obtain measurement of post voiding bladder volume. Post-void residual (PVR) urine volume is the volume remaining in the bladder immediately after completion of voiding. The instrument is commonly used in the acute care, rehabilitation, long-term care environments, urology, and gynaecology departments of hospitals. The method is a noninvasive alternative to bladder palpation and intermittent catheterization used to assess bladder volume, urinary retention, and PVR volume.

## Principle

The measurement of PVR urine volume is an important aspect of assessment of continence of patients with spinal cord and brain disorders that lead to bladder dysfunction. The effectiveness of the voiding technique can be determined by the rehabilitation team from the



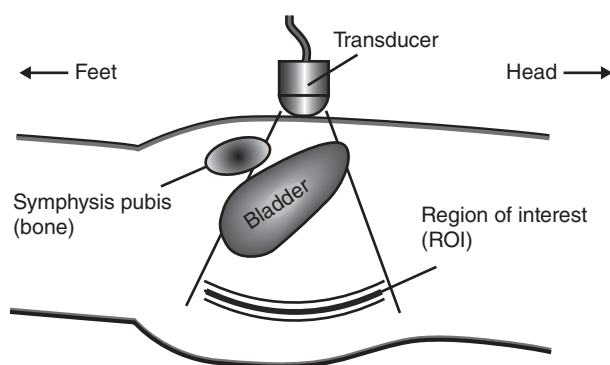
measurement of PVR urine volume. The voiding dysfunction of a patient is usually evaluated by using uroflowmetry, which is a noninvasive test. The measurement of PVR urine volume by uroflowmetry test can help to determine whether additional testing is required.

PVR is generally measured either by sterile catheterization or bedside ultrasound bladder scanners. There are many disadvantages associated with the catheterization procedure. It causes patient discomfort, carries a risk of urethral trauma, and is time-consuming. In contrast, ultrasound method offers advantages in terms of convenience, efficiency, and safety and can be performed with a portable device. Also, the bladder ultrasound technique that minimizes medical waste and supplies is noninvasive and time efficient. The technique helps to determine bladder wall thickness and bladder wall mass, both of which are associated with urine outflow obstruction. Measurement of PVR is also useful in evaluating voiding dysfunction and identifying potential bladder outlet obstruction.

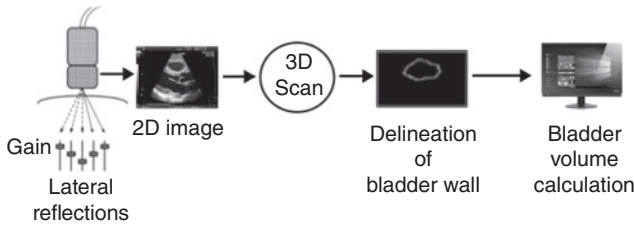
Ultrasound is an established technology based on reflections of ultrasonic waves from various structures inside the body when a beam of ultrasound is directed towards them. This helps to noninvasively visualize, monitor, and perform measurements of various structures in the human body. For bladder volume measurements, the bladder can be differentiated from surrounding tissues by ultrasonic reflections. Its volume can then be calculated based on bladder wall detection and a clinically established algorithm.

The last decade has seen significant developments in bladder ultrasonography. Portable, battery-powered self-contained ultrasound devices are now available commercially, which are specifically meant for measurement of total bladder volumes and PVR urine volumes. They comprise of a handheld scanhead (ultrasound transducer) and a control console with a display screen. Just as in conventional ultrasound scanners, the scanhead is placed on the patients' abdomen and directed towards the bladder as shown in Figure 39.1. The control circuit, after processing the received ultrasound waves, automatically calculates and displays the bladder volume. Portable three-dimensional (3D) ultrasound devices have been shown to provide highly accurate measurement of bladder volume.

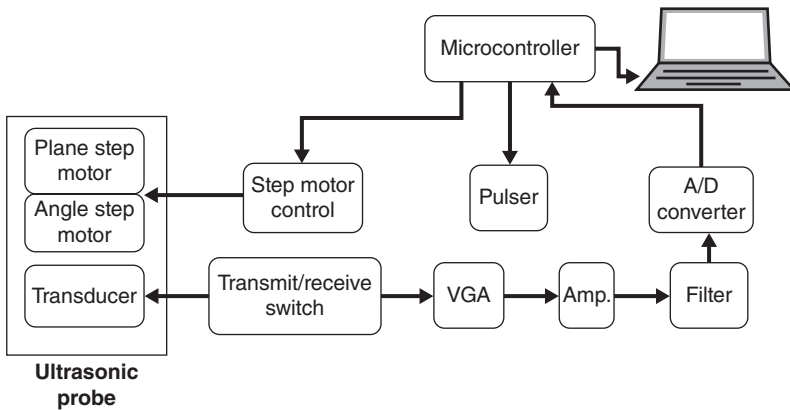
The bladder scanner is basically a B-mode ultrasonic instrument that is portable and battery operated. It uses a single element transducer operating at around 3.0 MHz and is steered mechanically to acquire a 120° cone of V-mode (multiple, aligned B-mode images) ultrasound data. Figure 39.2 shows a schematic block diagram of the bladder scanner.



**Figure 39.1** Set-up for ultrasonic bladder volume measurement.



**Figure 39.2** Principle of ultrasonic bladder volume measuring system.



**Figure 39.3** Block diagram of ultrasonic bladder volume measurement system.

The instrument measures ultrasonic reflections on multiple planes inside the body to differentiate the bladder from surrounding tissues and produce a 3D image. The 3D scan is achieved by performing 12 planar scans rotated  $15^\circ$  apart. The bladder volume is then computed using the detected 3D geometry. The principle of 3D imaging technology is shown in Figure 39.3. A microprocessor automatically calculates and displays bladder volume on an liquid-crystal display (LCD) screen. The operator simply applies ultrasound, applies and directs the scanhead towards the bladder, and initiates the scan.

In the ultrasound bladder scanner from M/s Verathon Medical, USA, the measurements are made using patented V-mode ultrasound technology. When the scan is initiated, within seconds, the V-mode technology measures ultrasonic reflections on multiple planes inside the body and produces a 3D image. Based on this image, the instrument calculates and displays the bladder volume and bladder mass. Volume measurements made with V-mode ultrasound are more accurate than those from conventional two-dimensional ultrasound, as they are based on a more complex, 3D image of the bladder.

The portable BladderScan(R) BVI 9500 Model from the same company, however, has a trifrequency transducer. The centre section of the transducer generates higher-frequency ultrasound at 7.3 MHz. This special design is for bladder wall thickness measurement, which can yield higher resolution information, and improves the

thickness measurement accuracy. The cross-sectional B mode images are obtained from 3 MHz signal and the harmonic ratio from 1.74 MHz transducer. The information obtained automatically calculates the urine volume via volumetric integration. At the same time, the 3D bladder surface area is also calculated based on the segmentations from every plane.

The device also incorporates patented Neural Harmonics technology that helps improve both speed and accuracy in bladder volume measurements. This technology is based on the principle of 'neural networks,' which applies a multispectral analysis to a data set giving clinicians definitive, intelligent diagnostic capabilities in bladder measurement. This technology helps achieve previously unattainable differentiation of the bladder, urine, and hypo-echogenic regions such as the uterus, thereby reducing error and minimizing uncertainty in measurements of bladder function as the measurements are based on more complex, multifaceted image of the bladder. Bladder volume, directional aiming, and battery status are all displayed on the LCD at the console. The results of the test can be printed on the thermal printer.

Modern bladder scanners also include aorta scan facility. The user selectable dual function allows to project ultrasound energy either into the lower abdomen to obtain an image of the bladder for measuring bladder volume or the mid abdomen to obtain an image of the abdominal aorta for aortic diameter measurement. In some of these instruments, the scanning probe is wirelessly connected to the console for data transfer. They provide a scanning depth of 23 cm.

## Specifications

*Maximum ultrasound during a scan:*  $\leq 5.0 \text{ mW/cm}^2$

*Ultrasound probe:* 3D sector scan, B-mode scan, scan angle:  $120^\circ$

*Transducer diameter:* 10–13 mm transducer

*Transducer frequency:* 2.5–3.0 MHz

*Penetration depth:* 15–23 cm

*Power source for scanhead:* Lithium ion battery pack

*Display:* 7" TFT-LCD

## Applications

Bladder ultrasound scanners find applications in a wide variety of patients including hospitalized patients, children, and elderly persons. Nursing homes and rehabilitation facilities often care for patients with urinary retention and urinary incontinence. The bladder scanner is therefore a fundamental clinical tool in these environments. There are clear advantages to using the bladder ultrasound device in inpatient/ambulatory care settings. These instruments are also used to determine bladder wall thickness and bladder wall mass, both of which have been associated with outflow obstruction.

## 40

# Blood Cell Processor (Apheresis System)

## Purpose

Blood cell processor or apheresis system is a machine with which blood can be removed automatically from a patient or donor and continuously separated into its components. The machine allows retaining the desired component of the blood while the residual component is retransfused to the patient or donor during or at the end of the process. Apheresis is one of the precious life-saving procedures in the field of transfusion medicine. Apheresis systems collect and separate blood components for donation. They can also remove or exchange substances in therapeutic procedures.

## Principle

Apheresis system employs centrifuge-based technology to separate the whole blood into its major components. The system draws the whole blood in a continuous flow from a donor or patient through a needle or catheter and delivers it to the centrifuge. An anticoagulant is added before centrifugation. The separation of the blood components follows allowing removal and collection of specific components. The residual blood is returned to the donor or patient. This completes the continuous flow extracorporeal circuit.

In therapeutic plasma exchange and red blood exchange procedures, appropriate replacement fluid (typically albumin or plasma) is continuously returned. The centrifuge spins at typical speeds of 2000–2500 rpm. The separation of the contents of the anticoagulated blood is based on the density or specific gravity of various components of blood. The efficiency of separation of the various blood components is determined by the dimensions of the centrifuge and its speed of rotation in revolutions per minute. The centrifuge creates centrifugal forces, as well as the dwell time, which is the amount of time that the blood spends in the centrifuge during the process.

The following are two types of centrifugation units:

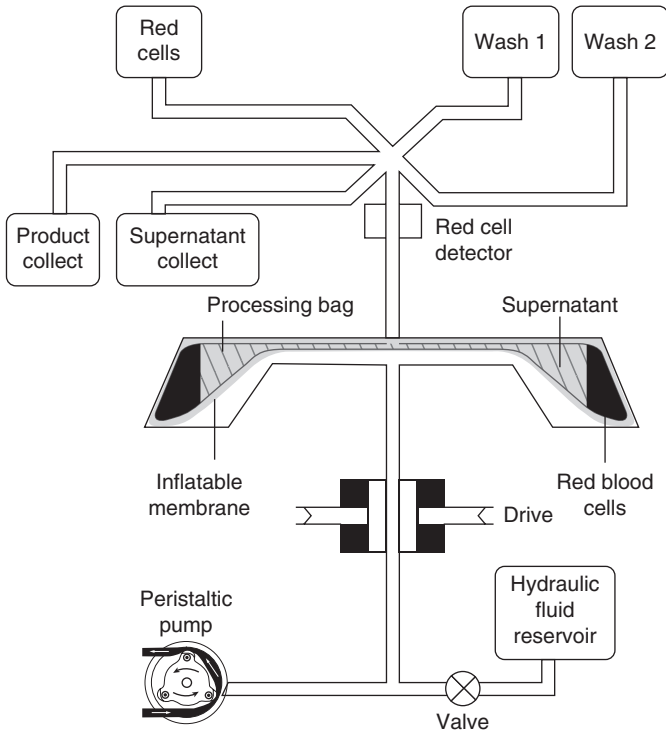
*Intermittent flow:* Intermittent flow centrifugation unit works in cycles and the blood is also collected in cycles. The desired component of the blood is spin separated and the rest of the components are returned to the donor. The procedure requires just a single venipuncture site. The blood is prevented from clotting by the pumping the anticoagulant automatically and mixing it with the blood in the apheresis machine.

*Continuous flow:* Continuous flow centrifugation involves the same steps of the process consisting of collection of blood, spinning it and returning it to the donor simultaneously by the machine. Here, the blood is withdrawn, processed, and returned to the individual continuously and not in cycles. It, however, requires two separate venipunctures for withdrawal and return of blood, although some systems

introduced recently need only single venipuncture. The continuous flow method operates on low extracorporeal volume and is thus preferred for the elderly and children.

A typical apheresis system consists of three major subsystems: (i) the apheresis machine itself comprising centrifuge, pumps, valves, etc., (ii) a sterile, single-use, disposable tubing set, and (iii) microprocessor-based electronics with embedded software. The fluid handling part of the machine is shown in Figure 40.1. Polyvinyl tubing is employed to draw blood from the patient and to send it back to the donor or the patient. The machine can be programmed from a display and control panel. Many essential features are incorporated in the machine to ensure safety of the person. These include pressure sensors, ultrasonic air-bubble detectors, optical fluid-level detectors, and dry-heat fluid warmers. The machines are microprocessor based and work under the programmed separation protocol. The centrifuge, pump, and other settings are automatically controlled by the software. Usually, rotary peristaltic pumps are employed to draw blood from the patient or donor and pump blood through the centrifuge.

The separation of blood components takes place in the centrifuge on density basis. Optical sensors are used to detect plasma–cell interfaces to minimize contamination



**Figure 40.1** Principle of operation of blood cell processor.

from other components. The blood products are moved into collection bags, anticoagulants are added, and fluids are replenished by the pumps. The replenishment of the fluids such as saline, serum albumin, plasma protein fraction, and fresh frozen plasma is necessary to maintain appropriate intravascular volume and pressure. The function of the fluid warmers is to help prevent hypothermia caused by infusing low temperature fluids.

Some machines such as the Spectra Optia apheresis system from M/s Terumo BCT, USA, also include bone marrow processing (BMP) protocol. In this process, filtered harvested bone marrow undergoes an apheresis procedure in which mononuclear cells (MNCs) are removed by means of centrifugal sedimentation and selective collection of the fraction rich in MNCs. The bone marrow is processed multiple times to ensure good recovery of the target cells. The Automated Interface Management (AIM) system in the system provides real-time interface monitoring, interpretation, and adjustment for efficient MNC collection. This is done by monitoring the interface position and thickness of separated blood components, up to 25 times/s with a resolution of approximately 10  $\mu\text{m}$ . The interface information is interpreted using optical detection software, and the pumps and valves are adjusted to manage the interface position and efficiently remove targeted components.

## Specifications

*Principle:* Continuous or intermittent flow separation

*Scope:* Universal cell separator for carrying out all apheresis procedures including stem cell apheresis and therapeutic plasma exchange

*Control:* Microprocessor-controlled fully automatic

*Safety features*

- Air detector in return line
- Flow control and monitoring
- Adjustable flow rates for draw and return
- Low extracorporeal volume
- Centrifuge leak detector
- Automatic validation of results
- Built-in contamination monitor for monitoring and preventing RBC contaminating in platelet collection and plasma exchange
- Monitor for haemolysis
- Donor's safety notifications alarms
- Memory for storing previous and current procedure information

## Applications

Blood cell processors find applications in blood banks, transfusion laboratories, cellular therapy laboratories, and manufacturing facilities.

## 41

## Blood Flow Detector: Ultrasonic Doppler

### Purpose

Ultrasonic Doppler blood flow detector is designed to detect blood flow in the arterial and deep venous systems of the extremities. These instruments are especially applied for diagnosis of deep venous thrombosis and valvular deficiency. With this instrument, the peripheral blood flow can be detected and monitored on the principal blood vessels of the arms and legs from varying audible frequency as blood flow velocity changes in these vessels.

### Principle

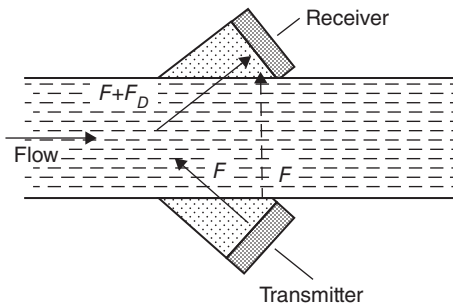
The ultrasonic blood flow detector operates on a well-known principle in physics called Doppler effect. The Doppler effect is widely used in medical ultrasound to generate images and sounds of flowing blood. It is a noninvasive technique and is based on the analysis of echo signals from the erythrocytes in the vascular structure. A small transducer probe transmits low intensity ultrasound beam into the body. The ultrasound beam is reflected back with slight change in frequency due to the movement of blood particles (Doppler effect). The frequency of the 'echo' is compared with the transmitted frequency, which provides information regarding forward or reverse flow, flow velocity, and the magnitude of the movement of blood. The reflected signal is received by the second transducer, amplified, and processed electronically to produce audible beeps on the built-in speaker or external earphone. A typical vascular Doppler blood flow detector is shown in Figure 41.1.

The Doppler principle is illustrated in Figure 41.2. When the transducer is placed on the skin and it is aimed at an angle,  $\theta$ , towards a blood vessel containing blood flowing with a



**Figure 41.1** Typical vascular blood flow detector.





**Figure 41.2** Ultrasonic probe with transmitting and receiving transducers placed on the opposite side of a flowing liquid.

velocity of  $u$  m/s, at any instant. The transducer transmits ultrasound waves of frequency  $f_o$ . The reflected ultrasound waves generated as a result of the moving erythrocytes (red blood cells) in the blood have a frequency  $f$ . The difference between these two frequencies,  $\Delta f$ , is related to the velocity of the flowing blood with the following equation:

$$\Delta f = f_o - f = \frac{2 f_o u \cos \theta}{v}$$

where  $v$  velocity of sound in the medium.

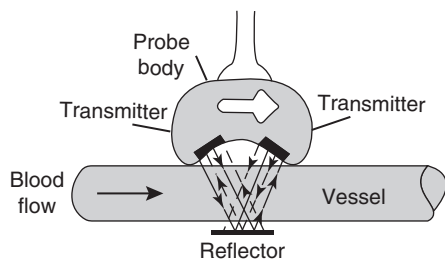
From this formula, it can be inferred that blood cells moving towards the transmitter of ultrasound beam add their velocity to the signal causing the reflected signal to be a higher frequency than the transmitted frequency. Conversely, when the blood cells move away from the transmitter, their velocity from the transmitted signal is subtracted, resulting in the reflected signal to be of lower frequency. The audio signal that is generated due to Doppler effect is the difference between the transmitted and the received frequency signals, which can be given to a recording device or to a speaker or headphone.

The ultrasound frequency used for blood flow studies is usually in the range of 2–10 MHz. The typical blood flow velocities in the arteries would vary at 0–5 m/s. Calculating from the above equation, it is found that the frequency differences will be in the range of 0–15 kHz, which falls in the audible range of sound frequencies and can be easily heard on a speaker.

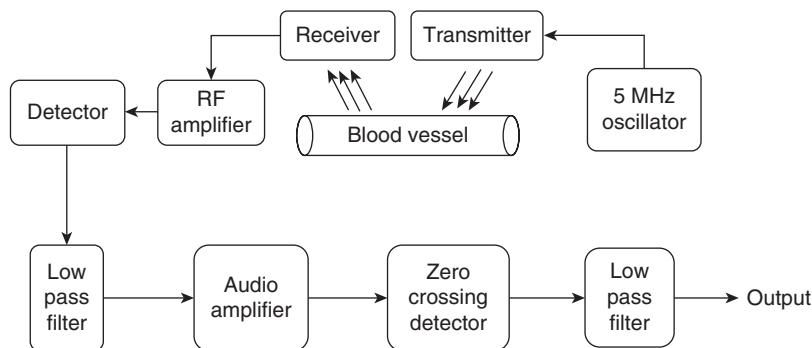
### Instrumentation

Ultrasound waves are generated by using a piezoelectric crystal, which is generally made of lead zirconate titanate. When a high frequency electric current passed through these crystals, it causes a change in the thickness of these crystals, resulting in the production of ultrasound waves. Conversely, when the reflected ultrasound waves from the moving blood cells strike the crystal, the ultrasound energy is converted back into electric current. Two types of configurations are used in piezoelectric elements. In one type, the transmitter and receiver are mounted on opposite sides (Figure 41.2) of the blood vessel, whereas in the other type the elements are placed side by side (Figure 41.3) at an angle on the same side.

Ultrasound Doppler blood flow detectors are self-contained, battery-operated, portable units. Figure 41.4 illustrates a simplified block diagram. A high frequency signal



**Figure 41.3** Ultrasonic probe with transmitting and receiving transducers placed on the same side of a flowing liquid.



**Figure 41.4** Block diagram of Doppler shift blood flow detector.

(2–10 MHz) generator supplies the required electrical energy to the piezoelectric crystal, which in turn produces ultrasound waves. The crystal is contained in the probe, which is connected to the instrument through an electrically shielded probe cable. These waves are transmitted into the area of interest by placing the probe over it.

The received signal is amplified in the radio frequency (RF) amplifier, followed by a detector that separates the upper and lower Doppler side bands for sensing flow direction. The signal is then amplified in the audio amplifier followed by a zero-crossing detector. The function of the zero-crossing detector is to convert the audio frequency amplifier output to a proportional analog output signal. It does this by emitting a constant area pulse for each crossing of the zero axis from negative to positive. The output of the zero-crossing detector is a series of pulses. These pulses are passed through a low pass filter to remove the high frequency components. The output is then made available as an audio signal, which can be heard on a built-in speaker or through the headphones.

Vascular testing uses two basic Doppler types: continuous wave (CW) and pulsed. The early instruments used a CW ultrasonic beam. Basically, a CW ultrasonic Doppler technique instrument works by transmitting a beam of high frequency ultrasound (2–10 MHz) towards the vessel of interest. Some instruments have multiple interchangeable probes of 2, 5, and 8 MHz. The 2 MHz probe is used for cardiac and foetal monitoring, whereas the 5 MHz probe is suitable for deep vein applications. For examining superficial vessels, the 8 or 10 MHz probes are employed. A highly loaded lead zirconate titanate transducer is usually used for this purpose. The transducer size may

range from 1 or 2 mm to as large as 2 cm or more. Most CW-based instruments use two piezoelectric crystals, one for continually transmitting and the other for continually receiving. On the other hand, pulsed Doppler instruments use a single crystal, which alternately transmits and receives ultrasound waves. Both have their respective advantages. CW-based instruments allow greater signal resolution and frequency response, whereas pulsed Doppler instruments provide more accurate determination of vessel depth. However, most of the noninvasive vascular testing instruments are of CW type.

## Specifications

*Ultrasonic frequency:* Interchangeable probes of 2, 5, and 8 MHz

*Audio output:* Maximum 1000 mW, adjustable

## Applications

Ultrasound Doppler blood flow detectors are employed for numerous vascular and arterial applications. Examples are study of cerebrovascular insufficiency, venous thrombosis, diagnosis of arteriosclerosis, and blood flow monitoring in case of carotid stenosis, acute varicose veins, and occlusive vascular and arterial diseases.

# 42

## Blood Gas Analyser

### Purpose

Blood gas analysers are used to measure the pH, partial pressure of carbon dioxide ( $p\text{CO}_2$ ), and partial pressure of oxygen ( $p\text{O}_2$ ) of the body fluids with special reference to the human blood. The measurements of these parameters are essential to determine the acid–base balance in the body. A sudden change in the pH and  $p\text{CO}_2$  could result in cardiac arrhythmias, ventricular hypotension respiratory problems, and even death. This shows the importance of the maintenance of physiological neutrality in blood and consequently the crucial role that the blood gas analysers play in clinical medicine.

### Principle

A blood gas analyser is a vital instrument that is used to measure the critical parameters that determine the acid–base balance in the human blood, serum, or plasma. The pH value is an indicator of the balance between the blood, renal (kidney), and lung (respiratory) systems and is one of the most tightly controlled parameters in the body.

The normal pH of the extracellular fluid lies in the range of 7.35–7.45, indicating that the body fluid is slightly alkaline. When the pH exceeds 7.45, the body is considered to be in a state of alkalosis. A body pH below 7.35 indicates acidosis. Both acidosis and alkalosis are conditions widely encountered in clinical medicine.

The  $p\text{CO}_2$  value of arterial blood is used to evaluate how well the body eliminates carbon dioxide, which is a by-product of metabolism. The  $p\text{O}_2$  value of arterial blood is a measure of how well the body is able to absorb oxygen in the lungs. In order to maintain pH,  $p\text{CO}_2$ , and  $p\text{O}_2$  within normal limits, throughout the wide range of body activities, the rate and depth of respiration vary automatically with changes in the metabolism.

pH,  $p\text{CO}_2$ , and  $p\text{O}_2$  are measured directly from the sample by using specific electrodes. The measurement of pH and  $p\text{CO}_2$  with respective electrodes are based on potentiometric principle. In these instruments, the voltage produced across a semipermeable membrane to hydrogen ions or  $\text{CO}_2$  gas is proportional to their concentration in the sample. The measurement of  $p\text{O}_2$  is done using an amperometric (current producing) electrode.

### **Blood pH Measurement**

The pH measuring system comprises a glass electrode, a reference electrode, and the liquid junction formed between these two electrodes.  $\text{H}^+$  ions in the sample under test exchange with the metallic ions in the glass membrane of the glass electrode, thereby creating a potential difference across the membrane. This potential difference, measured by the glass electrode, is then compared with the reference electrode, which is directly proportional to the concentration of  $\text{H}^+$  in the sample. The reference electrode may be made of Ag/AgCl or Hg/HgCl (calomel).

**Electrodes for Blood pH Measurement** Several types of electrodes have been described in literature for the measurement of blood pH. They are all of glass electrode type but made in different shapes so that they may accept small quantities of blood and yield accurate results. Typically, a microelectrode for clinical applications requires only 20–25  $\mu\text{l}$  of capillary blood for the determination of pH. The electrode is enclosed in a water jacket with circulating water at a constant temperature of  $38^\circ\text{C}$ . The water contains 1% NaCl for shielding against static interference. The capillary is protected with a polyethylene tubing. The internal reference electrode is silver/silver chloride and the calomel reference electrode is connected to a small pool of saturated KCl, through a porous pin. An accuracy of 0.001 pH can be obtained with this electrode against a constant buffer. Figure 42.1 shows the constructional details of a typical blood pH electrode and the measurement set-up used in practice. Quite often, combination electrodes comprising both measuring and reference electrodes offer single-probe convenience for all pH measurements. Several instruments offer the ability to measure pH in small containers with as little as 250  $\mu\text{l}$  of the sample. Microcapillary glass electrodes are preferred when it is required to monitor pH continuously, for example, during surgery. These types of electrodes are especially useful when a very small volume of the sample is to be analysed.

The pH of blood is found to change linearly with temperature in the range of  $18$ – $38^\circ\text{C}$ . The temperature coefficient for the pH of blood is 0.0147 pH unit/ $^\circ\text{C}$ . This necessitates the use of a highly accurate temperature-controlled bath to keep the electrodes with the blood sample at  $37 \pm 0.01^\circ\text{C}$ . A circuit diagram for controlling temperature of the bath

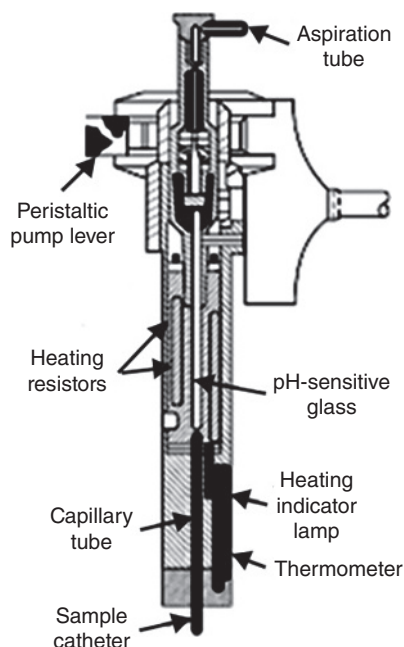


Figure 42.1 Microcapillary blood pH electrode.

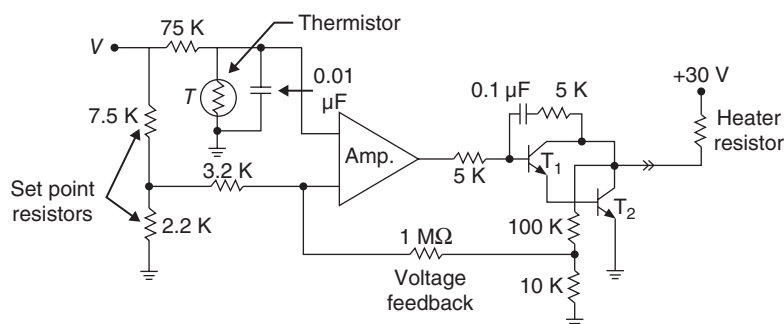


Figure 42.2 Temperature control circuit for thermostated chamber for blood pH measurement.

is shown in Figure 42.2. It is advisable to keep both the glass and the reference electrode at a temperature of 37°C.

The glass electrode exhibits a high electrical resistance, of the order of 100–1000 MΩ. The EMF measurement, therefore, necessitates the use of measuring circuits with high input impedance. The input impedance of the measuring circuit must be at least  $10^{12} \Omega$ . Further, the high resistance of glass electrodes renders them highly susceptible to capacitive pick-up from AC mains. In order to minimize such effects, it is advisable to screen the electrode cable. The screen is usually grounded to the case of the measuring instrument.

The error caused in pH measurements due to temperature effect can be compensated either manually or automatically. In automatic adjustment, a variable resistor, which is usually a thermistor or wire wound resistance that has an approximate desired resistance temperature coefficient, is inserted in the circuit. During measurement, it is placed

in the test solution. The use of an automatic temperature compensator will ensure that the pH meter is operating with a correct mV/pH conversion ratio. The pH meter is usually equipped with controls for calibration and temperature compensation.

### Measurement of Blood $p\text{CO}_2$

The blood  $p\text{CO}_2$  is the partial pressure of carbon dioxide of blood taken anaerobically. It is expressed in mmHg and is related to the percentage  $\text{CO}_2$  as follows:

$$p\text{CO}_2 = \text{Barometric pressure} - \text{Water vapour pressure} \times \% \text{CO}_2 / 100$$

At  $37^\circ\text{C}$ , the water vapour pressure is 47 mmHg, so at 750 mm barometric pressure, 5.7%  $\text{CO}_2$  corresponds to a  $p\text{CO}_2$  of 40 mm.

All modern blood gas analysers use a  $p\text{CO}_2$  electrode, which basically consists of a pH-sensitive glass electrode having a thin film of Teflon membrane stretched over it, with a thin film of an aqueous sodium bicarbonate ( $\text{NaHCO}_3$ ) solution separating the membrane from the electrode surface. The Teflon membrane is permeable to  $\text{CO}_2$  but not to any other ions, which might alter the pH of the bicarbonate solution. The technique is based on the fact that the dissolved  $\text{CO}_2$  changes the pH of an aqueous solution. The  $\text{CO}_2$  from the blood sample diffuses through the membrane to form  $\text{H}_2\text{CO}_3$ , which dissociates into  $(\text{H}^+)$  and  $(\text{HCO}_3^-)$  ions in the space between the membrane and the electrode tip. The free hydrogen ions produce change in pH, which is a function of the  $\text{CO}_2$  concentration in the sample. The EMF generated is found to give a linear relationship between the pH and the negative logarithm of  $p\text{CO}_2$ . The meter, although actually measuring  $[\text{H}^+]$ , is calibrated in  $p\text{CO}_2$ . The electrode is calibrated with the known concentration of  $\text{CO}_2$ . The response time of the  $\text{CO}_2$  electrode is of the order of 0.5–3 minutes. Figure 42.3 shows the construction of a typical  $p\text{CO}_2$  electrode.

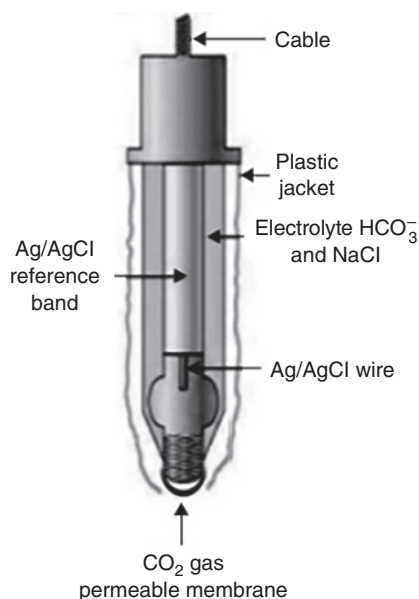


Figure 42.3 Blood  $p\text{CO}_2$  electrode.

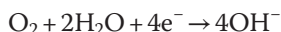
### Blood $pO_2$ Measurement

The partial pressure of oxygen in the blood or plasma indicates the extent of oxygen exchange between the lungs and the blood and, normally, the ability of the blood to adequately perfuse the body tissues with oxygen. The partial pressure of oxygen is usually measured with a polarographic electrode. There is a characteristic polarizing voltage at which any element in solution is predominantly reduced, and in the case of oxygen, it is 0.6–0.9 V. In this voltage range, it is observed that the current flowing in the electrochemical cell is proportional to the oxygen concentration in the solution.

The Clark polarographic electrode consists of a platinum cathode, a silver/silver chloride anode connected to an external voltage source. The cathode and anode are immersed in a KCl buffer. A polypropylene membrane selectively permeable to gases separates the buffer from the blood sample. The  $O_2$  combines with water in the buffer, producing current in proportion to the number of oxygen molecules. The current is measured and expressed as partial pressure of oxygen. Figure 42.4 shows the construction of a typical Clark-type oxygen electrode. The entire unit is separated from the solution under measurement by the polypropylene membrane.

Oxygen from the blood diffuses across the membrane into the electrolyte filling solution and is reduced at the cathode. The circuit is completed at the anode, where silver is oxidized, and the magnitude of the resulting current indicates the partial pressure of oxygen. The reactions occurring at the anode and cathode are as follows:

Cathode reaction:



Anode reaction:

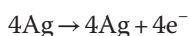
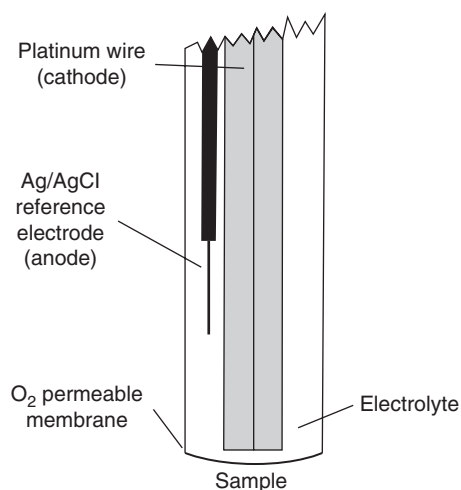


Figure 42.4 Blood  $pO_2$  electrode.





The Clark electrode for measuring  $pO_2$  has been extensively studied and utilized. It is found to be of particular advantage for measuring blood samples. The principal advantages are that (i) sample size required for the measurement can be extremely small, (ii) the current produced due to  $pO_2$  at the electrode is linearly related to the partial pressure of oxygen, (iii) the electrode can be made small enough to measure oxygen concentration in highly localized areas, and (iv) the response time is very low, so the measurements can be made in seconds. In comparison, it takes a very long time if the measurements are made by chemical means.

The platinum cathode of the oxygen electrode tends to become contaminated or dimensionally unstable with time and use. The result is usually an inability to calibrate and slope the electrode on any  $pO_2$  range. The manufacturers usually recommend application of ammonium hydroxide on the tip of the electrode (10% solution), with a gentle, rotary motion using a swab. The silver chloride gets dissolved in ammonium hydroxide and then flushed with distilled water. It is found that zero electrode current is not given by a solution having zero oxygen tension but occurs at a definite oxygen tension, which is called the 'electrode constant'. So, for calibrating the electrode, it is necessary to know this constant for that particular electrode.

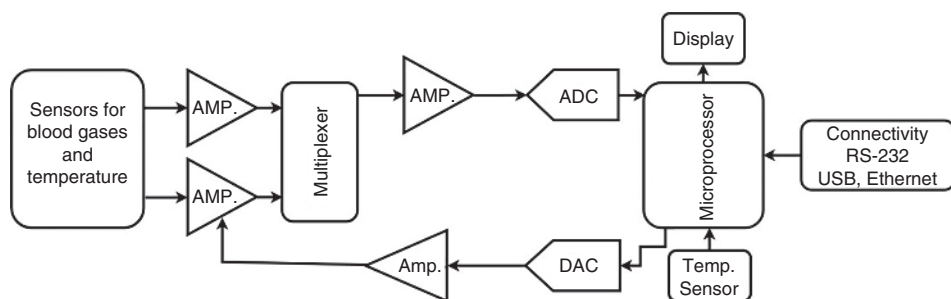
The polarographic electrodes usually exhibit ageing effect by showing a slow reduction in current over a period of time, even though the oxygen tension in the test solution is maintained at a constant level. Therefore, the electrode needs frequent calibration. This is probably associated with the material depositing itself on to the electrode surface. The effect due to ageing can possibly be avoided by covering the electrode with a protective film of polyethylene, but it has the undesirable effect of increasing the response time.

The measurement of current developed at the  $pO_2$  electrode due to the partial pressure of oxygen presents special problems. The difficulty arises because of the extremely small size of the electrical signal. The sensitivity (current per mmHg of oxygen tension) is typically of the order of 20 pA approximately per mmHg for most commercial instruments. It is further subject to a constant drift and is also not independent of the sample characteristics. Measurement of oxygen electrode current is made by using high input impedance, low noise, and low current amplifiers. Field effect transistors usually form the input stage of the preamplifiers.

### ***Instrumentation***

Blood gas analysers are designed to measure pH,  $pCO_2$ , and  $pO_2$  from a single sample of whole blood. The size of the sample may vary from 25  $\mu$ l to a few hundred microlitre. The estimations take about one minute. With built-in calculators, the instruments can also compute total  $CO_2$ ,  $HCO_3$ , and base excess. A typical block diagram of a blood gas analyser machine is shown in Figure 42.5. Blood collected from the patient is introduced into the analyser, which aspirates the blood into a measuring chamber. In this chamber, separate sensors/electrodes are used for pH,  $pCO_2$ , and  $pO_2$  measurement. The instrument contains three separate high input impedance amplifiers designed to operate in the specific range of each measuring electrode. A separate module houses and thermostatically controls the three electrodes. It also provides thermostatic control for the humidification of the calibrating gases.

A vacuum system provides aspiration and flushing service for all three electrodes. Calibrating gases are selected by a special push button control and passed through the



**Figure 42.5** Block diagram of a typical blood gas analyser.

sample chamber when required. Two gases of accurately known  $O_2$  and  $CO_2$  percentages are required for calibrating the analyser in the  $pO_2$  and  $pCO_2$  modes. The gases required are  $O_2$  value of 12% Cal and 0% slope and  $CO_2$  value of 5% Cal and 10% slope. These gases are used with precision regulators for flow and pressure control. Two standard buffers of known pH are required for calibration of the analyser in the pH mode. The buffers that are used are 6.838 (Cal) and 7.382 (slope). It is generally recommended that the sample chamber should control 7.382 buffer when in the standby mode.

The outputs from multiple sensors and calculators are driven through a multiplexer to an analog-to-digital converter (ADC). The data is processed in the microcontroller, which is connected to a PC or other instruments through RS-232, USB, or Ethernet. A digital-to-analog converter (DAC) is used to calibrate the sensor amplifiers to maximize the sensitivity of the electrodes. Modern blood gas analysers mostly employ a touch screen in combination with a graphical user interface (GUI) to make the programming process more intuitive. After measurement, the blood is automatically expelled into a waste container and the entire sample path is cleaned so that it is ready for the next sample. Results are usually printed, displayed, transmitted to the requesting department, and also sent to the laboratory information system.

Many of the blood gas analysers have a provision for checking the membrane of  $pO_2$  and  $pCO_2$  electrodes. In the check position, a potential is applied across the membrane. Any leak in the membrane of sufficient magnitude will result in a considerable lowering of the resistance, which may be from 100 M $\Omega$  to 500 k $\Omega$ . The change in resistance can be used to have a change of potential to switch on a lamp to light on the front panel of the instrument. This would indicate that a new membrane is needed.

The measurement of saturated  $O_2$  ( $sO_2$ ) is also included in some of the blood gas analysers. This is done by measuring oxyhaemoglobin versus total haemoglobin by spectrophotometry. The instrument takes multiple absorbance readings at various respective wavelengths and computes the  $sO_2$ .

Most of the modern blood gas analysers combine in them the facility to measure some other important electrolytes such as  $Na^+$ ,  $K^+$ , and  $Ca^{2+}$ . These measurements are made using respective ion-specific electrodes (ISE). Also, portable blood gas analysis instruments are available for point-of-care testing. Depending on combination and configuration, several parameters can be measured in human whole blood, serum, plasma, acetate, and bicarbonate containing dialysis solutions and quality control QC materials: pH, blood gas ( $PO_2$ ,  $PCO_2$ ), electrolyte ISE ( $Na^+$ ,  $K^+$ ,  $Cl^-$ ,  $Ca^{2+}$ ), haematocrit (Hct), metabolite glucose, and lactate. The glucose is measured as it oxidizes to form gluconolactone using atmospheric

oxygen and the glucose–oxidase (GOD) enzyme. Similarly, lactate oxidizes to form pyruvate using the lactate oxidase enzyme. The generated  $\text{H}_2\text{O}_2$  is determined amperometrically by using manganese dioxide/carbon electrode. The measurement of urea is done by breaking urea into ammonia and carbon dioxide through urease. Ammonia and carbon dioxide react through hydrolysis with physiological pH to form ammonia or bicarbonate ions. The ammonia ions can be determined using ammonia ion-selective electrode. This measurement requires a reference electrode such as those used in ion-selective electrodes.

## Specifications

### *Measurement range*

*pH*: 6.00–8.00 (Resolution: 0.01 pH)

*pCO<sub>2</sub>*: 5–250 mmHg (Resolution: 1 mmHg)

*pO<sub>2</sub>*: 0–700 mmHg (Resolution: 1 mmHg)

*Calculated parameters*: TCO<sub>2</sub>, HCO<sub>3</sub>, base excess

### *Sample volume*

*Syringe*: 85 µl nominal

*Capillary*: 60 µl nominal

*Analysis time*: 50 seconds

*Note*: In case the instrument has provision for electrolyte analysis, the range of measurement are as follows:

- (i) Na<sup>+</sup>, approximate range of 80–250 mmol/l.
- (ii) K<sup>+</sup>, approximate range of 0.1–20 mmol/l.
- (iii) Ca<sup>2+</sup>, approximate range of 0.25–5 mmol/l.

## Applications

Blood gas analysers are used to perform the most common blood tests on patients in intensive care units (ICUs), respiratory therapy, and point-of-care diagnostics.

## 43

## Blood Gas Monitor: Transcutaneous

### Purpose

Transcutaneous blood gas monitor is used to measure skin surface pO<sub>2</sub> and pCO<sub>2</sub> to provide an assessment of arterial partial pressure of oxygen and carbon dioxide, which is vital for assessing ventilation and oxygenation in critically ill patients. A transcutaneous monitor

can help in detecting noninvasively and continuously changes in respiratory status more quickly than blood gas analysis by blood sampling. The technique enables clinicians to monitor mainly neonates or paediatric patients without invasive arterial access. In addition, they are useful for patients with respiratory and cardiovascular disease and during anaesthesia and surgery as such patients are required to be monitored continuously for their carbon dioxide and oxygen status.

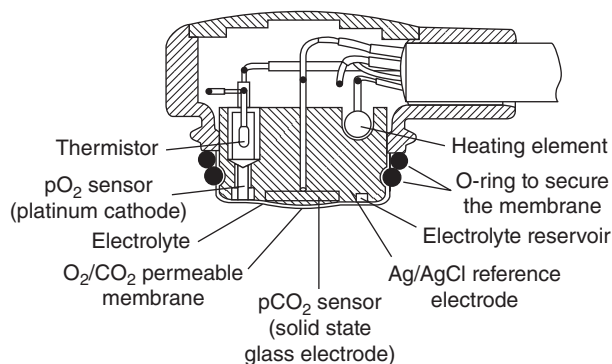
## Principle

The analysis of arterial blood gases is an accurate method for measurement of partial pressure of oxygen ( $\text{PaO}_2$ ) and partial pressure of carbon dioxide ( $\text{PaCO}_2$ ) and is most commonly used in the hospital set-up. However, this method gives results only for that time of collection. Thus, with the invasive method, the blood gas values are available only intermittently and indicate the status of the patient at the time of withdrawal of the blood. Also, the technique is associated with the risk of infection and discomfort. It is therefore advantageous to continuously monitor blood gases noninvasively so that timely corrective action can be taken based on the real-time instantaneous changes in blood gases. The method is mostly used as a supplement or, in some cases, as an alternative to periodically drawing and analysing arterial blood.

The basis for measuring partial pressure of  $\text{O}_2$  and  $\text{CO}_2$  from the skin surface relies on the diffusion of gases through the skin due to difference in partial pressures between blood and outermost surface of the skin, which is very low under normal conditions. However, when the skin is locally heated to about  $43^\circ\text{C}$ , it arterializes the underlying blood and the skin becomes much more permeable to the gases, which enhances diffusion of blood from the capillaries to the skin. A specially designed sensor placed on the surface of the skin is employed to measure transcutaneous partial pressures of oxygen and carbon dioxide. Several studies have shown a good correlation between transcutaneous blood gas measurement and arterial values.

## Instrumentation

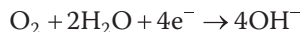
In modern instruments, the transducers for  $\text{O}_2$  and  $\text{CO}_2$  measurements are housed in one casing as shown in Figure 43.1. The sensors are similar in design to the electrodes used in laboratory type of arterial blood gas analysers. A combined Clark-type and a Severinghaus-type sensor also called Stow–Severinghaus sensor is placed on the skin. The sensor also includes a heating element for inducing hyper-perfusion by local heating of the skin to  $42-45^\circ\text{C}$ , ideal temperature being  $43^\circ\text{C}$ . The sensor heat dilates the underlying capillaries and increases the gas diffusion through the lipid structure of the skin, thereby allowing carbon dioxide and oxygen to diffuse up to 20 times more quickly from the capillaries through the skin to the sensor. The oxygen generates a current and the carbon dioxide a potential in the sensor. These signals are converted by the monitor and showed as  $\text{TcPCO}_2$  and  $\text{TcPO}_2$  values on the screen.



**Figure 43.1** Diagram showing a cross section of the Radiometer E5280 transcutaneous sensor for  $pO_2$  and  $pCO_2$  measurement. *Source:* Courtesy of M/s Radiometer Medical, Denmark.

### Transcutaneous Oxygen Measurement

Transcutaneous oxygen reflects a local noninvasive measurement reflecting the amount of  $O_2$  that has diffused from the capillaries, through the epidermis. The sensor used is based on the Clark-type electrode at the measuring site. This electrode is basically an electrochemical cell. Oxygen from the skin passes through the sensor membrane and reaches the cathode, which consists of platinum. Here, oxygen is reduced as a result of the current-generating process as follows:



The silver/silver chloride ring surrounding the platinum cathode is the anode where the following oxidation reaction takes place:



The reduction of oxygen generates a current that is converted by the monitor into a voltage and a digitized  $TcPO_2$  value in mmHg.

When oxygen transfers from capillaries to the sensor cells of the matrix, a 'diffusion corridor' is formed because of the local heating of the skin cover, and the electrochemical reaction causes an electric current of several tens of nanoamperes. The amplifier connected to the cathode measures the current and transforms it into a value proportional to the partial pressure of oxygen in the sensor/membrane interface. The said value is displayed on the monitor in mmHg.

The principal requirement of the anode unit is increasing the contact area and reducing the current density. In the tests, the gas diffusion membrane that is usable in transcutaneous sensors is replaced by single-use 3–5  $\mu m$  thick polypropylene or polytetrafluoroethylene (PTFE) film after its previous soaking in electrolyte solution. The film directly contacts the skin covering, which is heated up to  $42^\circ C$  by the heat source integrated in the sensor. Thus, a 'diffusion corridor' is formed and  $O_2$  from the capillaries penetrates the sensor cells.

In construction, the  $TcPO_2$  monitor consists of a combined platinum and silver electrode covered by an oxygen-permeable hydrophobic membrane, with a reservoir of phosphate buffer and potassium chloride trapped inside the electrode. A small heating

element is located inside the silver anode. The oxygen monitor consists of a  $\text{TcPO}_2$  channel, for which high and low alarm limits can be set, a temperature display channel, and a heat channel.

Transcutaneous measurement of arterial  $\text{pO}_2$  is based on the principle of oxygen polarography. The  $\text{O}_2$  molecules dissolved in an electrolyte are reduced at the surface of cathode of a noble metal such as platinum. A constant polarizing voltage of about 600 mV is applied between cathode and a reference silver/silver chloride electrode resulting in continuous flow of electrons between the cathode and the anode. The resulting current would be linearly proportional to the number of  $\text{O}_2$  molecules in the blood, when the electrode is operated in the plateau region of the polarogram.

$\text{TcPO}_2$  measurements usually require at least two to three sites, preferably four or more, to provide a good picture of the oxygenation status of the skin. The prerequisite for accurate correlation of an arterial  $\text{PO}_2$  value with a transcutaneous  $\text{PO}_2$  value is creation of constant local vasodilatation by heating the skin. In addition, the heat will dissolve the lipid structure of the dead, keratinized cells in the epidermal layer making the skin permeable to gas diffusion. This causes maximal blood flow in the skin with little or no difference between the  $\text{PO}_2$  value at the arterial and venous ends of the capillary.

### ***Transcutaneous Measurement of Carbon Dioxide***

In principle,  $\text{TcPCO}_2$  measurement is in fact a pH measurement.  $\text{CO}_2$  from the skin diffuses through the membrane of the sensor into an electrolyte solution. Here it reacts with water, forming carbonic acid that immediately dissociates into  $\text{HCO}_3^-$  and  $\text{H}^+$  according to the following equation:



As  $\text{HCO}_3^-$  in the electrolyte solution is kept at a fixed level, changes in the  $\text{H}^+$  concentration will always be equivalent to changes in pH. These pH changes alter the voltage between the glass sensor and the reference sensor. The measured pH is converted into a carbon dioxide reading by the Henderson–Hasselbalch equation and is shown as a  $\text{TcPO}_2$  value in mmHg.

The transcutaneous oxygen/carbon dioxide ( $\text{TcPO}_2/\text{TcPCO}_2$ ) transducer heats the skin. When the skin underneath the sensor is heated to  $44^\circ\text{C}$ , it effectively increases local blood perfusion so that  $\text{O}_2$  and  $\text{CO}_2$  can diffuse to the skin surface more easily. The transducer contains an electrolyte solution, which is held in place by two gas permeable membranes. The  $\text{O}_2$  and  $\text{CO}_2$  diffuse out of the skin and pass through the membranes into the electrolyte solution where the electrochemical reactions take place.

Transcutaneous  $\text{pCO}_2$  sensor consists of a glass pH electrode with a concentric silver/silver reference electrode. A buffer electrolyte is placed on the surface of the electrodes. A Teflon membrane, which is stretched over the electrode, separates the sensor from its surroundings. When the  $\text{CO}_2$  molecules diffuse through the membrane into the electrolyte, hydrogen and bicarbonate ions are formed. This results in potential generation between the glass pH electrode and the reference electrode. The measured pH is proportional to the negative logarithm of the  $\text{pCO}_2$ .

The modern instruments generally use a combined small sensor for  $\text{pO}_2$  and  $\text{pCO}_2$  measurements as shown in Figure 43.2. The sensor is just about 20 mm in diameter.



**Figure 43.2** A typical sensor for transcutaneous blood gas monitoring.

The sensor consists of a silver cylinder, into which a heating element and a temperature sensor is embedded. A fine platinum wire passes through the silver ring forming a part of the  $pO_2$  sensor. Also, a solid state pH sensor is mounted at the surface of the silver ring. A thin electrolyte layer (diluted bicarbonate solution) is placed in the sensor chamber over the slightly convex silver cylinder. The electrolyte is held in place with a tightly stretched Teflon membrane fixed with the help of O-rings. Oxygen from outside the sensor diffuses across the semipermeable membrane into the electrolyte, which generates a small current proportional to the  $pO_2$ . Similarly, the  $CO_2$  diffusing into the electrolyte lowers the pH of the solution and a glass electrode measures the changes in pH, which correspond to the  $pCO_2$  to which the sensor is exposed. The electrode's output is converted into a signal, which the instrument records as  $pCO_2$ .

The sensor is attached to the patient's skin by special adhesive fixing rings. Some contact gel is applied in the well of the fixation ring before the sensor is secured in place. This arrangement excludes stray air stopping it from reaching the sensor and also provides good thermal contact with the skin.

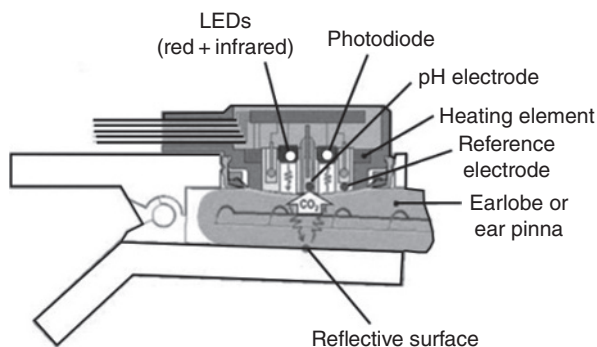
It is observed that the sensor changes its sensitivity over a period of time, requiring frequent calibration. The calibration is carried out by exposing the sensor to a calibration gas mixture having highly accurate  $CO_2$  and  $O_2$  known composition.

Blood gas measurements on 24/7 basis is essential for premature babies. However, the sensor is required to be heated up in order to work with the necessary precision. Thus, there is a need for keeping a track of how long a sensor has been applied to the skin to avoid burning the sensitive skin of the neonate. A smart algorithm that links temperature and time automatically prevents burns and informs healthcare professionals when they need to reposition the sensor. The transcutaneous blood gas monitor, Model TCM 5 (Figure 43.3) from M/s Radiometer, provides for automatic control of the sensor temperature and how long the sensor has been applied



**Figure 43.3** Blood gas analyser. Source: Courtesy of M/s Radiometer Medical, Denmark.





**Figure 43.4** The sensor combines an optical sensor for the measurement of  $SPO_2$  with a Stow–Severinghaus-type  $CO_2$  sensor and is also equipped with a heating element. *Source:* With permission M/s Radiometer Denmark.

to the skin. The instrument has provisions for storing and sharing data through connectivity to major patient monitoring systems. An integrated data memory allows for downloading of patient measurements to a PC or export to a USB stick for detailed analysis on a PC.

However, with the introduction of pulse oximetry to measure oxygen saturation ( $SPO_2$ ), the use of transcutaneous monitoring of oxygen has diminished in clinical practice. New-generation monitors now incorporate a combined  $TcPCO_2$ – $SPO_2$  sensor as shown in Figure 43.4. Like other similar devices, the pulse oximeter measures oxygen saturation by measuring the difference in absorption of selected light wavelengths by oxyhaemoglobin and deoxyhaemoglobin. It utilizes two LEDs: one LED emits red light (658 nm wavelength) selectively adsorbed by deoxyhaemoglobin, while the other one emits infrared light (880 nm wavelength) selectively absorbed by oxyhaemoglobin. The sensor also contains a photodetector, which converts light into an electronic signal proportional to the incident light intensity and sends it to the monitor for calculation. The pulse oximeter uses reflection technique for measurement by having the LEDs and the photodetector positioned on the same side of the transducer.

Transcutaneous measurement of  $CO_2$  is again based on the principle that this gas has a high tissue solubility and diffusion through the skin and that the application of local heat dilates blood vessels and enhances skin permeability. The  $TcPCO_2$  component of the sensor consists of a Stow–Severinghaus type electrode, a potentiometric sensor combining a silver/silver chloride reference electrode, and a glass pH electrode. Over the sensor surface, there is an electrolyte solution, provided within a thin hydrophilic spacer and coupled to the skin via a highly gas permeable hydrophobic membrane.  $TcPCO_2$  determines a pH change of this electrolyte solution by diffusing through the skin to the sensor.

## Specifications

$pCO_2$  range: 5–250 mm

$pO_2$  range: 0–2000 mmHg

Accuracy: Better than  $\pm 2$  mmHg at 25 °C

Polarization voltage:  $-680 \pm 5$  mV



*Sensor heating power range:* 10–500 mW

*Displayed accuracy:*  $\pm 3\%$

*Sensor temperature:* 37.0–45.0°C in steps of 0.5°C

## Applications

Transcutaneous monitoring of oxygen and carbon dioxide provide essential measurements for neonatology, paediatrics, operating room, intensive care unit (ICU), pulmonary/respiratory medicine laboratory, or wards. They are used wherever there is a need to monitor the adequacy of arterial oxygenation and/or ventilation and the need to quantitate the response to diagnostic and therapeutic interventions. Besides, transcutaneous blood gas monitoring is appropriate for continuous and prolonged monitoring during mechanical ventilation, continuous positive airway pressure (CPAP), and supplemental oxygen administration.

## 44

### Blood Glucose Meter

#### Purpose

Blood glucose meter is used to measure blood glucose concentration as and when desired. It is also employed to test for transient high or low glucose levels in situations such as during surgery. The objective of these measurements is to maintain blood glucose near normal levels. The glucose meter is a point of care testing device used widely by people with diabetes mellitus in the comfort of their homes. The measurements can be taken multiple times in a single day, but every time a new test strip is required. The glucose concentration is measured in units of milligram per decilitre (mg/dl) in the United States and Canada or millimole per litre (mmol/l) in Europe.

#### Principle

A glucose meter is a small handheld device with a digital LCD display and a slot to insert a disposable test strip containing a sensor for glucose and a couple of push buttons or keypad to enter external information. Some recent models have alarms, memory functions, and wireless connectivity to transfer data to a computer or to a clinician for telemedicine purposes. After the test strip is inserted in the slot, a drop of blood is added onto the small area and the blood flows in by capillary action. The device begins the measurement process automatically when the meter senses blood on the strip and displays a reading within a few seconds. A 'beep' sounds, signalling that testing has begun. In some devices, a digital display on the screen 'counts down' the seconds till the concentration of glucose is displayed.

## Test Strips

Most present-day glucose meters are based on the use of electrochemical test strips to perform the measurement. The two most common methods used in electrochemical measurement of glucose are the amperometric method and colorimetric method.

In the *amperometric method*, the test strip contains an enzyme electrode containing a reagent such as glucose oxidase. When a drop of blood is added at the strip, glucose undergoes a chemical reaction in the presence of enzymes and electrons are produced during the chemical reaction. The flow of these electrons results in the flow of current through working and reference electrodes. The measured current is proportional to the concentration of glucose in the sample (blood). The effect of varying ambient temperatures on the rate of reaction is compensated by separately measuring the temperature. The size of the drop of blood needed by different models varies from 0.3 to 1  $\mu\text{L}$ .

Each test strip consists of about 10 layers, which include a stiff plastic base plate, and several other layers containing chemicals. These layers are suitably separated by the spacers to allow a small amount of blood to enter. The layers containing chemicals are those which carry a layer of the immobilized enzyme, glucose oxidase, and another layer containing microcrystalline potassium ferricyanide. There is also a layer containing two silver electrodes. The enzyme glucose oxidase reacts with the glucose in the blood sample creating gluconic acid. The gluconic acid then reacts with ferricyanide to form ferrocyanide. The electrode oxidizes the ferrocyanide, and this generates a current that is directly proportional to the glucose concentration. The rate of enzyme reaction depends upon temperature, humidity, and altitude and, therefore, they may affect the glucose measurements. A pore free silicone rubber membrane is used between the electrode and the enzyme layer to prevent electrochemical interference and electrode poisoning from endogenous biochemicals.

The test strip has the following three electrodes as shown in Figure 44.1.

- *Working electrode*: Electrons are produced on the working electrode during the chemical reaction.
- *Reference electrode*: This electrode is held at a constant voltage ( $-0.4\text{ V}$ ) with respect to the working electrode to aid the desired chemical reactions.
- *Counter (trigger) electrode*: This electrode is used to supply current to the working electrode.

Most of the glucose meter designs use only two electrodes, (i) working electrode and (ii) reference electrode. A precise reference voltage ( $V_{\text{REF}}$ ) is applied to the reference electrode maintaining a precise potential difference across the working electrode and the reference electrode. This voltage acts as the stimulus to drive the test strip's output current.

In the *colorimetric method*, a sensor detects the optical properties of the test strip as it reacts with a blood sample. The principle used is that of colour reflectance to sense



Figure 44.1 Glucose test strip terminals.

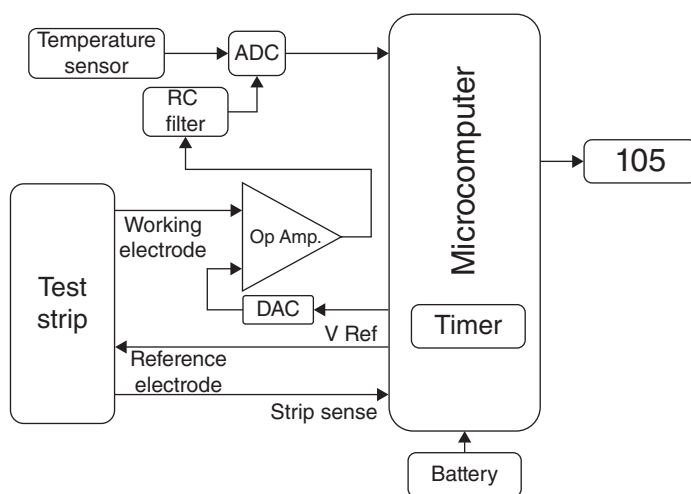
the colour intensity in the reaction layer of the test strip by the photometry. Here, the blood sample is exposed to a membrane covering the reagent pad, which is coated with an enzyme glucose oxidase. The reaction results in a colour change and the intensity of this colour change is directly proportional to the amount of glucose in the blood sample. An LED is used as a light source and the reflected light from the sample is detected by a photodiode, which measures the light's intensity and converts it to an electrical signal.

### Instrument

Figure 44.2 illustrates the block diagram of a typical blood glucose meter. The output generated by the test strip is a current that represents the glucose concentration. As a first step, this current requires to be converted to voltage so that it can be filtered and processed. This conversion is done using a current to voltage converter using an operational amplifier. It is followed by a low pass filter with a cut-off frequency of 8 Hz that is designed to minimize high frequency noise.

The filtered signal is then given to a 12bit analog-to-digital converter (ADC). The digital signal is processed by a microprocessor and the value of glucose concentration is displayed on the LCD in units of mg/dl or mmol/l. The internal EEPROM can store up to 32 glucose readings that can be viewed later on the LCD. The power to the glucose meter is given from on-board lithium battery.

The glucose meter is usually a small, palm-sized, battery-powered meter, just about 5 cm × 9 cm and 1.5 cm thick with a display screen size of about 3 cm × 4 cm. Figure 44.3 shows a typical blood glucose meter being used for measurement of glucose level in blood. The test strips can be inserted into a small opening on the top or bottom edge of the device. A lancet device with a needle projecting from one end of the device is used to prick the patient's finger. The working of this device involves just pressing a button on the device, which releases the needle to prick the surface of the finger and draws blood. The time taken for a reading to be generated is approximately five seconds for the electrochemical method, making this blood glucose sensor device more efficient.



**Figure 44.2** Block diagram of a blood glucose analyser.

**Figure 44.3** Typical blood glucose analyser in use for measurement of blood glucose.



Modern glucose measuring instruments are made using just one chip that integrates all the requirements of a glucose meter. The chip includes the analog front end having transimpedance amplifiers with a gain stage, a precision ADC, and an accurate voltage reference. Multiple precision digital-to-analog converters (DACs) are incorporated to properly bias the sensor. Other essential components include LCD drive, real-time clock (RTC), and user interface. The in-built temperature monitoring ensures consistent performance across temperature in the range 0–50 °C.

Presently, there are many commercial meters that give results as ‘plasma equivalent’, even though they are designed to measure whole blood glucose. The plasma equivalent is calculated from the whole blood glucose reading using an equation built into the glucose meter. Glucose levels in plasma are generally 10–15% higher than glucose measurements in whole blood. Therefore, it is important for patients and their healthcare providers to ascertain whether the meter gives its results as ‘whole blood equivalent’ or ‘plasma equivalent’.

## Specifications

*Measurement technology:* Oxidase electrochemical sensor

*Sample:* Drop of whole blood

*Minimum sample volume:* 1.0 µl

*Measuring range:* 20–600 mg/dl

*Test time:* 5 seconds

*Memory capacity:* 500 blood glucose test results with date and time

*Power saving:* Turns off automatically 2 minutes after last user action

## Applications

The blood glucose meter is usually used by diabetics at home to measure the amount of sugar (glucose) in the blood. This helps in determining daily adjustments of insulin dose for treatment. With this device, it is convenient to know if the person is having dangerously high or low levels of glucose and to understand how the diet and exercise are changing the glucose levels. Glucose monitors are also used in emergency testing of glucose levels of patients.

## 45

## Blood Grouping Machine

### Purpose

Automated blood grouping machine is used to determine a person's blood type by performing tests such as ABO grouping, Rh typing, antibody screening, and cross matching. These tests are done to determine factors that can cause transfusion reactions such as red cell haemolysis, anaphylaxis, and other immunologic and nonimmunologic effects. So, the test becomes essential in case of blood transfusion or blood donation. Since all blood types are not compatible, it is essential to ensure that the antibodies do not attack the donor blood in the recipient of the transfused blood.

### Principle

After severe blood loss, the blood volume can be restored by the intravenous injection of certain fluids. However, in most cases, whole blood is the best replacement for lost blood. But blood transfusion is only safe if the blood of the donor and the receiver are carefully matched. There are a number of components surrounding blood cells. *Antigens* are chemical structures attached to the surfaces of red blood cells (RBCs). *Antibodies* are proteins floating in blood plasma. Incompatibility between the blood of two persons is due to the presence of substances called *agglutinogens (antigens)* in the red cells in the donor, which react with *agglutinins (antibodies)* in the serum of the recipient. In the human blood, the two most important agglutinogens are designated by the letters A and B.

Antibodies or agglutinins for these two factors are found in the serum of normal persons and are called anti-A and anti-B. If red cells containing one of the agglutinogens A or B is mixed with serum containing the corresponding anti-A or anti-B agglutinin, then agglutination or clumping of the donor red cells will take place. Pre-transfusion testing is thus necessary in order to prevent transfusion of incompatible donor red cells that might result in an immune-mediated haemolytic transfusion reaction. Blood grouping or blood typing in respect of ABO and Rh thus forms a crucial test before a blood transfusion is performed to ensure compatibility and it can be more critical in emergency situations, due to the condition of the patient.

Blood grouping systems can be divided into four groups depending upon the presence or absence of the two antigens A and B. The possible combinations are A, B, AB, or O as shown in Table 45.1, which shows the presence of different antigens or antibodies in the various groups. For example, a person with factor B in his/her red cells always has the antibody anti-A in his/her serum, but never anti-B. Blood containing red cells with no antigens (Group O) always contains both the antibodies anti-A and anti-B. Persons with Group O are often called universal donors because in theory, their red cells would not clump by any recipient. Persons with Group AB are sometimes called universal recipient, because having no antibody, they can safely receive blood of any group. Besides ABO grouping, RBCs are also tested for Rh grouping (Rh factor) and

**Table 45.1** The principle antigens and antibodies of the ABO system.

| ABO blood group | Antigen present on the red blood cells | Antibodies regularly present in the serum/plasma |
|-----------------|----------------------------------------|--------------------------------------------------|
| O               | Neither A or B                         | Anti-A and anti-B                                |
| A               | A                                      | Anti-B                                           |
| B               | B                                      | Anti-A                                           |
| AB              | A and B                                | None                                             |

anti-K. According to ABO and Rh blood grouping system, the person can belong to any one of the following eight blood groups: A positive, A negative, B positive, B negative, AB positive, AB negative, O positive, and O negative.

### **Blood Group Testing**

Blood group testing can be done manually or with automatic instrumentation systems. In the manual method, the blood sample is mixed with antibodies that attack type A and B blood and observed to see how it reacts. If the blood cells clump together when mixed with antibodies against type A blood, for example, then it is type B blood. The blood sample is then mixed with an anti-Rh serum. If the blood cells clump together in response to the anti-Rh serum, it means that it is Rh+ blood. These manual methods are no doubt cumbersome and are not amenable to a blood bank, which receives a large number of samples.

Fully automated blood typing methods have emerged in the last two decades due to rapid technological advances. They are quickly replacing the manual tube methods with their advantages of quality, flexibility, efficiency, and reliability. The semi-automated or automated systems are based on techniques such as column agglutination technique (CAT), solid phase red cell adherence assay (SPRCA), and erythrocyte-magnetized technique (EMT). All these technologies are amenable to automation. Documentation, traceability, and archiving of results are the major advantages offered by automation.

**Column Agglutination Technology** The column agglutination test system, also known as gel test, comprises a 5 cm × 7 cm plastic card with six to eight built-in microtubes supplied by the manufacturer. Each microtube contains pre-dispensed gel, diluent, and reagent, if applicable. The microtubes have a broad reaction chamber in the upper part, while the lower part, which is long, narrow portion, contains either a clear gel or a glass microbead matrix. Serum/plasma and RBCs are added to the reaction chamber of the microtube and incubated at 37°C. The gel card is then centrifuged, which brings the RBCs in contact with antiglobulin reagent contained in the lower half of the microtube. The sensitized red cells agglutinate in the gel/bead matrix and get trapped, while unsensitized cells form a pellet at the bottom of the microtube. The reactions may be graded from 1+ to 4+. The card reader provides objectivity to the grading.

The CAT requires special incubators and centrifuges to accommodate the cards. A bar code reader is an essential part of the equipment, which also has three cameras to record sample, reagent, and card identification. A camera in the system performs image analysis and processing by specially designed algorithm to display the results. During processing, the monitor continuously displays updated information on the progress of

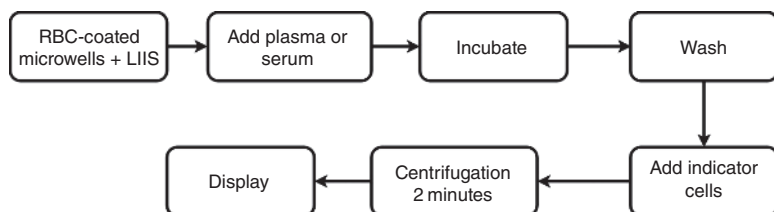
the batch. The display shows which tubes have been processed and also indicates whether any errors have been encountered. Once a batch is complete, microplates and gel cards are removed for incubation, centrifugation, and reading. The automated platforms based on the column agglutination technology are available from BIO-RAD (Switzerland), Ortho-Clinical Diagnostics (USA), and Grifols (Singapore).

**Solid Phase Red Cell Adherence Assay (SPRCA)** This is a technique in which red cells are first immobilized onto a solid support medium polystyrene, to the microwells before starting the test. Figure 45.1 illustrates the test procedure for SPRCA principle. Patient serum or plasma and low ionic strength solution (LIIS) are then added to the RBC-coated microwells and incubated at 37 °C. After incubation, the microwells are washed to free them from residual serum, and indicator red cells are added. This is followed by centrifugation for two minutes, which brings the indicator red cells in contact with antibodies bound to the immobilized red cell layers. This centrifuge spins at rates ranging from 500 to 18 000 rpm. Finally, the results are read, digitally displayed, and interpreted. When the test is positive, complexes form between the indicator red cells and the sensitized, immobilized cells. As a result of antibody bridging, the indicator cells adhere to the immobilized cells as a second immobilized layer. In case antigen–antibody interactions are not detected (negative test), the indicator red cells do not bind to the immobilized cells and pellet to the bottom of the wells as tightly packed cell buttons. A popular instrument The IMMUCOR based on SPRCA principle is available from Galileo/NEO (USA).

**Erythromagnetic Technology** The principle of this technology is based on the use of paramagnetic particles that are adsorbed on the surface of RBCs. The antibodies are allowed to react with the antigens on RBCs in a microplate well. When a magnetic force is applied at the bottom of the plate using an external magnet, these cells are pulled to the bottom of each well. A final phase of shaking reveals positive or negative reactions. By using this technology, the magnetic force replaces centrifugation step, which is completely eliminated during the analytical process. This technology may also be adapted to antibody screening and identification. The QWALYS 3 from DIAGAST (France) is based on the erythromagnetic technology.

### Instrumentation

A typical modern blood group analyser is a microprocessor-controlled instrument designed to fully automate immunohaematology in vitro diagnostic testing of human blood. A typical example of a blood grouping machine from M/s Beckman Coulter is shown in Figure 45.2.



**Figure 45.1** Principle of test procedure for solid phase red cell adherence assay.





**Figure 45.2** Automated blood grouping machine model PK7300. *Source:* Reproduced with permission from Beckman Coulter.

The machines automate test processing, result interpretation and data management functions using a microplate-based platform. The analyser has provisions for sample identification, automated recording of reagents, sample dilutions, reagent addition and mixing, incubation and centrifugation, and image acquisition and analysis. The data can also be compiled and transmitted to the laboratory information system (LIS) through data management software. The analysers usually perform the following tests: ABO + RhD blood grouping, including reverse grouping and weak D testing; Rh phenotyping (C, c, E, e) and Kell blood grouping (K); antibody screening and identification; direct antiglobulin testing; and cross matching. The analyser generates results from individual images that are generally verified by visual inspection and editing by a qualified person.

The sample identification is done using bar code labels for tubes and microplates that are read by a laser scanner. Eight tubes with bar code labels are placed in a specially designed sample handling rack, which also contains the bar-coded microplate, which is to be used for testing. This constitutes the processing station about which the information read by the laser scanner and transmitted to the system's microprocessor for storage. The processing station containing the donor samples and the associated microplate is then placed in the sample preparation device, which is programmed to deliver 25 µl of each reagent and sample to the assigned wells on the microplate. This is achieved through an automated probe attached to an arm with motion in three directions.

After the completion of the programmed 10 minutes incubation period, the prepared plates are ready for centrifugation, reaction reading, and interpretation. The microplate reactions are automatically assigned by the microprocessor to the correct blood samples. The reader evaluates all 96 wells of a 96 well microplate, using either a tungsten halogen light source or LED to measure absorbance for each well at 410 nm. These optical density readings are then transmitted to the microprocessor, which interprets these data based on the predetermined thresholds stored for comparison. The microprocessor executes all processing tasks. The display terminal is used to request program functions and display options and information selected by the operator. The dot printer generates a permanent hard copy of serologic test results with statistical analysis of the data.

## Specifications

*Analytical method:* Agglutination method

*Channels:* 12

*Throughput:* 300 samples/h with 4 dilution cups

*Sample tubes:* Diameter, 12 and 15 mm; height, 55 and 102 mm

*Reagent tray:* Up to 16 special reagent bottles

*Reaction vessel:* Microplate with 120 wells per plate, non-disposable

*Incubation time:* 20–60 minutes

*Incubation temperature:* Room temperature to 40°C

*Parameters:* ABO grouping; Rh antigens; Kell photometer: Light intensity of each well measured by a colour charge coupled device (CCD) camera

## Applications

Automated blood grouping systems are mostly used in hospital blood banks and blood transfusion/donor centres for blood typing prior to a blood transfusion or when classifying a person's blood for donation. Blood typing is especially important for pregnant women before attempting transfusion.

# 46

## Blood Pressure Measurement (Invasive Method)

### Purpose

The direct method of pressure measurement is an invasive technique requiring percutaneous cannulation and is mostly used when the highest degree of absolute accuracy, dynamic response, and continuous monitoring is required. The method is also used to measure the pressure in deep regions inaccessible by indirect means. The measurement gives not only the systolic, diastolic, and mean pressures but also a visualization of the pulse contour and such information as stroke volume, duration of systole, ejection time, and other variables. A variety of invasive vascular pressure monitors are available for trauma, critical care, and operating room applications. These monitors are either standalone or part of multi-parameter vital signs monitors.

### Principle

Arterial blood pressure is most accurately measured invasively by using an arterial line. The technique involves direct measurement of arterial pressure by placing a cannula needle in an artery, usually radial, femoral, or brachial. The cannula is connected to a

sterile, fluid-filled system, which is connected to a pressure transducer. This method has the advantage that pressure can be constantly monitored beat by beat.

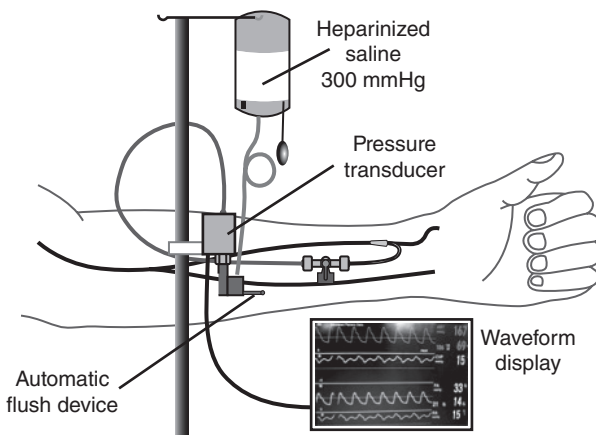
For direct measurement, a catheter or a needle-type probe is inserted through a vein or artery to the area of interest of pressure measurement. Two types of probes are generally used. One type is the catheter tip probe in which the sensor is mounted on the tip of the probe and the pressures exerted on it are converted to the proportional electrical signals. The other is the fluid-filled catheter type, which transmits the pressure exerted on its fluid-filled column to an external transducer. This transducer converts the exerted pressure to electrical signals. The electrical signals can then be amplified and displayed or recorded. Catheter tip probes provide the maximum dynamic response and avoid acceleration artefacts, whereas the fluid-filled catheter-type systems require careful adjustment of the catheter dimensions to obtain an optimum dynamic response.

Once an arterial catheter is in place, it is also convenient for drawing blood samples to determine the cardiac output (by dye dilution curve method), blood gases, and other chemistries. Problems of catheter insertion have largely been eliminated and complications have been minimized. This has been due to the development of a simple percutaneous cannulation technique: a continuous flush system that causes minimal signal distortion and simple, stable electronics that the paramedical staff can easily operate.

### Fluid-Filled System

A typical set-up of a fluid-filled system for measuring blood pressure is shown in Figure 46.1. Before inserting the catheters into the blood vessel, it is important that the fluid-filled system be thoroughly flushed. In practice a steady flow of sterile saline is passed through the catheter to prevent blood clotting in it. As air bubbles dampen the frequency response of the system, it should be ensured that the system is free from them.

The infusion or flushing system comprises a bag of either plain 0.9% saline or heparinized 0.9% saline pressurized to 300 mmHg and attached to the fluid-filled tubing via



**Figure 46.1** Typical invasive blood pressure measuring arrangement.

a flush system. The system provides a slow infusion of fluid at a rate of about 2–4 ml/h to maintain the patency of the cannula. The flush system also enables a high pressure flush of fluid through the system to keep the tubing clear and to check the damping and natural frequency of the system.

The arterial system is accessed using a short, narrow cannula made of polyurethane or Teflon to reduce the risk of arterial thrombus formation. The most commonly used site of insertion of cannula is radial artery as it usually has a good collateral circulation and is easily accessible. Fluid-filled tubing is attached to the arterial cannula, which provides a column of non-compressible, bubble-free fluid between the arterial blood and the pressure transducer for hydraulic coupling. A three-way tap is incorporated to allow the system to be zeroed and blood samples to be taken. The fluid in the tubing is in direct contact with a flexible diaphragm of the transducer, which in turn moves strain gauges in the pressure transducer, and converts the pressure waveform into an electrical signal.

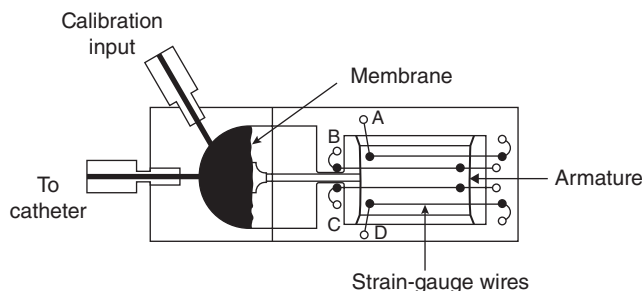
There could be some cases when cannulation could result in complications such as thrombosis, infection, and bleeding. Thus, patients with invasive arterial monitoring require very close supervision, as there could be a danger of severe bleeding if the line becomes disconnected. The technique is generally used for patients where rapid variations in arterial pressure are anticipated.

### Instrumentation

A direct pressure measuring device consists of three basic components:

- A transducer or device that detects the pressure and converts the pressure value to an electrical signal.
- An amplifier that increases the magnitude of the signal from the transducer.
- A monitor to display the signal and a recorder to provide a permanent record.

**Transducers** Commonly used for direct measurement of pressure is the displacement-type strain gauge transducer. The transducer is usually linked directly to the patient's heart and hence complete safety of the patient must be ensured. It is for this reason that the construction of the transducers should be such that they provide patient-safe isolation. Figure 46.2 shows the simplified construction of one such transducer. The transducer must have three modes of isolation: (i) external isolation of the case with a plastic sheath, which provides protection from extraneous voltages, (ii) standard



**Figure 46.2** Simplified constructional details of blood pressure transducer.

internal isolation of the sensing (bridge) elements from the inside of the transducer case and from the frame, and (iii) additional internal isolation of the frame from the case and the diaphragm, in case of wire breakage. Thus, isolation of the patient/fluid column from electrical excitation voltage is ensured, even in the event of failure of the standard internal isolation.

Strain gauge transducers are sensitive to temperature changes and typically vary  $0.1 \text{ mmHg}/1^\circ\text{C}$ . This implies that they require frequent checking of the zero-pressure baseline for drift due to temperature. Solutions flushed through the transducers can also cause temperature variance and consequent baseline drifts. The room in which the measurement set-up is arranged should be maintained at a fairly constant temperature. For best operational performance, the transducers should not be exposed to a temperature higher than  $65^\circ\text{C}$  (maximum for short duration) or  $50^\circ\text{C}$  for extended periods of time.

Pressure transducers are commonly used in intensive care units (ICUs), cardiac catheterization, and other situations in which there is a possibility of a defibrillator being used on the patient. If the transducer breaks down with the application of a defibrillating shock, the current to earth through the transducer would be a few milliamperes, assuming that the catheter impedance is  $1 \text{ M}\Omega$ . This is probably not significant as far as the patient is concerned, in view of the very high current flow in between the defibrillator paddles. However, there is a possibility of irreversible damage, which may be done to the transducer. Transducers, therefore, should be able to withstand high voltages arising from electrocautery or defibrillator procedures. The minimum breakdown voltage for this purpose should be  $10000 \text{ VDC}$ .

Physiological pressure transducers need to be sterilized before every use. This is a costly and time-consuming exercise and results in transducer wear and tear due to repeated cleanings and sterilization. This problem has been overcome by designing a pre-sterilized disposable dome with a built-in membrane that provides a sterile barrier between the patient and transducer. The transducer should be thoroughly cleaned as soon as practicable after each application and maintained in a clean condition for optimum long-term service.

One of the commonest type of abuses of physiological transducers is applying a pressure in excess of the working pressure either by standing on the pressure line or by flushing out the transducer with the output closed. A weight of  $2 \text{ kg}$  applied to a  $1 \text{ ml}$  disposable syringe is known to produce a pressure of about  $10000 \text{ mmHg}$ . The calibration of the transducers should not substantially change (more than  $1\%$ ) after the maximum rated pressure is applied. The diaphragm rupture pressure values are different for pressure transducers of different makes and are usually in the value range of  $3000\text{--}10000 \text{ mmHg}$ .

**Amplifiers** The signal received from the pressure transducer, being small in amplitude, is amplified by a factor of about  $1000$  times before it can be digitized and given to a microprocessor for processing and display. The amplifier is followed by filter circuits to remove interference signals from other physiological signals and undesirable environmental noise picked up by the transducer. The amplifier should introduce minimum temperature drift and distortion in the amplified signal and give a linear output. Most monitors have a built-in electrical calibration arrangement that provides a known pressure value. This calibration must be checked before measurement process is initiated.

**Display** After the signal is digitized and processed in the microprocessor, the pressure signal is displayed in the form of a waveform of pressure versus time and numerical and graphical display. The waveform is analysed to extract clinically significant parameters

such as morphology; position of the dicrotic notch or 'swing,' which can give information regarding filling status and to calculate cardiac output; and other cardiovascular parameters.

### ***Frequency Response and Damping***

The frequency components of a normal pressure pulse consist of a zero frequency (DC) component, a fundamental component at the heart rate and harmonics of the fundamental rate. To record a pressure pulse without any distortion, the measuring system should be capable of recording all the frequency components with equal amplification and phase shift. The range of uniform frequency response starting from DC is determined from an estimation of the highest heart rate expected and the number of harmonics to be taken into account. It is established that the blood pressure pulses contain from 6 to 20 significant harmonics, but generally it is accepted that frequencies up to 10th harmonics produce significant components in the pressure pulse. If we assume the heart rate to be 90bpm, the same shall be the rate of the arterial blood pressure waves. This means that the upper frequency response should be at least 15 Hz for a heart rate of  $90 \text{ min}^{-1}$ .

Fluid column systems usually have a very low natural frequency to be commensurate with the requirements, due to their large inertia and compliance. Therefore, to accurately record the pressure pulses, some form of compensation is necessary to improve the frequency response of the system. This compensation is called *damping*. Damping is inherent in any system that tends to slow down the rate of change of signal between the patient and pressure transducer. This can be caused by occlusion of the arterial system, a bubble interrupting the saline column, or using a soft cannula and tubing. Some damping is however useful, as it helps to reduce the resonant frequency of the pressure transducing system. The amount of damping in a system is indicated by the 'damping factor'. The damping factor in a system can be as follows:

- *Under-damped*: The system is under-damped when resonance occurs causing the signal to oscillate and overshoot (damping factor:  $<0.7$ ).
- *Over-damped*: In over-damped systems, the signal takes a long time to reach equilibrium but it will not overshoot (damping factor:  $>1.0$ ).
- *Optimally damped*: The system responds rapidly to a change in signal by allowing only a small amount of overshoot (damping factor:  $0.7$ ).
- *Critically damped*: No overshooting occurs in a critically damped system but the system may be too slow (damping factor:  $1.0$ ).

The damping can be varied by introducing an adjustable constriction into the flow line.

### ***Central Venous Pressure (CVP) Measurement***

Central venous pressure (CVP) measurement made with needle cannulation technique proves extremely useful in the management of acute circulatory failure and in the maintenance of blood volume in difficult fluid balance problems. CVP is usually measured from a catheter located in the superior vena cava. The CVP reflects the pressure of the right atrium and is sometimes referred to as right atrial pressure. The catheter can also be placed in the right atrium. Major peripheral veins used as entry sites for CVP monitoring are the brachial, subclavian, and jugular veins.

Catheters used for CVP monitoring are usually 25–30 cm long. Long catheters, as they remain in place over extended periods of time, are susceptible to the formation of fibrin sheaths along their outer surfaces. Besides this, air can be aspirated into a catheter that is situated in an area of low pressure (as compared to the atmospheric pressure), resulting in thromboembolic complications. A continuous infusion of heparin solution will reduce this tendency. Also, it should be ensured that there is no possibility of air intake.

Venous pressure measurement can be made by using a strain gauge transducer and a similar electronic signal processing circuitry. The transducers should be of higher sensitivity to give more accurate results at lower pressures. Since the blood pressure is always referred to as the atmospheric pressure at the height of the heart, a correction must be applied while making venous pressure measurements to compensate for the difference of level between the heart and the site of measurement. A correction of 7.8 mmHg is applied for every 10 cm. The site of measurement is below the height of the heart.

Development of the Swan-Ganz catheter, a balloon tipped, flexible catheter that can be flow-directed from a peripheral vein into the pulmonary artery, has made routine clinical monitoring of pulmonary artery pressure possible. Information about pulmonary artery wedge pressure or end diastolic pressure in the pulmonary artery gives a good indication of the left atrial pressure. This is a very valuable parameter in predicting and treating left ventricular failure in myocardial infarction in patients undergoing cardiac surgery.

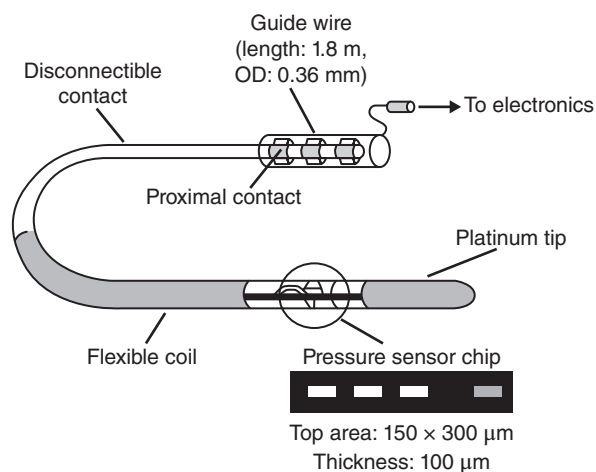
### ***Catheter Tip Pressure Transducers***

Fluid-filled catheter and external pressure transducer arrangements for the measurement of intravascular pressures have limited dynamic response. The problem has been solved to some extent, by the use of miniature catheter tip pressure transducers. The transducer is 12 mm long and has a diameter of 1.65 mm. It is mounted at the tip of a No. 5F Teflon catheter, 1.5 m long. The other end of the catheter carries an electrical connector for connecting the transducer to a source of excitation and a signal conditioner. A hole in the connector provides an opening to the atmosphere for the rear of the diaphragm. The active portion of the transducer consists of a silicon-rubber diaphragm with an effective area of  $0.75 \text{ mm}^2$ . Pressure applied to the diaphragm is transmitted by a linkage to two silicon strain gauges, which form a half bridge, while the other half is constituted by the electrical circuit.

Millar Mikro-Tip pressure catheter, which is commercially available from Millar Instruments Inc., Houston, Texas, United States, provides an ideal solution for measuring arterial and ventricular blood pressure, spinal pressures, or airway pressures. They are available in sizes from 1F (0.33 mm) to 7F (2.33 mm) in diameter. The pressure transducer has a standardized output of  $5 \mu\text{V/V/mmHg}$ .

The catheter tip pressure transducers do not remain stable over variations in temperature and with long-term clinical use. Safety problems may also be experienced due to the direct connection between external electronic devices and the heart. To overcome these problems, fibre optics-based catheter tip pressure transducers for the measurement of intracardiac pressures have been developed. The pressure is detected by the photo-electric transducer whose output voltage is proportional to the applied pressure. Comparison of waveforms and frequency analysis of waveforms reveal that the fibre optic catheter has characteristics by no means inferior to the tip transducer-type catheter.





**Figure 46.3** MEMS-based catheter tip pressure sensor.

A pressure sensor for measuring blood pressure in the coronary arteries is shown in Figure 46.3. The sensor is used in balloon dilatation and for monitoring of the blood pressure in 'real time' during the surgery. Dimensions of the chip are  $0.1 \text{ mm} \times 0.15 \text{ mm} \times 1.3 \text{ mm}$ . The fabrication of the chip is based on surface micromachining in silicon and piezoresistive micro-electro-mechanical sensors (MEMS). The transducer consists of a flexible diaphragm, connected to a MEMS piezoresistive element with an electric current applied across it. As pressure is applied to the diaphragm, it deforms and stretches the MEMS element, which changes resistance, altering the electrical output from the system. The sensor can be fitted on a small catheter used for balloon dilatation. An important advantage with the piezoelectric sensor is the electrical contact to the instrument, allowing the catheter to be used as combined pressure sensor and guide wire for balloon dilatation. By being able to measure the pressure drop in the coronary arteries, the diagnosis can be much more precise than only relying on the X-ray image of the heart.

## Specifications

*Transducer type:* Strain-gauge resistive bridge

*Impedance range:* 200–2000  $\Omega$

*Transducer sensitivity:*  $5 \mu\text{V/V/mmHg}$

*Excitation voltage:* 4.85 V pulsed DC at 181 Hz

*Bandwidth:* Digital filtered, DC to 20 Hz

*Zero drift:*  $\pm 1 \text{ mmHg}$  without transducer drift

*Numeric accuracy:*  $\pm 2 \text{ mmHg}$

*Pressure range:* –30 to 300 mmHg

*Pulse range:* 25–250 bpm

## Applications

Intra-arterial invasive blood pressure monitoring is a commonly used technique in the ICU and is also often used in the operating theatre on patients who are likely to display sudden changes in blood pressure, or in whom close control of blood pressure is required or in patients receiving drugs to maintain the blood pressure. Direct arterial blood pressure monitoring is also indicated in case of patients with shock, critical illness, and peripheral vasoconstriction and for intra-operative and post-operative monitoring of high risk patients.

## 47

## Blood Pressure Measurement (Noninvasive Methods)

### Purpose

Noninvasive blood pressure (NIBP) apparatus is an essential device in the clinical practice to assess pumping efficiency of the heart and the resistance of the peripheral vasculature as an indicator of physiologic changes in blood volume. Blood pressure measurement is the most frequently used diagnostic test especially in cases of cardiac emergencies to monitor the status of the patient. The measurement is done in real time noninvasively without cannulating the human body. NIBP apparatus can be standalone or a part of the vital signs monitors that are used in intensive care unit (ICU) to measure basic physiologic parameters of critically ill patients.

### Principle

Blood pressure represents the pressure of circulating blood on the walls of blood vessels, especially in large arteries of the systemic circulation. The maximum pressure reached during cardiac cycle is called *systolic pressure* and the minimum pressure occurring at the end of a ventricular relaxation is termed as *diastolic pressure*. The mean arterial pressure over one cardiac cycle is approximated by adding one-third of the pulse pressure (difference between systolic and diastolic values) to the diastolic pressure. It is measured in millimetres of mercury (mmHg), above the surrounding atmospheric pressure, which is considered to be zero for convenience. It is one of the vital signs, along with respiratory rate, heart rate, oxygen saturation, and body temperature that are usually measured on sick patients. Normal resting blood pressure in an adult is approximately 120 mmHg (16 kPa) systolic and 80 mmHg (11 kPa) diastolic, abbreviated '120/80 mmHg'.

There are three commonly used approaches for measuring blood pressure. These are for clinical purposes, self-monitoring by the person at home, and 24 hours of ambulatory monitoring. NIBP measurements for clinical purposes can be taken manually by

the clinician by doing one measurement each time the patient visits the clinic. Traditionally, blood pressure is measured noninvasively using a mercury sphygmomanometer and is generally considered as the gold standard. Due to the ban on the use of mercury devices, mercury-based devices are being phased out in many countries. This has resulted in the development of alternative methods, of which aneroid devices are the leading contenders. The aneroid sphygmomanometer consists of a bellow system connected to a needle to indicate the pressure on a dial. However, calibration of the aneroid sphygmomanometers against a mercury sphygmomanometer every six months is advised.

Self-monitoring is normally carried out by individuals using portable electronic devices. Such devices can measure blood pressure usually from the upper arm, but devices that work on wrist or finger are also available. The 24 hour ambulatory monitoring is generally done to predict the cardiovascular risk in the patient and is mainly used for diagnosing hypertension.

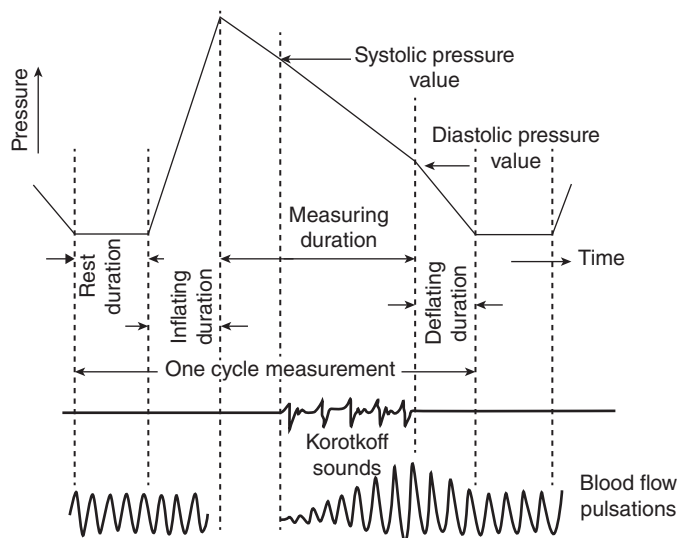
### ***Automatic Methods***

Automatic methods use the classical method of making measurement of blood pressure by the use of a cuff over the limb containing the artery. This technique was introduced by Riva-Rocci for the determination of systolic and diastolic pressures. Initially, the pressure in the cuff is raised to a level well above the systolic pressure so that the flow of blood is completely terminated. Pressure in the cuff is then released at a particular rate. When it reaches a level, which is below the systolic pressure, a brief flow occurs. If the cuff pressure is allowed to fall further, just below the diastolic pressure value, the flow becomes normal and uninterrupted. The problem here finally reduces to determining the exact instant at which the artery just opens and when it is fully opened.

***The Auscultatory Method*** A number of automated blood pressure measuring instruments have been designed, which use the Riva-Rocci method. They operate in a manner analogous to that employed by a human operator but differ in the method of detecting the pulsations of blood flow at the systolic and diastolic levels. The method given by Korotkoff and based on the sounds produced by flow changes is the one normally used in the conventional sphygmomanometers. The sounds first appear when the cuff pressure falls to just below the systolic pressure as shown in Figure 47.1. They are produced by the brief turbulent flow terminated by a sharp collapse of the vessel and persist as the cuff pressure continues to fall. The sounds disappear or change in character at just below diastolic pressure when the flow is no longer interrupted. These sounds are picked up by using a microphone placed over an artery distal to the cuff.

Frequency bands that best discriminate the Korotkoff sounds at systole and diastole from the sounds immediately preceding these events need to be defined for achieving a high degree of reliability in the automatic electronic blood pressure instruments. From the analysis of Korotkoff sounds, it is found that a maximum increase in amplitude at the systolic transition occurs in the 18–26 Hz band. Similarly, a maximum decrease in spectral energy of diastolic Korotkoff sounds, at auscultatory cessation, was observed within a 40–60 Hz passband.

The automatic method consists in putting a cuff around the upper part of the patient's arm and applying a microphone over the brachial artery. The compressed air required



**Figure 47.1** Principle of blood pressure measurement based on Korotkoff sounds.

for inflating the cuff is provided by a pumping system incorporated in the apparatus. Usually inflating is done to a preset pressure level, well beyond the systolic value at the rate of approximately 30 mmHg/s. The pressure in the cuff is then decreased at a relatively slow pace at the rate of 3–5 mmHg/s.

While air is allowed to leak from the cuff, the Korotkoff sounds are picked up by a special piezoelectric microphone. The corresponding electrical signals are fed to a pre-amplifier. The amplified signals are then passed on to a bandpass filter having a bandwidth of 25–125 Hz. With this passband, a good signal-to-noise ratio is achieved when recording Korotkoff sounds from the brachial artery beneath the lower edge of the cuff. The system is designed that the appearance of the first Korotkoff sound switches in the systolic manometer and locks the reading on the indicating meter. In a similar way, the diastolic value is fixed by the last Korotkoff sound. The cuff is completely deflated, automatically, after an interval of two to five seconds after the determination of the diastolic value.

Instruments operating on this principle are subject to serious errors, particularly in restless patients, unless steps are taken to ensure protection against artefacts. One method is to design the control system in such a way that when pressure is registered, the first sound must be followed by a second one within the preset interval. If this is not the case, the recorded value is automatically cancelled and the measurement starts again with the subsequent sounds. The measuring accuracy of such type of instruments is not very high and the error is usually of the same order ( $\pm 5$  mmHg) as is obtained in clinical sphygmomanometers.

A number of shortcomings limit the application of the Riva-Rocci method. Probably the most serious among them is that the measurement is not continuous. Even for a particular single measurement, a number of heart cycles intervene between the determination of the systolic and diastolic pressures. Moreover, large errors are common since the pressure applied to the exterior vessel wall is not necessarily identical to that

in the cuff but is attenuated by the intervening tissue and an exact state of flow cannot be precisely determined. This problem is so severe that in most of the measurements made with instruments based on this principle, the diastolic pressure value is less reliable than the systolic.

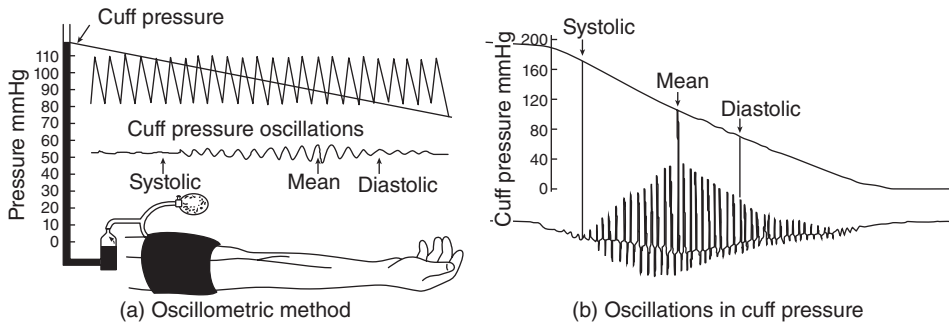
The automatic built-in pump system of inflating and deflating the cuff must be provided with safety devices so that the patient does not experience any discomfort in case of system failure. Provision should be made for immediate switching off of the pump when the pressure in the cuff reaches the preset maximum over-systolic value and in no case should the pressure in the cuff be allowed to exceed 300 mmHg. An additional arrangement must switch off the pump at any pressure after 20 seconds from starting and deflate the cuff at a constant rate. These devices shall ensure that the pressure in the cuff will not reach too high a value and that no pressure is kept longer than approximately 20 seconds.

**Oscillometric Measurement Method** Most of the patient monitoring systems presently are based on the oscillometric principle for NIBP measurement. This method has distinct advantages over the auscultatory method. Since sound is not used to measure blood pressure in the oscillometric technique, high environmental noise levels such as those found in a busy clinical or emergency room do not hamper the measurement. In addition, because this technique does not require a microphone or transducer in the cuff, placement of the cuff is not as critical as it is with the auscultatory method. The oscillometric method works without a significant loss in accuracy even when the cuff is placed over a light shirt sleeve. The appropriate size cuff can be used on the forearm, thigh, or calf as well as in the traditional location of the upper arm. Figure 47.2 is a typical instrument based on the oscillometric principle.

The oscillometric technique operates on the principle that as an occluding cuff deflates from a level above the systolic pressure, the artery walls begin to vibrate or oscillate as the blood flows turbulently through the partially occluded artery and these vibrations will be sensed in the transducer system monitoring cuff pressure. As the pressure in the cuff further decreases, the oscillations increase to a maximum amplitude and then decrease until the cuff fully deflates and blood flow returns to normal. The cuff pressure at the point of maximum oscillations usually corresponds to the mean



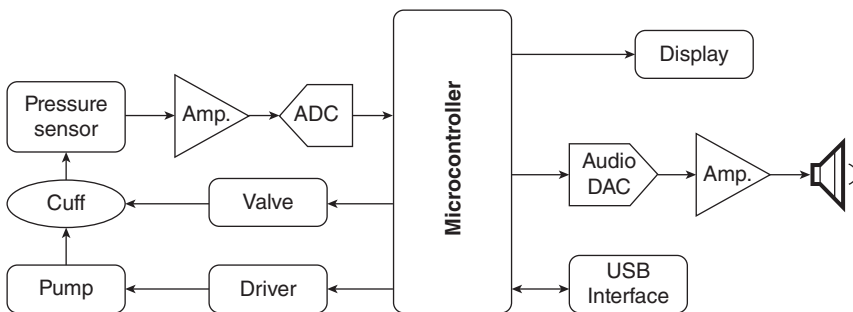
**Figure 47.2** Noninvasive blood pressure monitor Model Mini-Torr Plus. Source: Image courtesy of M/s Smiths Medical.



**Figure 47.3** Illustration of oscillometric method of blood pressure measurement. (a) Inflating the cuff in a conventional way of blood pressure measurement much above the systolic pressure level. (b) Generation of oscillometric (pressure) pulses generated in the cuff during inflation or deflation.

arterial pressure. The point above the mean pressure at which the oscillations begin to rapidly increase in amplitude correlates with the diastolic pressure as illustrated in Figure 47.3. These correlations have been derived and proven empirically but are not yet well explained by any physiologic theory. The actual determination of blood pressure by an oscillometric device is performed by a proprietary algorithm developed by the manufacturer of the device and there is no generic oscillometric technique. The oscillometric technique has been successfully used in ambulatory blood pressure monitors and home monitors. Measurement sites for oscillometric blood pressure measurement include the upper arm, forearm, wrist, finger, and thigh. However, the standard location for blood pressure measurement is the brachial artery.

Most of the patient monitoring systems are based on the oscillometric measuring principle for blood pressure measurement. Figure 47.4 shows the major functional parts of an NIBP measuring system. An air pump is used to automatically inflate the patient cuff. The pump is of a membrane type and is enclosed in a foam rubber-filled casing to attenuate noise. The pneumatic unit includes damping chambers to (i) prevent a rapid increase of pressure caused by the pump, (ii) slow down the pressure change in the measurement of infant, and (iii) smooth down rapid pressure pulses caused by the bleed valve. A safety valve prevents accidental cuff over-pressurization and operates nominally at 330 mmHg. A bleed valve is incorporated to release the cuff



**Figure 47.4** Block diagram of automatic blood pressure measurement system.

pressure. The opening of the valve is pulse-width controlled between 100% (valve fully open) and 0% (valve fully closed). The driving signal frequency is 40 Hz. For quickly deflating the cuff, an exhaust valve is provided. The magnetic solenoid valves and the air pump are controlled by a driver circuit. A watchdog timer prevents a prolonged inflation. The operation of the pump and the operation of the valves are all under microprocessor control.

A piezoresistive pressure transducer is connected to the cuff. It measures the absolute pressure of the blood pressure cuff and the pressure fluctuations caused by the arterial wall movement. The pressure transducer is excited by a constant current source. The output signal from the pressure sensor is conditioned with an op-amp circuit or by an instrumentation amplifier before data conversion by an analog-to-digital converter (ADC). The systolic pressure, diastolic pressure, and pulse rate are then calculated in the digital domain using a method appropriate for the type of monitor and sensor utilized. The resulting systolic, diastolic, and pulse rate measurements are displayed on a liquid crystal display (LCD). The microcontroller along with its associated memory circuits allow the control of the whole measuring procedure. Some portable blood pressure monitors have the ability to upload data to a computer for further analysis and tracking of measurements over time. This data transfer is usually done through a USB interface. Most of the automatic NIBP monitors are used as vital sign monitors with the real-time measuring and display of two or more of the vital signs.

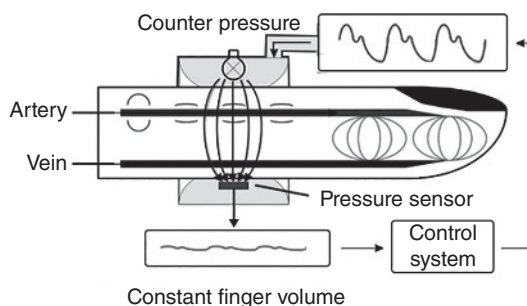
Based on the oscillometric principle, battery operated blood pressure monitors are available for home use as shown in Figure 47.5. Cuffs are available in various sizes, and it is important that a properly sized cuff is used when making BP measurements. The suggestive length of the blood pressure cuff is about 80% and the width at least 40% of the circumference of the upper arm. If measurements are made with an inappropriately sized cuff, it may result in erroneous estimation of the true pressure values.

**Vascular Unloading Technique (Finger Monitor)** This technique is used in placing a cuff over the finger and works on the principle of unloaded arterial wall. Inside the pressure



**Figure 47.5** Portable home use digital blood pressure monitor.





**Figure 47.6** Principle of the vascular unloading technique for measurement of blood pressure.

cuff, the blood volume in the finger arteries is measured using photoplethysmograph comprising a light source and a light detector. This is shown in Figure 47.6. The resulting output signal is used to drive a servo loop, which alters the cuff pressure to keep the output constant. For example, during systole, when the blood volume increases in the finger, the control system increases cuff pressure, too, until the excess blood volume is squeezed out. On the other hand, during diastole, when the blood volume in the finger decreases, the cuff pressure is reduced to maintain the overall blood volume to be constant. The continuously changing external pressure that is required to keep the arterial blood volume constant directly corresponds to the arterial pressure.

NIBP monitors have been widely in use in operating rooms and critical care units to closely monitor blood pressure in patients of all ages. Despite their widespread use, doctors continue to discuss and deliberate over the accuracy and reliability of automated NIBP devices when compared to other methods of blood pressure measurement.

## Specifications

*Pressure range:* 0–300 mmHg

*Pulse rate range:* 40–240 bpm

*Automatic measurement cycles:* Adjustable from 1 to 180 minutes

*Memory:* Up to 400 measurements

*Cuff sizes:* Adult, paediatric, infant

## Applications

Blood pressure is an important parameter in assessing the functional integrity of the cardiovascular system. As majority of blood pressure measurements do not require continuous monitoring, noninvasive techniques are used in most cases, which maximizes patient comfort and safety, thus making them a preferred choice for routine examinations and monitoring.

## 48

# Blood Recovery System

### Purpose

Blood recovery system, commonly known as a cell saver, is used to perform a medical procedure involving recovery of blood lost during surgery and re-infusing it into the patient. In other words, it is a form of autotransfusion in which the patient receives his/her own blood instead of donor blood, so that there is no possibility of risk of contracting outside diseases. Also, since the blood is recirculated, any amount of blood can be given back to the patient. Blood recovery system is mostly employed for surgeries where medium- to high-volume blood loss is likely to occur, such as trauma cases.

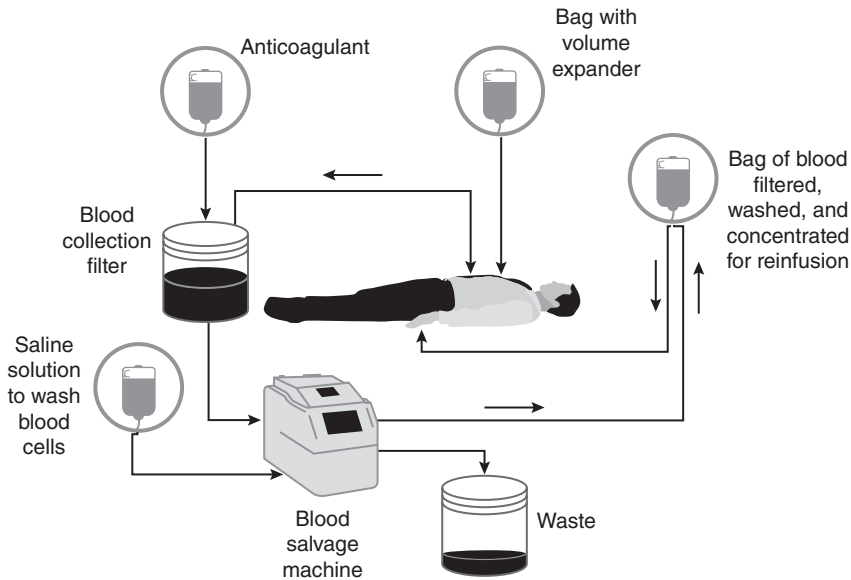
### Principle

Autologous blood is widely established as the preferred choice for transfusion, whenever and wherever possible. The term autologous blood refers to blood that is derived from the same person. An autologous blood transfusion refers to the procedure that involves a patient receiving his or her own blood. The blood can be autologously collected before a surgery, or alternatively, it can be collected intra-operatively or post-operatively using a blood salvage device.

### *The Process*

The principle involved in the blood recovery system is simple involving use of intra-operative cell salvage machine. The process carried out in the machine involves three steps: collection and anticoagulation, processing, and reinfusion back to the patient instead of being thrown away. Figure 48.1 illustrates the process of salvaging of blood. The first step is to collect the patient's blood from a collection reservoir during surgery. The blood is then filtered to remove any debris contaminating the blood. An anticoagulant is then added to the collected blood to prevent it from clotting. The collected blood is then processed using a centrifuge. During this phase, the red blood cells (RBCs) are separated from the rest of the material collected from the patient. After the separation, the RBCs are then washed to remove the dead RBCs that can no longer carry oxygen. The anticoagulant is also washed out during this stage. After completion of the wash cycle, the compacted RBCs are returned into another collection bag for reinfusion into the patient.

**Blood Collection and Anticoagulation** Utilizing a special double lumen suction tubing, blood is aspirated from the operative field at vacuum levels of less than 150 mmHg. This is to avoid possible skimming of the surface of the blood in order to minimize blood cell



**Figure 48.1** Block diagram of blood cell saver process.

trauma. It is mixed with an anticoagulant (heparin) solution near the tip of the suction cannula and the anticoagulated blood is collected into a sterile blood collection reservoir. Collected blood is filtered in a sterile reservoir that contains filter and has a capacity of between 2 and 31 of fluid. When a sufficient volume (500–600 ml) of blood has been collected, processing may start.

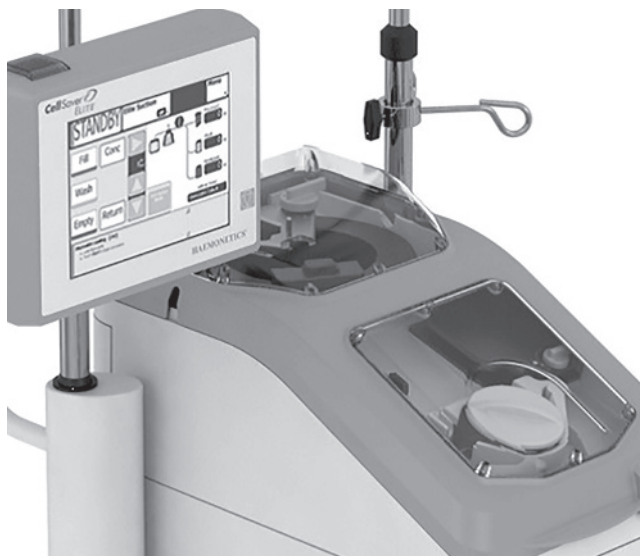
In the *processing phase*, cell salvage systems use semi-continuous flow centrifugation. The blood is centrifuged typically at 5600 rpm. Fluids are moved in and out of the centrifuge bowl by a three-roller, occlusive pump, capable of a flow rate of 1000 ml/min at its maximum speed. The application of centrifugal force separates the components of the fluid according to their weight so that the higher density RBCs are packed against the outer wall of the spinning bowl, while the supernatant plasma floats inwards towards the core of the bowl. The lighter fraction is forced out the effluent tubing from the bowl and into the waste bag.

The *wash phase* begins when the wash bowl is appropriately filled with RBCs. This is detected by using an optical sensor, which initiate penning the wash line. This causes saline solution to enter the bowl and wash the RBCs. At this stage, the pump begins counterclockwise rotation, allowing the transfer of the reservoir contents to the wash bowl. During the wash cycle, normal saline is pumped into the spinning bowl that displaces less dense material than the RBCs including clotting factors, platelets, plasma-free haemoglobin, any plasma-bound antibiotics, intracellular enzymes, plasma, platelets, white blood cells, and anticoagulant solution (heparin) away from the outer wall of the bowl and subsequently into the waste reservoir bag.

Once the minimum wash volume of saline has been introduced and the effluent line sensor has detected adequate washing, the wash line will be clamped and the reinfusion

line will be opened. The washed and packed cells suspended in saline are then pumped into the reinfusion bag from where it goes to the arterial line of an extracorporeal circuit for reinfusion to the patient. At that time, the centrifuge bowl comes to a complete stop before the pump begins a clockwise rotation to empty the bowl. Once the bowl is emptied, the cycle is ended and a new cycle can begin. It may be noted that over filling of the reinfusion bag, or reinfusion under pressure may cause the bag to rupture. The reinfusion bag may contain a significant amount of air requiring careful monitoring during reinfusion to avoid the potential of air embolism. Therefore, it is recommended to use a separate blood bag attached to the reinfusion bag. This second bag can then be disconnected, air purged from it, and then tied off before giving for reinfusion, thus reducing the chances of an air embolism. In such a case, any air in the reinfusion bag must be purged utilizing the purge facility provided in the machine. According to the guidelines issued by the American Association of Blood Banks, the blood should be reinfused within four hours from washing.

The blood recovery machines (Figure 48.2) consists of two groups of components: (i) the machine components and (ii) the disposable set elements. The machine controls the fluid pathway facilitated by the disposable set. The key component of the disposable set is the centrifuge bowl, in which the RBCs are separated, washed, and packed. The centrifuge bowl consists of two subassemblies: an inner assembly, which remains stationary, and an outer assembly, which rotates. The outer assembly rotates with the centrifugation chamber where the blood is processed. The stationary inner assembly contains the inlet and outlet ports. The machine components include the control panel elements and the hardware elements. The machine is equipped with a pole for hanging the saline solution, reservoir bag, reinfusion bag, anticoagulant solution, and transfer packs with the help of movable pole hooks.



**Figure 48.2** Blood cell saver machine. *Source:* Image Courtesy : M/s Haemonetics UK. Ltd., UK.

Modern blood salvaging machines are based on the use of the microprocessor technology, which incorporates a high level of automation in the processing of autologous blood. The microprocessor receives data from a variety of sensors to automatically control the processing of blood. A photoelectric RBC sensor in the centrifuge well, an ultrasonic air detector on the tubing line and an optical effluent line sensor provide information to the microprocessor, which then regulates the cycles of the device based on this information. The use of *level sensors* in the reservoir and initiation of device operation has minimized operator interaction and surveillance. This has also reduced processing time while maintaining the quality end product. The *ultrasonic air detector* monitors the flow in the tubing. In case air in the pump tubing is detected, the pump is stopped, the appropriate tubing is clamped and a message is sent to the display.

The centrifuge well *optical sensor* monitors the RBC level in the bowl. The *effluent line sensor* monitors the quality of the effluent blood as it leaves the bowl. The machine provides easy and quick access to an emergency protocol to allow high speed blood processing (800 ml/min) while continuing with automatic operation in high blood loss procedures. The *clamped line sensor* monitors pressure levels in the line to the reinfusion bag. If the bag is inadvertently clamped, the clamped line sensor will cause the pump to stop. An electronic *fluid detection system* is incorporated to detect the presence of liquid. The device safety system automatically stops the centrifuge and pump if there is contact between liquid of any sort and the fluid detector(s) located inside the centrifuge well and to the left of the bowl. A *reservoir level sensor* monitors the weight of the reservoir throughout the procedure to estimate the volume of fluid it contains.

Several devices are available commercially to assist in salvaging the patient's own blood in the perioperative environment. These are used frequently in cardiothoracic and vascular surgery, in which blood usage has traditionally been high.

## Specifications

*Red blood cell recovery:* >80%

*Haematocrit:* 50–60%

*Heparin removal:* >95%

*Free haemoglobin removal:* >95%

*Pump speed:* 25–1000 ml/min

*Centrifuge speed:* 2500–5600 rpm

*Typical processing time:* 5 minutes

## Applications

Blood recovery machines find applications in areas that may include specific types of surgery such as open heart and vascular surgery, total joint replacement and spinal surgery, liver transplantation, and selected neurosurgical procedures.

## 49

# Blood Rheometer

### Purpose

Blood rheometer is a device that is used to study the deformation and flow of blood under certain forces. The basic objective is to understand flow properties of blood and its formed elements, as well as the coupling of blood and the blood vessels in living organisms. In other words, blood rheometry deals with the interrelationship between force, deformation, and flow of blood.

### Principle

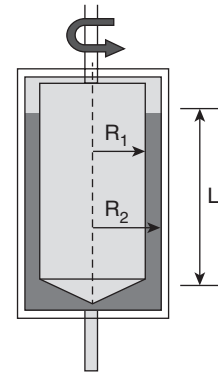
Blood rheology is the study of flow and deformation of blood usually refers to its behaviour as a viscous fluid in the flow through large arteries, veins, and the heart. In both small and large vessels, there are two rheological parameters that describe the flow properties of blood: viscosity and elasticity. Viscosity is simply defined as the property of a rheological fluid to resist the flow. In other words, the viscosity of blood is highly shear dependent so that the apparent viscosity increases at low rates of flow and decreases as the shear rate increases at high flow rates. The measurement of blood viscosity is described in the Chapter 51.

The ability of the red blood cells (RBCs) to deform when an external shear stress is applied is an essential property for the cells to pass through the smallest capillaries of the microcirculation. The measurement of deformability of RBC has assumed great importance in diagnostics because many pathologies have been found to be associated with impaired RBC deformability. For example, the deformability of RBC is considered necessary for the purposes of oxygen delivery in the microcirculation system. In case there is even a small fraction of rigid cells in the blood, it is likely to harm the exchange of respiratory gases. The rheological properties of blood can be measured using a *rheometer*.

There are three types of commonly used rheometers for blood: the concentric cylinder rheometer (Couette rheometer), the cone and plate rheometer, and the capillary rheometer. These instruments allow measurement of mechanical properties of whole blood over a wide range of shear rates. However, in practice, the range of each rheometer is limited so that more than one rheometer may have to be used when blood properties are to be studied over a wide range of shear rates.

#### **Couette Rheometer**

As shown in Figure 49.1, the Couette rheometer consists of two concentric cylinders. The test fluid is placed in the annular space between the two concentric cylinders. The outer cylinder is called 'cup' and the inner cylinder as 'bob'. The fluid motion is generated by rotating the outer cylinder at a fixed angular velocity, thus producing a shearing

**Figure 49.1** Schematic diagram of Couette rheometer.

force that is transmitted to the fluid, causing it to deform or flow. The inner cylinder is maintained stationary by a torque ( $T$ ) that can be measured by a torsion spring. The magnitude of the applied  $T$  necessary to maintain the relative rotation rate can then be used to obtain the shear stress and shear rate. A typical Couette rheometer is shown in Figure 49.2. The sample cup is kept at a constant temperature by Peltier effect, jacketing and providing tube fittings for connection to a constant temperature circulating bath. The system is accurate to within  $\pm 1.0\%$  of full-scale range. Reproducibility is within  $\pm 0.2\%$ . Working temperature range is from 0 to  $100^\circ\text{C}$ .

**Figure 49.2** Rotating rheometers based on Couette principle. *Source:* With permission courtesy of M/s Lamy rheology.



**Cone and Plate Rheometer**

Figure 49.3 illustrates the principle of cone and plate rheometer. It is basically a precise torque meter, which can be driven at discrete rotational speeds. The torque measuring system consists of a calibrated beryllium–copper spring that is connected to the drive mechanism to a rotating cone. The blood is loaded between the cone and flat plate and driven by the rotation of the cone. The system senses the resistance to rotation caused by the presence of sample fluid (blood) between the cone and a stationary flat plate.

The resistance to the rotation of the cone produces a torque that is proportional to the shear stress in the fluid.

The instrument is very simple in construction. The stationary plate forms the bottom of a sample cup, which is removable. The cup is usually filled with 0.5–2.0 ml of sample blood depending on the cone in use. The cup can be remounted without disturbing the calibration. Various cone spindles are available for use with the instruments.

**Capillary Rheometer**

A capillary rheometer is designed to measure shear viscosity and other rheological properties. The test region of a capillary rheometer comprises a cylindrical rigid tube of radius  $R$  and length  $l$ . Figure 49.4 shows the essential components of a capillary rheometer. Generally, capillary rheometers are used to measure the shear viscosity and elasticity of viscous materials at high shear rates. The design and operational principle of a capillary rheometer are suitable to provide rheological data under these processing conditions. The

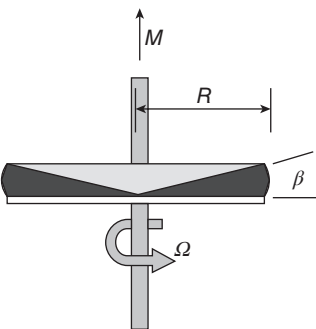


Figure 49.3 Principle of cone and plate-type rheometer.

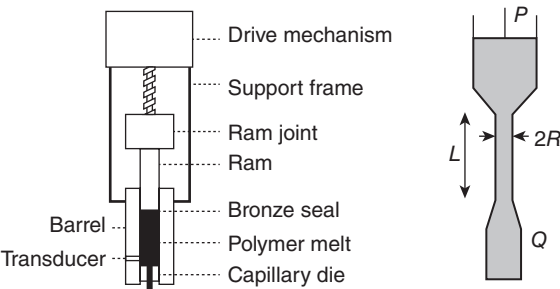


Figure 49.4 Working principle of capillary-type rheometer.

basic components of a capillary rheometer comprise a barrel, piston, capillary die fitted inside the barrel, pressure gauge, and force transducer. The test fluid (blood) is driven through this cavity by a piston attached with a force transducer at a specified rate.

The pressure transducer allows to measure the pressure within the barrel of the capillary. Measurements of viscosity are then made by applying a steady pressure drop across the test region in order to generate a flow with constant volumetric flow rate. Using the measured pressure and known controlled flow rate, one can calculate the viscosity of the test sample. The shear rate of the sample through the die can be controlled by controlling the velocity of the piston. For fluids with shear rate-dependent viscosity, the viscosity will vary over the cross section. As a result, an explicit relationship between viscosity and the measurable parameters of the apparatus only exists for a small number of cases, constant viscosity and power-law fluids being the most obvious examples.

## Specifications

*Measuring principle:* Rotating rheometer based on Couette principle

*Rotation speed:* From 0.1 to 100 rpm

*Precision of speed:*  $\pm 1\%$

*Torque range:* 0–0.0006 mNm

*Temperature control:* Sensor PT 100/Peltier element, range 10–60°C, resolution 0.1°C

## Applications

The study of blood rheological behaviour is very important for understanding blood flow, which helps to detect and consequently to treat some cardiovascular disease. In fact, the most obvious use of blood rheology in clinical medicine is in identification of diseases, which show any change in rheology.

# 50

## Blood Time–Temperature Indicator

### Purpose

The blood time–temperature indicator (BTTI) is a device designed to monitor the accumulated time–temperature history of blood bags during storage and transportation. The device allows to indicate exposure to excessive temperature and time especially of blood. The device gives useful information regarding blood temperature during transit from the highly controlled environment of the blood bank for usage or storage at a different destination. BTTI is simply a tool to assist personnel handling blood components to decide to use or discard a particular blood consignment to ensure safety of the

blood supply. Time–temperature indicators are also commonly used on food, pharmaceutical, and many other medical products such as vaccines or ophthalmic solutions.

## Principle

As per the prevalent regulations and guidelines issued by most of the countries, human blood should be stored at 2–6°C, and in no case it should exceed 10°C when stored or transported. The blood should not be kept outside the prescribed limits under any circumstances for a period of 30 minutes or more. BTIs provide a signal when a threshold temperature has been exceeded and also allow an easy-to-read visual signal indicative of the amount of time a product has spent above the threshold temperature. The indicator gives irreversible performance and provide a permanent record of temperature exposure even after temperature has returned to acceptable level.

There is a variety of time temperature indicators available commercially that are based on different technologies. These devices operate on physical change, chemical change, electrochemical or electromechanical indication, electronic readout devices, etc. However, most of them are based on colour change of the indicating device when subject to rise in temperature. For example, one device is based on the migration of dye through a filter paper, while the others contain pouches with bacterial fluids that change colour when certain time–temperature combinations have been reached. Once activated, the labels show clearly and irreversibly when the temperature of individual blood bags has breached the regulatory 10°C/50°F temperature abuse point. This implies that the blood cannot be returned to the blood bank for future use.

## The Devices

WHO in consultation with some manufacturers has developed a BTTI device to monitor the temperature of a consignment of blood, especially during transportation. It is based upon the migration of a chemical through a paper wick. The BTTI is an indicator on a card that upon activation shows colour changes when the cumulative temperature of exposure exceeds +10°C. The BTTI has four windows labelled 1–4 that will turn blue upon undue thermal exposure, as shown in Figure 50.1.

The first three windows monitor whether the blood has been exposed cumulatively to a temperature of +10°C or above. As soon as +10°C is exceeded, the first window starts to turn blue. If the temperature remains above +10°C or at every successive exposure to this temperature, the blue colour will migrate through windows 1, 2, and 3. The higher the temperature, the faster the blue colour will spread through these windows. Window 4 will start to show traces of blue immediately the temperature in the container exceeds +17°C. The coloration in the windows is irreversible. The BTTI does not indicate temperatures below +10°C. The dual temperature indicator



Figure 50.1 Blood time–temperature indicator.

incorporates both a 10°C time–temperature indicator and a 34°C go/no-go threshold indicator whose separate window shows blue if the temperature exceeds 34°C.

Another design of BTTI is from the 3 MTM Monitor Mark TM, which is a rectangular flat laminate containing layers of paper, film, adhesive, and other components. The device as shown in Figure 50.2 has an overall size of 95 mm × 19 mm. The heart of the device is a porous wick indicator track strip, one end of which is positioned over a reservoir pad containing a blue-dyed specialty chemical having a desired melt point. The meltable solid travels down a porous wick when heated above the melting point. The time interval is a function of the travel of the colour down the wick. Before activation, a removable activation strip separates the indicator track from the reservoir. The indicator is activated by pulling and removing the activation strip. This provides contact between the reservoir pad and the end of the porous wick indicator track. At this point, the indicator track is just a plain white colour.

A pressure-sensitive adhesive on the underside of the indicator allows convenient attachment to most clean, dry surfaces. Upon exposure to temperatures exceeding the threshold response temperature, the chemical in the reservoir melts and begins to migrate along the track. Thus, blue colouring first appears at the left edge of the first viewing window and gradually moves left to right to the end of the track. The rate of the blue colour movement is dependent on the temperature. The appearance of any blue colour in the indicator's first window signals that the indicator's preset threshold temperature has been exceeded. A paper board layer over these components contains viewing windows and is topped with a clear protective film over layer.

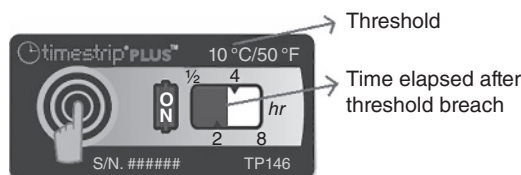
M/s Timestrip® has introduced a small, finger pressure-activated label that can be applied to blood bags the moment they are taken out of refrigeration units and packed into cool boxes for use by theatre technicians or emergency response teams. Once activated, the labels show clearly and irreversibly when the core temperature of individual blood bags has breached the regulatory 10 °C/50 °F temperature abuse point, which stipulates that blood cannot be returned to the blood bank for future use.

The principle of this indicator applies in using a mixture that will melt from solid to liquid form when an ascending temperature threshold is breached and return to solid form if the temperature falls again to its freeze point. When in liquid form, the mixture will move laterally through a porous membrane at a known rate. The progress of the liquid will be visible through a viewing window. If the threshold is breached, the blue colour will progress to the viewing window with the time markers. Each movement is irreversible, so the cumulative time of any temperature breaches is shown by how far the blue colour has moved along the time markers. Figure 50.3 shows a typical BTTI based on this principle.

Since all of the available temperature indicators are applied to the blood bag surface, they do not measure core temperature. There is no way to measure core temperature of a blood unit during temporary storage and transport except for inserting a temperature



Figure 50.2 Time–temperature indicating strip.



**Figure 50.3** Blood time–temperature indicator from M/s Timestrip. The device will indicate how long a product has been exposed to higher temperatures.

probe into the ‘core’ of the bag. The strip also helps in observing the time taken to complete the transfusion.

## Specifications

*Threshold temperature:* 10 °C

*Temperature accuracy:*  $\pm 1$  °C

*Storage conditions:* Storage temperature of 22 °C at 20–80% RH

*Shelf life:* 2 years from date of manufacture

*Size:* 19 mm  $\times$  32 mm  $\times$  0.5 mm

## Applications

Time–temperature indicators are used to monitor any product subject to time–temperature exposure outside the prescribed range. They are basically used primarily on the secondary package such as case, box, etc., and are often used to monitor storage and distribution conditions. The devices help blood banks to develop and validate their standard operating procedures by monitoring the transport temperature of blood. The indicators monitor temperature exposure, not product quality. Their purpose is to signal when product quality should be checked.

# 51

## Blood Viscometer

### Purpose

Blood viscosity meter or blood viscometer is a device that is used to measure the viscosity of blood or its resistance to flow. It represents the thickness and stickiness of an individual’s blood. Viscosity is a direct measure of the ability of blood to flow through the blood vessels and determines how much friction the blood causes against the

vessels. Blood viscosity is correlated with all known risk factors for cardiovascular disease and is a strong independent predictor of cardiovascular events.

The unit of viscosity in the metric system is the *poise* and is generally expressed as dyne-second per  $\text{cm}^2$ . In the metre, kilogram, and second (MKS) system, poise is replaced with the pascal-second. Viscosity values for biologic fluids traditionally are given in centipoise (cP), which is equal to 1/100 of a poise and is a more convenient unit.

## Principle

Almost all the viscometers measure blood viscosity at a given shear rate. There are different kinds of testing for blood viscosity. It can be measured either from serum/plasma or whole blood. Plasma viscosity measurements have significant role in the clinical management of patients that are prone to hyperviscosity syndrome. However, plasma viscosity measurement does not take into account the haematocrit and blood cell deformability. On the other hand, whole blood viscosity measurement is more realistic as it takes into account the haematocrit value. However, the measurements on whole blood are more complex as whole blood is a non-Newtonian liquid and changes its viscosity with the applied shear stress. Moreover, the blood viscosity rises and falls with every cardiac cycle similar to blood pressure.

The fluids that have the same viscosity at different shear rates are known as Newtonian fluids, over the shear rate range they are measured. On the other hand, the non-Newtonian fluids such as blood having different viscosities at different shear rates can be categorized into two types: (i) *time independent*, which means that the viscosity behaviour does not change as a function of time when measuring at a specific shear rate, and (ii) *time dependent*, which means that the viscosity behaviour changes as a function of time when measuring at a specific shear rate. Blood viscosity decreases at high shear stress due to the deformation of red blood cells (RBCs), while it increases at low shear stress. Whole blood comprises a plasma and formed elements such as RBCs, white blood cells, and platelets. The blood velocity thus mainly is determined by the viscous properties of plasma, the fraction of RBCs (haematocrit) in the blood, and viscoelastic properties of the formed elements.

## Instruments

The blood viscometers generally measure the viscosity of blood over a wide range of shear rates. This is achieved by controlling either shear stress or shear rate of blood using rotational objects. Stress-controlled blood viscometer applies a constant torque, which corresponds to constant rotational speed in a rotational viscometer. In a rate-controlled system, applied torque is controlled by a stress-sensing device so that a constant rotational speed is achieved.

Most of the blood viscometers operate on the same principle as that of blood rheometers and can be classified accordingly by the shape of the cylinder such as a concentric cylinder, a cone plate, and a parallel plate viscometer.

*Cylinder-type viscometer* uses two concentric cylinders in which the inner cup rotates and the outer cylinder is stationary. This type of viscometer is used to measure precisely time-independent shear rate.

**Cone and plate viscometer:** Here, an inverted cone having very shallow angle ( $\sim 5^\circ$ ) is rotated and the shear rate under the plate is maintained consistently and independent of a flow curve.

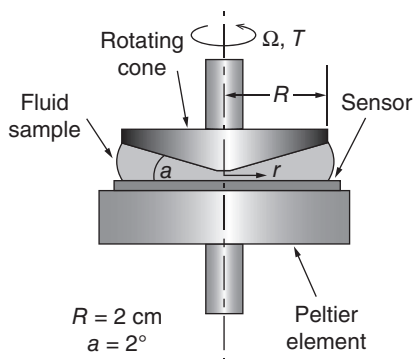
**Parallel plate viscometer:** This type of viscometer is a simplified version of the cone and plate viscometer. It has an advantage of flexible space between two parallel plates. The blood is confined and rotated in narrow space between two circular parallel plates.

### Cone–Plate Viscometer

In its simplest form, a spindle, which is immersed in the test fluid, is rotated through a calibrated spring. The drag exerted by the viscous fluid against the spindle is measured by the spring deflection using a rotary transducer, which provides a torque signal. An optical signal pick-up inside the device is used to detect the torque value of the calibrated spring. The device will display the average value for both torque (%) and viscosity in cP. The shear rate of a given measurement is determined by the size, shape, and rotational speed of the spindle, the size and shape of the container used, and the distance between the container wall and the spindle surface.

The viscosity of blood is dependent on shear rate and the spindle geometry conditions. The viscosity readings will thus be affected by the specifications of the viscometer spindle and chamber geometry. Suppose that if one reading is taken at 5 rpm and a second at 50 rpm, the two viscosity values produced will be very different as they are taken at different shear rates. The faster the spindle speed, the higher the shear rate. All viscosity measurements of fluid flow properties are generally made under laminar flow conditions. Laminar flow is where all particle movement is in layers directed by the shearing force. This means that for rotational systems, fluid movement must be circumferential.

Figure 51.1 shows a schematic of the principle of cone–plate viscometer. The blood is placed on a horizontal plate and a shallow cone placed into it. The cone is nearly flat with a reference angle between  $0.8^\circ$  and  $3^\circ$ , with its tip just touching a flat plate. The test liquid is contained in the small gap between the cone tip and the plate. Either the cone or the plate is rotated at a constant speed, and the torque exerted on the other member is measured and translated into the viscosity of the fluid. However, typically the plate is rotated and the force on the cone is measured using a torsion bar, which is basically a thin piece of metal that twists with the movement of the cone. The response of the



**Figure 51.1** Principle of cone–plate blood viscometer.



torsion bar and the degree of twist give the shear stress, while the rotational speed and cone dimensions give the shear rate. Since the cone has a very small reference angle relative to the plate, the test fluid required is of a very small amount. The conical design provides a constant shear rate at all locations under the cone because as the linear velocity increases along the length of the cone radius, the gap between the cone and plate increases.

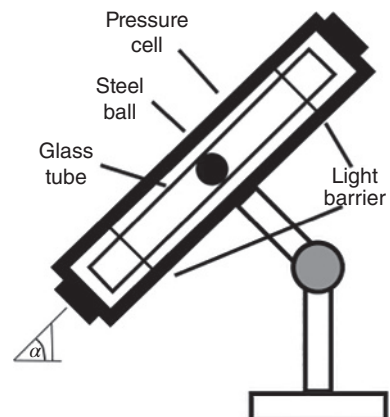
### ***Rolling Ball Viscometer***

The viscometer designed on the rolling ball principle measures the rolling time of a ball through the liquids. A schematic of the measuring principle is shown in Figure 51.2. The principle is based on the use of gravity as the driving force. A ball is made to roll through a closed capillary filled with the fluid, which is inclined at a defined angle. While the gravity pulls the ball downwards, the buoyancy and the viscosity of the liquid oppose the gravitational force. The stronger the viscous force, the slower the ball rolls. The time taken by the ball to travel a defined measuring distance determines the fluid's viscosity. The time taken between two measuring points is determined by photoelectric means. The driving force can be varied by varying the inclination angle of the capillary. The rolling ball viscometers usually operate at  $10^\circ$  and  $80^\circ$  inclination angles. For calculating the viscosity of the blood from the rolling time, it is necessary to consider the influence of gravity and buoyancy of the fluid. Therefore, both the density of the liquid and the density of the ball need to be known to obtain accurate viscosity results.

### ***MEMS-Based Blood Viscometer***

Microvisk, United Kingdom, has developed a portable microelectromechanical sensors (MEMS)-based blood viscometer shown in Figure 51.3, which uses micro-cantilever devices that are produced on a wafer scale where thousands of identical microchips are processed together as flat structures on the surface of silicon wafers. At the final stage of production, the micro-cantilevers are released to deflect above the supporting surface,

**Figure 51.2** Principle of rolling ball blood viscometer.





**Figure 51.3** Typical MEMS-based blood viscometer from M/s Microvisk, United Kingdom. The system consists of a small disposable strip and a reader.

forming 3D microstructures. These highly deformable and flexible micro-cantilevers, controlled by complementary metal oxide semiconductor (CMOS)-type signals, form the fluid microprobe used in determining the rheometric properties of minute (nanolitre volume) samples. When a current is passed through the structure each layer deflects in a different way. As one structural layer expands more, another expands less, which leads to each cantilever moving up and down in response to immersion in a gas or in a liquid such as blood. The speed of blood clotting and its rheometric changes associated with the clotting process can therefore be monitored in a one-stage process based on physical changes rather than on chemical changes.

The Microvisk system is relatively simple as it comprises a small disposable strip onto which blood is placed and a handheld reader into which it is inserted for analysis and display of results. The strip itself is an active component, which contains a small amount of thromboplastin to initiate the clotting reaction and a micromachined cantilever that is responsible for sensing the change in the viscosity of the blood over time. The cantilever is held rigid at one end and flexes at the other and comprises a pair of polyamide strips that each have a different coefficient of expansion. Sandwiched between these two polyamide layers are a heater and a piezoresistive element.

When a sample of blood is placed on the strip, the small amount of dried thromboplastin contained on it is made soluble and the blood starts to coagulate. Once placed inside the reader, the heating element on the strip is thermally cycled, which causes the cantilever to oscillate due to the different coefficients of expansion of each of the polyamide strips. As the blood becomes more viscous, it presents more of a resistive effect to the oscillating cantilever, causing a corresponding change to the output from the piezoresistive layer between the polyamide strips. By measuring the changes in resistance in the piezoresistive layer due to the increase in blood viscosity, the reader can calculate the time it takes the blood to change from a solution to a gel, which is then displayed.

## Specifications

*Principle:* Cone–plate method

*Measurement range:* 0–50 mPa s

*Shear rate range:* 1–200 seconds

*Test speed:* Whole blood/plasma  $\geq 60$  samples/h

*Sample quantity:* 0.5 ml

*Preheating time:* 15 minutes

## Applications

A growing number of research studies have indicated that blood viscosity has an important role as predictor of cardiovascular events in the adult population. The increased blood viscosity is associated with all known risk factors for cardiovascular disease that include high blood pressure, cholesterol, diabetes, gout, and rheumatoid arthritis, etc. The blood viscosity meter finds important applications in the clinical field.

# 52

## Blood Warmer

### Purpose

A blood warmer is a device that is used to warm blood or fluids prior to transfusion to a patient. They are designed to reduce the risk of hypothermia associated with the infusion of cold blood products. These devices are mostly employed in emergency settings, operating rooms, and intensive care units. Their main use is for the cases requiring rapid transfusion rates or massive transfusion.

### Principle

The blood is generally stored in blood bank refrigerator at 4°C, whereas the normal body temperature of a human is 37.5°C. So, if blood transfusion is required, it will be quite risky to directly infuse cool blood in a patient. The blood drawn from the bank therefore requires heating before it is infused to minimize adverse thermal reactions in patients. This is done by comparing the blood bag temperature and the patient body temperature, providing heating to blood accordingly. The infusion temperature is determined by the condition of the patient, the duration of infusion, and the total volume of blood to be administered.

Blood warmers are inline devices, which are usually mounted on the IV pole between the blood bag and the patient's venous line. Several types of blood warmers are available, which operate on different principles. The simplest one is the *dry heat* type in which the bag or

the tubing is placed between two aluminium heating plates. The *water bath* consists of a heated water reservoir and the blood is warmed as it passes through a bag or coil of polyvinyl chloride tubing immersed in the reservoir. Then, there are warmers, which use a countercurrent water bath heat exchange system. Still, there are other systems based on infrared, microwave, and convective air heating, but they are not very popular commercially. The temperature of the heating element is controlled either by using a thermostat or electronically. The warmers generally have a high temperature indicator with audible alarm.

### Temperature Control

A simplified block diagram of a typical electronic temperature control circuit is shown in Figure 52.1. The temperature of the blood bag is sensed by a thermistor. Thermistors are constructed of semiconductor material and have negative temperature coefficient, which means that their resistance decreases with the rise in temperature. They are used as one arm of a Wheatstone bridge configuration and provided with temperature compensation. Temperature of the patient body is also sensed using thermistor as a sensor.

The electrical output from the two temperature sensors then goes to two instrumentation amplifiers. These amplifiers provide a gain of 1000 in two stages. The differential amplifier circuit provides error signal by detecting temperature difference of both blood and patient channels. The output of the differential amplifier is converted to the corresponding value of current in the voltage-to-current converter circuit. The current is then given to the heating coil.

The heating coil is used to perform the heating operation on the cold blood of the blood bag. It is constructed by using a very thin coil coated with mica and wound on a stainless steel tube. As the heating efficiency increases with the increase in the number of turns, it should be ensured that there is no overlapping of coil turns; otherwise, there would be damage to the coil material due to excessive heating. All modern blood warmers are microprocessor-controlled devices designed specially to avoid intra- and post-operative hypothermia. They allow the operator to set the warmer temperature between 37 and 41 °C in increments of 0.5 °C.

Figure 52.2 illustrates another simplified diagram of a blood warmer. The temperature of the reservoir is compared with the set temperature. The error signal generated is used to control the power to the heating element. The devices are provided with special grooves as shown in Figure 52.3 to ensure that the tube is always kept in the required position and

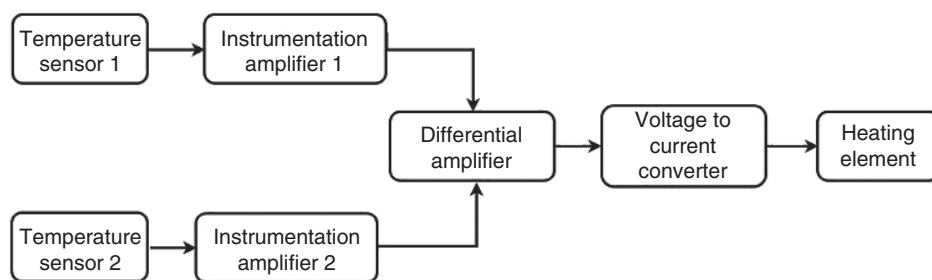
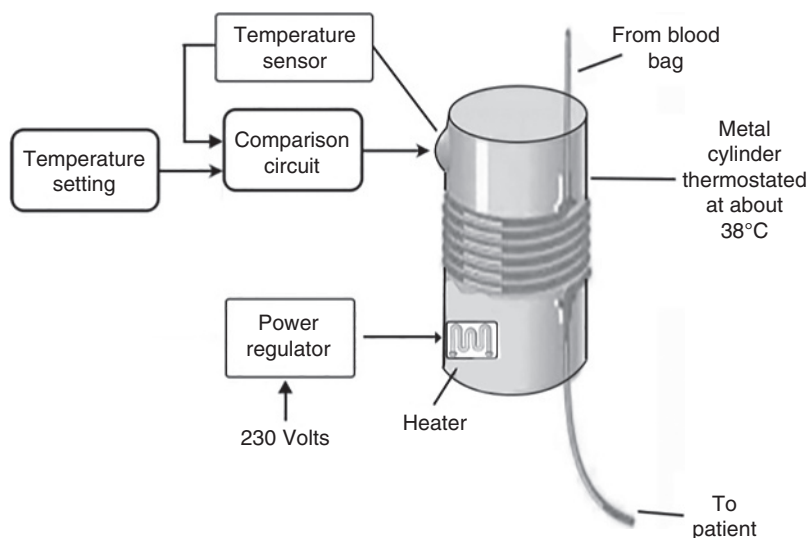


Figure 52.1 Detailed block diagram of blood warmer.



**Figure 52.2** Simplified block diagram showing the principle of a blood warmer.



**Figure 52.3** Typical blood warmer from M/s Biegler, Austria, with several loops to allow several infusions to be warmed at the same time.

also allows several infusions to be warmed at the same time. The primary temperature control circuit limits the recirculating solution to 40°C maximum. If there is a malfunction of this circuit, a second 'watchdog' circuit will stop the recirculating solution pump. In case the temperature reaches 41.2°C, visual and audible alarms are issued.

As a matter of safety, some warmers include an air detector that monitors for presence of air in the disposable gas vent filter assembly. An ultrasound signal is continuously passed through the fluid-filled gas vent filter assembly. When a bolus of air displaces the fluid, the ultrasound signal is interrupted, and the clamp automatically



**Figure 52.4** Blood and fluid warmer. The temperature is maintained by surrounding the sterile intravenous line with a layer of warmed recirculating solution. *Source:* Image courtesy of M/s Smiths Medical.

closes off the patient line. In such a situation, audible and visual alarms are activated, which alerts the doctor about the stoppage of fluid flow due to the presence of air. The operator then has to follow a sequence of steps to purge the system of air before infusion of fluids can be resumed.

The HOTLINE® Warmer from M/s Smith Medical shown in Figure 52.4 operates by delivering blood and intravenous fluid at the set temperatures by surrounding the sterile intravenous line with a layer of warmed recirculating solution. The recirculating solution supply is heated to  $39.5 \pm 0.5^\circ\text{C}$  and circulated through the outer lumen of the fluid warming set, which surrounds the intravenous line. The recirculating solution temperature is continuously monitored to ensure that the fluid warming set is never exposed to any damaging or dangerous temperatures. The recirculating solution temperature and visual alarms are indicated on the display panel. The fluid warming systems in most of the blood warmers suffer from cool-down effect between the warmer and the patient connections. This problem is obviated by providing active warming of the patient line all the way to the patient connection. The device allows blood and intravenous fluid to be delivered to the patient at gravity flow rates of 50–5000 ml/h. The other features include automatic adjustment of temperature to flow rate, an audible alarm system, and portability.

## Specifications

*Temperature:* Can be set from 37 to  $41^\circ\text{C}$  in  $0.5^\circ\text{C}$  increments

*Safety features:* Multiple independent cut-off from  $42^\circ\text{C}$

*Alarms:* Low and high temperature

*Warm-up time:* 40 seconds max.

## Applications

A blood warmer is frequently used in emergency units, operating rooms, and intensive care units in hospitals for blood or plasma transfusion to patients to avoid hypothermia.

## 53

### Body Fat Analyser

#### Purpose

Body fat analyser is intended to measure body fat weight and body fat percentage, which is the percentage of fat in the body in relation to total weight of the body. The human body is mainly composed of water, with fat having the next largest percentage. The other constituents of the body comprise proteins and carbohydrates, which are in the form of muscles and minerals.

#### Principle

The body fat analyser measures the body fat percentage by bioelectrical impedance analysis (BIA) method. The method depends upon the fact that tissues that contain much water such as muscles, blood vessels, and bones show high electric conductivity, but not the fat tissues.

Therefore, by measuring electric impedance of the body tissues, it is possible to determine the ratio of fat tissue in comparison to other tissues in the body. The body impedance is measured by applying extremely low level electric current ( $500\mu\text{A}$ ) to the human body at a frequency of about 50 kHz. The application of electric current at these high frequencies and at such low amplitudes is quite safe for the human body.

The parameter that is measured is impedance, and it is not the body fat percentage. The body fat is empirically calculated by taking into account scale reading and based on the basic data on human body, gathered by researchers from a large number of subjects. Along with measurement of impedance, the conditions specific to users are considered while developing equations and assumptions for calculating body fat. The user specific conditions are gender, age, height, and weight, which contribute to the formula employed for calculating the body fat percentage. Some devices allow to set age and gender on the machine before the measurement results are read, to provide more accurate measurement results. Using equations and assumptions about average hydration and body water content, handheld BIA monitors display body fat percentage.



### **Types of Body Fat Analysers**

Body fat analysers can be categorized into handheld devices and standing scales types. In a handheld body fat analyser such as shown in Figure 53.1, when the device is held in both hands, an imperceptible electrical current passes through the body. In this arrangement, the electric current passes from one hand to the other hand through the body. In this type of device, the electrodes should be held firmly while standing in a firm posture. In a standing body fat scale illustrated in Figure 53.2, the person stands on the weighing scale-type device and the entry and exit of electric current are through the feet after travelling through the legs to complete the circuit. The person should stand firmly on the electrodes with the feet covering the electrodes. A handheld BIA device gives about 5% accuracy, whereas the body fat scales are accurate to only about 80%. There are body fat analysers that provide hand-to-foot measurements. Such a device is shown in Figure 53.3. These devices give more accurate readings because foot-to-foot measurements tend to underestimate body fat because they do not travel across the stomach like hand-to-foot measurements, and this is where many people carry their extra weight. All types of body fat analysers have digital displays. The device handles (electrodes) should be held with bare hands or the person should stand barefoot when doing the body fat analysis.



**Figure 53.1** Typical body fat analyser.



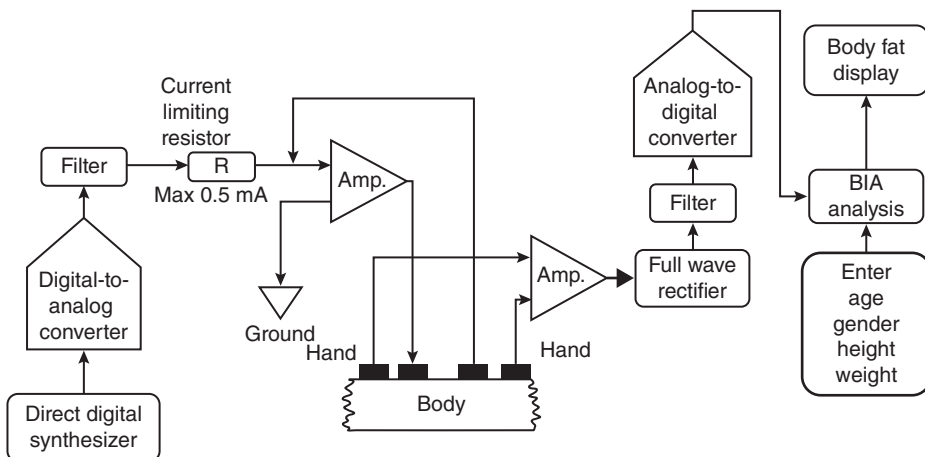
**Figure 53.2** Body fat scale.



**Figure 53.3** Body fat analyser with both hand and foot operations.

### Instrumentation

Figure 53.4 is a block diagram of the body fat analyser. It uses the established four-electrode system used in bio-impedance measurements on the human body. A high frequency constant current pulse source circuit provides the output to electrodes A and B, which are typically located on the respective left- and right-hand bars of a handgrip device. Current flows between terminals A and B when a person places their right and left hand of the bar to establish contact through contact electrode plates M and N also respectively positioned on the left and right handgrip bars.



**Figure 53.4** Block diagram of a body fat analyser.

The high frequency generator is a basic direct digital synthesizer (DDS) that consists of a frequency reference (often a crystal), followed by a digital-to-analog converter (DAC). The current source delivers a  $500\mu\text{A}$  sinusoidal current to the human body at a frequency of 50 kHz. The voltage electrodes sense voltage levels between two distinct positions and this voltage information is acquired from the contact electrodes by op-amps. Subsequently, the bipolar signal is rectified by a rectifier circuit. The output then goes to an analog-to-digital converter (ADC module). From this measurement, the total body impedance is computed using pre-input data concerning the body weight, height, age, and sex of the person holding the handgrip to determine the percentage of body fat-to-body mass ratio of the person being tested. The circuit uses amplification, filtration, and rectification stages wherever required. The whole circuit works under the control of an 8 bit microcontroller. The microcontroller, based on the measured signal strength, determines body fat/body mass ratio and displays it on seven segment LCD display.

The body fat analysers are not very accurate devices and give only an estimate of the body fat. Several factors such as body type, body temperature, hydration, and recent exercise can have a significant impact on the readings. The results can also get affected by having wet or sweaty feet during measurement. So the body fat scale should be utilized only as a means of tracking trends rather than believing it to be an absolute number for body fat amount. Also, the body fat analyser is based on the fluid content in the body to assess the fat composition. This means that the hydration level, which gets affected by the consumption of water, alcohol, caffeine, food, etc., should be at the right level. It is therefore recommended that the body fat measurements should be taken in the morning on an empty stomach to ensure repeatable and more reliable results. For women, body fat in the range 20–30% and, for men, in the range 10–20% is generally considered good.

## Specifications

### *Display*

*Body fat %:* 5.0–50.0%

*Body fat % assessment:* Low/normal/high

### *Input data*

*Height:* 100.0–199.5 cm

*Body weight:* 10.0–199.8 kg

*Age:* 10–80 years old

*Gender:* Male/female

## Applications

The main applications of body fat analysers are aimed at fitness professionals, gym centres, nutritionists, dieticians, and other healthcare professionals including physical therapists who treat patients and clients undergoing wellness or weight loss programs.

## 54

# Bone Cutting Machine

### Purpose

A bone cutting machine is used in orthopaedic surgery, to cut and shape the bones. The application is particularly complex in the case of total knee joint replacement, when the femur and the tibia are to be precisely cut and shaped to ensure that they firmly mate with the artificial joint.

### Principle

The normal procedure of bone cutting is to manually cut the bones using a bone saw and mechanical jigs. However, powered surgical saws are preferred for their efficiency and precise control over the cutting process. These are high powered machines that have a high torque density to meet the toughest requirements in a small lightweight package. They consist of slotted brushless direct current (DC) motors. The magnetic coil design of these motors provides extremely high peak torque to enable surgeons to saw through the toughest bone with a small size motor. The motors are so encased that they are sterilizable. They are designed for high efficiency to work even in batteries to give maximum battery life. A typical battery-operated bone cutting machine is shown in Figure 54.1.

The shape of the machine is ergonomically designed to provide low noise to allow steady and quick cutting with no damage for soft tissue. A variety of different thickness



**Figure 54.1** A typical battery-powered bone cutting machine.

or the length of the saw blade are available to meet various requirements. Typically, the blade lengths are 70, 90, and 100 mm and common thickness are 0.8, 1.0, 1.2, and 1.27 mm. Highly advanced machines in which the cut plane is determined by a 5 degree-of-freedom mechanism and the cut is made by two translational and one rotational degrees of freedom have been reported in literature.

## Specifications

*Operation:* Fully motorized

*Frequency of saw:* >15 000 rpm

*Highest temperature:*  $\leq 30^{\circ}\text{C}$

*Noise:*  $\leq 75\text{ dB}$

*Weight:* 1300 g

## Applications

Bone cutting machine find applications in orthopaedic departments.

# 55

## Bone Density Measurement: Dual Energy X-ray Technique

### Purpose

Dual energy X-ray absorptiometry (DEXA)-based bone density measuring system is presently an established technique for measuring bone mineral density (BMD). The main use of DEXA is the diagnosis of osteoporosis, which results from reduction in bone mass and increase of bone fragility, which in turn indicates the possible increased risk of a fracture. Osteoporosis is considered as one of the serious public health problems because of its prevalence and the associated cost for its management. DEXA also helps determine the treatment and monitor the response of the patient to treatment.

### Principle

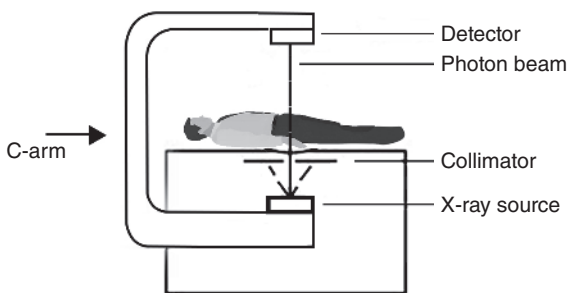
The primary purpose of bone density measurement using DEXA is to detect quantitative reduction in bone mass related to metabolic bone diseases such as osteoporosis and to assess efficacy of treatment noninvasively. Determination of the bone mineral content (BMC) in the skeletal system, particularly the lumbar spine and hips, using DEXA, is the most commonly used modality in clinical practice. The forearm can also be studied when it is not convenient to make measurements on hip or spine.

A DEXA scanner consists of a whole body scanner frame, an X-ray source and detector, and a control computer. The other main components include different types of filters, collimators, and software having analysis algorithms. The subject is positioned on top of the scanner frame, in a supine position as shown in Figure 55.1. The machine produces two X-ray beams, each having different energy levels. One beam is high energy, while the other is of low energy. The attenuation coefficients of different radiation energies through the body consisting mainly of two materials, bone and soft tissue, are measured. The absorption of the low and high energy X-rays is then compared. DEXA is based on the variable absorption of X-ray by the different body components and thus the contribution of soft tissue to X-ray absorption can be identified and subtracted for bone measurements. In this way, BMC and BMD can be measured.

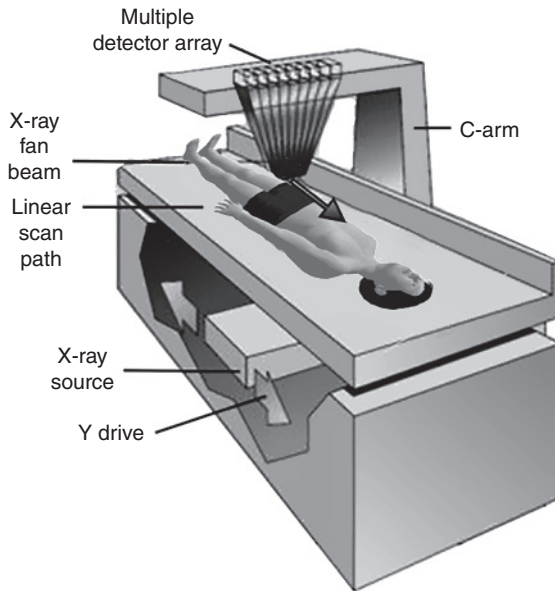
The X-ray beams can be produced by two methods. In some systems, the X-ray generator generates radiation of high (140 kVp) and low (70 kVp) kilovoltage alternately while moving across the surface of the body under examination. In other designs, the generator emits a constant beam, while a rare-earth filter separates high energy from low energy photons. The X-ray beam shape can be a pencil beam produced with a pinhole collimator that can be detected using a single detector. Alternatively, the beam may be of fan beam shape produced using a slit collimator and require a multiple detector. The fan beam system reduces the acquisition time and gives better quality images. DEXA systems make use of low radiation doses on the order of 1–10 mSv and usually they do not require lead shielding of the room or special protection measures for the technicians. In general, the pencil beam scan-based DEXA systems use slightly lesser X-ray dose.

Figure 55.2 illustrates the schematic of a DEXA system, which is designed to measure the area and length of a bone, BMC, and BMD. The BMD is calculated by dividing the BMC by the area of the bone. The radiation source is collimated to a pencil beam and aimed at a radiation detector placed directly opposite to it. Fan beam systems use a linear detector array and collect 10 or more pixels at a time. Thus, these systems are much faster than pencil beam systems for similar imaging properties. Typical time for acquiring images of the spine or hip is less than 30 seconds and 3 minutes for the whole body. The patient is positioned on a table so that the area under measurement lies in the path of the X-ray beams. The X-ray source and detector, which are coupled, are made to scan back and forth across the regions of interest in the body. The whole body can also be scanned to measure whole body bone mass and soft tissue body composition.

The system has a C-arm, which supports an X-ray source at the lower end beneath the patient table. The C-arm also supports an X-ray detector at the upper end



**Figure 55.1** Schematic representation of X-ray source and detector system in dual X-ray absorptiometry device.



**Figure 55.2** Scan path pattern for DEXA densitometer using pencil beam format.

positioned above the patient table. The X-ray detector is a multi-element solid state detector. The source and detector assembly move in a raster pattern and trace a series of transverse scans of the patient. During the scanning process, dual energy X-ray data are collected by the X-ray detector. The raster motion is generated by actuators that operate under the control of a translation controller. The X-ray source, the X-ray detector, and the translation controller all work under the control of a computer, which may include the necessary software to execute a stored program using proprietary algorithms. The analysis algorithm is designed to discriminate bone from soft tissue in a variable way.

In addition, the system calculates various parameters that includes the BMC, which is the quantity of calcium estimated by the energy absorbed by it in a specific region. However, the BMD, being much more relevant, represents the mean quantity of mineral per unit area. It is calculated dividing the BMC by unit area ( $\text{g}/\text{cm}^2$ ). The measurements of the attenuations at two energies allows to calculate the bone density per unit projected area of two different types of tissues to be studied. The attenuation values of soft tissues are subtracted by an algorithm providing only the attenuation values of bone. Generally, the density information is processed and displayed in real time during a scanning session. The display may include one or more monitors to display the present patient information, the scanned image, and the age-related image for diagnosis and analysis. The data acquired from the scan is used to compute a T-score and/or a Z-score, which are defined as follows:

**T-score:** This number compares the density of each scanned bone of a young healthy adult of the same gender. A score above  $-1$  is considered normal. A score between  $-1$  and  $-2.5$  is classified as osteopenia (low bone mass). A score below  $-2.5$  is defined as osteoporosis. The T-score provides an assessment of your risk of developing a fracture.



*Z-score:* This number indicates the amount of bone a person has compared with other people in the same age group and of the same size and gender. The Z-score takes into account other factors such as age and ethnicity.

When using DEXA bone density technique to diagnose osteoporosis, the common measurement sites include the lumbar spine, the proximal hip, and the forearm. As per the standard protocol, two sites, typically the spine and hip, are scanned. Optimization of the patient's position on the DEXA table is very important for correct measurements. Incorrect positioning is one of the main causes of errors in the estimation of BMD. Inadequate placement of the region of interest is another important source of errors.

## Specifications

*X-ray characteristics:* Constant potential source at 100kV

*Tube current:* 0.2–2.5 mA

*Detector:* Solid state ceramic digital detector array

*Scanning method:* Narrow-angle fan beam technology

*Power supply:* High frequency pulsing power supply

*Connectivity:* DICOM14 and HL7, picture archival and communication systems (PACSs), and radiology information system (RIS)/hospital information system (HIS)

## Applications

DEXA is a fast and reliable technique of choice in the diagnosis and monitoring of osteoporosis since it objectively measures the most relevant parameters. It finds applications in orthopaedics to provide accurate BMD and BMC values. Bone assessment in the region surrounding an implant is now possible using DEXA technique.

# 56

## Bone Density Measurement: Ultrasound Method

### Purpose

Bone density measurement using ultrasound technique is another way to assess the bone mineral density (BMD) with the objective of evaluation of patients at risk for osteopenia and osteoporosis. However, the ultrasound-based machines are usually portable and fall in the category of point-of-care screening or testing.

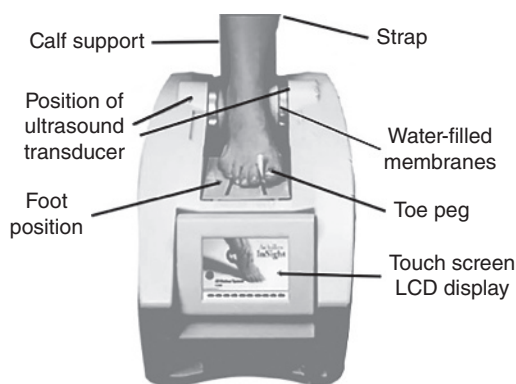
## Principle

BMD has been generally measured using dual energy X-ray absorptiometry (DEXA) by comparing the image density of the skeleton to the surrounding soft tissues. The mineral density of bone is estimated by the degree of grey colour of the X-ray image in the bone region. However, DEXA has not become a standard tool in the clinic of a primary care physician as it is expensive and inconvenient and involves X-ray exposure.

Another commonly used method for BMD measurement is based on the use of ultrasound as an alternative to DEXA. Quantitative ultrasound (QUS) technique has become quite popular in recent years due to its several advantages that it is non-ionizing, relatively less expensive, and simple to use. Ultrasound employs high frequency sound waves for measurement of BMD. The ultrasound waves are produced by piezoelectric crystals mounted in the transmitting and receiving transducers. The measurement is usually done on the heel, shin, or finger. The process is quite simple and involves asking the person to place the bare foot in the device as shown in Figure 56.1.

Most devices choose the heel as the measurement site because it has a large volume of trabecular bone between relatively flat faces and is readily accessible for transmission measurements. The transducers are acoustically coupled to the heel by elastomer transducer pads using ultrasound coupling gel, which is applied to the transducer pads. This ensures a good acoustical contact with the skin over the bone being tested. The heel is positioned between a pair of ultrasound transducers, with one transducer transmitting the ultrasound signal and the other transducer receiving the signal after passage through the heel. The inbuilt computer calculates the bone density by measuring as to how fast the sound waves pass through the heel. The measurement and generation of the report just takes less than a minute.

The ultrasound frequency applied in QUS generally range between 0.2 and 1.5 MHz. There are two types of QUS techniques in use depending on the axis the ultrasound waves can take to travel through the bone. These can be either horizontal or longitudinal.



**Figure 56.1** Bone density measurement technique with ultrasound-based machine. The heel is placed in between the two ultrasound transducers. *Source:* Adapted from Vishwanath, S.B., Kumar, V., Kumar, S., et al. (2011). Correlation of periodontal status and bone mineral density in postmenopausal women: A digital radiographic and quantitative ultrasound study. *Indian Journal of Dental Research* 22: 270–276.

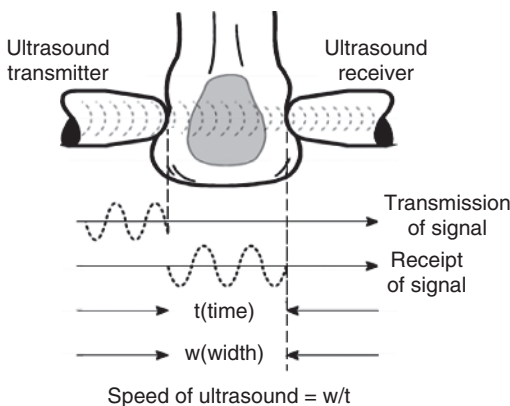
Horizontal transmission uses probes that measure the speed of sound (SOS) on the cortical layer of the bone at a fixed distance, whereas the longitudinal transmission is more often used in clinical practice and is mainly applied to the heel bone (calcaneus). Calcaneus is considered the most reliably reachable location due to the presence of a large semi-flat region of almost exclusively cancellous bone, which can give accurate and reliable results.

From the signal measured by the receiving transducer, two parameters describing the nature of the received sound waves can be simultaneously determined: SOS and broadband ultrasonic attenuation. It has been observed that broadband ultrasonic attenuation is reduced in patients with osteoporosis, because there are fewer trabeculae in the calcaneus to attenuate the signal. Similarly, SOS values are reduced in patients with osteoporosis because, with the loss of mineralized bone, the elastic modulus of the bone is decreased.

### Speed of Sound Method

During passage through the bone, the speed and amplitude of the ultrasound wave gets attenuated with the changes detected by the receiving transducer. Since the SOS in bone tissue is higher than in soft tissue, this information is directly related to the amount of bone in the ultrasound path. Ultrasound speeds of 2800–3000 m/s are typical in cortical bone, whereas speeds of 1550–2300 m/s are typical in trabecular bone. In addition, time differences between the arrival times of the first arriving signal and a more energetic guided wave component can be used to gauge the amount of bone.

Many commercial QUS devices measure the SOS through the heel. SOS is determined by measuring the width of the heel, and the time delay between the initial transmission of the sound waves from the transmitting transducer and the receipt of the sound waves by the receiving transducer as shown in Figure 56.2. The system measures the time ( $t$ ) the ultrasound signal takes to go through the heel and the transducer pads minus the propagation time measured with the pads touching each other and with no heel interposed. The width of the heel ( $w$ ) is measured using a micrometre attached to the transducers.



**Figure 56.2** Principle of measurement of speed of sound for bone density measurement.

The SOS value is then equal to  $w/t$  and is measured in metres per second (m/s). The range observed with in a typical population is approximately 1450–1700 m/s, with young/healthy subjects having higher SOS values than older or osteoporotic subjects.

### ***Broadband Ultrasound Attenuation (BUA) Method***

An ultrasound pulse passing through bone is strongly attenuated as the signal is scattered and absorbed by trabeculae. Attenuation is measured in decibels. The rate of ultrasound attenuation, or loss of energy, over a given frequency range is referred to as the rate of 'broadband ultrasound attenuation'. Its value increases linearly with frequency, and it is usually expressed as decibels per megahertz (dB/MHz). The slopes of the frequency spectrum reflect the density and structure of bone. It has been observed that the SOS is reduced and broadband ultrasound attenuation (BUA) is decreased with reductions in bone density and trabecular number, correlating well with the physical density of the bone under study leading to a diagnosis of osteopenia or osteoporosis. The range of BUA observed in a typical population is approximately 30–130 dB/MHz, with young/healthy subjects having higher BUA results than older or osteoporotic subjects.

Attenuation of the ultrasound pulse depends upon a number of factors such as scattering, diffusion, absorption, transmission, reflection, etc., and therefore has a complex relation with the amount and material properties of bone. Also, attenuation shows a linear relationship to frequency in the 0.2–0.6 MHz range, with the bone attenuating high frequency sound waves much more than low frequency sound waves. The slope of the attenuation curve with respect to frequency has been shown to depend on bone mineral content (BMC) and BMD.

Just like DEXA, bone density measurements are reported as a value in  $\text{g}/\text{cm}^2$  and as a T-score or Z-score, which reflects the bone density measurement in relation to other people in a similar group, termed as reference population. The reference population for the T-score is young adults of the same sex as the patient, while the reference population for the Z-score is a group of the same age and sex as the person being tested.

Commercial machines for quantitative real-time bone assessment are usually handheld and portable and can operate on rechargeable batteries. These devices are constructed around microprocessors or a digital signal processor, using high resolution A/D converter that samples the ultrasound signal at 30 MHz. In one design, the pulser produces a 300 V 400 ns pulse that excites the 2.25 MHz 12.7 mm diameter transmitting transducer. The 12.7 mm coaxially located receiver transducer operates at 1 MHz that receives the ultrasound signal after it has propagated through the heel of a foot. Both the transducers are flat and unfocused. The combination of the higher frequency transmitter with the lower frequency receiver allows to increase the bandwidth of the overall system. A high resolution electronic calliper (0.03 mm) is included in the device that measures the distance between the transducers. The adjustment of gel pads is automatic for optimal foot positioning. The device measures the SOS and BUA, thus allowing to calculate the bone quality index (BQI).

With the developments in QUS, several new diagnostic parameters have emerged from experimental results conducted both *in vitro* and *in vivo*. These parameters have shown potential for assessing not only bone quantity but also bone quality in terms of structure and strength.

## Specifications

*Measurement site:* Calcaneus (heel bone)

*Measurement method:* Ultrasound pulse penetration

*Measuring parameter:* SOS and BUA

*Measurement time:* 10 seconds

*Measurement precision:* 0.5% or better

*Measurement type:* Dry type (acoustic gel)

*Ultrasound frequency:* 500 kHz

## Applications

The applications of ultrasound-based BMD measurements are same or similar to the DEXA machine. These include diagnosis of bone loss and osteoporosis and predict risk of bone fractures. Current clinical practice recommends BMD testing every two years.

# 57

## Bone Healing Stimulator: External

### Purpose

An external electrical bone healing stimulator is a device that provides electrical stimulation from outside the body to augment bone repair and growth. This therapy is utilized to promote bone healing in difficult to heal fractures or fusions when satisfactory healing is not occurring naturally.

### Principle

The human bone has the inherent property of healing itself when broken or injured as it is actually a living tissue like skin. The bone healing process of the body is aided by the broken bone by creating its own electrical field. This means that the application of an external electrical stimulus can augment the body's natural bone healing process. So, electrical bone growth stimulators serve as supplementary therapy to help enhance the body's bone healing process. The stimulator sends low level electrical signals to the fusion site which activate the body's natural bone healing process.

Electrical stimulation can be applied either from the outside of the body (noninvasive) or from the inside of the body (invasive). Noninvasive (external) devices are worn outside of the skin. They employ treatment coils applied externally around the fracture or fusion site and are provided with stimulating electrical pulses from an

external power supply. Another version of external stimulator is in which the bone growth stimulator generates a weak electrical current within the target site using pulsed electromagnetic fields (PEMFs) or combined magnetic fields (CMFs). This type device uses either inductive coupling or capacitive coupling. With inductive coupling, PEMFs are delivered by a pair of external magnetic coils placed parallel to each other on top of the cast at the non-union site. When the stimulation is delivered through capacitive coupling, the electrodes are placed directly over the treatment site.

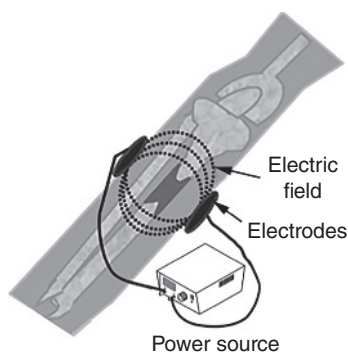
External bone growth stimulator is usually portable, lightweight, and powered by a battery. Patients feel no discomfort and may move about and complete their daily activities as they normally would with the device.

### ***Capacitive Coupling Devices***

These devices use an external power source generating potentials of 1–10 V at frequencies at 20–200 kHz and providing fracture site electric fields of 1–100 mV/cm. Stimulation with these parameters has shown to be efficient for bone stimulation. The treatment involves connecting the two wires from the power source to the electrodes that are applied on the skin at the fracture site of the bone to be stimulated. The capacitive coupling signal treats the bone fracture within the area of the electrodes as illustrated in Figure 57.1. The treatment provided by capacitive coupled devices is for 24 hours but requires daily changing of the battery. It is likely that the units may cause irritation of the skin from the electrodes. Capacitive coupling electrical stimulation is generally used for treatment of appendicular non-unions and spinal fusions. The mechanism of action with capacitive coupling is that the low voltage alternating current (AC) applied to the site increases the flow of calcium ions into osteoblasts, i.e. the cells that form a new bone. Figure 57.2 illustrates a typical capacitive coupling-based commercial device.

### ***Pulsed Electromagnetic Field (PEMF) Devices***

This type of device promotes healing by inducing weak pulsing electrical currents at the non-union fracture site as shown in Figure 57.3. The signals are generated by a low energy electromagnetic field created by passing specific electrical current pulses through a flexible treatment coil, which is externally applied to deliver the current. The

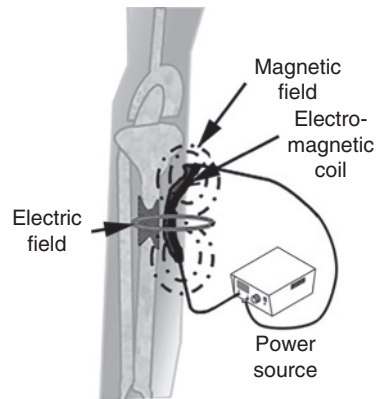


**Figure 57.1** Capacitive coupling method of bone healing.

**Figure 57.2** Noninvasive spine fusion stimulator system.



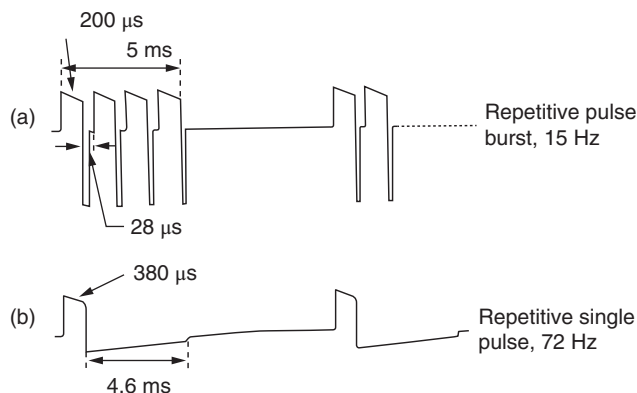
**Figure 57.3** Pulsed electromagnetic method of bone healing.



stimulating pulses are provided by a microprocessor-controlled unit, which is programmed to the patient's specific fracture needs. The signal generated by the control unit is a complex waveform that is often biphasic and quasi-rectangular, varying in amplitude and frequency as shown in Figure 57.4. Electromagnetic fields varying from 0.1 to 20 G have been used to create an electrical field at the fracture site of 1–100 mV/cm. The microprocessor and memory controls the level of the magnetic field as well as monitors and records the patient use.

The device operates on nickel metal hydride, rechargeable batteries that allows for its ambulatory use. The control unit contains the operating electronics and includes an audible and visible self-checking alarm mechanism to alert the patient if the unit is not functioning properly. It has a sufficient memory to store the patient's daily usage information, which can allow the physician to review their treatment regimen during the follow-up visit of the patient. A liquid crystal display (LCD) is used to display the device status regarding treatment record and daily treatment time countdown. The treatment coil is an encased wire coil that may be incorporated into a cast, over a cast, or brace, or when a cast is not utilized, may be applied directly to the skin. The coil receives the





**Figure 57.4** Typical shape of induced current waveform pulse burst: (a) wave train and (b) single pulse.

electrical current from the control unit and then delivers the therapeutic electromagnetic signal to the non-union fracture site. Figure 57.5 shows a typical PEMF device from M/s Biomet, United States. In semi-noninvasive devices, the control unit and the anode are placed externally, and the cathodes are inserted percutaneously into the fracture site.

When the coil is energized, it creates low level electromagnetic signals, which after reaching a fracture site are converted into an electrical signal in the bone. This enhances the treatment of non-unions, based on the bioelectrical principles of bone healing. In this way, the technique mimics the body's normal physiologic processes. Under the circumstances, when the human bone is bent or broken, it generates an electrical field. This low level electrical field activates the body's own repair mechanism, which, in turn, stimulates bone healing. The PEMF stimulators are designed to generate a uniform, low level PEMF similar to the electrical field generated by the body. The application of PEMF directly to the fusion site thus helps activate and augment the body's natural healing process to enhance bone fusion. A waist belt is provided to secure the treatment coil relative to the patient's fusion site during treatment.

The treatment system has been found to be very safe and has been widely adopted because of its proven success in the absence of any known risks. The treatment does not



**Figure 57.5** Bone healing system from M/s Biomet, United States, with flexible treatment coil.

require surgery and has no side effects. All areas of the body and all fracture types can be accommodated by the bone healing system. Furthermore, the treatment can be easily and conveniently done by patients at home.

### **Combined Magnetic Field (CMF) Devices**

CMF devices employ a combination of static direct current (DC) and AC to produce both static and time-varying magnetic fields produced by an external coil system. A magnetic field sensor placed in the middle of the coil monitors the static magnetic field and the sensor data is used to maintain the static magnetic field at 200 mG. The dynamic field is a sine wave, having a frequency of 76.6 Hz and an amplitude of 400 mG peak to peak, which is superimposed in parallel with the static field. The device is worn about 30 minutes daily. Patient compliance is ensured due to ease and brevity of the application. The device may be worn over a cast, external fixation, orthopaedic brace, or clothing without lessening its effectiveness.

A typical CMF device is the SpinaLogic® bone growth stimulator from M/s DJO, Vista, CA, United States, as shown in Figure 57.6. It consists of an electronic control box containing the signal generator, transducer coil embedded in the patient interface to match the curvature of the lumbar spine, and a battery pack. The patient interface also carries a magnetoresistive element to provide feedback as to the magnitude of the earth's magnetic field which ranges from 25 to 65  $\mu\text{T}$ . When projected in two dimensions, the shape of the interface is an ellipse with a major axis of 0.24 m and a minor axis of 0.19 m. It also includes a microprocessor and memory that controls the level of the magnetic field as well as monitors and records the use of the device by the patient. The status of the device is displayed on the LCD screen.

When the specified current is supplied to the coil, an extremely low frequency and extremely low intensity magnetic field is generated that combines both AC and DC components. Specifically, the magnetic field oscillates sinusoidally at a frequency of 76.6 Hz with an AC component of  $40.0 \pm 8.0 \mu\text{T}$ , peak to peak, and a DC component of  $20.0 \pm 2.0 \mu\text{T}$ .



**Figure 57.6** SpinaLogic bone growth stimulator. The electronic control module (ECM) and the transducer coil are shown. The module includes a signal generator that produces an electrical signal, which is transmitted to the treatment transducer. The transducer coil is an elliptically shaped copper wire coil that converts the electrical signal into an electromagnetic field. *Source:* Photograph Courtesy of M/s DJO, LLC USA.

The electrical signal is converted into a magnetic field by the transducer coil. The coil is so placed that it faces the spine and the magnetic field is directed at the fusion site. During treatment, the transducer coil is secured in place by the waist belt. A magnetic field sensor placed in the middle of the transducer coil monitors the static magnetic field and sends the information to the microprocessor. Using the sensor data, the microprocessor works to maintain the static magnetic field at 200 mG. The dynamic field is a sine wave, having a frequency of 76.6 Hz and an amplitude of 400 mG peak to peak, which is superimposed in parallel with the static field.

The main advantage of an external stimulator versus internal stimulator is that the external device is usually less expensive treatment option and does not require second surgery to remove the device. However, the disadvantage is that there may be less patient compliance with wearing the external stimulator, and if the patient does not wear the device, the benefits from the treatment will not be available.

A spine bone fusion stimulator, which applies both combined and pulsating magnetic fields has been introduced by M/s OrthoLogic Corp., Phoenix, Arizona, United States. The combined effect of this device, called the OrthoLogic 1000, offers the advantage that it needs to be worn just only 30 min/d, compared to 10 h/d with standard PEMF therapy. Also, the device uses magnetic fields that are of lower energy (peak amplitude 400 mG) than standard PEMFs (peak amplitude greater than 20 G). A stimulator for ambulatory applications that work on rechargeable battery has been is the Biomet® SpinalPak® Stimulator. The device has an audible and visible self-checking alarm mechanism to alert the patient if the device is not functioning properly. It is designed to store the patient's daily therapeutic treatment data, which may be downloaded and read with the patient compliance software. Ultrasonic bone growth stimulation has also been studied for accelerating healing of stress fractures.

A number of factors including age of the patient, health status, medical history, and bones condition affected by the damage are taken into consideration by the surgeon before deciding the use of internal or external stimulator. Other differences include the type of electrical current or magnetic field generated by the device and how stimulation is transmitted to the spine.

## Specifications

*Type:* Combined magnetic field

*Static magnetic field (DC):*  $\pm 200 \text{ mG} \pm 20 \text{ mG}$

*Operating range:* 400 mG peak to peak  $\pm 80 \text{ mG}$ , maximum 2% harmonic distortion at  $76.6 \text{ Hz} \pm 1.0 \text{ Hz}$

*Ambient magnetic field:*  $\pm 600 \text{ mG}$

*Power source:* 9 V battery

## Applications

The electrical bone healing systems are used for the treatment of fracture non-unions, failed fusions, and congenital pseudarthrosis.

## 58

### Bone Growth Stimulator: Implantable

#### Purpose

The implantable spinal fusion or bone growth stimulator is designed for use as an adjunct therapy to surgical spinal fusion procedure. Its purpose is to help enhance the body's bone healing process by providing stimulation through electrical and/or magnetic fields that is known to promote osteogenesis, which is the body's way of growing bony tissue. It thus facilitates the healing of non-union fractures and lumbar spinal fusions.

#### Principle

The invasive (implantable) devices are surgically implanted or stimulating current is directly given to the non-healing fracture or bone fusion site by surgical placement of electrodes. The cathode is placed at the site of the bone defect and the anode in the soft tissue close by. The stimulating direct current (DC) current at the cathode can be varied between 5 and 100  $\mu\text{A}$ . Usually, two to four stimulating electrodes are used. Since the stimulator is totally implanted, the treatment is continuous at the non-union site. Once the healing is complete, the stimulator can be removed as an outpatient procedure. Treatment with direct current has the advantage that the patient compliance required is minimal. However, the technique being invasive carries with it the risk of infection, tissue reaction, and soft tissue discomfort.

The stimulator consists of a waveform generator, either battery-powered or AC-powered, a user interface with visual and/or audible alarms, and electrodes or coils to deliver the stimulation at the desired site.

With internal or implantable bone growth stimulators, the device is usually implanted at the time of the spinal fusion surgery. The device is quite small and is implanted in a soft pocket of tissue under the skin in the lower back to the side of spine as shown in Figure 58.1. The specially designed electrodes are anchored near the bone and connected

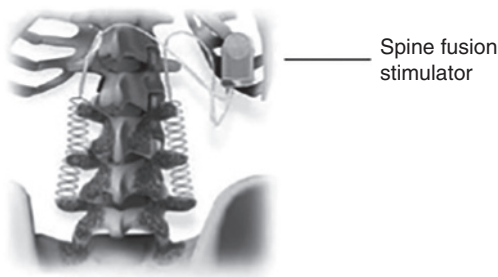
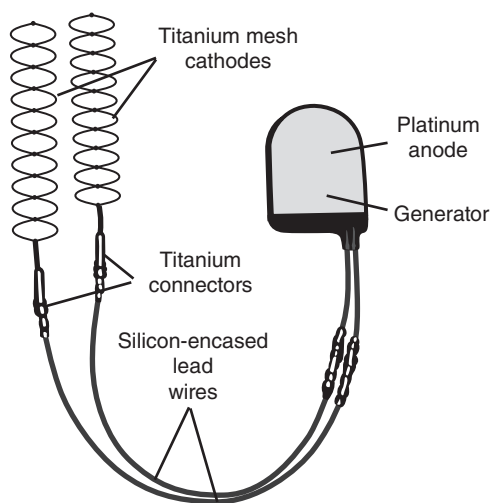


Figure 58.1 Spinal fusion implantable stimulator in place in the body.

to the stimulating pulse-producing circuit. Usually, direct current electrical stimulation is applied through surgically implanted cathode at the fracture site. By this method, constant stimulation is provided at the fracture site, but there is an increased risk associated with implantable leads.

A typical example of an implantable spine fusion stimulator is shown in Figure 58.2. The device consists of two titanium cathodes connected to a DC stimulation generator through dual silicone insulated lead wires. The generator electronics and the power source are encased in medical-grade titanium cover. A circular area on the generator plated with a  $5 \pm 1 \mu\text{m}$  thick platinum functions as the anode. The device is a constant current generator and the entire electronics circuitry is powered by a lithium manganese dioxide battery. The device produces constant current output for a minimum period of six months. The electronics and battery are hermetically sealed within the generator case to prevent leakage. The generator weighs just 10 g and has dimensions of  $45 \text{ mm} \times 22 \text{ mm} \times 6 \text{ mm}$ .

The device is available with either a 40 or a  $60 \mu\text{A}$  output signal. The lead wires, which are about 15 cm in length, consist of a silicone-insulated braided strand of stainless steel wire. These leads are attached to the generator and the cathodes with the help of titanium connectors that can be disconnected at either site. The cathodes are composed of insulated wire leads that terminate as bare wire leads, which are embedded in pieces of bone grafted onto the lateral aspects of fusion sites. There are two cathode configurations, which are the mesh and the preformed wave. The mesh-configured cathode is made from two strands of 0.01 in. diameter titanium wire formed into alternating loops and twists. The preformed wave is made from three strands of 0.01 in. diameter titanium wire. The use of each configuration is dictated by the specific fusion application and preference of the surgeon. The field of influence is approximately 5–8 mm around the cathode. An implant tester is provided with each device that allows to test the device intra-operatively prior to implantation. The main advantage of implantable stimulator is that the stimulus is provided constantly without the involvement of the patient so that



**Figure 58.2** Typical direct current spinal fusion implantable stimulator.

compliance is not a problem. However, it requires two operations, one to implant the implantable device and the other to remove the device when it has served its purpose.

## Specifications

*Output signal:* 60  $\mu$ A

*Over-current limit:* 70  $\mu$ A

*Generator case size:* 39 mm  $\times$  27 mm  $\times$  4.7 mm

*Weight:* 10 g

*Platinum-plated anode area:* 600 mm<sup>2</sup>

*Cathode size (wave configuration):* 1 cm  $\times$  4 cm

*Cathode size (mesh configuration):* 1 cm  $\times$  4 cm

## Applications

An electrical bone growth stimulator is applied as an adjunct to spinal fusion surgery to help enhance the chances of achieving a successful bone fusion. This is particularly recommended if the patient has risk factors for fusion and is vulnerable to bone healing problems.

# 59

## Bone Healing Stimulator: Ultrasound

### Purpose

An ultrasonic stimulator is a noninvasive device that is designed to emit low intensity, pulsed ultrasound to accelerate the healing time of a bone fracture. The ultrasonic waves produced by the device deliver mechanical pressure to the bone tissue at the fracture site, which is considered to promote bone formation in a manner comparable to bone responses to mechanical stress. Although low intensity pulsed ultrasound (LIPUS) has been in clinical use as a potential adjunctive therapy for accelerating fresh fracture healing, but its role both in terms of its mechanism of action and its efficacy in the clinical setting remains a subject of discussion.

### Principle

LIPUS has been extensively studied as a technique to accelerate healing of fresh fractures, delayed unions, and non-unions. Non-union is permanent failure of healing following a broken bone, which is a serious complication of a fracture and may occur when

the fracture moves too much, has a poor blood supply, or becomes infected. In such a case, the normal process of bone healing gets interrupted or stalled. A non-union that does go on to heal is called a delayed union.

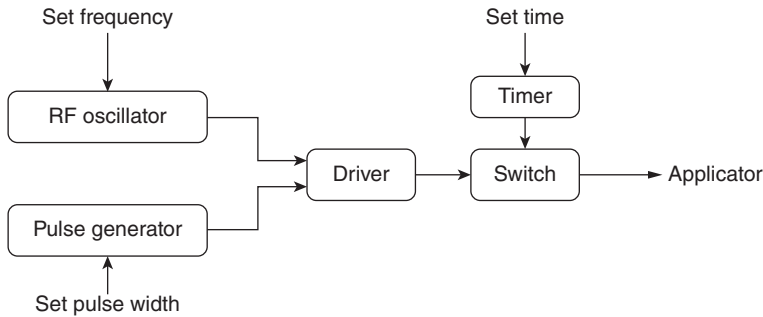
Although the exact biological effects of the ultrasound are still under study and investigation, the healing effects are generally attributed to the mechanical stress delivered to the bone by the acoustic waves. The numerous studies have suggested that ultrasonic stimulation enhances bone healing by increasing the incorporation of calcium ions in cultures of cartilage and bone cells and stimulates the expression of numerous genes involved in the healing process. The device is typically applied by the patients to the fracture site about 20 min/d until the fracture is healed. Since the device operates at an intensity of  $30 \text{ mW/cm}^2$ , which is much less than some diagnostic ultrasound equipment, there is no substantial increase in the temperature of the tissue. Thus, there is no need to move the probe continually by the operator, as is usually required for treatment with conventional ultrasound.

The ultrasound bone healing stimulator consists of two main components: (i) a signal generator and (ii) a small transducer mounted on a separate fixture strap and connected to the generator by a cable. The low intensity, pulsed ultrasound is generated by an ultrasonic stimulator, which is basically a noninvasive device. The strap is placed around the fractured bone, and the transducer is secured directly over the fracture site by a fixture on the strap. The ultrasound signal is emitted by a transducer that is applied to the skin surface at the fracture location using ultrasound conductive coupling gel. When the device is intended for use with cast immobilization, a hole is cut to allow access of the transducer to the skin. The device is programmed to deliver ultrasound in 20 minute sessions, which can be self-administered daily by the patient in their home. A typical commercial ultrasound-based bone healing stimulator is shown in Figure 59.1.

Several studies have been conducted to evaluate different ultrasound intensities and frequencies for bone healing, but most clinical studies have utilized an ultrasound signal frequency of 1.5 MHz, pulse at 1 kHz, and power level of  $30 \text{ mW/cm}^2$ . The radius of the transducer is 11 mm. The device delivers acoustic radiation in the form of pulsed, low intensity ultrasound as per the pre-programmed settings.

**Figure 59.1** Ultrasound-based bone healing stimulator.  
*Source:* Image Courtesy of M/s Bioventus, USA.





**Figure 59.2** Block diagram of an ultrasonic generator for bone healing stimulation.

Figure 59.2 is a simplified circuit diagram of the signal generator. The heart of the circuit is the radio frequency (RF) oscillator, which generates a signal whose frequency can be varied in the 1.5–2 MHz range. The pulse generator circuit produces pulses with a repetition frequency between 100 and 1000 Hz. The pulse width is also kept variable between 10 and 2000  $\mu$ s. The output of the oscillator and that of the pulse generator are both coupled to a driver circuit, which modulates the oscillator output with the pulse generator signal. The driver circuit also amplifies the resulting signal to provide sufficient power to the transducer. The transducer element is usually made of conventional piezoelectric material such as plumbium zirconium titante-4 (PZT-4). The transducer will give maximum coupling efficiency, if the front face of the transducer element is secured to a layer of araldite whose thickness is equal to one quarter of the wavelength. The timer circuit controls the time duration for which the treatment is to be given. An alarm circuit is included to alert the operator or the patient that the treatment is over.

## Specifications

*Frequency:* 1.5 MHz

*Pulse period:* 200  $\mu$ s

*Interval period:* 800  $\mu$ s

*Duty cycle:* 20

*Effective radiating area:* 3.88 cm<sup>2</sup>

*Spatial-averaged temporal-averaged intensity:* 30 mW/cm<sup>2</sup>

*Spatial-peak temporal-averaged intensity:* 65 mW/cm<sup>2</sup>

## Applications

Ultrasound bone healing stimulator finds applications to accelerate healing of fresh fractures, fusions, or delayed unions at some of the high-risk sites.



## 60

**Brachytherapy: Intravascular****Purpose**

Intravascular brachytherapy (IVB) is a minimally invasive technology that employs controlled dose of ionizing radiation ( $\gamma$  or  $\beta$  radiation) to treat discreet lesions within a vessel or stent. The objective of this treatment is to improve lumen patency and consequently arterial blood flow to reduce the chances of renarrowing (restenosis) caused by stent placement within the artery. This may result in the reduction of the need for multiple percutaneous interventional procedures. IVB is delivered via wires or catheters and has been mostly utilized in the coronary arteries. It is also sometimes referred to as intracoronary brachytherapy.

**Principle**

The field of brachytherapy has been in practice for decades in the field of radiation oncology for treatment of intracavitary and interstitial cancers, whereas IVB is a relatively new subspecialty dealing with small vessels. In the conventional brachytherapy, the target is mostly a few centimetres away from the radiation source, while in the IVB, the target (vessel wall) is just located within 1–5 mm from the radiation source. Intracoronary brachytherapy includes several techniques to deliver radiation locally to coronary blood vessels by means of catheters or stents.

***The Delivery System***

Beta-Cath 3.5F (1.17 mm) system has been a popular device from M/s Novoste, Norcross, Georgia, which is intended to deliver beta radiation to the site of successful percutaneous coronary intervention for the treatment of in-stent restenosis in coronary arteries with discrete lesions. It is a second-generation device, which has an equivalent radioactivity to the earlier 5F (1.59 mm) system but is smaller in diameter and fits easily inside a 1.91 mm guide catheter.

The device comprises four components: the delivery catheter, transfer device, the source train, and the system accessories. The sources are stored in a handheld transfer device and are advanced by a closed-loop hydraulic system that uses sterile water to send and then return the source train. The system is designed so that the transfer device and the delivery catheter are exclusively compatible. The purpose of *delivery catheter* is to provide the path through which the *source train* is delivered to and retrieved from the site of interventional injury. The *transfer device* stores and shields the source train when not in use and controls the hydraulic delivery and return of the source train during the treatment procedure.

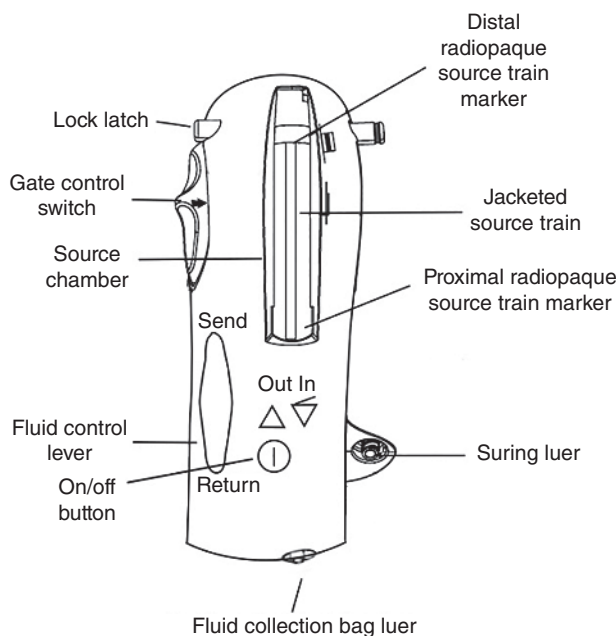
The *source train* consists of a wire jacketed series of individual, cylindrical, and sealed sources containing  $\text{Sr}^{90}/\text{Y}^{90}$  and an inactive radiopaque marker at each end. The source train provides the radiation dose during the treatment procedure.

The *system accessories* are the ancillary components of the system that ensure sterility and facilitate operation of the system and allow temporary storage of system components in the event of a disrupted clinical procedure and enable transport of the system components.

Figure 60.1 shows a simplified diagram of a typical delivery device Beta-Cath 3.5F from M/s Novoste, Norcross, United States. This is a handheld battery-powered device that is used to store the radioactive source train. The device can carry the source train of only one length. This implies that three separate delivery devices would be required if it is desired to accommodate the 30, 40, and 60 mm source trains. The movement of the source train into and return from the delivery catheter is controlled using hydraulic pressure. A number of pressure sensors are used that provide the feedback on the pressure to send, hold, or return the source train. The fluid flow and direction of the source train movement is controlled by a fluid control lever. A treatment counter tracks the number of procedures or test runs completed. The system allows a maximum of 125 transfers. Source train transfer depends on hydraulic pressure. Several electronic pressure sensors are used to provide the operator with feedback on the pressure required using a saline-filled syringe to send, hold, or return the source train.

### Radioactive Source

The system employs Strontium-90/Yttrium-90, which is a pure beta emitter with maximum energy of 2.27 MeV and an average of 0.934 MeV. The long half-life (29.1 years) of the source facilitates treatment planning as the dose rate remains almost unchanged



**Figure 60.1** Various controls on the Beta-Cath 3.5F system of M/s Novoste, Norcross, United States.

during the life cycle of the device (six months). Each seed is 2.5 mm long and 0.38 mm in diameter for the 3.5F system. The radioactive source train consists of a quartz source container for shielding and a hydraulic system operated by an external syringe. It is a wire jacketed 'train' having 12 (30 mm source train), 16 (40 mm source train), or 24 (60 mm source train) seeds, each 2.5 mm. The jacketed design is a major improvement over the initial design to eliminate seed movement that provides uniform dose distribution. A radiopaque mark is provided on each side of each source train to provide visualization under fluoroscopy.

### ***Delivery Catheter***

The delivery catheter comes in two diameters, with an outer diameter of 5F (slightly less than 2 mm in diameter) and 3.5F (just more than 1 mm in diameter). The 5-F system comes in three lengths of 30, 40, and 60 mm source trains, while the 3.5-F system comes in only two lengths of 30 and 40 mm. In the 3.5F system, the source delivers beta radiation through a closed-end catheter with a total length of 180 cm and diameter of 1.6 mm. A catheter with a longer length of 267 cm is also available. The catheter has three lumina: the first contains the guide wire, the second is for transportation of the sources to the distal tip, and the third is for the return fluid. By pressing the syringe on the delivery device, the source can be advanced to the distal tip.

When the return lever is operated, the fluid is passed through the third lumen and the source train is retacked to the quartz container. All source train lengths (30, 40, or 60 mm) that reach most distal radiopaque marker located inside the delivery catheter can be accommodated in the catheter. The catheter is preloaded with an indicator of source train, which is used for the nonradioactive dummy source. This helps in the measurement and positioning of the delivery catheter to ensure adequate radiation coverage. The delivery catheter is connected to the delivery device with a special proprietary connector. The dose prescription is given relative to the source axis at 2 mm radial distance.

The device is equipped with a long-life user-exchangeable battery, device sensors, indicators, and electronic interlocks for safety. Safety interlocks are designed to ensure jacketed radiation source train containment. Jacketed source train allows uniform unit dosing with vessel conforming and proprietary fast hydraulic movement. All fluids are contained in a closed system. The advantage of the system is the relatively short treatment times (three to five minutes) and the absence of radiation exposure to catheterization laboratory staff.

## **Specifications**

*Jacketed radiation source train*

*Isotope:* 90 Strontium

*Half-life:* 28.8 years sealed source

*Dimensions:* 2.5 mm × 0.38 mm (length × diameter)

*Source train jacket:* Stainless steel

*Delivery catheter*

*Total length/working length:* 180 cm/135 cm

*Outer diameter:* 3.5F (1.17 mm/0.046 in.)

## Applications

Intravascular coronary brachytherapy can help reduce the rate of restenosis after angioplasty procedures, may prevent narrowing of the arteries or grafts after stent insertion, or bypass grafts.

# 61

## Brachytherapy Machine

### Purpose

Brachytherapy is a procedure of treating cancer by inserting radioactive material directly into the affected area. The method allows a high dose of radiation to be given to the tumour, while reducing the radiation exposure in the surrounding healthy tissues. In a way, brachytherapy is radiation therapy delivered at a short distance from the tumour. It is localized, precise, and comparatively safer when compared with the conventional form of external radiation therapy that projects radiation from a machine outside the body. So, brachytherapy may cause fewer side effects than does external beam radiation.

### Principle

Brachytherapy is one form of radiation therapy for treatment of cancer. Radiation therapy involves the use of ionizing radiation, to kill cancer cells and shrink tumours. The radiation therapy is conventionally delivered externally involving high energy X-ray beams generated by a machine by directing the beam at the tumour from outside the body. This is known as external beam radiation therapy (EBRT). Brachytherapy, on the other hand, is internal radiation therapy, allowing a physician to use a higher total dose of radiation to treat a smaller area placing a radioactive material directly inside or next to the tumour. The treatment takes shorter time than is possible with external beam radiation treatment. While treating cancer, it is essential that the radiation treatment to be tightly focused on tumours to minimize serious side effects. Brachytherapy allows the maximum radiation dose to be given to cancerous tissues while minimizing exposure to the surrounding healthy tissue.

Most brachytherapy is performed by  $\gamma$  rays in the photon energy range from 20 keV to 1.0 MeV. Brachytherapy thus involves radiation sources that produce  $\gamma$  rays, which have the

same effect on cancer cells as X-rays. The  $\gamma$  ray sources are encapsulated in an inert non-radioactive metal that filters out low energy photons and  $\alpha$  and  $\beta$  particles. Different types of radioactive material may be used according to the type of brachytherapy. Common types of radiation sources used in brachytherapy are iodine, palladium, cesium, and iridium.

### **Types of Brachytherapy**

There are three different forms of delivering brachytherapy treatment: (i) interstitial, (ii) intracavitary, and (iii) skin therapy. In *interstitial* brachytherapy, the radioactive sources are implanted inside and throughout the affected site such as the prostate or breast. In *intracavitary* brachytherapy, the sources are placed in the body cavities very close to the tumour such as the cervix, uterus, or vagina. It could even be a body lumen such as the trachea or oesophagus. The radiation source can also be placed in the blood vessels such as for the treatment of coronary in-stent restenosis, known as intravascular brachytherapy. In *skin* therapy, the sources are placed directly on the skin surface.

### **Dose Rate**

The dose rate of brachytherapy is defined as the intensity at which the radiation is delivered to the surrounding medium. It is usually expressed in grays per hour (Gy/h). The dose rate is categorized into the following types:

*Low-dose rate (LDR) brachytherapy:* Consists in implanting radiation sources that emit radiation at a rate up to 2 Gy/h. Low-dose-rate interstitial and intracavitary implants are usually temporary. It means that the radioactive sources are left in place for a period of time, usually a few days, and then removed. When the implants are permanent, they are left in place without removal. Here, small radioactive 'seeds' are permanently implanted near or in the tumour. The radioactive material is typically placed by hand or machine under guidance of an imaging technique, such as ultrasound or computed tomography (CT).

*Medium-dose rate (MDR) brachytherapy:* The dose rate involved is between 2 and 12 Gy/h.

*High-dose rate (HDR) brachytherapy:* The rate of dose delivery exceeding 12 Gy/h is termed as high-dose rate therapy. Most of the high-dose-rate brachytherapy treatments are temporary and the radiation sources are administered using discrete fractions. They are removed from the patient at the end of each treatment session. The technique is preferred for more high-risk but localized cancers. The radioactive material is inserted into the brachytherapy device with the help of a computer-controlled machine.

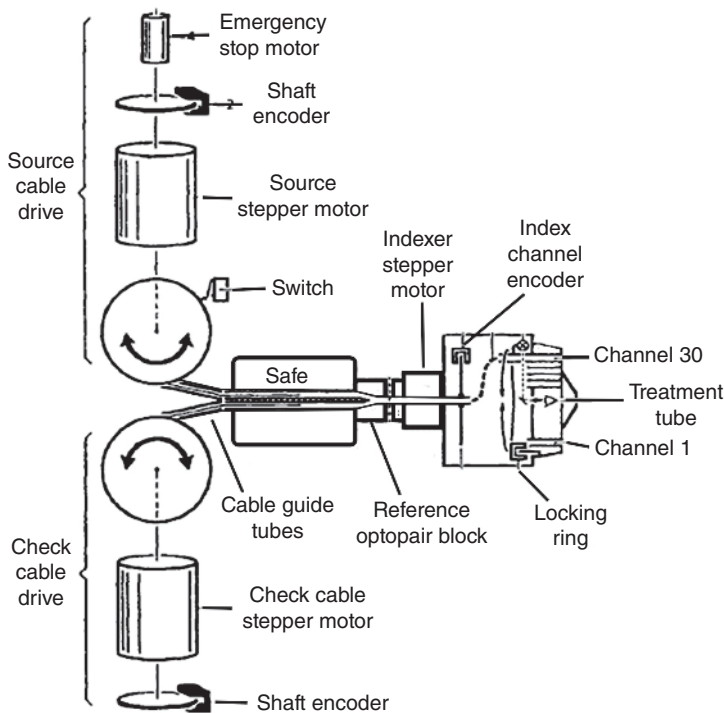
### **Treatment Delivery**

The radiation sources encapsulated within a non-radioactive capsule can be delivered to the site manually. However, manual delivery of brachytherapy is generally discouraged due to risk of radiation exposure to clinical staff. A more common delivery procedure involves the use of a technique termed as '*afterloading*' which involves the accurate positioning of non-radioactive applicator in the treatment site, which is subsequently loaded with the radiation source. This is known as the remote afterloading system (RAL).

The RAL is a computer driven system that transports the radioactive source from a shielded safe located inside the afterloader directly into the applicator placed into or next to the tumour in the patient. A computerized treatment planning program calculates the source position and the amount of time needed to deliver the desired dose of radiation to the tumour and precisely how long the source has to stay and radiate at the target position. The source is driven back into the safe upon termination or interruption of the treatment. X-rays, ultrasound, MRI, or CT scans are generally employed to assist the physician in positioning the radiation source. This process is only performed once staff members are removed from the treatment room. The device may move the source by one of several methods, most commonly pneumatic air pressure or cable drives. These systems provide protection from radiation exposure to healthcare professionals by securing the radiation source in a shielded safe.

### Afterloading Machine

Figure 61.1 illustrates a schematic of the HDR RAL. The heart of the system is the *shielded safe* that contains the radiation source and provides the desired dose rate. HDR brachytherapy employs a high intensity radiation source, which is passed through needles to the tumour site. The radioactive source in an HDR RAL is usually 3–10 mm in length. The safe is provided with adequate radiation shielding to house the source while not in the treatment mode. Once the treatment mode is initiated, the source is driven



**Figure 61.1** Schematic diagram of a single stepping source remote afterloading system (RAL).

out of the safe according to a planned program. In case the treatment is terminated due to any reason, the source is driven back to the shielded safe.

Source drive mechanism consists of a stepper motor connected to the reel containing the drive cable guide tube. When a command is issued to initiate the treatment, the stepper motor moves and causes the source cable to advance from the shielded safe. The source moves along a path constrained by transfer tubes to the first dwell position in the applicator. The source remains at that position for a predetermined dwell time as determined by the treatment planning system. After completion of the dwell time, the source goes on to the next dwell positions and then to the target position.

When the treatment is complete, the source is retracted into the safe. In a multichannel system, the source is then redirected to travel to the second channel. The process is repeated for all the subsequent treatment channels. A typical machine may have 6 channels, and the system can be upgraded to 18 or 30 channels. An optical encoder is used to verify the programmed movement of the source. The encoder compares the angular rotation of the stepper motor or cable length ejected or retracted with the number of pulses sent to the drive motor. The obstruction or constriction in the catheter can be detected from the

increased friction in the cable movement. If a fault develops and the stepper motor fails to retract the source, a high torque direct current (DC) emergency motor comes into action to retract the source. The exit from and return of the source to the safe is confirmed by using photoelectric sensor comprising of an infrared source and light-sensitive detector. The afterloaders are mostly equipped with check cables or dummy sources to check the integrity of the catheter system with an exact duplicate of the radioactive source. After a successful 'dry run' with the dummy source, the radioactive source is then pushed to the site for treatment.

An array of applicators are available for different applications and treatment sites. Their designs vary from vendor to vendor corresponding to the design of their transfer tubes and HDR RALs. The source travel and dwell sequence to be used in each channel can be selected by the operator from the treatment control console. Since the machine contains high intensity radioactive sources, they are provided with many safety features and operational interlocks to prevent undesirable source movement and safeguards against system failure.

A typical multichannel scalable afterloading machine to meet the evolving needs of brachytherapy centres consists of the treatment unit, remote treatment monitoring, and control devices, as well as quality assurance tools. The basic machine can be of six treatment channels, for example, and scale up to 18, 30, or even 40 channels as the need arises. With the 40-channel configuration, large implants for interstitial breast or prostate treatments can be performed without needing to reconnect catheters during treatment.

The treatment unit's forward stepping source ensures that the radioactive source is precisely placed at the defined dwell positions and that no unnecessary radiation exposure occurs at the tip of the treatment channel, thus ensuring the safety of the procedure. The source is paused at dwell positions every 2.5, 5, or 10 mm, depending on the clinical preference. The source movement is precisely controlled resulting in positioning of the source with an accuracy of  $\pm 1$  mm at each dwell position.

The operation of the machine involves first placing thin catheters in the tumour. The catheters are then connected to the HDR afterloader. The machine contains a single highly radioactive iridium pellet at the end of a wire. The pellet is pushed into each of the catheters one by one under computer control. The computer controls how long the

pellet must stay in each catheter (dwell time) and where along the catheter it should pause to release its radiation (dwell positions). With a few well-placed catheters in the tumour, a very precise HDR brachytherapy treatment can be provided that takes only a few minutes. After a series of treatments, the catheters are removed, and there are no radioactive seeds left in the body.

These devices have a subsystem comprising a shielding safe for storage of the radioactive source when not in use, drive mechanism and channel selection mechanism, and controlling electronics, which is connected to a personal computer for the entry of treatment program data. All these devices are using a radioactive source sealed in a stainless steel capsule connected to a stranded cable.

A typical example of remote-controlled brachytherapy afterloading system is Flexitron from M/s Elekta, Sweden, which is shown in Figure 61.2. It comprises of the following:

*Treatment delivery unit (TDU):* It houses the radioactive source in its built-in shielding safe, the microcomputer-controlled driving mechanism and channel selector mechanism.

*Treatment communications console (TCC):* For treatment program data entry, data storage, and data displaying.

*Treatment control panel (TCP):* It comprises the basic operator elements for start and stop treatment and for displaying device status and used and remaining treatment time.

The TDU houses the shielding safe for storage of the radioactive source and the source drive mechanism for moving the radioactive source into treatment positions within an applicator and back into the safe. There is a channel selector mechanism for selecting one out of 40 treatment channels. The TDU source drive mechanism and the channel selector mechanism are controlled by microprocessor-based electronics.



**Figure 61.2** Brachytherapy treatment unit – Flexitron. *Source:* Photo Courtesy of M/s Elekta Sweden.



Sensors are applied and their signals are input for the embedded microprocessor for safe and reliable operation. The TDU is designed for positioning the source at 401 separate dwell positions in each of the 40 treatment channels, and together with dwell time settings for each individual dwell position, it enables the creation of isodose shapes targeted to the patient's anatomy and geometry in order to irradiate the target patient body site and spare the healthy surrounding tissue.

Dwell positions can be programmed at 1 mm intervals. The maximum source out-drive distance is 1400 mm from the channel selector front plate. Dwell times are programmable with increments of 0.1 second. Maximum dwell time is 999.9 seconds per position. Minimum dwell time is 0.1 second per position. A dwell position is skipped if its dwell time is 0 second. Before the radioactive source is moved into a treatment channel, a check cable is first moved into it. A check cable is of a similar construction of a source cable, but without radioactive isotope. It is a measure to check the treatment channel for free passage of the source immediately after the check.

The TDU is connected to TOO via a serial data communications link to receive the patient treatment program and to return data of the performed patient treatment. TOO allows for manually entering a patient treatment program or for electronically transferring a patient treatment program from Brachytherapy Treatment Planning System. During patient treatment TOO displays treatment progress and logs patient treatment data and machine performance data in separate log files. TDU is connected via another serial communications port to TOP. TOP is a touch screen device that is directly controlled from the TDU embedded microprocessor. TOP allows for starting the patient treatment when all conditions are fulfilled.

The Flexitron device has built-in provisions for operation with two radioactive sources and one check cable. The channel selector mechanism enables the use of check cable and two radioactive sources simultaneously. The Flexitron device contains an appropriate dimensioned shielding safe and appropriate shielding capability for housing two sources.

## Specifications

*Sources:* 10 Ci of  $^{192}\text{Ir}$

*Source dimensions:* L 3.5 mm; OD 1.1 mm

*Number of channels:* 18

*Source extension:* 1500 mm

*Source step size:* 2.5, 5, or 10 mm

*Dwells per channel:* 48

*Speed of source:* 50 cm/s

## Applications

Brachytherapy HDR RAL systems are mostly used to treat gynaecological cancers but also tumours of the prostate, breast, oesophagus, lung, and bronchus, as well as the lip and oral cavity. The technique can be used alone or in conjunction with other cancer treatment procedures such as EBRT.

## 62

### Breast Biopsy System

#### Purpose

A breast biopsy system is used to obtain a small amount of breast tissue from a suspicious area in the breast for diagnostic purposes. The diagnosis is done under a microscope in a laboratory. Breast biopsy is a procedure to establish or negate the presence of cancerous cells in the breast. The biopsy is performed surgically or, more commonly, by using a hollow needle under image-guidance. This is a less-invasive technique, which is usually done by a radiologist. The biopsy provides the ability to obtain samples of tiny abnormalities that can assist in early detection and accurate diagnosis of cancerous or benign cells.

#### Principle

There are several procedures for performing breast biopsy for obtaining a tissue sample from the breast. The particular procedure is chosen based on the size, location, and other characteristics of the breast abnormality. The following are the commonly used procedures:

*Fine-needle aspiration biopsy:* This method involves the use of a very thin, hollow needle attached to a syringe that is used to withdraw or aspirate a small amount of tissue from a suspicious area. The extracted fluid can then be examined by a pathologist to confirm whether the abnormality is benign or cancerous. The needle used for fine needle aspiration biopsy is usually much thinner than the one used for blood tests in the clinical laboratory.

*Core needle biopsy:* This method makes use of a larger needle to sample breast abnormalities observed in ultrasound scan or mammogram or felt by the doctor. The needle is inserted into the lesion through a small skin incision made by the physician. The modern method to do a core biopsy is known as vacuum-assisted procedure.

*Image-guided biopsy:* Minimally invasive biopsies are conducted using computer-generated images to accurately identify breast abnormalities. This enables the physician to exactly pinpoint and map the area to be biopsied, without making large incisions. Three imaging techniques are usually employed for breast biopsies: (i) stereotactic X-ray, (ii) ultrasound, and (iii) magnetic resonance imaging (MRI).

*Stereotactic biopsy:* Stereotactic breast biopsy is a procedure that employs mammographic X-rays to precisely identify the area of concern and to assist in guiding the biopsy needle to the precise location. This method ensures that the area that is biopsied is the exact area where the abnormality had been observed on the mammogram. The technique is known as stereotactic because it requires two images to be taken

from slightly different angles of the same location. Two different types of needles are used to collect samples of breast tissue in the stereotactic technique: (i) a vacuum-assisted device (VAD) that can suck out several cell samples with only one insertion and (ii) a core needle that collects one sample of breast tissue per insertion.

*Ultrasound-guided core needle biopsy:* This method uses core needle biopsy whose insertion is guided by an ultrasound imaging system that produces precise images of body structures. The procedure is performed on patients in an upright or reclined position. A handheld ultrasound transducer is used, which is moved back and forth across the breast to generate images of the abnormal breast tissue. While viewing the images on a computer monitor, the doctor will make a small incision to insert the needle into the breast to retrieve sample tissue specimens.

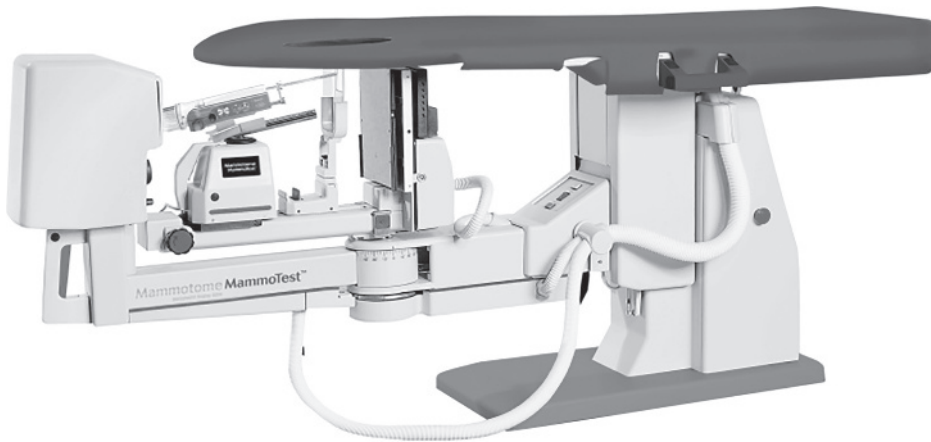
*MRI-guided core needle biopsy:* This is again a core needle biopsy technique done under guidance of an MRI that is capable of capturing multiple cross-sectional images of the breast and combines them, using a computer, to generate detailed 3D pictures. The MRI images allow to determine the exact location for the biopsy.

*Vacuum-assisted biopsy:* Vacuum-assisted biopsy method is a percutaneous ('through the skin') procedure that depends upon stereotactic mammography or ultrasound imaging for guiding the biopsy needle. Stereotactic mammography is based on the use of mammograms (X-rays) taken from two different angles and displays real-time images on the computer monitor screen to pinpoint the exact location of a breast abnormality. The computer coordinates of the abnormality as seen on the screen assists the physician to guide the needle to the exact location in the breast. Similarly, with ultrasound, the radiologist can watch the needle on the ultrasound monitor to help guide it to the area of interest.

A small incision or cut is made in the skin, and a special biopsy needle is inserted into the breast. By using a vacuum-powered instrument, several tissue samples can be taken. The vacuum draws tissue into the centre of the needle while a rotating cutting device takes the samples. The samples are retrieved from the centre of the biopsy needle following the procedure and sent to a laboratory for examination. The biopsy procedure is performed under any of the imaging guidance methods such as mammogram, MRI, or ultrasound. The method allows the area of abnormality to be precisely identified using imaging guidance so that only samples from the region of concern are removed.

### **Instrumentation**

Vacuum-assisted breast biopsy systems are available commercially. They are usually referred to by the brand name. For example, Mammotome is the brand name of the system produced by M/s Devicor Medical Products, Inc. as shown in Figure 62.1. The system comprises of a disposable sterile probe and a reusable, non-sterile driver. A piercing tip is mounted at the distal end of the probe to penetrate breast tissue. The sterile probe also contains a tissue sampling chamber with a vacuum line at its bottom. The chamber is located just below the tip and opens along one side of the probe shaft.



**Figure 62.1** Mammotome breast biopsy system. *Source:* Image courtesy of M/s Leica.

The Mammotome uses a vacuum system that draws tissue into a sampling chamber, a rotating cutter that excises the tissue, and a second vacuum system that transports tissue back through the probe without the need to withdraw it each time. The aperture can be rotated 360°, allowing for multidirectional tissue sampling. After rotation of the probe, the process is repeated until samples are harvested in all directions around the needle tip. The system allows for a single needle insertion yielding large tissue cores without fragmentation. The procedure can be done under ultrasound guidance, where tissue acquisition can be monitored by ultrasound, as well as stereotactic method.

The system has a control unit that maintains aspiration at constant values (23–25 mm/Hg), and of a driver where a 8–11G needle is placed. The system is linked to a computer where calculations are done regarding radiographic acquisitions according to stereotactic geometry principles, numerical values regulating placement, and excursion of the needle to the lesion are transmitted to the driver. Figure 62.2 is a typical vacuum-assisted Mammotome biopsy probe system.

The system works under the control of a microprocessor. The other important system components comprise of LCD controller, motor controllers, and motor and solenoid drivers. The vacuum is controlled through a closed-loop control circuit consisting of a vacuum sensor, which helps in maintaining vacuum through



**Figure 62.2** The Mammotome biopsy probe. *Source:* Image courtesy of M/s Leica Biosystems, Deutschland GmbH Germany.

appropriate feedback. One motor drives the cutter rotation and another motor drives the cutter translation. A motor watchdog stops each motor in the event of a motor driver failure.

A new development in the field of breast biopsy is the 3D real-time biopsy machine. This machine allows to take many frames/second with additional mini oblique views,  $\pm 1.5^\circ$  with respect to major oblique view that could be either  $+15^\circ$  or  $-15^\circ$ . The  $+15^\circ$  or  $-15^\circ$  provide a good stereo view of the tip of the needle and the area of interest. The swinging of  $\pm 1.5^\circ$  provides two additional views around the stereo axis of  $\pm 15^\circ$ . When these two images are combined on a special monitor and using special glasses, the image of the compressed breast as 3D volume with the needle in position can be observed. The intervention is quicker and simpler and causes less stress on the operator and trauma on the patient.

Some biopsy devices such as Mammotome MammoTest from M/s Devicor Medical Products, Inc. offers a complete X-ray-based biopsy workstation that uses stereotactic positioning technique. The system comprises of a table and a built-in X-ray unit as well as a processor for exact localization of suspected tissues. The table enables optimal positioning of the patient through manual adjustment of the horizontal and vertical positions as well as motorized height adjustment. The biopsy device can be positioned precisely under the computer-controlled guidance system. The system permits  $360^\circ$  needle access to the entire breast.

There are several advantages of performing breast biopsy with a VAD. Due to small size of the probe, the incision is just about the size of a match-head. Further, this technique allows several samples to be acquired through one incision, resulting in a highly accurate breast cancer diagnosis. Also, a breast biopsy with this device can be performed in an outpatient setting, and the entire procedure generally takes less than an hour. It is a patient-friendly technique that causes minimal pain, scarring, and recovery time for the patient.

## Specifications

*Needle length (without cannula):* 136.0 mm

*Needle length (with cannula):* 122.0 mm

*Needle diameter:* 2.6 mm

*Aperture length:* 18.4 mm

*X-ray generator:* High frequency, automatic exposure control, kV range: 20–35 kV; mA range: 15–125 mA

*X-ray detector:* CsI, size 5 cm  $\times$  5 cm, image matrix: 1024  $\times$  1024

*Display:* 19 in. TFT colour display, image matrix: 1280  $\times$  1024

## Applications

The breast biopsy system finds applications in the radiotherapy departments and are intended to provide breast tissue for histological examination for diagnosing any abnormality in the breast.

## 63

### Breast Pump

#### Purpose

A breast pump is a mechanical device that is designed to extract milk from the breasts of a lactating woman. The purpose is to collect the milk so that the baby can have it when the mother is not around. The pump is also useful if the baby cannot latch or feed directly from the breast. In that case, the milk can be pumped and the baby can be given breast milk from a cup or bottle. Pumping also means that the woman need not be on call for every feeding even when at home. There are many more reasons in using the breast pump. For example, the woman could be suffering from mastitis or need to drain the breast to help healing.

#### Principle

A breast pump works by creating and releasing suction on the nipple, which draws milk out from the breast. Breast pumps may be manual devices operated by hand or foot movements or electrical devices powered by electricity or batteries. A well-designed breast pump mimics the sucking action of a baby and does not cause pain during its operation. Some breast pumps allow the milk to be collected in the same bottle that will feed the baby eliminating the need to transfer the breast milk. All breast pumps have a breast shield or a flange that cups the breast. The shields are available in varying sizes depending on the type of pump. It is important that the right size of the shields is chosen suitable for the nipples. Several types of breast pumps are available in the market, but technically they fall into the following two categories:

*Manual breast pumps:* Manual breast pumps use a pressing motion and create the suction for these pumps with a hand. They are operated by squeezing or pulling a handle in a repetitive fashion, which allows the user to directly control the pressure and frequency of milk extraction. Some pumps are easy to operate with one hand, while others require two hands. Although manual pumps are small and inexpensive, they can be tiring as they require significant effort to operate. The breast pump must be noiseless and small, preferably about the size of a bottle, making it a good choice for travel or for occasional pumping. They also allow for only one breast to be pumped at a time. Foot-powered breast pumps, which use the same collection tubing and breast horns as electric breast pumps, are powered by a foot pedal. This avoids the need for an electrical supply with privacy.

*Electric breast pumps:* These pumps are operated by a motor that creates suction through plastic tubing to a horn that fits over the nipple. The electric pumps provide higher levels of suction making the pumping action much faster. The pump also allows pumping of both breasts at the same time. Electric breast pumps are in general

much larger than manual pumps, but portable versions are also available. Some electric pumps are intended for multiuser operation, which requires only an additional kit for each user. The parts of the pump coming into direct contact with the milk are sterilizable for preventing contamination.

The electric breast pumps may be of open or closed collection systems. However, most electric breast pumps are of *open collection* type that allows for the free passage of air/suction and results in more flow of air/suction. Here, the suction is directly passed to the mother's breast unlike indirectly with closed diaphragm systems. The system incorporates bacterial and viral filters to prevent any contamination or overflow into pump motor. These pumps are considered more effective by most women as they can compensate better for different tissue elasticities and sizes and shape of the breast. The open collection systems are single-user devices, and their usage virtually eliminates the chance of cross-contamination of the pump from mother to mother. The cross-contamination is also protected as the parts that generate the suction are external to the pump.

A *closed collection system* includes a barrier or diaphragm that separates the pump tubing from the horn. The milk is extracted due to vacuum created by lifting of the diaphragm by the pump motor. The diaphragm removes the possibility of milk to overflow into the pump tubing. In the closed collection systems, the milk is not exposed to the pump motor or air, and therefore, these systems are considered as more hygienic than open collection systems. However, the diaphragm must be cleaned as condensation or milk may cause bacterial contamination, defeating the very purpose of the closed system. Electric breast pumps are of two types, for personal use and hospital grade pumps:

*Personal electric breast pumps:* These portable pumps are usually battery operated and come with a carrying case so that they can be taken to the workplace. The pumps may have battery packs or built-in batteries. Most of the pumps have a cooler storage for transporting unused milk back home. The device can have a single or double pumping arrangement.

*Hospital grade electric breast pumps:* These are heavy-duty pumps and are equipped with powerful motors that allow a greater amount of 'sucks' per minute. They are larger in size and are intended for multiple users. They are suitable for initiating lactation and building milk production. The double pumping system has the advantage of saving time, as the woman is able to express milk from both breasts at the same time. A typical hospital grade pump is shown in Figure 63.1.

The use of an electric breast pump is quite simple. A breast shield or flange is put over the nipple, and the machine is turned on. The machine will start sucking the milk into an attached container. The flange is made of soft silicone that provides a secure seal and comfortable fit for more efficient pumping. The pump uses two-phase technology by providing stimulation and expression modes. Stimulation mode gently stimulates the breast to initiate milk flow and expression mode to maximize milk flow. The pumps allow adjustable suction levels with selectable suction speed. It usually takes 10–15 minutes to pump both breasts with a good electric pump and up to 45 minutes with a hand pump. The pumps are microprocessor based, and the digital controls allow to set the pumping program to the speed and rhythm most effective for a particular action.



**Figure 63.1** Hospital grade breast pump.



## Specifications

*Vacuum range:* 0–300 mmHg

*Cycle length:* 38–54 rpm

*Weight:* 2 kg

*Motor life:* 1500 hours

## Applications

The breast pumps are used by women for several reasons. The most important use of the pump is to express breast milk, which can be later bottle fed to their child by a caregiver. Also, a breast pump may be used to relieve engorgement, a painful condition whereby the breasts are overfull, possibly preventing a proper latch by the infant. The pump may also be used if the baby does not latch properly, or cannot nurse for physical reasons. Expressing milk for donation is another use for breast pumps.

# 64

## Bronchoscope

### Purpose

A bronchoscope is a device that is designed to see the inside of the body airways and lungs. Bronchoscopy plays a key role in the diagnosis and treatment of pulmonary disease.



The procedure helps to diagnose, and often to treat, various conditions of the airways and lungs. For example, a bronchoscopy can enable the clinician to deliver medication to the lungs or remove an object that is caught in the airways, like a piece of food. Laser therapy via the bronchoscope allows treatment of obstructive endobronchial tumours.

## Principle

A bronchoscope allows the doctor to view all of the structures that make up the respiratory system. These include the larynx, the trachea, and the smaller airways of the lungs, which include the bronchi and bronchioles. The bronchoscopy procedure consists in putting the bronchoscope (a thin lighted tube) in the nose or mouth and moving it down the throat and trachea (windpipe), and into the airways. The clinician can then see the voice box (larynx), trachea, large airways to the lungs (bronchi), and smaller branches of the bronchi (bronchioles). Pulmonary infection is a major cause of morbidity and mortality, and bronchoscopy enables quick access to secretions and tissue for diagnosis.

There are two types of bronchoscope: rigid and flexible. Earlier, rigid bronchoscopes were used. However, flexible bronchoscopes have now become more popular and are mostly used in practice.

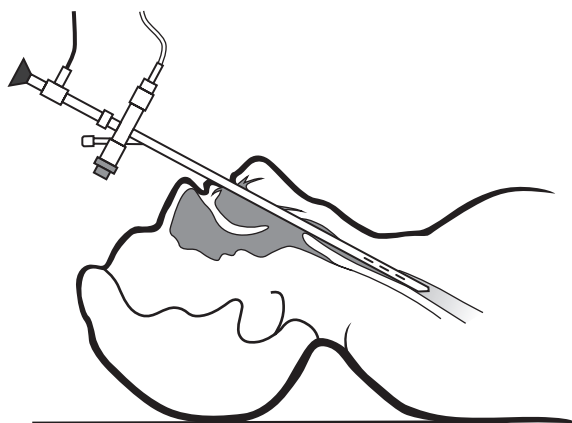
### *Rigid Bronchoscope*

The rigid bronchoscope has three main components: the barrel, the multifunction head, and the optics including light source.

**The Barrel** *The barrel* is a straight, rigid hollow metallic thin tube having the same diameter from the proximal to the distal end, although some may have a bevelled or tapered distal tip. Most rigid bronchoscopes are round, while a few are of oval shape when visualized in cross-section. A small internal channel is provided in some rigid bronchoscopes, through which the rigid telescope passes. Others are simply an empty tube. The proximal end of the scope is connected to the multifunction head that permits ventilation and instrument access. The light source is attached to the proximal end of the device or to the telescope lens directly depending on the design of the device.

Rigid bronchoscopes are available in various lengths that range from 33 to 43 cm. A very short tube is employed for paediatric cases, and a long or extra-long tube is used for adults. The inner diameter of the adult rigid bronchoscope varies from 7 to 13 mm, while the external diameter ranges from 2 to 14 mm and wall thickness from 2 to 3 mm. The size of the bronchoscope plays a crucial role in making clinical decisions in bronchoscopy. The rigid bronchoscope operates with several accessories such as graspers, dilators, biopsy forceps, stent delivery devices, catheters, and suction devices.

**The Multifunction Head** The multifunction head connects to the proximal portion of the barrel. The head has separate ports for ventilation and procedural instruments or for simultaneous suction. The ventilation can be volume ventilation or jet ventilation. With jet ventilation, the operator can maintain an open circuit and easily introduce and remove instruments, whereas in volume ventilation, the cap must remain to ensure adequate ventilation.



**Figure 64.1** Rigid bronchoscope in use.

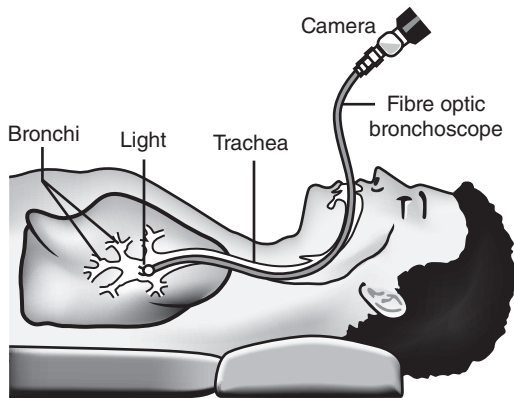
**Optics and Light Source** The rigid bronchoscope optics contains only direct viewing telescope and a light source. For optimum view, the telescope is integrated directly in the bronchoscope tube. For intubation, the clinician can either use a telescope and camera to direct the rigid scope or directly visualize down the barrel with the naked eye using the light source built into the barrel. Single-chip or three-chip video cameras can be easily connected to the proximal end or eyepiece directly. It is necessary to have several direct viewing lenses in the 4 and 5.50 mm diameter telescopes. Smaller diameter telescopes are necessary for paediatric cases. There is an integrated irrigation channel to irrigate the distal lens of the bronchoscope during an operation if it becomes cloudy due to secretions or blood. The device provides 12° direction of view, with integrated lens irrigation and protective sheath.

Rigid bronchoscopy is most commonly used to manage patients who have obstruction of either their trachea or a proximal bronchus. The large lumen of the rigid bronchoscope facilitates suctioning and the removal of debris, or interventional procedures such as insertion of airway stents. Special procedures, such as dilating the airway or destroying a growth using a laser, are usually done with a rigid bronchoscope.

Modern rigid bronchoscopes are designed for both diagnostic and therapeutic applications, such as biopsy, tumour resection, foreign body removal, and stent placement and removal. The accessories designed for the rigid bronchoscope are usually larger and stiffer than those built for the working channel of the flexible bronchoscope. Figure 64.1 shows as to how the rigid bronchoscope is used in practice.

### **Flexible Bronchoscope**

A flexible bronchoscope is the most commonly used type of bronchoscope. It consists of a fibre optic system that transmits an image from the distal tip of the instrument to an eyepiece or video camera at the opposite end. This is shown in Figure 64.2. The position of the distal tip of the instrument can be manipulated or oriented using Bowden cables connected to a lever at the handpiece, allowing the doctor to navigate the instrument into individual lobe or segment bronchi.



**Figure 64.2** Flexible bronchoscope in use.

A flexible bronchoscope is longer and thinner than a rigid bronchoscope. The tube is about 1 cm wide and about 60 cm long. The device has a mechanism to flex or extend its distal end, which facilitates insertion through the curved airways. The insertion tube can be rotated left or right up to  $120^\circ$  by simply turning a ring on the control section of the bronchoscope. This allows easier operation and smoother insertion while reducing operator fatigue. The  $210^\circ$  angulation range provides smoother insertion into the upper lobe bronchi.

A video bronchoscope has a miniature charge-coupled device (CCD) mounted at the distal tip of the bronchoscope to capture and transmit images. This has replaced the image guide and eyepiece system that was found in earlier bronchoscopes. The images can be recorded, printed, stored on digital media, or transmitted to another location for multiple viewing. Video bronchoscopy is an ideal tool for teaching and documenting procedures. Most flexible bronchoscopes also include a channel for suctioning or instrumentation.

The flexible bronchoscopy system as illustrated in Figure 64.3 comprises of (i) a flexible bronchoscope, (ii) a light source, and (iii) an image processor. The light source and the image processor are connected by a cord to the control handle (handpiece) of the bronchoscope. The flexible bronchoscope has further three parts as follows:

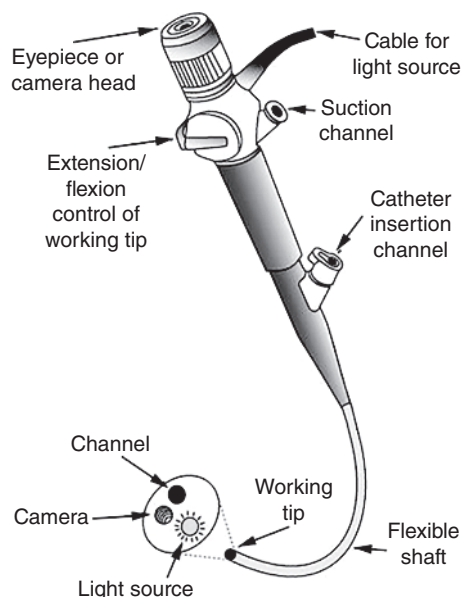
*The control handle:* It is designed to be held by the operator. It consists of a lever that allows you to flex or extend the distal tip of the bronchoscope. It is also provided with a suction port and an opening through which instruments such as forceps, brushes, etc. can be inserted into the working channel.

*The flexible shaft:* The shaft carries cables that allow flexion and extension of the distal tip of the bronchoscope by manipulating the lever on the handle. It also contains lighting cables and imaging cables. A working channel is also provided through which airway contents can be aspirated and catheters or other instruments can be passed.

*The distal tip:* The part of the bronchoscope that enters the patient's airway is the distal or working tip. The tip contains the camera to capture the image, the light source, and the opening of the working channel.

*Light source:* The light source typically transmits a broad spectrum white light. However, the use of narrow spectrum light sources greatly improves the visualization of vessels on the mucosal surface.

**Figure 64.3** Different parts of a flexible fibre optic-based bronchoscope.



*Image processor:* The image of the illuminated airway is transmitted to the doctor either by fibre optic transmission or digitized video transmission. In early days, fibre optic transmission was used for image transmission. The image of the airway could be viewed by the doctor by directly looking into an eyepiece at the proximal end of the scope. The image can also be transmitted from the eyepiece to a video monitor for better viewing. Using image processing techniques, the intensity, colour, brightness of the light, and other features of the captured image can be optimized. In small portable flexible bronchoscopes, the light source is located on the bronchoscope, and an eyepiece on the control handle allows to visualize the airway directly, without any video monitor.

Most of the modern bronchoscopes use a miniature CCD camera located at the distal tip for transmission of the image. The camera acquires real-time images and then transmits them to a video processor for display on a video monitor. The images obtained with this technique are of high resolution, sharper, and magnified, with a wider field of vision.

Flexible bronchoscopy is the technique of choice nowadays for most bronchoscopic procedures as it causes less discomfort for the patient than rigid bronchoscopy. It usually does not require general anaesthesia, offers a better view of the smaller airways, and allows the doctor to remove small samples of tissue (biopsy).

### ***Special Types of Flexible Bronchoscopes***

There are several variants of conventional flexible bronchoscopes, which are summarized as follows:

- ***Endobronchial ultrasound (EBUS):*** It consists in using a flexible bronchoscope that has a small ultrasound probe mounted into its distal end. It allows real-time ultrasound images of the tissue adjacent to the airway, facilitating drawl of samples for diagnosis. The bronchoscope is slightly larger than a standard scope and is therefore always passed through the mouth rather than the nose.

- *Electromagnetic navigation bronchoscopy*: The technique uses a special catheter with a sensor probe that is inserted through the working channel of a regular flexible bronchoscope. The probe is steered through the distal airways, guided by an electromagnetic guidance system. This allows peripheral lung masses or abnormal areas to be sampled that cannot be accessed by regular bronchoscope directly.
- *Ultrathin bronchoscopy*: This procedure is performed with a bronchoscope that has an external diameter of only 2.8 mm.
- *Fluorescence bronchoscopy*: The technique utilizes special imaging equipment that enables the airways to be viewed with blue light of a certain wavelength. This technique allows to show up some abnormalities within the airways that may be otherwise invisible under normal white light.

## Specifications

### *Rigid bronchoscope*

*Telescope*: Straight forward 0°, diameter: 4.5 mm length 50 cm, autoclavable with fibre optic light transmission

*Inner diameter*: 6, 8, 10, 12, and 14 mm

*Outer diameter*: 10, 12, 14, 16, and 18 mm

*Length*: Around 42 cm

*Light source*: Halogen lamp, 12 V, 50 W

*Camera*: Single chip

*Optical forceps*: Foreign body forceps, with alligator jaws; universal forceps, biopsy forceps, grasping forceps, for soft foreign bodies

*Fibre light cable*: 2.3 m long

### *Flexible bronchoscope*

*Field of view*: 120°

*Depth of field*: 2–50 mm

*Insertion tube*: Distal end outer diameter 3.1 mm

*Instrument channel*: Inner diameter 1.2 mm

*Minimal viewing distance*: 1.5 mm from the distal end

*Angulation range*: Up 180°, down 130°

*Biopsy channel size*: 2.2 mm

*Light source*: Xenon light source

## Applications

Bronchoscope are used both for diagnostic and therapeutic applications. They are used to view abnormalities of the airway, to take tissue samples (biopsy) for examination, to suck out secretions, and to insert medicines into the lungs. Their therapeutic applications include removing secretions, blood, or foreign objects lodged in the airway, performing laser resection of tumours, stent insertion, and treatment of specific disorders such as control of bleeding from focal lesions.

## 65

### Cabinet: Warming

#### Purpose

Warming cabinets are required to store and warm sterile intravenous and surgical irrigation fluids, linens, and blankets. These cabinets provide a safe and accurate method of determining and maintaining the fluid temperature to the manufacturer's recommendations. The blankets, when gently heated in these cabinets, can help to restore body temperature post-surgery, assist thermo-regulation of patients, and reduce the risk of hypothermic reaction, post-operative discomfort, and stress in patients.

#### Principle

The blanket and fluid warming cabinets are available in a wide variety of configurations: standard or dual compartments, dedicated single compartments for fluids or blankets, glass or solid doors, and mobile or fixed units. They include several safety features to allow accurate temperature control and LED temperature display in both centigrade and Fahrenheit, individually for each compartment. Audible and visual alarm systems that get triggered in case of over-temperature are included. The alarm is also initiated if the door is left open, which reduces the possibility of loss of heat.

The cabinets are designed to provide efficient heating and prevent accidental overheating of the stored material. Modern cabinets have provisions for digital data recording and USB port so that the stored temperature data can be easily downloaded on to a PC or laptop. The stored data can generate reports that include date and time, temperature setting, actual temperature, door status, over-temperature status, and under-temperature status.

#### Construction

The warming cabinet is a fully sealed chamber constructed from polished 16-gauge stainless steel with rounded corners for easy cleaning and to give good appearance. While smaller warming cabinets usually have a single compartment, the larger ones have dual compartments. The outer cabinet is given tough powder coat paint finish to make it corrosion resistant. The cabinet has double panel glazed door with a 16 mm gap between panes to provide insulation and safe external temperature to ensure cool to touch exterior surface. The inner door closes positively onto a silicone gasket, whereas the outer door has a magnetic gasket to provide a good seal.

Doors are of double-wall construction with 38 mm thick insulation between the walls. They are made in solid vinyl coated galvanized steel material with stainless steel inside and include optional tempered double pane glass window(s). Temperature monitoring probes are inserted safely into the chamber through a rear access port. Adjustable perforated polyester powder-coated steel shelves are provided for storage of 2 and 11

bottles and bags. Different sized cabinets are available to have different capacities for fluid and blankets. The cabinets can be fixed or made mobile by using 4 castors of which 2 are fixed type while the other 2 are swivel and lockable. Cabinet controls are all digital and similar for single and dual compartment configurations.

### Heating

The heating element consists of a profiled resistive wire whose operation is controlled by a microprocessor based circuit. A schematic diagram of the control circuit is shown in Figure 65.1. Even temperature throughout the chamber is ensured by a fan that assists air circulation and convection heating. An efficient temperature controller circuit allows fast temperature recovery that keeps heat loss to a minimum after door opening. Heating chamber compartment is insulated with 25 mm thick fibre glass blanket.

### Temperature Control

In the double compartment cabinets, the upper compartment operates in the range 90–110°F (32.2–43.3°C), and the lower compartment is in the range 90–160°F (32.2–71.1°C). In single compartment cabinets, the temperature range is set to 90–160°F (32.2–71.1°C). The temperature accuracy in upper or single compartment is  $\pm 3^\circ\text{F}$  ( $\pm 1.7^\circ\text{C}$ ), and for lower compartment \, it is  $\pm 5^\circ\text{F}$  ( $\pm 2.8^\circ\text{C}$ ) when warming irrigation solution. The temperature controller allows temperature stability to within  $0.1^\circ\text{C}$  in all parts of the warming cabinet. A thermistor or thermocouple is used for sensing the temperature. The controller displays digitally both the target and actual temperatures in real time.

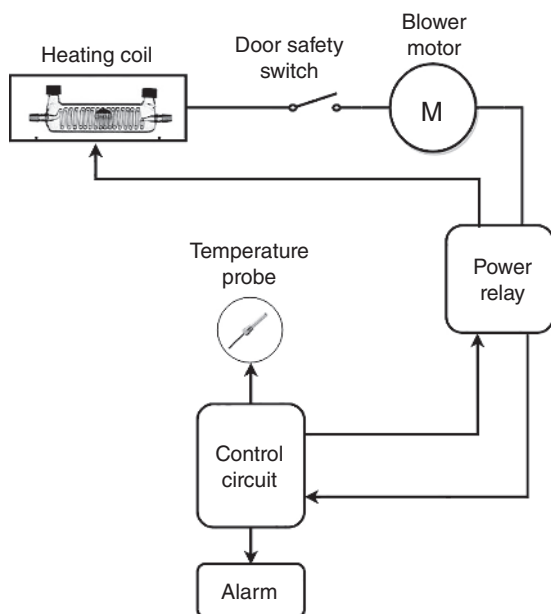


Figure 65.1 Heating control system in a warming cabinet.

## Safety

In case of under- and over-temperature, if the electronic cutout fails, the heating element is disconnected by an independent safety bimetallic cutout. An alarm visually and audibly alerts the operator if there is an over-temperature condition and the chamber temperature is greater than 10°F (5.5°C) above set temperature. An additional safety measure is to make the controller operation password protected so as to prevent any unauthorized manipulation of the set point and alarm thresholds.

## Specifications

*Size:* From 4.2 to 15.8 cf capacity, door option: steel or dual-pane tempered glass

*Compartments:* 1 or 2

*Depth:* 18 or 24 in."

*Temperature range:* From 90°F (32°C) to 160°F (71°C)

## Applications

They find applications throughout the healthcare facility: operating rooms, general wards, emergency wards, intensive care units, labour and delivery rooms, and other patient areas as a method of choice for patient warming.

# 66

## Camera: Spot Film

### Purpose

Spot film cameras are used to photograph the image on the output phosphor of the image intensifier tube. These cameras produce images that are separated by a specific time interval and exhibit the changes in the anatomy and pathology as a sequence of static events that can be viewed in sequential order. They are also called large format or rapid sequence cameras.

### Principle

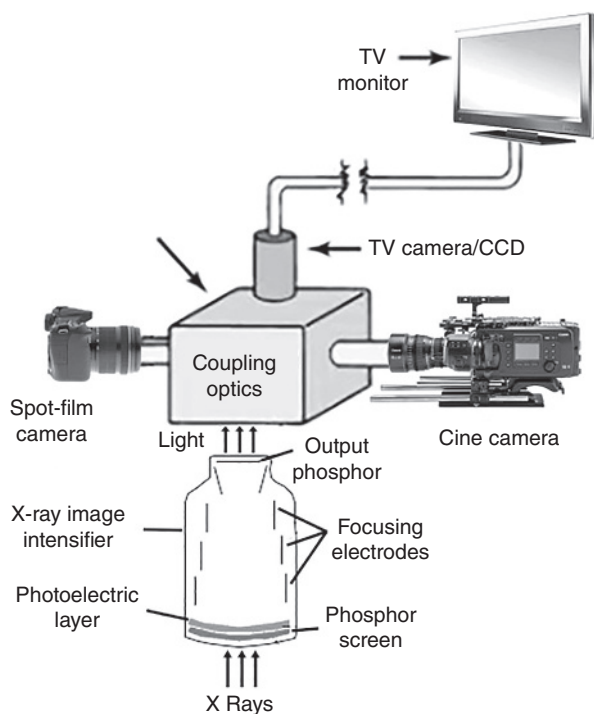
Cinefluorography is a popular technique for filming the images on the output phosphor of the image intensifier. This method has many useful applications where dynamic studies of physiological phenomena are undertaken. The image is recorded on 16 or 35 mm film. However, individual cine frames do not record all the information available on the



image intensifier output phosphor. In order adequately record the high definition image on the output phosphor, larger film format is necessary. Therefore, spot film cameras utilizing 70, 90, 100, or 105 mm have been developed. Conventional photographic cameras are unsuitable for filming from the image intensifier where the object-to-image ratio is in the range of 1 : 1 or less. The location of the camera in an image intensifier system is shown in Figure 66.1.

Spot cameras are very close in design to cine cameras. These cameras are capable of recording from 1 to 12 frames (pictures) per second, which is a slower rate than cine cameras. The film size used is a matter of personal choice, but the larger film format gives better image quality. However, the larger film size requires higher patient dose. They use either roll or cut film depending upon the design of the camera. These devices do not contain a shutter, as the image is recorded from the image intensifier by using pulsed X-ray beam. When the beam becomes on, the image is produced; and when the beam is off, no image is produced on the output phosphor and no image will be recorded by the camera.

The spot camera is basically a static imaging system. It is used with an optical lens system that also includes a beam splitting mirror. When the spot film exposure switch is operated, the split mirror comes into position and diverts some of the beam towards the spot camera and exposes the film in the same way as a conventional photographic camera. After the exposure, the shutter is closed and the film is advanced to the next



**Figure 66.1** Position of spot film camera in the X-ray image intensifier chain.

position for the sequence to repeat. The roll film is developed in the conventional processor in a similar way of developing a sheet film. Since the camera records the image from the output phosphor of the image intensifier, the patient dose is just 1/2 that for a cassette-loaded spot filming system.

Cassette spot filming is a standard technique in conventional fluoroscopic imaging. Spot film images are taken to record a patient's anatomy at specific moments during the fluoroscopic examination. This is primarily a static imaging process in which a static radiographic cassette is used to obtain an image. The cassette is positioned between the patient and the image intensifier. As this imaging method uses radiographic mode, it requires a much higher radiation dose to the patient than is required in spot film cameras. However, the resolution of spot filming is better than photospot film cameras or digital spot cameras.

## Specifications

*Format:* Full field, 1 on 1; 2 on 1 longitudinal; 3 on 1; 4 on 1; 6 on 1; 9 on 1

*Cassette sizes:* 18 cm × 24 cm to 35 cm × 35 cm

*Longitudinal motion:* 74 cm

*Lateral motion:* 25 cm

## Applications

Photospot cameras are used to record the image intensifier output on rolled or cut film to produce radiographic images.

# 67

## Capnograph

### Purpose

A capnograph is a device designed to measure the concentration or partial pressure of carbon dioxide (CO<sub>2</sub>) in the respiratory gases. Its main application has been as a monitoring tool during anaesthesia and intensive care. The measurement of carbon dioxide concentration is done in each breath of the respiratory cycle, and the results of measurement are usually presented as a graph of expiratory CO<sub>2</sub> (mmHg) plotted against time. The plot may also show the inspired CO<sub>2</sub>, which is of interest when rebreathing systems are being used. Most of the modern capnographs include a pulse oximeter in the same housing for monitoring spot oxygen saturation (SpO<sub>2</sub>), pulse rate, and derived respiration rate.

## Principle

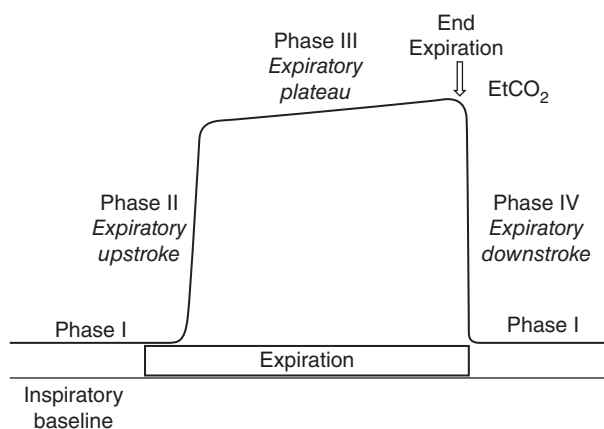
Monitoring of carbon dioxide levels in human breath is of vital importance because changes in carbon dioxide levels can indicate hypoxia of a region or whole body when it is deprived of adequate oxygen supply, leading to irreversible brain damage. An important application of  $\text{CO}_2$  measurement is in intensive care unit or when a patient is undergoing surgery where artificial ventilation is being used and it is required to balance the ventilation as per requirement of the patient. Reduced production of carbon dioxide is observed during anaesthesia and hypothermia, whereas during fever and shivering, there is an increase in carbon dioxide production.

Capnography provides information about  $\text{CO}_2$  production, pulmonary (lung) perfusion, alveolar ventilation, respiratory patterns, and elimination of  $\text{CO}_2$  from the anaesthesia breathing circuit and ventilator. From these parameters, the anaesthetist can evaluate respiration rate, adequacy of ventilation, verification of correct endotracheal tube placement, and airway patency. capnographs are also used to measure carbon dioxide production as a measure of metabolism. Thus, monitoring expired carbon dioxide concentration provides useful information about respiratory system, cardiovascular system, metabolism, and integrity of the breathing system.

*Capnography* is primarily a technique for graphic display of instantaneous  $\text{CO}_2$  concentration versus time (time capnogram) or expired volume (volume capnogram) during a respiratory cycle. *Capnograph* is the machine that generates a waveform, and the *capnogram* is the actual recorded waveform. *Capnometry* is the measurement and numerical display of maximum inspiratory and expiratory  $\text{CO}_2$  concentrations during a respiratory cycle. *Capnometer* is the device that performs the measurement and displays the reading.

### Capnography Waveform

The capnography waveform shows the concentration of  $\text{CO}_2$  in the breath as a function of time as shown in Figure 67.1. The waveform has a generally uniform square-like morphology with consistent frequency, which is calculated to determine respiratory



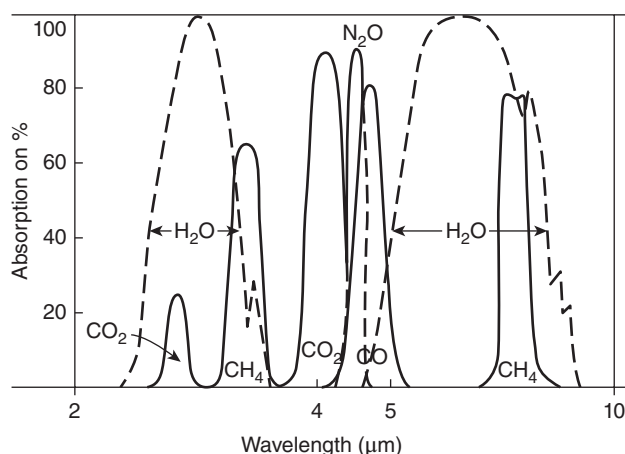
**Figure 67.1** Normal capnography waveform.

rate. Phase I in the diagram represents the waveform baseline. This phase represents the inspiratory phase of the respiratory cycle. Phase II shows the rise in  $\text{CO}_2$  as the dead space ventilation mixes with alveolar gas known as expiratory upstroke. This is followed by Phase III which represents the alveolar plateau. The end tidal  $\text{CO}_2$  is measured at the end of expiration, just before inspiration. Phase IV is the end of the waveform segment and the beginning of inspiration. The shape of the curve will get affected by the presence of some obstructive conditions in the lungs or some other form of lung disease.

For healthy adults, the breathing pattern occurs approximately every 3–5 seconds, which indicates a normal respiratory rate between 12 and 20 breaths/min. The baseline of the waveform is normally at near zero. This is because inspired air contains very little  $\text{CO}_2$ , which could be less than 0.5%. The waveform consists of four phases during each breath cycle, before the waveform returns to the baseline. For a normal healthy adult, the amplitude of the waveform is about 35–45 mmHg at the peak that represents the end tidal  $\text{CO}_2$  ( $\text{EtCO}_2$ ) value.

### Instrumentation

The most popular method of measurement of  $\text{CO}_2$  is based on the absorption of infrared radiation by gases having polyatomic asymmetric molecules. This means that water vapour ( $\text{H}_2\text{O}$ ), carbon dioxide ( $\text{CO}_2$ ), carbon monoxide ( $\text{CO}$ ), and nitrous oxide ( $\text{N}_2\text{O}$ ) will absorb infrared radiation, whereas there is no absorption by the symmetrical binary gas molecules such as oxygen ( $\text{O}_2$ ) and nitrogen ( $\text{N}_2$ ). The absorption bands for various gases in the infrared spectrum from 2 to 10  $\mu\text{m}$  are shown in Figure 67.2. It may be noted that  $\text{CO}_2$  has a strong absorption band for the infrared wavelength from 3.5 to 4.7  $\mu\text{m}$ , with a strong absorption at 4.26  $\mu\text{m}$ . By using bandpass filter to eliminate the other infrared wavelengths emitted by the infrared source, the detector can measure the absorption caused by the amount of  $\text{CO}_2$  present in a gas. The detector used for infrared radiation typically uses lead selenide detector.



**Figure 67.2** Infrared absorption bands for infrared radiation wavelengths from 2 to 10  $\mu\text{m}$ . The  $\text{CO}_2$  peak lies at 4.26  $\mu\text{m}$ .

Capnography uses non-dispersive infrared (NDIR) spectroscopy method to continuously measure the amount of  $\text{CO}_2$  during every breath, the amount of  $\text{CO}_2$  present at the end of exhalation ( $\text{etCO}_2$ ), the amount of  $\text{CO}_2$  present during inhalation ( $\text{FiCO}_2$ ), and the respiratory rate. A beam of infrared light is passed across the gas sample to fall on a sensor. The presence of  $\text{CO}_2$  in the gas results in reduction in the amount of light falling on the sensor due to absorption of light by  $\text{CO}_2$ . Because the absorption is proportional to the concentration of the absorbing molecule, the concentration can be determined by comparing its absorption to that of a known standard. A sample of the inhaled and exhaled gases from the ventilator or directly from the patient via an oral/nasal cannula is delivered into the monitor for  $\text{CO}_2$  measurement. The sampling flow rate is 50 ml/min that reduces liquid and secretion accumulation and decreases the risk of obstruction in the sample pathway. The optimal gas flow is considered to be 50–200 ml/min, which ensures that the capnographs are reliable in both children and adults.

Once inside the  $\text{CO}_2$  sensor, the gas sample passes through a 15  $\mu\text{l}$  micro-sample cell. This extremely small volume allows to be quickly flushed and gives fast rise time at high respiration rates. The IR source illuminates the micro-sample cell and the reference cell. The IR light source generates only the specific wavelengths characteristic of the  $\text{CO}_2$  absorption spectrum, and therefore, no compensations are necessary due to the presence of  $\text{N}_2\text{O}$ ,  $\text{O}_2$ , anaesthetic agents, and water vapour present in the inhaled and exhaled breath. The IR passing through the micro-sample cell and the IR passing through the reference cell are measured by the IR detectors. The microprocessor calculates the  $\text{CO}_2$  concentration by comparing the signals from both detectors.

Figure 67.3 shows a block diagram of a capnometer. It consists of an airway adapter, a sensor, and a processor. The airway adapter, a hollow aluminium casting with sapphire windows, is inserted in series with the ventilator plumbing. The sensor is snapped over the airway adapter windows, and the measurement is made directly on the artificial

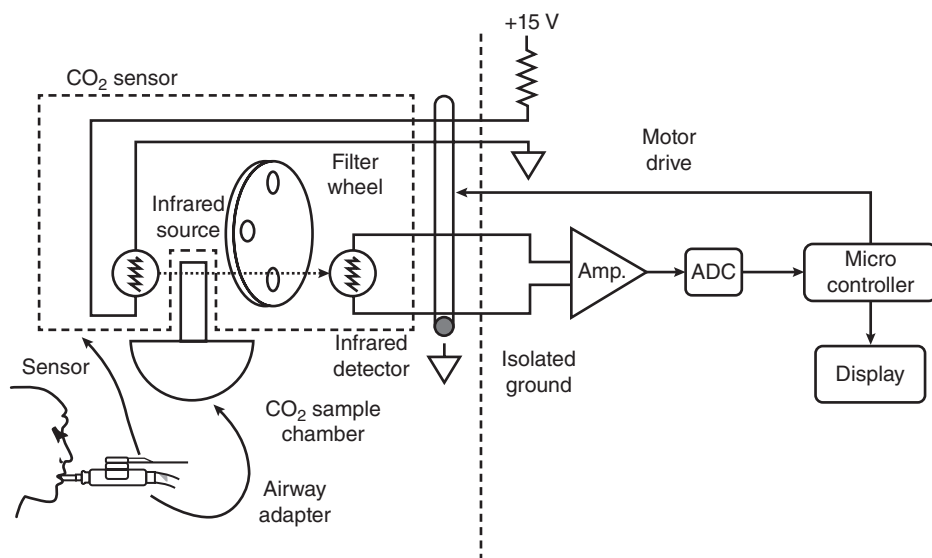
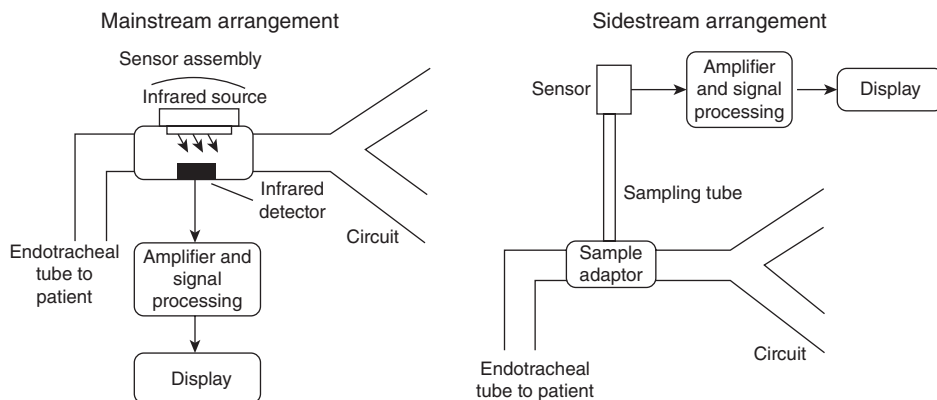


Figure 67.3 Block diagram of a capnometer.



**Figure 67.4** Configuration of mainstream and sidestream arrangement in a capnograph.

airway through which the patient is breathing. This sensor contains all the optical components necessary to make the infrared measurement and is connected to the processor. The processor powers the sensor, processes the return signal, and presents the data via LED displays. The microprocessor performs numerous tasks that greatly simplify the use of the system. Compensations for interfering gases and total pressure are also performed by the processor. The sampling gas pump, flow regulator, sampling system including the connector to the sampling port, and water trap or other important components that constitute the capnograph all operate under the control of the microprocessor. The gas that is withdrawn from the patient generally contains anaesthetic gases. So, the exhausted gas from the capnograph is usually routed to a gas scavenger.

A capnometer can be either of mainstream or sidestream configuration as illustrated in Figure 67.4. Mainstream devices measure respiratory gas ( $\text{CO}_2$ ) directly from the airway, with the sensor located on the airway adapter at the hub of the endotracheal tube. Sidestream devices measure respiratory gas via nasal or nasal–oral cannula by aspirating a small sample from the exhaled breath through the cannula tubing to a sensor located inside the monitor. In other words, a sidestream capnometer transports a portion of a patient's respired gases from the sampling site, through a sampling tube, to the sensor, whereas a mainstream capnometer does not transport gas away from the sampling site. Current generation mainstream devices, besides being relatively light and low in dead space, have generally demonstrated better performance than sidestream system in terms of signal fidelity and end tidal measurements.

The measurement of  $\text{CO}_2$  in respiratory gases has become an integral part of anaesthesia monitoring. Changes in carbon dioxide levels exhaled by the patient during surgery can indicate that there is a problem with the anaesthesia, or a surgical complication is likely to emerge. By keeping track of the amount of  $\text{CO}_2$  exhaled by the patient breathes over time or with the volume of each breath, an anaesthesiologist can become cautious to the emergent signs of a problematic complication. In such situations, capnography plays an important role as this noninvasive technique provides information about  $\text{CO}_2$  production, pulmonary perfusion, and alveolar ventilation. It also shows respiratory patterns as well as elimination of  $\text{CO}_2$  from the anaesthesia circuit and ventilator. Capnography provides a rapid and reliable method to detect life-threatening conditions and to circumvent potentially irreversible patient injury.



**Figure 67.5** Typical capnograph. Source: Image courtesy of M/s Smiths Medical.

### Portable CO<sub>2</sub> Meters

Portable CO<sub>2</sub> analysers such as shown in Figure 67.5 are specifically designed for the verification of incubators in research and pharmaceutical markets. They are also used for checking medical gases before administering to the patient, air quality monitoring, and verifying heating, ventilation and air conditioning (HVAC) system performance and air ventilation control.

Portable analysers use the well-defined infrared principle for measurement of percent levels of carbon dioxide. The instrument has an infrared sensor comprising an infrared source, a detector, and an optical path. The infrared sensor is generally a self-contained unit with the necessary electronics that processes the signal from the sensor and displays the carbon dioxide concentration on the digital display.

Earlier, most infrared CO<sub>2</sub> sensors used a miniature incandescent light bulb as the infrared source. However, they suffer from instability issues, and therefore, the infrared sensors used in modern instruments incorporate a semiconductor light source and detector that are both temperature controlled and highly stable. The portable instruments come with the capability of multi-parameter measurement. The parameters include O<sub>2</sub>, relative humidity, and temperature. They provide data logging and USB connectivity to PC to download data, graphic display, analyse, and export it.

### Specifications

*Measurement range:* 0–10% at standard temperature and pressure

*Display range:* 0–100 mmHg; 0–13 kPa; 0–10% CO<sub>2</sub>

*Accuracy:*  $\pm 2$  mmHg

*System response time:* 90% in 2.46 s

*Averaging:* 4-breath average

*Sampling flow rate:*  $50 \pm 10$  ml/min

*Respiration rate:* 0–150 breaths/min

*SpO<sub>2</sub> (optional):* Range from 0 to 100% SpO<sub>2</sub>

*Accuracy:*  $\pm 2\%$  at 70–100%

*Pulse rate:* Range from 30 to 250 bpm

## Applications

Capnographs are employed to measure the respiratory gasses of patients undergoing anaesthesia or intensive care, or in emergency rooms. They are even being used in the on-site emergency and trauma fields to aid in patient assessment and treatment in the prehospital environment. Since they provide a breath-by-breath measurement of a patient's ventilation, capnographs can quickly indicate a worsening trend in a patient's condition with an early warning about the patient's respiratory status.

## 68

### Carbon Monoxide Analyser

#### Purpose

Carbon monoxide (CO) analysers are generally used as breath monitors by the emergency services to identify patients suspected of having CO poisoning. Carbon monoxide is a colourless, odourless, and tasteless gas, which is otherwise difficult to detect but is highly toxic. The breath monitoring of suspected exposure to CO can assist in providing treatment to the patient at site more rapidly and improve their chances of survival. Carbon monoxide analyser is also used for checking air quality. Monitoring of carbon monoxide is also essential in several industrial situations including the chemical, food, and medical industries. CO monitors measure carbon monoxide in parts per million (ppm) in air or breath. They have become popular because they allow for noninvasive testing and are inexpensive to use.

#### Principle

Breath carbon monoxide is the level of carbon monoxide that is detected in the exhaled air of a person. It is usually measured by a breath carbon monoxide monitor. The breath carbon monoxide level has been found to show a close relationship with the level of CO in the blood. Due to this correlation, the level of CO in the blood can be indirectly measured through a breath sample. Figure 68.1 is a typical breath carbon monoxide monitor.

#### *Carbon Monoxide Detectors*

A carbon monoxide detector is designed to detect the presence of the CO gas in a breath sample. Three types of CO sensors are in common use: biomimetic sensor, metal oxide semiconductor (MOS), or electrochemical sensor.

**Biomimetic Sensors** Biomimetic CO detectors are biotechnology based and work in a similar way the haemoglobin reacts to CO in biological organisms. They use gels that change colour after absorbing a certain amount of carbon monoxide. Basically, a





**Figure 68.1** Typical commercial breath CO monitor, displaying a breath concentration reading with its corresponding blood concentration. Source: [https://en.wikipedia.org/wiki/Breath\\_carbon\\_monoxide](https://en.wikipedia.org/wiki/Breath_carbon_monoxide).

biomimetic sensor monitors infrared (IR) light that is passed through a disc of synthetic haemoglobin that darkens in the presence of CO. Thus, as CO concentrations increase, the light is obstructed. This can either be seen directly or connected to an IR source of photons such as an IR LED and then monitored using a photodiode. Biomimetic detectors are low cost and draw low current to operate, giving an operational life of six years to the sensor. Though expensive than other sensors, the technology is used with larger facilities like hospitals. The drawbacks include a long recovery time after alarm and susceptibility to false alarms if environmental conditions fluctuate.

**Semiconductor Detectors** The MOS detector consists of a tin dioxide semiconductor that is heated to about  $400^{\circ}\text{C}$  by an electric current at periodic intervals. When tin dioxide reaches its operating temperature, its resistance changes in the presence of carbon monoxide. The change in resistance is measured to indicate the concentration of carbon monoxide. In construction, thin wires of the semiconductor tin dioxide are mounted on an insulating ceramic base to form part of an integrated circuit.

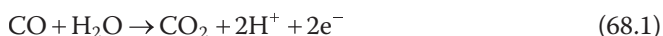
Semiconductor detectors have a long lifespan and can respond quickly to CO. However, due to requirement of heating, the sensor has a large power demand and usually operates from the power mains. A battery-powered, pulsed sensor is available, but they have battery working life of only a few months. Besides, these detectors are susceptible to false alarms in the presence of some common household chemicals or gases other than CO.

**Electrochemical Detectors** An electrochemical detector is a type of fuel cell that produces a signal current that is precisely related to the amount of carbon monoxide. The amount of current produced gives a measure of the concentration of carbon monoxide. A typical example of an electrochemical-type gas sensor from M/s Figaro is shown in Figure 68.2. The cell is basically an amperometric fuel cell with two electrodes. It consists of a semipermeable diffusion membrane, two electrodes, namely, working or sensing electrode,



Figure 68.2 CO gas sensor from M/s Figaro, Japan.

a counter electrode, and an ion conductor (a reservoir of acid electrolyte) in between them. When CO comes in contact with the working electrode, oxidation of CO gas takes place on the working electrode through chemical reaction with water molecules in the air as follows:



Carbon monoxide is oxidized at one electrode to carbon dioxide, while oxygen is consumed at the other electrode. When the working electrode and the counter electrode are connected through a circuit, the protons ( $\text{H}^+$ ) generated on the working electrode will flow towards the counter electrode through the ion conductor. In addition, generated electrons move to the counter electrode through the external wiring. A reaction with oxygen in the air will occur on the counter electrode is shown in Figure 68.3 and is as follows:



The overall reaction is given as follows:



The gas sensor operates like a battery with gas being the active material for this overall battery reaction. By measuring the current between the working electrode and the counter electrode, the electrochemical cell can be utilized as a gas sensor.

The sensor output current is measured by connecting it to an external circuit. The gas flowing towards the working electrode is controlled with diffusion film, and output current flowing across the external circuit will be proportional to gas concentration.

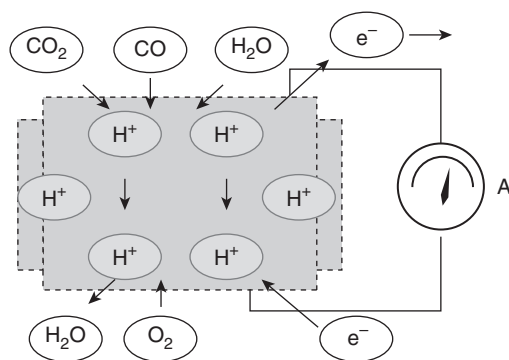
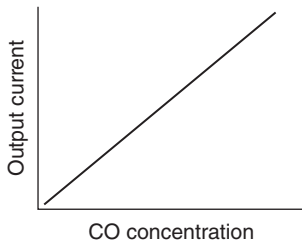


Figure 68.3 Principle of electrochemical-type gas sensor.



**Figure 68.4** Relationship between CO concentration and sensor output current.

The linear relationship of gas concentration to sensor output (Figure 68.4) makes this technology ideal for CO sensing application.

In some electrochemical cells, the carbon monoxide sensor consists of three electrodes immersed in an electrolyte (usually acids or dissolved salts). The three electrodes are the working electrode, the reference electrode, and the counter electrode. The counter-electrode is provided to complete the circuit of the electrochemical cell, whereas the reference electrode provides a stable electrochemical potential in the electrolyte. The three-electrode design gives increased selectivity to the measured gas compared with two-electrode designs. The CO fuel cell requires a bias voltage of 220 mV that is to be supplied permanently to the reference electrode. The circuit is powered by an internal 950 mAh lithium cell with an operational life greater than the life of the electrochemical fuel cell.

The CO sensor is also equipped with a chemically selective filter. This filter removes potentially interfering gases before they reach the working electrode. With the filter operating properly, the sensor will have minimal response to interfering gases. The fuel cell technology can be modified to give sensors that will respond to the different gases of interest. This is accomplished by using different working electrodes, bias potentials, and chemically selective filters.

### ***Instrumentation***

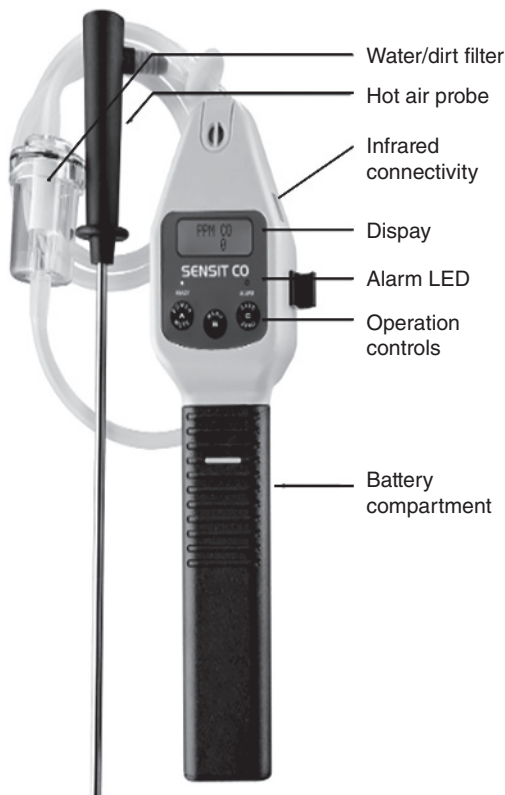
Breath CO monitors that are commercially available display a breath CO concentration reading with its corresponding blood concentration. They mostly use an electrochemical gas sensor and a digital display in numeric format of test results on LCD. The handheld CO monitors consist of a microcomputer unit that incorporates a CO sensor and have a mouthpiece adapter with integral one-way valve. A disposable cardboard mouthpiece is used to facilitate blowing of breath into the device. The device operates on a single alkaline PP3 battery.

The current output signal from the electrochemical sensor is conditioned using a current to voltage converter and amplifier and given to an analog-to-digital (A/D) converter and then to the microprocessor. The circuit that controls the potential of the working electrode and converts the signal current to a voltage is called a potentiostat. When the device is switched on, the microprocessor records the baseline reading on the A/D input and uses this value to auto zero the instrument. To make the measurements, the subject is asked to breathe in maximally, hold the breath for 20 seconds, and then expire fully through the mouthpiece connected to the microcomputer unit.

with the mouthpiece adapter. The microprocessor will record the peak value obtained and display the reading. The value can be displayed either as ppm concentration in the expired air or as the equivalent percentage carboxyhaemoglobin (%COHb) calculated with built-in software.

The MOS-type CO gas sensors have also been developed for the measurement of low gas concentrations. The technology allows this device to measure gases at the ppb level. The gas concentration is detected by measuring the resistance change of MOS-type sensing device. The chemical reaction of gases and adsorbed oxygen on the tin dioxide surface varies depending on the reactivity of sensing materials and working temperature of the sensor.

The CO monitors used for flue gas emissions are also available with additional oxygen sensor, which measures percentage of oxygen in air within a range of 0–25% volume. The range of CO measurements is 0–2000 ppm. Such devices use a diaphragm-type pump to draw in the air samples. Alarms are sounded in case of flow block, low battery power, and sensor failure and when dangerous levels of CO accumulate in an environment. Carbon monoxide detectors are just like smoke detectors, but instead of recognizing signs of fire, they detect levels of carbon monoxide. A typical CO monitor for testing air quality is shown in Figure 68.5.



**Figure 68.5** Portable CO analyser for testing air quality.

## Specifications

*Concentration range:* 0–500 ppm (breath CO monitor)

*Concentration range:* 0–2000 ppm (air quality CO monitor)

*Sensitivity:* 1 ppm

*Sensor life:* >1 year

*Sensor drift:* <2% per month

*Response time:* <60 seconds for 90% of reading

*Power supply:* Single 9 V PP3

## Applications

Carbon monoxide analysers are used in clinics where lung-function testing is done for estimating lung diffusing capacity. A breath CO monitor when employed as an aid to smoking cessation acts as a motivational, validational, and educational tool. The device is often termed as the stethoscope of tobacco treatment as it provides reliable information on smoking status of a person without relying solely on the person's self-report. They find extensive applications in air quality monitoring.

## 69

### Cardiac Monitor: Bedside

#### Purpose

A cardiac monitor is a device designed to display the electrical activity of the heart as a wave pattern on a monitor screen. The device continuously monitors the cardiac activity and allows the detection of changes in heart rate, rhythm, and conduction. It is usually used as a bedside monitor in cardiac care and intensive care units and is an essential equipment for the detection of life threatening arrhythmias. The cardiac monitors are available in many forms, which range from simple handheld devices for remote monitoring to sophisticated patient monitoring systems used in hospitals.

#### Principle

The most important physiological parameters monitored of critical care patients in the intensive care unit or otherwise are the heart rate and the shape of the electrical waveform, commonly known as electrocardiogram (ECG), produced by the heart. The information on these parameters can lead to detection of the presence of arrhythmias or changes in the heart rate that might be indicative of a serious condition. Thus, a cardiac monitor is specifically useful for monitoring patients having some cardiac problem.

Cardiac monitoring is different from hemodynamic monitoring, which monitors the pressure and flow of blood within the cardiovascular system. Both types of monitoring are usually performed simultaneously on critical heart patients. A typical cardiac monitor comprises of the following:

- *Electrodes*: Disposable type pre-gelled AgCl electrodes used with conductive gel to pick up the ECG signal. These electrodes have average impedance of  $\leq 2\text{ k}\Omega$  and DC offset voltage of  $\leq 100\text{ mV}$ .
- *Signal processing*: Amplifier and a LCD for the amplification and display of the ECG waveform and heart rate, which allows direct observation of these parameters.
- *Heart rate computation*: A heart rate meter to indicate average heart rate in numerical form with audible beep or flashing light or both with each beat.
- *Alarm system*: An alarm system to produce signal in the event of abnormalities occurring in the heart rate.

The cardiac monitor is basically similar to the conventional oscilloscope used for the display of waveforms in electronic laboratories. They have the usual circuit blocks like vertical and horizontal amplifiers and the time base for display of time varying ECG with respect to time. However, they differ in two important aspects as compared with the conventional oscilloscopes. The ECG is a low frequency signal, and therefore, the cardiac monitor operates at slower sweep speeds. The monitor also includes memory so as to display a continuously moving ECG trace.

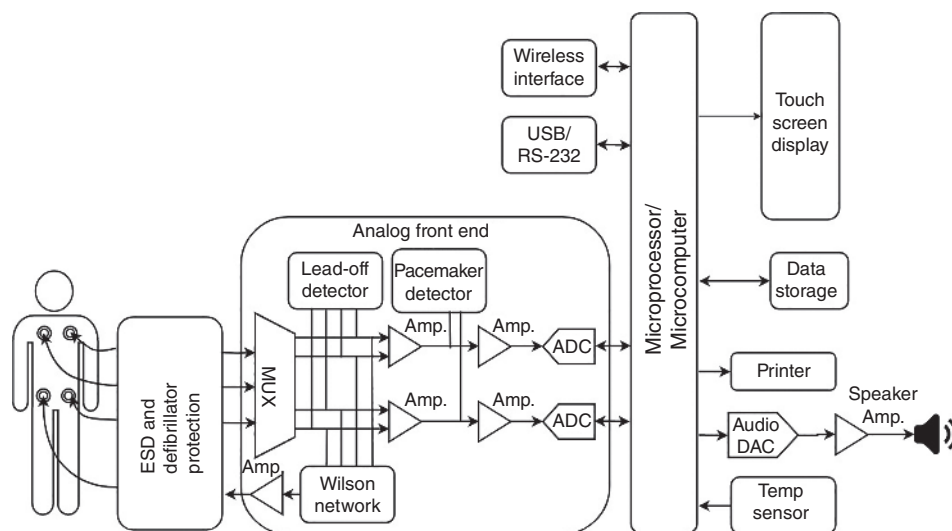
Most of the present-day cardiac monitors are designed to be used at the bedside. They are also available as portable units that can operate on storage batteries. The display screen is mostly about 50 cm, and the unit is usually mounted on one side of the bed at a height at which it is possible to conveniently observe the waveforms from a distance. Cardiac monitors with a smaller screen size of about 20 cm are often mounted on anaesthesia trolleys for continuous monitoring of the ECG of anaesthetized patients.

The cardiac monitor provides a visual display of the patient's heart rhythm, which is particularly useful information during heart attacks, when patients can develop lethal cardiac arrhythmias. The monitor sounds an alarm if the patient's heart rate goes above or below a predetermined number. Computerized ECG monitoring and analysis are now an integral part of bedside monitors. They normally make use of multiple microprocessors that run sophisticated arrhythmia analysis software. However, most of the present-day monitors include automatic monitoring of blood pressure, temperature, pulse oximeter, and respiration rate and are appropriately called vital signs monitors.

Figure 69.1 illustrates a block diagram of a general ECG monitoring instrument. It comprises of several integrated circuits that can be divided into the following sections:

- Analog front end (AFE)
- Power management
- Communications
- Software algorithms

The AFE captures the ECG signal, carries out necessary signal conditioning, and digitizes the signals. The rest of the system analyses, displays, prints a hard copy, stores, and transmits the data via radio frequency (RF) link.



**Figure 69.1** Block diagram of a cardiac monitor. ESD, electrosurgical and diathermy protection.

Source: Courtesy M/s Maxim Integrated, USA.

### **Analog Front End (AFE)**

AFEs in the cardiac monitor share the same basic requirements as that of ECG machine but differ in the number of leads, fidelity of signal, interference for rejection, and so on. While the cardiac monitors have facilities for display of 12-leads, but are generally operated as a 5-, 3-, or 1-lead systems. The essential requirements of AFE include the need to reject interference from strong RF sources, pace signals, lead-off signals, respiration signals, common-mode line frequency, signals from other muscles, and electrical noise. All this is performed on several channels simultaneously. Besides, most cardiac monitors are required to recover quickly from a defibrillation event, which can saturate the front end and charge capacitors. This creates a long recovery time for capacitive coupled circuits.

### **Input Circuit**

The complete input circuit used in present-day cardiac monitors has three main circuit blocks: (i) low pass filter circuit, to suppress RF interference from electrosurgery machines, (ii) high voltage protection circuit, similar to electrocardiographs, to provide voltage clamp in the presence of defibrillator pulses, and (iii) over voltage protection circuit (iv) leads off detection.

### **Electrosurgery Interference**

Electrosurgery machines generate RF signals within a range of 0.4–5 MHz with peak-to-peak amplitudes of 100–1000 V, pulse modulated at rates from 1.5 to 25 kHz for coagulating or 120 Hz for cutting. Cardiac monitors are often used in operation theatres, where the RF is applied through a pointed scalpel at the point of incision, and the

return path for the current is through a wide area electrode on the opposite side of the patient's body. RF interference occurs due to any one of two possible modes. The first and usually the most severe is due to conduction, i.e. the RF energy is actually carried via the patient into the monitor. The second is radiation, by which the RF energy is transmitted through the air and is induced into the circuits of the monitoring instrument and its leads and cables. The ECG signal, on the other hand, is of the order of 1 mV with frequency components below 100 Hz. The ECG input amplifier, the ECG electrode-skin interface, and the scalp-tissue interface are the main sites where interference occurs. Moreover, the common mode RF signal gets converted into a normal mode signal by an imbalance in the capacitance between input to ground and the differential amplifier input.

In order to reduce interference caused by electrosurgery and RF emissions, it is very essential to use filters at the input of leads of the monitoring instruments. To reduce the interference to acceptable levels, the ratio of amplifier sensitivities to the ECG signal (1 mV at less than 100 Hz) and to the electrosurgery machine (100 V at 1 MHz or so) should be at least  $10^5$ . If we use a filter having a cut-off frequency above 10 kHz, a three-pole filter is needed to achieve this level of reduction. Five poles are used in the monitors, three provided by the resistor capacitor (RC) filters within the instrument and two provided by the electrosurgery filters and the conductor-to-shield capacitance of the cable (usually 1000 pF). The imbalance in capacitance from each input of the differential amplifier to the ground also injects a differential RF signal that can be rectified and can produce interference. The imbalance necessary to provide a 100 mV signal is very small, of the order of 0.001 pF at 1 MHz. To minimize this problem, a guard is used, which besides shielding the input circuits from electromagnetic radiation also helps in equalizing the capacitance from input to ground of each amplifier input.

### ***Leads Off Detector***

The 'leads off' detector circuit usually works on the principle that loss of body contact of either the RA or LA electrode causes a rather high impedance change at the electrode/body contact surface, consequently causing a loss of bias at the appropriate amplifier input. This sudden change makes the amplifier to saturate, producing maximum amplitude waveform. This waveform is rectified and applied to a comparator that switches on an alarm circuit (leads off) when the waveform exceeds a certain amplitude.

### ***Quick Recovery Circuit***

In order to avoid problems due to DC drift and supply voltage variations, ECG amplifiers are usually constructed with at least one stage of AC coupling. The circuit employs a high-value series capacitor in between two amplifying stages; a high value is used to maintain a good low frequency response. The presence of this capacitor, however, creates the problem of a very long recovery time after an over voltage appears at the input of the amplifier due to conditions like leads off, excessive patient movement, defibrillator operation, etc. This problem is overcome by using a quick recovery circuit. This circuit basically provides a fast discharge of the coupling capacitor once it has been excessively charged to return to zero level.



### ***Common-Mode Rejection Ratio (CMMR)***

The ability of the amplifier to reject common voltages on its two input leads is known as common-mode rejection (CMR) and is specified as the ratio of common-mode input to differential input to elicit the same response. In addition to the millivolt-level ECG signal, there is a DC offset signal that is hundreds of millivolts, with channel-to-channel common-mode voltages differing by over a volt. Some of the 50/60 Hz common-mode interference can be cancelled with a high-input-impedance instrumentation amplifier, which removes the AC line noise common to both inputs. To further reject line power noise, the signal is inverted and driven back into the patient through the right leg by an amplifier. Only a few microamps or less are required to achieve significant CMR improvement. In addition, 50/60 Hz digital notch filters are used to reduce this interference further.

### ***Frequency Response***

The frequency range of interest for the ECG varies somewhat with the application but is usually around 0.05–100 Hz. Some monitors have two selectable frequency response modes, namely, monitor and diagnostic. In the ‘monitor’ mode or ‘filter-in’ mode, both the low and high frequency components of an electrocardiogram are attenuated. It is used to reduce baseline wander and high frequency noise. The monitor mode bandwidth is generally 0.4–50 Hz (3 dB points). In the ‘diagnostic’ mode, the instrument offers expanded bandwidth capability of 0.05–100 Hz.

### ***Pacemaker Signal Detection***

Filters after the instrumentation amplifiers remove the pacemaker signals before the ECG signal is digitized by the analog-to-digital converter (ADC). The pace signal is passed through a high pass filter, amplified, and detected by a comparator circuit.

### ***Multiplexer***

A separate ADC is used for each lead, or one ADC can be multiplexed with simultaneous sampling to digitize multiple leads. Powerful ADCs with a resolution of about 20–24 bits at a rate of 200 kbps are used to simultaneously digitize the signals on all nine electrodes. When multiple ADCs are used, all the ADC channels must be tightly matched.

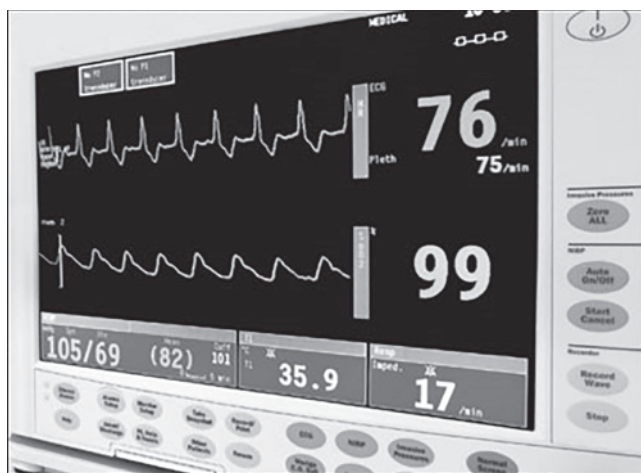
### ***Microprocessor/DSP***

A microprocessor or preferably a digital signal processor (DSP) is used to calculate the signal for each lead, isolate the pace signal, isolate the lead-off/respiration signals, and filter out unwanted frequencies. The DSP also calculates values for a digital-to-analog converter (DAC) driving the right leg drive (RLD) electrode. The output from the DSP goes to LCD display, a hard copy printer, and an RF link. In addition, ECG may be duplicated at a central console at nursing monitoring station via a wired or wireless connectivity. Although most cardiac monitors are commonly used in emergency rooms and critical care areas, cardiac monitoring at central station allows for continual observation of several patients simultaneously.

In the modern cardiac monitors, flat-panel LCD technologies are preferred for display of alphanumeric and graphic information. Flat panels offer advantages of wide-angle visibility (up to 170°) and brightness, resistance to physical shock, and immunity to electromagnetic disturbances. They provide high contrast, high resolution images and data, as well as resistance to glare in high-ambient-light environments such as ambulatory surgical units, emergency rooms, operating rooms, and intensive care units. LCDs employ line-addressed, dot matrix imaging, rather than the complex, pixel-by-pixel raster pattern of cathode ray tubes (CRTs). They are available in formats ranging from 278 × 128 pixels to 1024 × 864 pixels, with preferred screen diagonals of 19 in. LCDs with touch screens are becoming more and more popular in cardiac monitors. A touch-screen display provides the ability for the user to make choices by simply touching icons or graphical buttons on the screen. There are several technologies for touch screens, including 4-, 5-, and 8-wire resistive, surface capacitive, projected capacitive, and surface acoustic wave (SAW).

Cardiac monitors are also available, which display more than one channel of information such as ECG and pulse waveform with digital heart rate display and alarm facility. The display should be minimum for a four second period. This is shown in Figure 69.2. They use time-multiplexing of complete sweeps to avoid the excessive bandwidth introduced by electronic switching or the chopper technique. Each channel, in these instruments, can be independently controlled for updating or freezing the information.

Texas Instrument has developed ADS1298 integrated circuit, which provides standard 12-lead ECG and integrated AFE along with 24-bit ADC. The ADS1298 reduces component count and power consumption by up to 95% and, thus, is very useful for portable ECG monitors. The Analog Devices AD8232 is another integrated signal conditioning block for cardiac monitors. It is designed to amplify and filter small biopotential signals in the presence of noisy conditions, such as those created by motion or remote electrode placement. The AD8232 can implement a



**Figure 69.2** Typical cardiac monitor with pulse oximeter. Source: Courtesy M/s Maxim Integrated, USA.

two-pole high pass filter for eliminating motion artefacts and the electrode half-cell potential. The user can select the frequency cut-off of all filters to suit different types of applications. To improve CMR of the line frequencies in the system and other undesired interferences, the AD8232 includes an amplifier for driven lead applications, such as RLD. The AD8232 is available in a 4 mm × 4 mm, 20-lead LFCSP package. Performance is specified from 0°C to 70°C and is operational from -40°C to +85°C.

### ***Power Management***

All cardiac monitors make use of switch mode power supplies (SMPSs). If noise is likely to affect sensitive analog circuits, a low dropout linear regulator can be used between the SMPS and the analog supply rail. This combination provides a good compromise between power consumption and noise injection from the supply.

### ***Connectivity***

Modern cardiac monitors have provisions for Ethernet and USB connectivity to meet the networking requirements of hospitals and clinics. Wired connectivity is perhaps the preferred method for connecting to the hospital network; however, the trend to go wireless is growing. Wi-Fi is the most widely used wireless standard in the hospitals due to its widespread availability making device integration relatively easy, but due to higher power consumption of Wi-Fi, cardiac monitoring devices working on solely on batteries include lower power wireless technologies such as Bluetooth, Bluetooth low energy, and ZigBee.

### ***Software Algorithms***

Most of the present-day cardiac monitors incorporate computerized software that recognises life-threatening cardiac arrhythmias that aid in the automatic analysis of the ECG signals and detect arrhythmias. Although detection of cardiac arrhythmias is the job of a highly trained clinician, algorithms that enable higher degrees of diagnosis accuracy and precision have now been developed. The software automatically identifies and labels the significant features of the ECG complex. It also calculates the amplitudes and timing intervals of various cardiac events and displays the results on the monitor. The heart rate variability (HRV) is analysed with the online R-R calculator and automated HRV analysis especially before, during, and after exercise or dosing.

Portable ECG monitors are now available as personal devices that record user's cardiac function in single lead and display the waveform. They are useful for daily health check. A typical portable cardiac monitor is shown in Figure 69.3. This device is intended for self-testing by adult users who might experience transient symptoms that may suggest cardiac abnormality so that irregularities in the heart may be detected and managed at an early stage. The pocket-sized device weighs only 100 g and can be used at home or outside for recording ECG. The stored recordings can then be shown to the doctor, who can examine and use the information to derive accurate diagnosis based on the symptoms.



**Figure 69.3** Personal cardiac monitor. *Source:* With permission from M/s Favourite Plus.

## Specifications

*Number of leads:* 12 electrographic standard leads, simultaneous acquisition

*Display:* At least one group of three leads simultaneously

*Display size:* Waveform and alphanumeric values

*Bandwidth:* 0.5–100 Hz

*Storage:* At least 40 ECG records

*Input impedance:*  $\geq 5 \text{ M}\Omega$

*Patient leakage current:*  $< 10 \mu\text{A}$

*CMR:*  $\geq 100 \text{ dB}$

*Alarms:* Ventricular fibrillation; tachycardia bradycardia, and electrode disconnection

*Software:* Arrhythmias detection and analysis; ventricular fibrillation detection and analysis; ventricular tachycardia detection and analysis; and ST segment analysis

Automatic equipment calibration

## Applications

Cardiac monitors are a common equipment used on hospitalized patients to continuously monitor cardiac activity and monitor heart rate and rhythm to identify heart irregularities.

## 70

### Cardiac Output Meter: Fick Method

#### Purpose

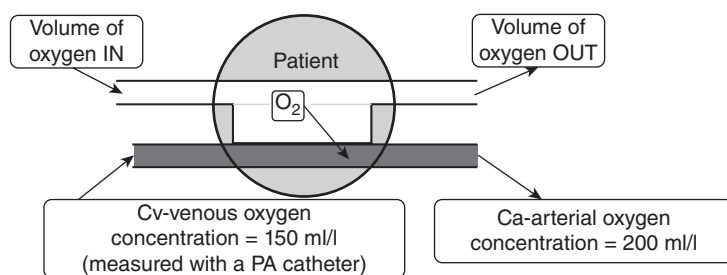
Cardiac output meter is a device to measure the volume of blood pumped by the heart per minute. It is the product of the heart rate and stroke volume. Cardiac output is an

important parameter for cardiac function monitoring that provides an estimate of whole body perfusion oxygen delivery and as a diagnostic tool in understanding the causes of high blood pressure. Cardiac output is of great significance in the management of critically ill patients in the intensive care units and of 'high risk' surgical patients in the operating room.

## Principle

Cardiac output is the quantity of blood delivered by the heart to the aorta per minute. It is a major determinant of oxygen delivery to the tissues. Cardiac output is the product of the heart rate and the stroke volume. Stroke volume of blood pumped from the heart with each beat at rest varies among adults between 70 and 100 ml, while the cardiac output is 4–6 l/min. During exercise, cardiac output may rise to 20 l/min or more. The stroke volume is determined by the filling pressure, the compliance of the ventricular wall during diastole, the arterial pressure, and the contractility of the ventricular wall. A fall in cardiac output may result in low blood pressure, reduced tissue oxygenation, acidosis, poor renal function, and shock. It is a reflection of the myocardial function, and when taken with other measurements such as blood pressure and central venous pressure, the rational treatment of cardiac disorders becomes clearer. There are several methods that are available for measurement of cardiac output. However, the Fick method is the most accurate method and is considered as a gold standard.

The Fick method is based on the principle first described by Adolf Fick in 1870. According to this principle, the blood through an organ can be calculated by continuously infusing a substance into the blood or removing a substance from it and measuring the amount of substance in the blood before and after its passage. The amount infused or removed per unit time is equal to the difference between the amounts in the blood arriving at and departing from the site of measurement. When the Fick principle is used for measurement of cardiac output, the indicator substance used is oxygen. The principle of the Fick method is shown in Figure 70.1. The oxygen consumption is a function of rate of blood flow and rate of oxygen picked up by the blood. It involves measurement of oxygen concentration of arterial and venous blood and measurement of  $O_2$  consumption. For example, the oxygen uptake in the lungs is the product of the blood flow through the lungs and the arteriovenous oxygen content difference. Therefore, cardiac output can be calculated using the equation:



**Figure 70.1** Principle of the Fick method of cardiac output measurement.

$$\text{Cardiac output} = \text{VO}_2 / (\text{CaO}_2 - \text{CvO}_2)$$

where  $\text{VO}_2$  is the oxygen consumption by the lungs and  $\text{CaO}_2 - \text{CvO}_2$  is the arterio-venous difference in oxygen. The cardiac output is calculated by measuring the oxygen contents of arterial and venous blood samples, whereas whole body oxygen consumption is measured by analysing expired air by spirometry. The  $\text{CvO}_2$  oxygen content of blood is measured by taking blood from pulmonary artery (deoxygenated) and for  $\text{CaO}_2$  oxygen content of blood, the sample is taken from a peripheral artery (oxygenated). The blood concentration of oxygen is expressed as ml  $\text{O}_2$ /ml blood, and the  $\text{VO}_2$  is expressed in units of ml  $\text{O}_2$ /min. If  $\text{CaO}_2$  and  $\text{CvO}_2$  are 0.25 and 0.20 ml  $\text{O}_2$ /ml blood, respectively, and  $\text{VO}_2$  is 250 ml  $\text{O}_2$ /min, then  $\text{CO} = 4000 \text{ ml/min}$ , or 4l/min. Ventricular stroke volume can be derived from the cardiac output divided by the heart rate.

The direct Fick technique based on measurement of oxygen uptake is rather complicated, difficult to repeat, and necessitates catheterization and, therefore, cannot be considered for clinical applications. Also, the method is cumbersome and time consuming and requires a facemask or endotracheal intubation, and is not suitable for bedside clinical use.

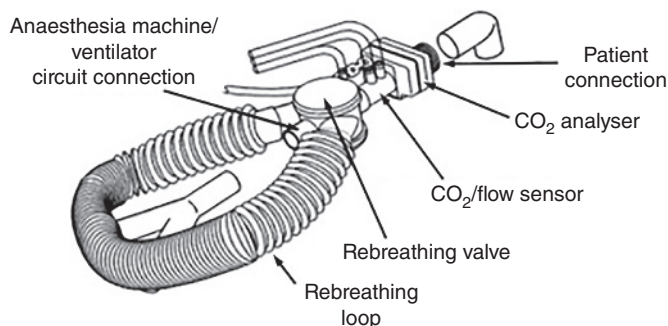
The Fick principle can be applied to all gasses that obey Henry's law and diffuse through the lungs, especially carbon dioxide ( $\text{CO}_2$ ). So, as an alternative method for cardiac output measurement, carbon dioxide production, instead of oxygen consumption, can be used in the Fick equation. In this case, the rate of carbon dioxide elimination by the lungs ( $\text{VCO}_2$ ) and the arterial and mixed venous carbon dioxide contents are substituted for the equivalent oxygen variables as per the following equation:

$$\text{Cardiac output} = \text{VCO}_2 / (\text{CvCO}_2 - \text{CaCO}_2)$$

where  $\text{VCO}_2$  is the  $\text{CO}_2$  production and  $\text{CaCO}_2$  and  $\text{CvCO}_2$  the arterial and mixed venous  $\text{CO}_2$  content in blood, respectively.

The technique has the advantage that right heart catheterization is not required to be performed by having the person rebreathe exhaled air until the carbon dioxide tension in the breathing circuit plateaus. This carbon dioxide tension is theoretically that of the mixed venous blood and can be used in the equation. This Fick technique has been indirectly modified by the change in carbon dioxide tension with partial rebreathing to approximate the mixed venous carbon dioxide tension. The measurement of cardiac output is accomplished by interpreting data collected by proprietary sensors that measure flow, airway pressure, and  $\text{CO}_2$  concentration and then combining these signals to calculate  $\text{CO}_2$  elimination. The partial rebreathing technique has been successfully validated in mechanically ventilated subjects in the operating room, intensive care, or emergency departments. However, the technique can be used only on patients connected to a ventilator and breathing circuit. A loop of dead-space tubing is intermittently added to the patient circuit, which facilitates the rebreathing of carbon dioxide. The cardiac output is derived by measuring carbon dioxide levels in the circuit and applying certain assumptions.

A commercial instrument for measuring cardiac output based on this technique is non-invasive cardiac output (NICO) from M/s Novamatrix Medical Systems, Inc.,



**Figure 70.2** NICO rebreathing loop and circuit attachment added to the patient's breathing circuit while performing the partial carbon dioxide rebreathing method of test.

Wallingford, CT, USA. The monitor employs a specific disposable rebreathing loop (Figure 70.2) with a  $\text{CO}_2$  sensor (infrared light absorption), a disposable air flow sensor (differential pressure pneumotachometer), and a pulse oximeter.  $\text{VCO}_2$  is calculated from the simultaneously measured minute ventilation by the differential pressure transducer and its  $\text{CO}_2$  concentration. The arterial  $\text{CO}_2$  ( $\text{CaCO}_2$ ) content is calculated from end tidal  $\text{CO}_2$  ( $\text{EtCO}_2$ ) after applying a correction based on the slope of the  $\text{CO}_2$  dissociation curve and the degree of dead space ventilation. The partial rebreathing reduces carbon dioxide elimination and increases  $\text{EtCO}_2$ . Measurements under normal and rebreathing conditions allow to omit the venous carbon dioxide content ( $\text{CvCO}_2$ ) measurement, and therefore the need for a central venous access is eliminated. It is also important to note that the patient must be under fully controlled mechanical ventilation if the NICO monitor is to be used.

## Specifications

*Ventilation modes:* Adult patients on controlled mechanical ventilation or patients breathing spontaneously with ventilation support

*Measurement frequency:* Every three minutes for a duration of 35 seconds

*Rebreathed volume:* 35 ml

*$\text{CO}_2$  sensor:* Infrared absorption principle

*Flow sensor:* Pneumotachometer

*Alerts:* Adjustable limits: Cardiac output,  $\text{EtCO}_2$ ,  $\text{SpO}_2$ , respiration rate, no respiration,  $\text{VCO}_2$ , and pulse rate

## Applications

Cardiac output is an important hemodynamic parameter that plays a key role in several physiological equilibriums. It is mostly used in the operating room, intensive care, or emergency departments of well-established hospitals and clinics.



## 71

**Cardiac Output Monitor: Indicator Dilution Method****Purpose**

Cardiac output measurement by indicator dilution method is an invasive technique that measures the amount of blood ejected by the heart every minute for peripheral circulation in the whole body. Measurement of cardiac function is an important tool for assessing the haemodynamic status of a patient in a critical care setting. Since accurate direct measurement of cardiac output is rather difficult as it requires collecting and measuring all of the blood pumped from the heart into the aortic outflow tract, it is necessary to adopt indirect methods for its measurement that would give reasonably equivalent accuracies. Indicator dilution method is one of the indirect methods used for this purpose.

**Principle**

The indicator dilution method for cardiac output measurement became popular after Hamilton, in 1948, who demonstrated that this technique is in agreement with the Fick method. Indicator dilution principle states that if we introduce into or remove from a stream of fluid a known amount of indicator and measure the concentration difference upstream and downstream of the injection (or withdrawal) site, we can estimate the volume flow of the fluid. The method involves injecting an indicator, which may be a dye, thermal, or saline solution into the venous blood, and its concentration is measured continuously in the arterial blood as it passes through the circulatory system. The cardiac output is determined by analysing the resulting time-dependent concentration curve.

Two methods are generally employed for introducing the indicator in the blood stream, viz, it may be injected at a constant rate or as a bolus. The method of continuous infusion suffers from the disadvantage that most indicators recirculate, and this prevents a maximum from being achieved. In the bolus injection method, a small but known quantity of an indicator such as a dye or radioisotope is administered into the circulation. It is injected into a large vein or preferably into the right heart itself. After passing through the right heart, lungs, and left heart, the indicator appears in the arterial circulation. The indicator dilution curves recorded in arterial blood consist of primary and secondary curves due to the initial circulation and then recirculation of the indicator. The presence of an indicator in the peripheral artery is detected by a suitable (photoelectric) transducer and is displayed on a chart recorder. In this way we get the cardiac output curve shown in Figure 71.1. This is also called dilution curve.

The dilution curve shows the concentration of the indicator in the blood plotted as a function of time. During the first circulation period, the indicator would mix up with the blood and will dilute just a bit. When passing before the detector, it would reveal a big and rapid change of concentration. This is shown by the rising portion



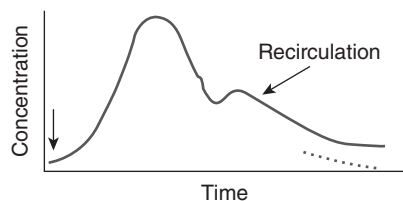


Figure 71.1 Indicator dilution curve.

of the dilution curve. If the circulation system had been an open one, the maximum concentration would have been followed by an exponentially decreasing portion so as to cut the time axis as shown by the dotted line. However, the complicating factor is the occurrence of some recirculation, with the result that the indicator would once again pass through the heart and enter the arterial circulation. A second peak would then appear. When the indicator is completely mixed up with blood, the curve becomes parallel with the time axis. The amplitude of this portion depends upon the quantity of the injected indicator and the total quantity of the circulating blood.

For calculating the cardiac output from the dilution curve, the area under the curve is integrated. Assume that

$M$  = Quantity of the injected indicator in milligram

$Q$  = Cardiac output then

$$Q = \frac{M}{\begin{array}{l} \text{Average concentration of} \\ \text{indicator per litre of blood} \times \text{Curve duration in seconds} \\ \text{for duration of curve} \end{array}} \text{ 1/s}$$

$$= \frac{M \times 60}{\text{Area under the curve}} \text{ 1/min}$$

Suppose 20 mg of the indicator was injected and the average concentration as calculated from the curve was 10 mg/l for a curve duration of 20 seconds. Then  $Q = 6 \text{ l/min}$ .

The area under the primary curve obtained by prolongation of the downslope exponential curve to cut the time axis encloses an area showing the time concentration relationship of the indicator on its first passage round the circulation and does not include any of the subsequent recirculations. It is, therefore, necessary to extrapolate to zero concentration before integrating. It demands a sophisticated algorithm to perform the exponential extrapolation for calculating the area.

### Dye Dilution Method

The dye dilution method for measuring cardiac output is based on injecting rapidly a known quantity of a dye at one site into the circulatory system and withdrawing blood at a distal site for determination of a concentration curve of the dye. The most commonly employed dye for recording the dilution curve is indocyanine green (cardiogreen). This dye is preferred because of its property of maximum absorption in

the infrared part of the spectrum (805 nm) where both reduced and oxygenated haemoglobins have the same optical absorption. The concentration of cardiogreen can be measured with the help of a densitometer. The more modern densitometers are usually equipped with computers. Dye cuvettes of as small volume as 0.01 ml are available.

The procedure consists in injecting the dye into the right atrium by means of a venous catheter. Usually 5 mg of cardiogreen dye is injected in a 1 ml volume. The quantity used may be 2.5 mg in the case of children. A motor-driven syringe constantly draws blood from the radial or femoral artery through a cuvette. The curve is traced by a recorder attached to the densitometer. After the curve is drawn, an injection of saline is given to flush out the dye from the circulating blood. There are, however, some problems relating to the use of the indicator indocyanine green. It has been experimentally determined that above the dye concentration of approximately 20 mg/ml of blood, the optical density rises less with an increase in dye concentration than below this level. Thus for optimum accuracy, the amount of dye chosen for injection should result in dye curves whose peak concentration is less than 20 mg/ml.

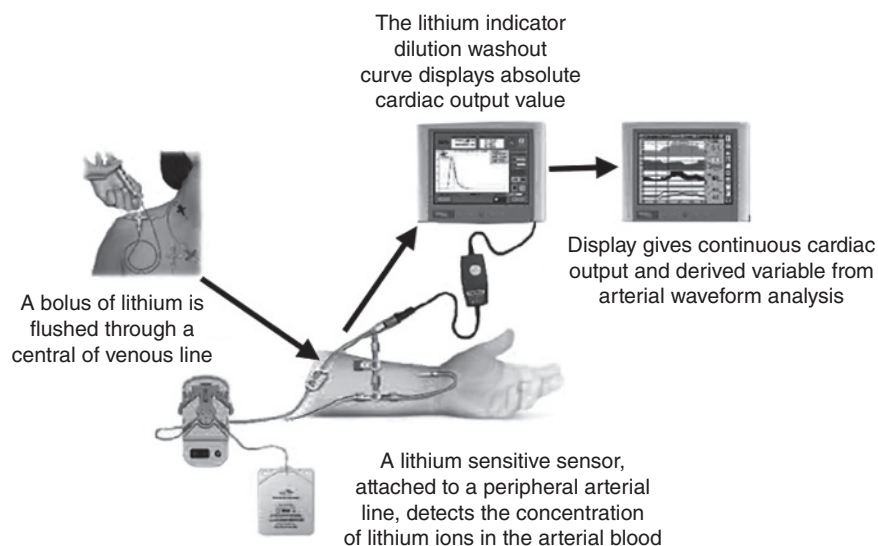
The dye dilution method is safe and may be used on an outpatient basis. A major advantage is that the arterial catheter can be used for determination of blood pressure during exercise, when all other methods based on arm cuff often give inaccurate results, particularly for diastolic blood pressure. However, the method does not allow measurement of 'beat-to-beat' changes in cardiac output and requires stable environment for approximately 10 seconds during exercise and 30 seconds at rest.

### ***Lithium Indicator Dilution Method***

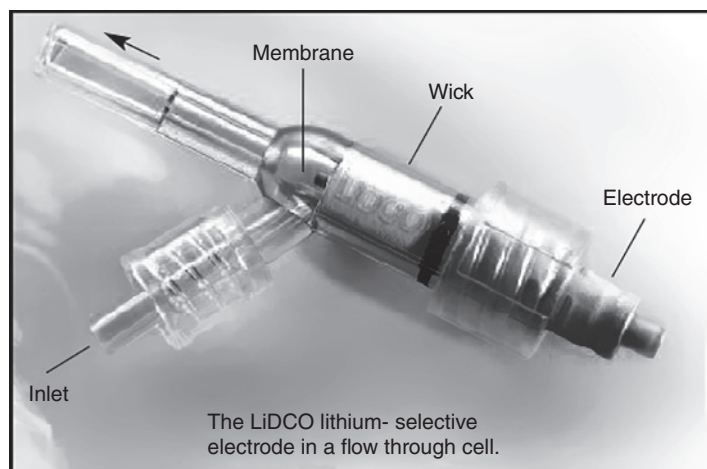
The use of indocyanine green dye as indicator requires frequent blood sampling and analysis of the dilution curve. The method is no longer used in practice being technically difficult and time consuming. The use of lithium as an indicator of cardiac output has since been extensively validated and found to be accurate and minimally invasive. The accuracy of this method is comparable with the established thermodilution technique. The dose of lithium chloride needed is in the range of 0.15–0.3 mmol boluses (maximum cumulative dose 20 ml) for an average adult is quite small and has no known pharmacological effects.

The cardiac output measuring process using lithium chloride as indicator is shown in Figure 71.2. In this method, a small dose of lithium chloride is injected via a central or peripheral venous line. The resulting arterial lithium concentration–time curve is recorded by withdrawing blood past a lithium sensor that is attached to the patient's existing arterial line. This measurement is then used to calibrate pulse contour analysis software, which provides continuous cardiac output data by analysing the arterial pressure waveform.

The *sensor* consists of a lithium-selective disposable electrode placed in a flow-through cell (Figure 71.3). The sensor is connected to a three-way tap on the arterial line and a small peristaltic pump restricts the flow through it to 4.5 ml/min. The flow-through cell is made of polycarbonate with a central lumen and designed with an eccentric inlet so that the blood swirls past the tip of the electrode. The electrical connection between the blood in the cell in the vicinity of the tip of the electrode and the remote



**Figure 71.2** Cardiac output measurement process using indicator dilution method.



**Figure 71.3** Constructional details of the LiDCO lithium-selective electrode in a flow-through cell.

Source: Reproduced with permission of M/s LiDCO Ltd, Cambridge, UK.

reference is made by a wick, which is soaked in saline when the cell is first primed. A reference material fills the electrode to provide a constant ionic environment and supports a membrane. The membrane is made of polyvinyl chloride and contains a lithium ionophore to make it selectively permeable to lithium ions.

The voltage across the sensor membrane corresponds via the Nernst equation to the plasma  $[Li^+]$ . A correction is required to be applied for plasma sodium concentration because when lithium is not present, the baseline voltage is determined by the sodium concentration. The voltage is measured using an amplifier that is optically isolated from

**Figure 71.4** Haemodynamic monitor Model LiDCO plus.  
 Source: With permission from M/s LiDCO Ltd,  
 Cambridge, UK.



the patient, digitized in an analog-to-digital converter and analysed by a proprietary software. The cardiac output is calculated continuously on beat-to-beat basis by analysis of the arterial blood pressure trace following calibration with an absolute cardiac output value. The device does not require recalibration for at least eight hours and more recently for 24 hours.

The instruments based on the use of lithium chloride, in addition to arterial blood pressure parameters and cardiac output, can also calculate and display some useful haemodynamic-derived parameters, which include body surface area, systolic pressure variation, pulse pressure variation, cardiac index, stroke volume, stroke volume index, stroke volume variation, systemic vascular resistance, and systemic vascular resistance index. One such instrument is the LiDCO™ plus haemodynamic monitor from M/s LiDCO Ltd, Cambridge, UK, and is shown in Figure 71.4. The advantages of this technique are that it is minimally invasive and may be used in conscious and unconscious patients.

Strictly speaking, the LiDCO monitor utilizes pulse power analysis rather than pulse contour analysis. The algorithm used is based on the law of conservation of mass for continuous cardiac output calculation. By following the assumption that net power has a linear relationship with net flow, an algorithm is used to calculate cardiac output.

## Specifications

*Output scaling:* 1 V /100 mmHg

*Range:* 0–2.5 VDC (0–250 mmHg)

*Accuracy:*  $\pm 3\%$  of full scale

*Signal to noise:* Better than  $-55$  dB

*Battery:* 3 V, 195 mA lithium battery

## Applications

The cardiac output monitor based on lithium chloride dilution indicator provides a valuable guide to fluid and inotropic therapy in high-risk patients in the intensive care unit, operating theatre, and other critical care areas. Because of the minimally invasive nature of the technology, the device may be used more readily than the pulmonary arterial catheter (PAC). It can be used in management of high-risk patients and patients with a history of cardiac disease and medical emergencies.

## 72

### Cardiac Output Method: Oesophageal Doppler

#### Purpose

The Doppler oesophageal cardiac output monitor provides a minimally invasive method for real-time assessment of cardiovascular status and displays cardiac output and stroke volume (SV), along with a visual and quantitative representation of aortic blood flow, preload (left ventricular end diastolic volume), contractility (inotropic status of the myocardium), and afterload (resistance or load against which the heart has to eject blood). In contrast, the methods like Fick-based technique such as dye or thermodilution are difficult to apply in the perioperative period, whereas the oesophageal Doppler is considered useful for most patients who should not be otherwise put to risk of the insertion of a pulmonary artery catheter.

#### Principle

Cardiac output can also be measured using ultrasound Doppler effect. The technique enables to measure blood flow velocity from which several haemodynamic parameters, including cardiac output and SV, can be derived. When ultrasound beam is directed from a ultrasound transducer towards descending aorta through a probe in the oesophagus, the blood flow through the aorta causes a Doppler shift in the frequency of the returning ultrasound waves. This frequency shift can be used to calculate flow velocity and volume, and effectively cardiac output.

The blood velocity  $V$  calculated from the Doppler equation is as follows:

$$V = \frac{C \times F_d}{2F_o \times \cos \theta}$$

where:  $C$  = Speed of ultrasound sound in tissue (1540 m/s)

$F_d$  = Doppler frequency shift

$F_o$  = Frequency of the emitted ultrasound

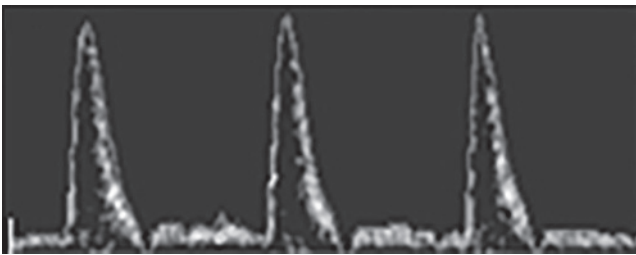
$\theta$  = Angle of insonation, that is angle between the emitted sound and the moving object, that is the angle of ultrasound beam in relation to the blood flow

It is obvious that in Doppler-based flow velocity measurements, the angle of insonation plays an important role. There would not be any Doppler shift if the angle of insonation is  $90^\circ$ . In fact, the Doppler shift is maximum if the angle of insonation is chosen to be as close to  $0^\circ$ . However, this is not practical in medical practice as this would result in considerable reflection from the blood carrying vessel walls. Therefore,  $45^\circ$  is the most commonly used angle in oesophageal Doppler, with the probe lying in the aorta and placed parallel to the aorta. The characteristic aortic velocity signal obtained in this way gives beat-to-beat real-time display of blood velocity against time as illustrated in Figure 72.1.

Accurate velocity measurement requires good alignment between the Doppler beam and blood flow and knowledge of the angle at which the ultrasound strikes the flowing blood. Alignment is optimal when the signal is the brightest on the spectral representation, when the aortic walls are well defined on M-mode echocardiography, and when peak velocity is maximum. The blood flow rate can be calculated by multiplying the flow velocity with the area of cross section of the vessel carrying the blood, which in our case is the aorta. The area of cross section of the aorta can be measured by the echo technique utilizing M-mode ultrasound, but this is seldom done in practice. Average human dimensions for the aorta are available from nomograms that consider sex, age, height, and weight and are generally provided in commercial instruments. However, these parameters may vary for individual patients considerably from the average. Therefore, lack of a precise area of cross section of the particular blood vessel poses a significant potential source of error. The probe position is also critical in minimizing measurement error for both blood flow measurement and aortic cross-sectional area measurement. Even small variation of the position of the ultrasound beam with respect to blood flow will result in underestimation of flow when using the Doppler equation. Also, the aforementioned equations are based on the assumption that the blood flow is laminar flow. Any turbulent flow in the aorta is likely to reduce the measurement accuracy.

The area under the systolic portion of the waveform is known as the *stroke distance*, which is the distance a column of blood moves along the aorta with each stroke of the heart. The SV is calculated from the measured value of the stroke distance and calibration constant derived from the nomogram. Cardiac output can then be calculated by multiplying the stroke value by the heart rate (HR).

An oesophageal ultrasound Doppler instrument for quick and continuous cardiac output and SV measurement has been introduced by M/s Deltex Medical, UK, which is

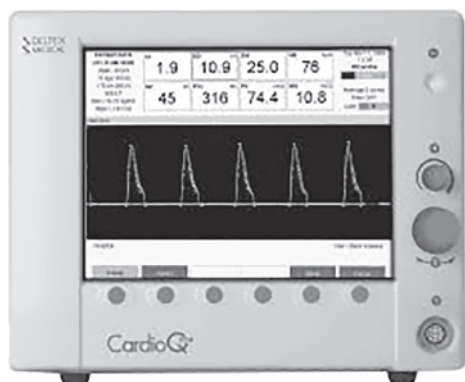


**Figure 72.1** Characteristic velocity waveform obtained in the descending aorta with oesophageal Doppler.

shown in Figure 72.2. In making measurements, a single use, small diameter (6 mm) probe is inserted into the oesophagus and a continuous Doppler signal is obtained, which is displayed as a blood flow velocity signal.

The instrument utilizes descending aortic flow to provide a real-time assessment of the left ventricular performance. The disposable probe emits a continuous ultrasound frequency 4 or 5 MHz. The probe tip shown in Figure 72.3 typically has two transducers. One transducer is used for emitting ultrasound, while the other continuously receives the ultrasound reflected by the moving blood. A proprietary algorithm converts the measured descending thoracic aortic blood flow velocity into total left ventricular SV. The algorithm takes into account the patient's age, weight, and height to generate the conversion factor and does not require any other measurement.

Cardiac output estimation using Doppler ultrasound is a minimally invasive technique that requires the insertion of a lubricated probe, orally or nasally, into the distal oesophagus. The angled tip of the probe containing ultrasound transducers is oriented towards the descending thoracic aorta. The position of the probe is optimized so as to generate a clear signal with the highest possible peak velocity. The probe may often require refocusing to ensure an optimal signal. The probe is inserted typically up to a depth of 35–45 cm for adults, depending on the route of insertion. The transducer is pointed towards the aorta by rotating it to obtain the optimal aortic velocity signal. The procedure thus requires a trained operator. The blood flow velocity is then calculated with the Doppler equation.



**Figure 72.2** Cardiac output monitor based on oesophageal Doppler. *Source:* Reproduced with permission of M/s Deltex Medical System, USA.



**Figure 72.3** Ultrasound Doppler probe. *Source:* Reproduced with permission courtesy of M/s Deltex Medical System, USA.



The accurate, portable, and noninvasive character of Doppler ultrasound allows its use in many settings with patients in the supine position. However, the measurement is affected by operator skill, anatomy, and subject movements, for instance, during breathing. Consequently, the technique suffers from a larger inter- and intra-observer variability. The precision of this measurement depends on the following three conditions: (i) the cross section must be accurate, (ii) the ultrasound beam must be directed parallel to the blood flow, and (iii) the beam direction may not undergo major alteration between measurements.

The cardiac output can also be measured using echocardiography, which is also a noninvasive technique. The technique involves using two-dimensional (2D) ultrasound and Doppler measurements together to calculate cardiac output. The 2D measurement of the diameter of the aortic annulus enables calculation of the flow cross-sectional area, which is then multiplied by the velocity time integral (VTI) of the trace of the Doppler flow profile across the aortic valve to determine the flow volume per beat (SV). The result is then multiplied by the HR to obtain cardiac output.

## Specifications

*Measured values:* HR, stroke distance, minute distance, peak velocity

*Derived values:* Cardiac output, cardiac index, stroke volume, stroke volume index, body surface area

*User inputs:* Patient sex, age, height, weight

*Operating mode:* 4.0 MHz continuous wave (CW) Doppler

*High pass filters:* 300, 900 Hz

*Blood flow velocities:* Up to 2 m/s

## Applications

Cardiac output measurement by oesophageal Doppler is made in many clinical settings, including the operating room, the intensive care unit, the post anaesthesia recovery unit, and the emergency or trauma department. The device is particularly applied in case of moderate- to high-risk patients undergoing surgery and critically ill patients with an unstable haemodynamic status.

# 73

## Cardiac Output Monitor: Pulse Contour Method

### Purpose

Cardiac output monitor based on the pulse contour method performs the same function of measuring amount of blood ejected by the heart every minute to the peripheral circulation. The method consists in calculating the cardiac output measurement by

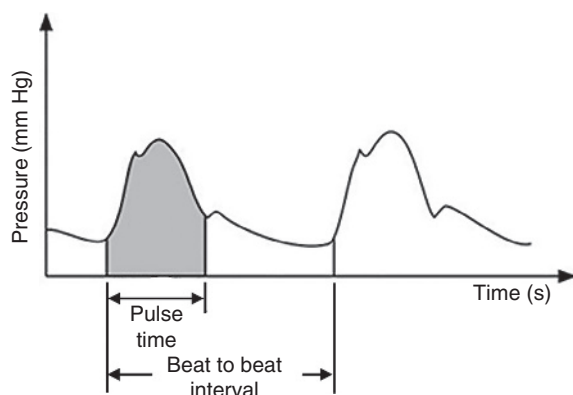


measuring beat-by-beat stroke volume multiplied by heart rate. The stroke volume is reflected by the area under the systolic part of the pressure curve of one heartbeat.

## Principle

It is often necessary to estimate cardiac output on a beat-to-beat basis particularly in critically ill patients. Thermal dilution measurements can be repeated more frequently than the other methods, but even then the measurements can only be made at certain intervals. The technique also requires the presence of well-trained operators for obtaining reliable measurements. These problems are overcome in a technique that is based on pulse contour analysis of the invasive arterial blood pressure curve illustrated in Figure 73.1. The input of the device consists of a pressure measurement, the arterial waveform. The method involves calculating the stroke volume for each pulse with pulse contour analysis and multiplying it with heart rate. The heart rate can be obtained by counting the number of upstroke of the pressure curve over time. However, calculating the stroke volume is quite complex since the pressure measurements must be converted into volume measurements. This technique is considered a minimally invasive procedure as it involves the insertion of an arterial catheter only.

The method is based on the analysis of the aortic pressure wave and estimates the left ventricular stroke volume from the pulse contour. The analysis of the pressure wave depends on simple hydraulic relationships between flow, pressure, and time. During the ejection phase, flow is ejected into the aorta, the total amount depending on the driving pressure, the duration of the ejection period, and the impedance to flow in the aorta. Referring to the figure, the area 'A' under the systolic portion of the aortic pressure wave is integrated, and it is divided by the patient calibrator ( $Z_{ao}$ : aortic characteristic impedance) to obtain a quantity that approximates the left ventricular stroke volume. Thus, changes in the area 'A' would reflect corresponding changes in stroke volume. Cardiac output is then computed for each beat as the instantaneous product of stroke volume and heart rate:



**Figure 73.1** Principle of pulse contour method of cardiac output measurement. Cardiac output is area under the curve multiplied by the heart rate.

$$\text{Stroke volume (SV)} = \frac{A}{Z_{ao}} (\text{cm}^3)$$

$$\text{Heart rate} = \frac{60}{T} \text{ (bpm)}$$

$$\text{Cardiac output} = \frac{(\text{SV}) \times (\text{HR})}{1000} = \frac{60 \cdot A}{1000 \cdot Z_{ao} T} (\text{l/min})$$

The instrument uses pattern recognition techniques to detect the onset and the end of ejection period and integrates the difference between the actual aortic pressure and the end diastolic pressure over that time period. The average value of  $Z_{ao}$  is found to be 0.140 for adults.

The method requires only one pressure measurement at any site in the aorta. The pressure signal can be obtained, both by catheter tip manometers and by ordinary catheter manometer systems. The pressure is usually measured in the aorta or near the aorta proximally in a major side branch such as the subclavian artery. However, in medical practice, the pressure waveform is not obtained from the aorta but from a peripheral artery (radial or femoral), which requires a backward filtering from the peripheral to aortic pressure. The cardiac output is calculated by analysis of the area under the systolic portion of the arterial pressure waveform, from the end-diastole to the end of the ejection phase that is related to stroke volume. Thus, a beat-to-beat analysis of cardiac output, averaged over a period of 30 seconds, is computed and displayed. For reliable operation of the computing circuit, the resonant frequency of the catheter manometer system must be 25 Hz or higher. This method offers a level of accuracy comparable with thermodilution method of cardiac output measurement.

The cardiac output computer consists of three modules: (i) the pressure transducer amplifier, (ii) the cardiac output computer, and (iii) dual numerical display and alarm limits. Quantities, which can be displayed, are mean systolic and diastolic pressure, cardiac output, stroke volume, and pulse rate. Two parameters must be set initially for each patient: (i) patient age and (ii) patient calibrator  $Z_{ao}$ . In addition, waveform display is also provided for visually checking the pressure curve shape and to ensure the correct triggering of the processing circuit. An algorithm is used to determine the cardiac output and produce a continuous read-out. The instrument can be used to monitor trends in cardiac output or for displaying absolute values of cardiac output after calibration.

The device based on this method is designed to display a range of user-defined physiological variables, which include cardiac output, cardiac index, heart rate, and stroke volume variation with respiration as an indicator of fluid responsiveness. Cardiac index is defined as the cardiac output from the left ventricle in one minute to body surface area. Cardiac index thus relates the heart performance to the size of the individual. Stroke volume variation is the difference between maximum and minimum stroke volumes over the respiratory cycle and results from the changes in preload with alterations in intrathoracic pressure.

A number of devices based on the pulse contour method are commercially available. Although their principle of working is the same, they use different methods of calculating cardiac output. For example, the PiCCO system from M/s PULSION Medical



**Figure 73.2** Cardiac output meter based on pulse contour method. *Source:* Courtesy of M/s Pulsion, Germany.

Systems, Munich, Germany, shown in Figure 73.2 employs both central venous (femoral or internal jugular) and arterial cannulation (femoral/radial). Indicator solution injected via central venous cannula and blood temperature changes are detected by a thermistor tip catheter placed in the artery. Thus, it combines pulse contour analysis with the transpulmonary thermodilution CO to determine hemodynamic variables. It requires manual calibration every eight hours and hourly during hemodynamic instability. An algorithm is used to determine the cardiac output by integrating the area under the curve of the arterial pressure versus time trace by using a proprietary algorithm. Another design also utilizes a blood flow sensor, attached to a standard arterial catheter. Cardiac output is calculated every 20 seconds using a special algorithm.

The pulse contour analysis devices depend upon an optimal arterial signal. Over- or under-damped traces are likely to lead to inaccurate cardiac output measurement, necessitating optimum damping coefficient. Besides, arrhythmias, aortic regurgitation, and the use of an intra-aortic balloon pump all affect the pulse contour and affect accuracy. While air bubbles or blood clots in the arterial cannula can be removed, kinking of the cannula may necessitate recalibration or even replacement of the arterial cannula followed by recalibration.

## Specifications

*Cardiac output range:* 0.25–25 l/min

*Measurement accuracy:* Mean error  $\leq \pm 3\%$  or 0.25 l/min

*Stroke volume (SV):* Range 1–250 ml

*Cardiac output index (CCI):* Range 0.1–15.0 l/min/m<sup>2</sup>

*Cardiac function index (CFI):* Range 1–15 l/min

*Cardiac power output (CPI):* Range 0.1–9.9 W/m<sup>2</sup>

## Applications

Cardiac output monitors play a vital role in assessing cardiac function and while making therapy decisions for critically ill patients. They are routinely used during and after major surgical procedures for a comprehensive evaluation of the hemodynamic status of the patient. The technology is well suited in situations where the hemodynamic is unstable and/or when mechanical ventilation is needed for severe hypoxemia.

## 74

### Cardiac Output Meter: Thermodilution Technique

#### Purpose

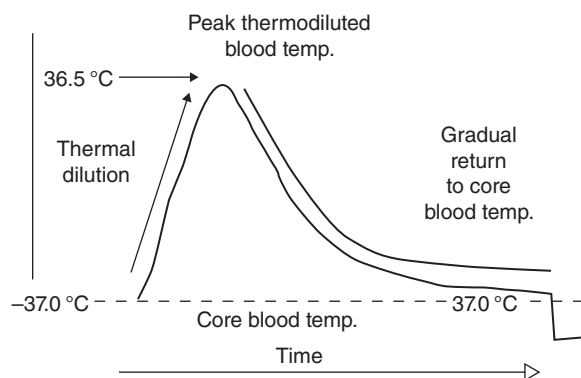
Monitoring cardiac output by thermal dilution method is principally the same as that of the indicator dilution method. The difference here is that instead of using lithium chloride as the indicator, a thermal indicator (cold bolus) is used, and the resultant fall in temperature of the circulating blood is evaluated. Cardiac output monitors based on this technique and using the Swan–Ganz or similarly designed thermodilution catheters are almost considered the gold standard for cardiac output measurement, against which all new monitors are compared.

#### Principle

The thermodilution technique of cardiac output measurement is based on the injection of a known quantity of cold bolus of a sterile solution into the patient's blood stream and recording its dilution in terms of the subsequent change in temperature of the blood measured at distal point of the blood stream, thereby generating a thermal dilution curve as shown in Figure 74.1. The dilution curve displays a sharp change in temperature at the beginning of the waveform. But the gradual downslope under the thermodilution curve indicate slow return of the blood temperature to its core value. As heat unlike dye mixes very well irrespective of laminar flow in the blood vessels, the thermo-indicator can be injected into the right atrium and the temperature recorded in the pulmonary artery. From the area under the recorded dilution curve, the cardiac output can be calculated as follows:

$$\text{Cardiac output} = \frac{\text{'a constant'} \times (\text{Blood temp.} - \text{Injectate temp.})}{\text{Area under dilution curve}}$$

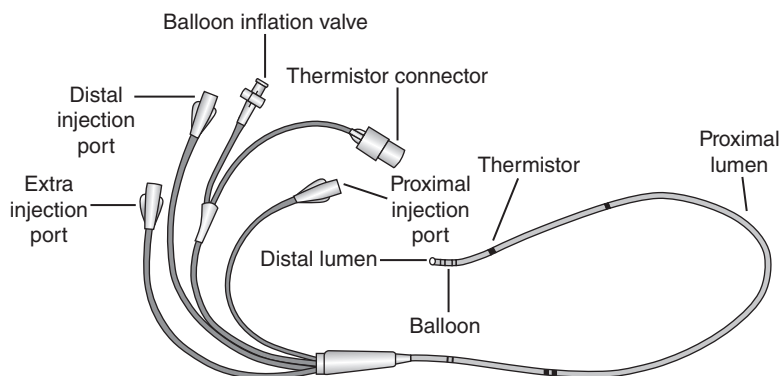
The measurement of cardiac output by thermal dilution became practical and convenient with the introduction of a multilumen thermistor catheter known today as the Swan–Ganz triple lumen balloon catheter in 1971. The balloon, located at or near the tip, is inflated during catheter insertion to carry the tip through the heart and into the pulmonary artery. One lumen terminates at the tip and is used to measure the pressure



**Figure 74.1** Thermal dilution curve. The curve shows fall in temperature with time as the blood circulation takes place in the body.

during catheter insertion. Later, it measures pulmonary artery pressure and, intermittently, pulmonary–capillary wedge pressure. A second lumen typically terminates in the right atrium and is used to monitor right atrial pressure (central venous pressure) and to inject the cold solution for thermal dilution. A third lumen is used to inflate the balloon. For thermal dilution, the pulmonary artery catheter carries a thermistor proximal to (before) the balloon. The thermistor is encapsulated in glass and coated with epoxy to insulate it electrically from the blood. The wires connecting the thermistor are contained in a fourth lumen as shown in Figure 74.2. Once the catheter is inserted into the vein, the balloon is inflated and the returning venous blood carries the catheter until its tip is positioned in the pulmonary artery, which can be checked by measuring the pressure at its tip. The pulmonary artery catheter is attached to the cardiac output computer, which displays a curve and calculates output and derived indices automatically.

This catheter has simplified the technique of cardiac cannulation making it feasible to do measurements not only in the catheterization laboratory but also in the coronary care unit. The acceptance of the thermal dilution technique over the past few years can only be attributed to the development of this catheter. In spite of its limitations, the thermodilution technique remains the most common approach in use today.



**Figure 74.2** Four-Lumen Swan–Ganz catheter.

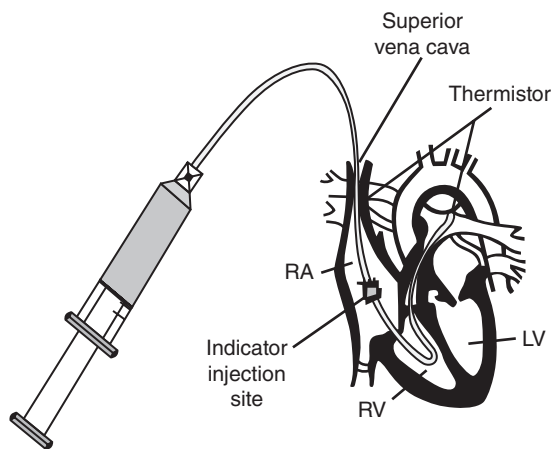
Figure 74.3 shows a typical cardiac output thermal dilution set-up. A solution of 5% dextrose (cold saline) in water at room temperature is injected as a thermal indicator into the right atrium. It mixes in the right ventricle, and the temperature is sensed in the pulmonary artery by means of a thermistor mounted at the tip of a miniature catheter probe. The circulating blood is rewarmed rapidly and no measurable recirculation takes place. The injectate temperature is also sensed by a thermistor, and the temperature difference between the injectate and the blood circulating in the pulmonary artery is measured. The reduction in temperature in the pulmonary artery due to the passage of the dextrose is computed by a simple computer, which consists basically of an electronic integrator and associated controls. The decrease in temperature is inversely proportional to the dilution of the injectate. The direct reading of cardiac output is displayed after being muted until integration is complete so as to avoid spurious indications during a determination.

It may be noted that the cardiac output is inversely proportional to the area under the thermal dilution curve. So, a good cardiac output will produce a curve with a small area, but a patient with insufficient cardiac output would produce a large area under the curve as temperature changes takes place over a longer period of time and results in creating a larger area under the curve.

Blood temperature is measured over a range of 30–40°C to an accuracy of  $\pm 0.2^\circ\text{C}$ . It is observed that normally encountered temperature fluctuation at the measuring point is 0.3–0.5°C. Therefore, the sensitivity of the measuring system is adjusted in such a way that a temperature variation in this range measured by the catheter tip gives a full-scale deflection on the recorder. The total quantity injected is normally 10 ml, which gives a full-scale deflection with the aforesaid sensitivity of the recorder.

### Block Diagram Description

Assuming that the injectate mixes thoroughly with the blood and that negligible net heat flow occurs through the vessel wall during the passage of the blood injectate mixture between the points of injection and measurement, the heat (or coolth) injected can

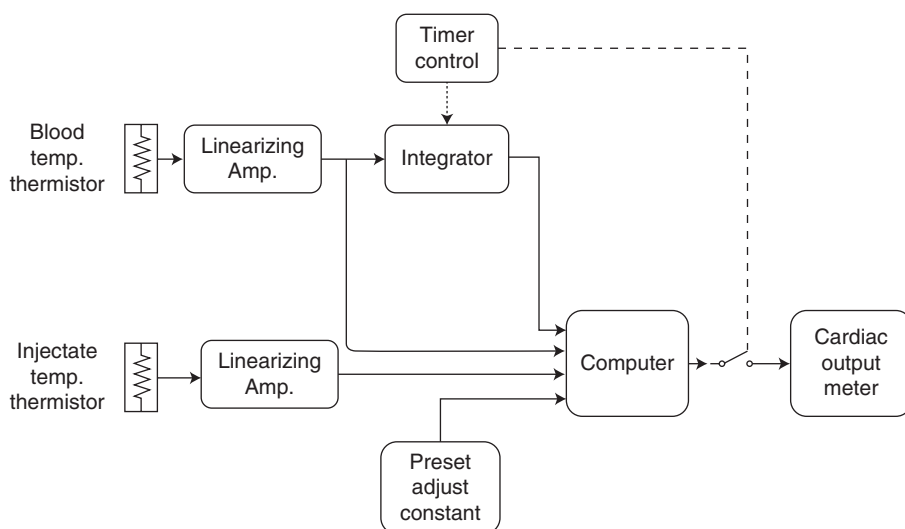


**Figure 74.3** Set-up for measurement of cardiac output based on thermal dilution method. LV, left ventricle; RA, right atrium; RV, right ventricle.

be equated to the heat (coolth) detected. Figure 74.4 shows a block diagram of the processing and computing circuit of thermal dilution method. The linearizing amplifier is based on the principle that a fixed resistance of suitable value placed in parallel with a thermistor will give a virtually linear relation over a limited range of temperature. The integrator responds to a  $\Delta T$  signal corresponding to a maximum temperature change of typically  $0.3^{\circ}\text{C}$  with reference to a temperature baseline, which itself may differ from one patient to another. The summing and multiplication/division operations required for the evaluation of cardiac output are performed by a simple computing circuit. The timer control unit generates the switching signals necessary for the proper integration of the  $\Delta T$  signal and for the display of the computed value of the cardiac output. The cardiac output is displayed in two ranges: 0–10 l/min and 10–20 l/min.

Since there is no significant recirculation of the thermal indicator, the electronic computation is relatively simple and the results are consistent. The calculations simply relate to the integral of the inscribed curve, the resting temperature in the pulmonary artery, the temperature of the injectate, and the number of constants. The system calibration is based upon the use of an injection of 10 ml of 5% dextrose solution at a temperature in the range of  $18\text{--}28^{\circ}\text{C}$ . Within this range, the injectate temperature is measured to an accuracy of  $\pm 0.02^{\circ}\text{C}$ .

In thermodilution cardiac output measurements, the basic source of inaccuracies result due to imperfect indicator mixing. This problem is circumvented by using a pneumatically controlled injector that can provide rapid and consistent injections. These injectors are powered by compressed air or  $\text{CO}_2$  from a pressurized cylinder or a hospital central gas system. Injection speed is usually set at 7 ml/s via standard 7F triple lumen thermistor catheter. Both injection and refill speed are usually kept adjustable. Slow return speed minimizes chances of air bubbles formation during refilling. Injection volume is also kept adjustable in the range 1–10 ml.



**Figure 74.4** Block diagram of thermal dilution method of cardiac output measurement.

As blood flow is pulsatile, injection can be delivered in any part of the heart cycle. However, dilution curve obtained in the pulmonary artery will appear different if injection was done in diastole or systole part of the heart cycle. Optimum injection moment is during diastole, and therefore, injectors are equipped with ECG synchronizer to ensure injection at the right moment. ECG synchronizer consists of an ECG amplifier with adjustable gain. A threshold detector senses appearance of R wave and the interval between two adjacent R waves is measured and stored in the memory. Delay of injection is set manually in a percentage of the cardiac cycle, which makes the synchronizer insensitive to variations in heart rate.

Modern cardiac output measuring instruments form a part of integrated systems that are designed to be used to measure, display, and log ECG with its own low level amplifier and two blood pressure channels in addition to measuring cardiac output and the associated parameters.

## Specifications

*Temperature sensor:* 4–7 k $\Omega$  thermistor

*Range:* 0–50°C

*ECG input:* Three lead: Left arm (LA), right arm (RA), right leg (RL); range: 50  $\mu$ V–2 mV peak-to-peak blood pressure inputs (2) (–100 to +300 mmHg range); resolution: 1 mmHg

*Transducer sensitivity:* 5  $\mu$ V/V/mmHg

## Applications

Cardiac output monitor based on thermal dilution method has the advantages of easy operation, no toxicity, unlimited sequence of measurements, and detection of a quantitative signal from a calibrated thermistor. Most monitors equipped with a computer unit provide a numerical cardiac output measurement within seconds. Otherwise its applications are similar to those of any other type of indicator dilution method.

# 75

## Cardiotocograph

### Purpose

Cardiotocograph is a diagnostic instrument that provides graphic and numeric information on foetal heart rate (FHR) and maternal uterine activity to help clinicians assess foetal well-being before and during labour, to determine any signs of foetal distress.



Some devices are designed to monitor maternal blood pressure and heart rate also before and during childbirth along with the measurement, record, and display of FHR and uterine contractions. Foetal monitors are bedside units that can identify conditions, which when uncorrected can lead to foetal and/or maternal mortality and morbidity.

## Principle

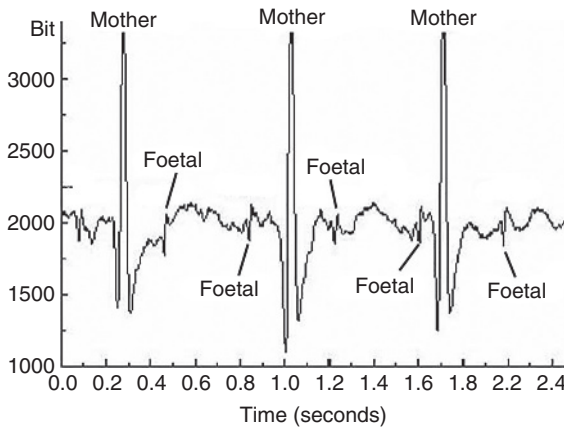
During the last four decades, several techniques, devices, and instruments have become available, which provide reasonably reliable information and data instantaneously about the condition of the foetus during its intrauterine life or at the time of delivery. In most cases, the condition of the foetus is assessed by studying the blood flow in the foetal heart and its heart rate, which is a widely studied parameter in maternity cases. The cardiotocograph is designed to monitor and record FHR on a beat-to-beat basis rather than on an average basis. Normally labour activity and FHR traces are usually recorded simultaneously on the same timescale. The following methods are commonly employed in most of the cardiotocographic monitoring during labour:

| Method                 | Foetal heart rate                                                                                                                       | Uterine contraction                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| Indirect<br>(external) | 1) Abdominal foetal electrocardiogram (AFECG)                                                                                           | Tocodynamometry (using tocotonometer to sense changes in uterine tension transmitted to the abdominal skin surface) |
|                        | 2) Foetal phonocardiogram                                                                                                               |                                                                                                                     |
|                        | 3) Ultrasound techniques (narrow beam and wide-angle transducer)                                                                        |                                                                                                                     |
| Direct<br>(internal)   | Foetal electrocardiogram (FECG) with scalp electrode (spiral, clip, or suction electrode attached to the presenting part of the foetus) | Intrauterine pressure measurement (using a fluid-filled intracervical catheter with strain gauge transducer)        |

### External Methods of Monitoring Foetal Heart Rate

**Abdominal Foetal Electrocardiogram (AFECG)** Monitoring the FECG is presently one of the most promising methods to assess foetal heart health. However, the main problem associated with this method is that FECG signals recorded from maternal abdomen have lower amplitude than those picked up at the same time from the mother maternal electrocardiogram (MECG). They are thus affected by noise and interferences not only from the MECG but also from the muscles of the mother, i.e. electromyographic signals.

FECG is recorded by suitably placing the electrodes on the mother's abdomen and recording the combined maternal and FECG. Figure 75.1 shows a typical recording of FECG picked up from the abdomen. The maximum amplitude of FECG (R wave) recorded during pregnancy is about 100–300  $\mu$ V. This magnitude is much smaller than in the typical adult electrocardiogram (ECG), which is about 1 mV in the standard lead connection. The amplitude is still lower in some stages of pregnancy and may not be even properly detected. The foetus heart rate is approximately twice that of the normal adult ranging approximately from 110 to 180 bpm, which is much faster than mother's



**Figure 75.1** Abdominal recording of foetal ECG.

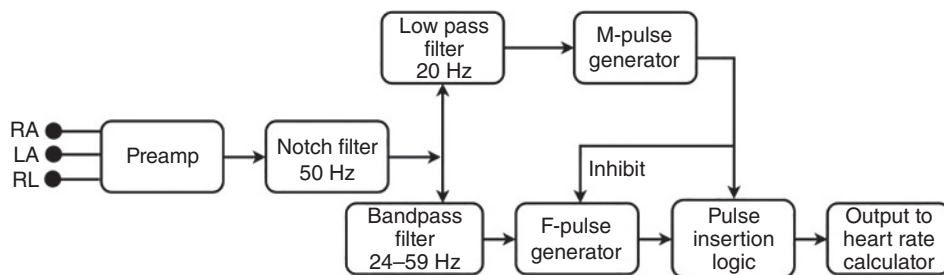
heart rate, which is about 60–100bpm. The FECG can be easily recorded from about sixteenth week of pregnancy.

To facilitate the diagnosis, specialized techniques of signal processing are applied. Frequency filtering is one technique that can improve the signal/noise ratio. This is based on the fact that mother's R wave has the greatest frequency content from 10 to 25Hz, while that of the foetus is greatest from 20 to 40Hz. Another technique is to suppress the MECG and enhance the FECG by subtracting the MECG from the composite signal picked up from the abdomen. In this case, the positioning of the electrodes is very critical, because the subtraction potential must be of the right potential, phase, and shape as the MECG in the recorded composite signal.

The frequency spectrum of each noise source partially overlaps that of the FECG, and therefore, filtering alone is not sufficient to achieve adequate noise reduction. The FHR is computed from the FECG by appropriately shaping the foetal QRS wave. The random sources of noise in the FECG signal recorded from the maternal abdomen include amplifier input noise, maternal muscle noise (electromyogram [EMG]), and fluctuations in electrode polarization potential, whereas maternal ECG is a periodic noise source. A method for dealing with this type of noise problem in FECG utilizes the technique of signal averaging to improve the ratio of signal to random noise. The maternal ECG component is effectively removed from each lead recording by creating an average maternal waveform at each of its occurrences in the recording.

Figure 75.2 shows a block diagram of the AFECG processing circuit for computing FHR. The electrodes are placed on the mother's abdomen, which pick up both maternal and FECG signals. These signals are amplified in a preamplifier, which has a very high input impedance ( $\geq 100\text{M}\Omega$ ), high sensitivity, and good common mode rejection ratio (up to 120 dB). The input stage is preferably isolated so that any earth leakage currents that may develop under fault conditions comply with the safety requirements. The pre-amplifier is a low noise instrumentation amplifier that has a wide dynamic range. Power line interference that is responsible for most of the common-mode interfering signal is suppressed by a notch filter following the input amplifier.

The signal path then splits into two channels: the maternal ECG channel or M channel and the foetal or F channel. Since the frequency spectrum of the FECG is different from the



**Figure 75.2** Block diagram of the abdominal foetal ECG signal processing circuit. LA, left arm; RA, right arm; RL, right leg.

maternal ECG, some initial signal separation is achieved by using the appropriate bandpass filtering in each channel. After filtering, the M signal is assured of being the largest signal component in the M channel, so it can be detected on the basis of peak amplitude.

Due to the overlapping of the FECG with the maternal ECG, about 20–50% of the expected foetal pulses are likely to be missed in the record. Therefore, a pulse train is generated in the F channel and is fed to logic circuits. These pulses determine the rate at which the F channel pulses should normally occur, and if the timing indicates that there should be an F pulse at a time when one is missing, a pulse is inserted into the F channel output pulse stream. However, the logic circuits will not insert two pulses in a row, so there is no danger that the instrument will continue to output normal pulses when no FECG is present.

**Ultrasound Doppler Shift Principle** The Doppler ultrasonic method provides useful diagnostic information about the blood circulation in the foetal heart. An important clinical instrument for obstetric applications, which makes use of this principle, is the foetus blood flow detector. The technique can be conveniently extended to derive the foetus heart from blood flow signals. In obstetric applications, the site of foetal heart varies from 5 to 20 cm below the surface of the abdomen. This depends upon the patient and the stage of pregnancy. For obstetric studies, ultrasonic frequency of about 2–2.5 MHz is usually employed. The level of ultrasonic energy transmitted into the body is generally kept between 10 and 15 mW/cm<sup>2</sup>. Assuming a maximum of 50% conversion efficiency, this implies that the transducer should be powered with an electrical energy below 30 mW/cm<sup>2</sup>.

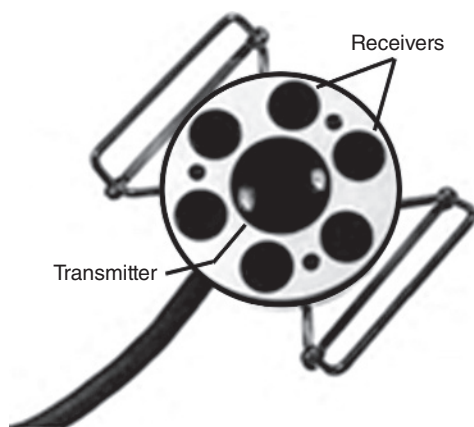
FHR monitoring using ultrasound is done externally by employing a transducer that transmits and receives ultrasonic waves. The Doppler shifted frequency of the received or reflected signal is proportional to the velocity of the reflecting structure, which in this case is the foetal heart walls. The transducer contains one or more piezoelectric elements that convert an electrical signal into ultrasonic energy that is transmitted into tissues. When this ultrasonic energy is reflected back from the tissues, the transducer reconverts it to an electrical signal that can be used to generate a waveform for computing FHR.

Two types of ultrasonic transducers for FHR measurement are in common use. They are the narrow beam and the wide-angle beam types. The narrow beam transducer uses a single ultrasound transmitter/receiver piezoelectric crystal pair in a probe. The typical transducer diameter is 25 mm. The transducer is held against the mother's abdomen wall. A small amount of gel or oil is placed between the probe and abdominal wall to obtain good acoustic coupling. The narrow beam transducer is very sensitive and

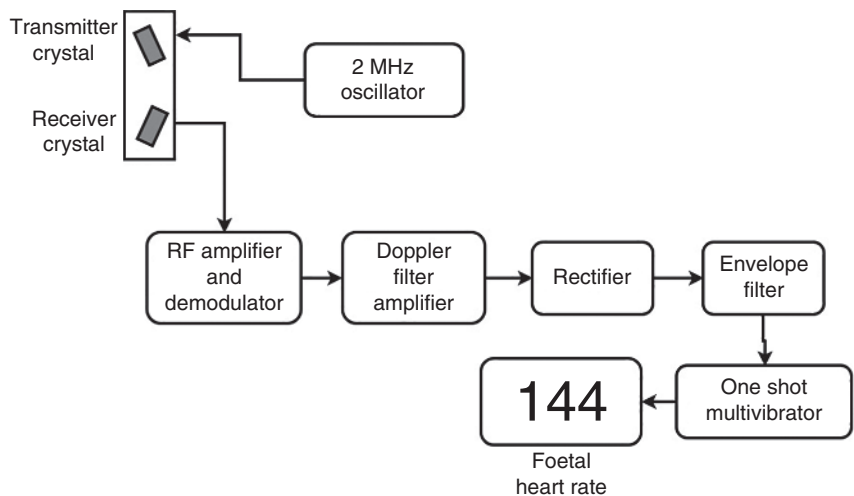
produces a good trigger signal for instantaneous heart rate determination. However, it takes time to detect a good signal, particularly if the foetus is moving. Therefore, frequent transducer repositioning is necessary.

To circumvent the problem of repositioning of the transducer, broad beam transducers have become available in many configurations. These transducers consist of a number of piezoelectric crystals mounted in such a way as to be able to detect foetal heart movements over a wider area. In one arrangement, the ultrasonic transducer is arranged in the shape of a cloverleaf so that it provides a large area of ultrasonic illumination, which allows the monitoring considerable lateral and descending foetal motion before requiring repositioning. The transducer has three crystals on the other side acting as transmitters, whereas the crystal placed at the centre acts as a receiver. An alternative arrangement is the array transducer that has one transmitter and six peripheral ceramic receiving crystals as shown in Figure 75.3. The transmitting crystal emits a  $40^\circ$  divergent beam so that at 10 cm from the skin surface, the beam covers an area of approximately 10 cm diameter. This construction ensures continuous recording of the foetal heart activity without the need to reposition the transducer, which is otherwise necessitated due to normal foetal movement. The transducer has a diameter of 6 cm and can be held in place either by a simple buckle or a stretch belt.

A block diagram of the ultrasonic Doppler shift based FHR measuring circuit is shown in Figure 75.4. This type of arrangement can be used both with a wide-angle beam and a narrow beam transducer. The reflected signal is amplified and mixed with the emitted signal in the demodulator. The output of the demodulator is the beat frequency that is proportional to the blood velocity in the foetus and mother. The beat frequency when amplified can be heard with a loud speaker. The reflected signal is some 90–130 dB lower in amplitude than the transmitted signal. The high overall gain in the receiving channel (+110 dB) requires special measures to minimize the effects of interference. The blood flow in the mother's blood vessels can be distinguished from that of the foetus due to differences in their pulse rates. Different parts of the foetus can be identified and examined due to the variations in blood stream velocity in different parts of the foetus.



**Figure 75.3** Multireceiver wide-angle ultrasound transducer for foetal monitoring.

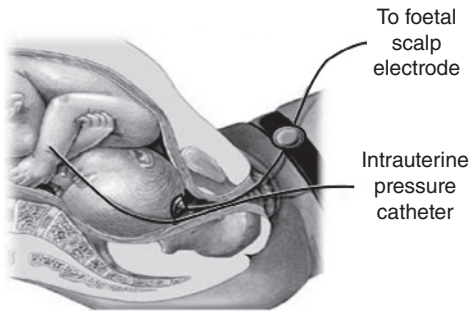


**Figure 75.4** Block diagram of ultrasound Doppler shift based foetal heart rate monitor.

The availability of the foetal heart Doppler signal from the twelfth week of gestation onwards, its usually good signal-to-noise ratio, and the lack of maternal interference makes it practical for measuring each and every heart beat interval. Modern cardioto-cographs use digital technology for generating ultrasound signal and microprocessors or digital signal processor for deriving the heart rate from the Doppler signal. Autocorrelation processor is used by some manufacturers for obtaining a reliable beat-to-beat record from ultrasonic Doppler foetal heart signals.

**Internal Methods of Monitoring Foetal Heart Rate**

**Recording Direct Foetal Electrocardiogram** After the cervix is dilated to about 2 cm or more, it is possible to attach an electrode directly to the presenting foetal scalp. Such electrodes are called scalp electrodes. The use of scalp electrodes shown in Figure 75.5 gives an excellent record of the electrocardiographic signals as the signal-to-noise ratio is much higher than in the abdominal recordings. QRS amplitudes of several hundred (50–300) microvolts are easily obtainable. The FECG is large enough to provide a reliable signal for computing FHR. Maternal ECG signals are rarely present in the direct



**Figure 75.5** Internal transducers for monitoring foetal heart rate and labour activity.

lead connections. For this reason, foetal monitoring with scalp electrodes is the most reliable method during the birth process. While this method has the advantage of producing very clean foetal heart frequency curves, its use is limited to only during delivery periods. The circuit arrangement for processing FECG signals is standard except for having capabilities for handling low level signals.

Three types of electrodes have been used for direct FECG studies, clip, spiral, and suction type. The clip is an adaptation of a surgical skin clip applied to the foetal scalp. It causes little damage to the foetal skin or vaginal tissue. The spiral electrode consists of a double small metallic spiral wire and can be 'screwed' into the upper layers of the skin of the presenting part. This electrode provides larger amplitude FECG signals than the clip electrode. The suction electrode is held on the scalp by suction. It is not preferred because it can get dislodged. Three electrodes are required for the direct detection of the ECG signal. One of the electrodes, called the scalp electrode, is attached to the presenting part of the foetus. The other signal electrode is fixed contacting the vaginal wall. The indifferent electrode is strapped to the maternal leg. Conducting jelly is used with the leg electrode to ensure good electrical contact with the skin. An applicator is provided for attaching the scalp electrode.

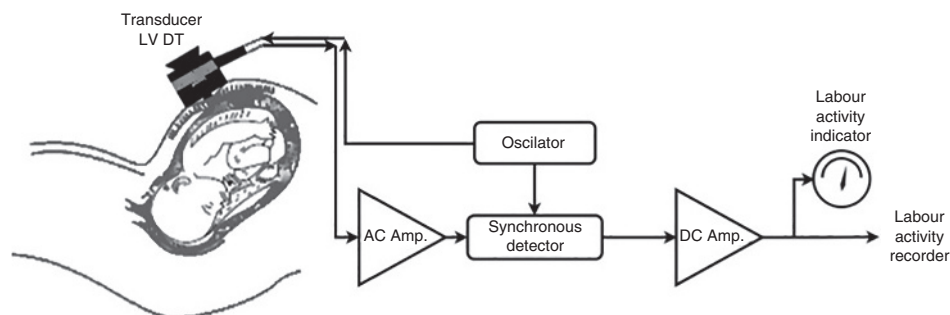
### ***Monitoring Labour Activity***

During labour, the uterus muscle starts contractions of increasing intensity in a bid to expel out the child. The intrauterine pressure can reach values of 150 mmHg or more during the expulsion period. A normal patient in spontaneous active labour will exhibit uterine contractions that occur at intervals of 3–5 minutes, with a duration of 30–70 seconds and peak pressure of 50–75 mmHg. Each uterine contraction acts as a transient stress to the foetus, which may be damaged by excessive contractility or by prolonged duration of labour. Therefore, the labour activity is often measured along with FHR at the time of delivery.

There are two methods of recording labour activity. It can be done in terms of the intrauterine pressure measured directly by means of a fluid-filled catheter placed within the uterus and connected to pressure transducer. The catheter is inserted into the uterus as illustrated in Figure 75.5 through a guide after the rupture of the foetal membranes. The pressure transducer converts the catheter pressure into an electrical signal, which can be displayed on the strip chart recorder. It is necessary to flush the catheter system to avoid any blockage and to maintain the frequency response.

Alternatively, relative indication of the labour intensity can be measured through an external transducer placed on the mother's abdomen. The external pressure-sensitive contraction transducer is called a tocodynamometer (toco), which is fixed to the skin by a band around the belly. The transducer has a protruding tip that is pressed to the mother's abdomen with a light force to ensure an effective coupling. The protruding tip gets displaced with the increase in tension in the uterus. This movement is converted into an electrical signal by a strain gauge in the transducer housing. The abdominal transducer provides a reliable indication of the occurrence frequency, duration, and relative intensity of the contraction.

A block diagram of the arrangement for measuring labour activity externally is shown in Figure 75.6. The transducer output is amplified in an AC amplifier. The low frequency labour activity signal is obtained from the synchronous detector and is further amplified by a DC amplifier. The activity can be either displayed on a digital display or recorded on a direct writing chart recorder.



**Figure 75.6** Cardiotocograph with external transducer for intrauterine pressure measurement.

### Recording System

Instantaneous ‘beat-to-beat’ rate is digitally displayed on the control panel of the device. A two-channel chart recorder is incorporated in instruments used for monitoring labour activity. One channel records FHR on a calibrated chart in beats per minute (50–210 bpm), while the other channel is used for recording uterine contractions calibrated 0–100 mmHg. The record is printed on thermo-sensitive z-fold paper using a high resolution thermal matrix printer. Heart rate, uterine activity, and foetal movement are recorded together with event marks, date, time, recorder speed, and mode. The standard chart speed is usually 1 or 2 cm/min. The chart paper is advanced by a direct-drive stepper motor eliminating the usual gear train.

### Specifications

*Ultrasound transducers:* Wide-angle multi-crystal monitoring transducer

*Mode:* Pulsed Doppler system with directional facility

*Operating frequencies:* 1.5 and 2.0 MHz

*External toco transducer:* Guard-ring tocodynamometer

*Nominal sensitivity:* 150 g full scale

*Foetal ECG with scalp electrode*

*Minimum signal threshold:* 30  $\mu$ V

*Intrauterine contractions (internal intrauterine pressure [IUP])*

*Pressure range (IUP):* 0–100 mmHg and 0–15.0 kPa

*Transducer sensitivity:* 5 mV/V/mmHg IUP

### Applications

The applications of cardiotocography to monitor the baby’s heart rate is extremely important if there are health concerns for the mother during late pregnancy due to bleeding, premature labour, high blood pressure, etc. Monitoring is also done if there are health concerns for the baby in respect of overdue pregnancy or any other abnormality, or baby is showing signs of distress. In a normal, low-risk delivery, cardiotocography is not usually required.



## 76

### Central Gas System

#### Purpose

The purpose of central gas system is to regulate and control the central supply of medical gases from cylinder manifolds or liquid tanks (vacuum-insulated evaporators) in hospital settings. Also known as medical gas pipeline system (MGPS), it is installed to provide a safe, convenient, and cost-effective method for the provision of medical gases for use at the point of requirement, thereby reducing the problems associated with the use of gas cylinders such as safety, portage, inconvenience, and noise.

#### Principle

Medical gases are required to be made available uninterrupted at all the designated locations in a hospital round the clock, 365 days in a year. In addition, the supply must meet the volume and quantity requirements of the gases at the desired pressure in a safe manner. This critical requirement is met by providing a proper pipeline distribution system for medical gases. The pipeline system is designed to deliver effectively the medical gases from the source of supply to the patient via a terminal unit near the bedside. The system provides a very economical and highly dependable life support service and makes better patient care in the critical areas of a hospital.

#### *Important Gases and Their Sources*

Centralized gas and vacuum supply service is a modern system of piped supply of medical gases from a central storage area called manifold room to all delivery points in a hospital. The important gases that are made available through a centralized gas system and their sources are described as follows:

**Oxygen:** Oxygen is the most vital gas that may be needed by any patient admitted anywhere in the hospital and so it is one of the most extensively used gases in hospitals. It is used for respiratory therapy and life support and in anaesthetic procedures. Oxygen is generally supplied from liquid cylinders or compressed gas cylinders or a liquid source such as a large vacuum-insulated evaporator. A combination of these sources can also be used to provide as a backup facility. In situations where liquid or cylinders are not available or expensive, oxygen can be supplied from an oxygen concentrator. In small medical facilities where there is a low patient capacity, oxygen is usually supplied by multiple standard cylinders.

Oxygen is usually supplied at a typical flow of 5–6 l/min. However, each terminal unit is designed to be capable of passing 10 l/min at standard temperature and pressure (STP) at a nominal supply pressure of 400 kPa.



**Medical air:** Medical air is mostly used in respiratory therapy as a power source for patient ventilators and for blending with oxygen. It is also used as the driving gas for nebulized drugs and chemotherapy agents. It is generally supplied from a special compressor or compressed air plant that includes high-quality drying and filtration equipment. Blending oxygen and nitrogen on-site to provide a high-quality product with minimum maintenance can also provide medical air. Medical air at a high pressure, termed as surgical air, is used to power a variety of surgical tools and other devices such as tourniquets. Medical air is usually provided at two different pressures as follows: (i) medical air that is used to drive ventilators and for other respiratory applications require the air at 400 kPa and (ii) surgical air that is used to drive surgical tools require a pressure of 700 kPa or higher at a flow rate between 200 and 350 l/min.

**Nitrous oxide:** Nitrous oxide is used for anaesthetic agent in surgery and occasionally for analgesic purposes when mixed with air, oxygen, and nebulized agents. Although in practice, the flow is limited 6 l/min, but each terminal unit should be capable of passing 15 l/min.

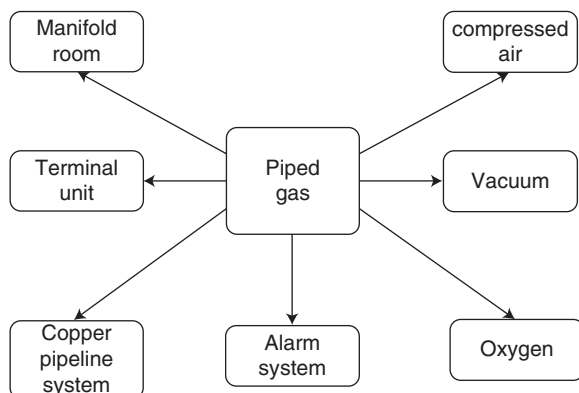
**Vacuum:** Medical vacuum in a hospital is provided to support vacuum equipment and evacuation procedures in most clinical areas by means of centrally sited vacuum pumps. Vacuum is also required for the surgical team and anaesthetist in the operating and recovery rooms. Continuous vacuum is maintained around 75 kPa.

**Other gases:** All other gases that may be required in specific cases are supplied from cylinders. For example, helium/oxygen mixture is used to treat patients with respiratory or airway obstruction and to relieve symptoms and signs of respiratory distress. Nitrogen is often used to provide pneumatic pressure in medical equipment and as a component of many gas mixtures. Carbon dioxide is used to inflate areas of the body for laparoscopy surgery, mixed with air or oxygen to stimulate breathing.

**Waste anaesthesia gas disposal:** The proper disposal of waste anaesthetic gas (nitrous oxide) and nebulized agents is a legal requirement, and for that scavenging systems are required to be installed. Although it uses the same vacuum pump as the medical vacuum system, the piping may be a separate line from the source or can be combined with the medical vacuum. Continuous vacuum must be maintained around 50–65 kPa.

### **Components of a Medical Gas Supply System**

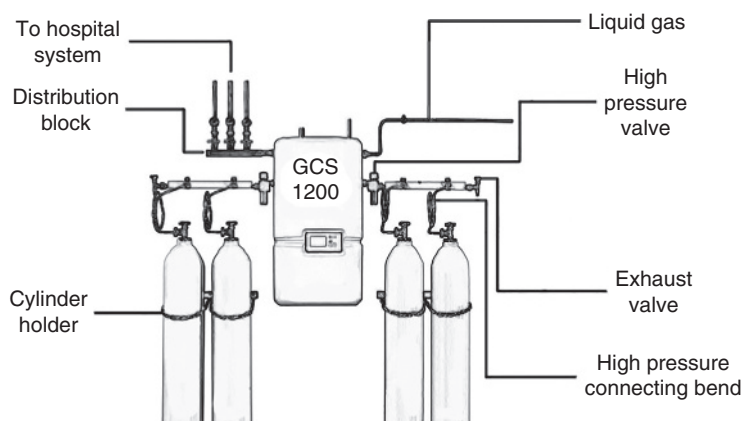
The medical gas system is designed to supply various essential medical gases with desired configurations, at controlled flow rates, and alarm functions. The functions of a medical gas supply system is shown in Figure 76.1. The system consists of source of supply of gases in a central supply room with control equipment and panels and gas distribution system involving piping arrangement, arrangement of suitable outlet valves and pendants at the point of use delivery connections near the bedside of the patient, and suitable monitoring and control equipment and alarms in case of any malfunction in the system.



**Figure 76.1** Various functions of a central medical gas system.

The main components of a medical gas system are shown in Figure 76.2 and are described as follows:

*Central gas manifold:* The central gas manifold system ensures that the supply of medical gases is made available without interruption. In case of an interruption or a gas source becoming empty, the supply automatically switches over to a functional or full gas backup source. The manifold system includes simply a cylinder manifold and a control panel. It is designed to supply the pipeline system with sufficient quantity of gas by cylinders and/or tanks. Accordingly, it normally consists of two-side cylinder supply with automatic changeover between empty and full side, and additional third source for emergency supply. The status of the manifold is continuously monitored



**Figure 76.2** Manifold in a centralized gas supply system.

for pressure level of each source and line pressure level and information forwarded to the central supervisory station.

An average cylinder manifold configuration consists of two equal banks of gas cylinders with a centrally located control panel, which provides a normal output pressure of four bar. The cylinders are usually divided into two groups: primary or duty bank and secondary or standby bank. The supply is automatically changes over to the secondary group when the primary group is nearly empty. The changeover is achieved through a pressure-sensitive device that detects when the cylinders are nearly empty.

The number of the cylinders depends on the expected demand. All cylinders in each group are connected to the manifold via a copper tailpipe with a gas-specific connection and seal. All the cylinders are connected through non-return valves to a common pipe. The non-return valve unit is intended to secure that gas does not flow back from the equipment and pipes through the central gas system. This valve unit consists of a non-return valve with flow direction arrow, lockable medical shut-off valves, nuts, and a gas-specific medical quick coupling for medical breathing air. This in turn is connected to the pipeline through pressure regulators. The gas supply should not be disrupted via the cylinder manifold in case of failure of the electricity. Either both banks or the default bank will continue to provide oxygen supply till power is restored.

The manifold must be housed in a well-ventilated room and built from a fireproof material, either brick or concrete. It should be located away from the main building of the hospital and should ideally have easy access of the delivery vehicles so that the cylinders have not to be carried over long distances. The room is temperature controlled at 10–40°C and is well-lit. Warning signs should be prominently displayed on the outside and inside of the manifold building. The manifold room should not be used as a general cylinder store, and the empty cylinders should be removed immediately from the manifold room.

*Pressure regulators:* Three types of pressure regulators are used in a medical gas supply system. (i) *Manifold pressure regulators:* They are used to reduce high cylinder pressure to a lower pressure within a source of supply of an MGPS. (ii) *Line pressure regulators:* They are employed to reduce the pressure supplied by manifold pressure regulators to the lower pressure required at the terminal units of MGPS. (iii) *Cylinder pressure regulators:* These regulators are used to reduce high cylinder pressure to a lower pressure suitable for use with medical equipment or for delivery of gas directly to a patient.

*Stabilizer unit:* A stabilizer is basically a pressure reduction unit whose function is to minimize the pressure variation in the hospital pipeline system to ensure a stable pressure from the terminal units in various buildings and departments at the hospital. The stabilizer can be delivered with pressure transmitter 4–20 mA, pressure transmitter 0–50 mV, or with contact gauge. Sometimes, it is required to deliver a higher pressure from the main gas manifold to compensate for small pipe dimensions. In such a case, the stabilizer can be mounted as close as possible to the first terminal unit, to ensure a correct pressure to the patient.

*Pipelines:* Pipeline is a system where medical gases and vacuum are delivered from central supply point to different supply points in the hospital. The pipes are made of special high-quality, phosphorus-containing, deoxidized, non-ferrous, and non-arsenical copper alloy, which prevents degradation of the gases it contains as well as has bacteriostatic properties. The fittings used must be copper to copper only, made with a special silver solder brazing alloy to reduce pipe corrosion. The size of the pipes depends upon the demand that they carry. Pipes with a 42mm diameter are usually employed for leaving the manifold, whereas the smaller 15mm concealed pipelines ultimately terminate as gas outlets. Exposed oxygen pipelines should not be installed in areas like kitchen, laundry, and rooms where combustible materials are generally stored.

*Terminal units:* Medical terminal units provide quick and easy connection of hospital ward gas equipment to the hospital gas source. These outlets are located at actual usage point and are usually flush fitting on walls. They are connected to source equipment through the distribution system. The outlets must be gas specific and non-interchangeable and are accordingly colour-coded and labelled with gas name and arranged in various gas orders (e.g. O<sub>2</sub>-N<sub>2</sub>O-air). The outlets have self-sealing sockets that shut down automatically that allows the servicing work to be done on individual units without shutting down the entire system. They are designed for making a quick connection and not to allow a cross connection to a different medical accidentally. A pin guide system also prevents a cross-connection mechanically. The outlets are fitted with locking system and non-return valves. The gas outlets are designed in accordance with ISO EN 9170-1, ISO EN 9170-2 international standards.

An emerging trend in hospital construction is the provision for patient headwall systems, which incorporate many services, besides medical gases, for the patient's care. These include emergency power, direct and indirect lighting, nurse-call system grounding outlets, patient-monitoring receptacles, etc. The headwalls presently available vary in shape, size, type, and cost from a simple over-the-patient-bed standard configuration to elaborate total-wall units.

*Alarm system:* Audio visual alarm systems are provided to warn the maintenance department when the supply pressure is down and the supply station is malfunctioning. A pressure monitoring system gathers the information about the supply source such as the amount of gas remaining in the right and left banks of manifold and the operating condition of supply station and the pressure of gas supplied at each area of section where the gas is used.

*Shut-off valve:* The shut-off valve box is installed on the ward for easy access and for quick shut-off action of the medical gases in a limited part of the central gas supply system. For example, in an emergency situation or during maintenance, it may be necessary to interrupt the gas supply, for which the shut-off valve is used. The valves are usually mounted in a box. The boxes carrying these valves are placed in such a manner that the gas can be shut off section wise. To achieve the demands of safety and maintenance, these boxes are fitted in every main line and placed before wards, operating rooms, and critical treatment areas. The boxes are equipped with unions to be soldered to the copper piping and are individually leak and pressure tested.

**Control unit:** It is necessary that the status of the proper availability of the medical gases at various floors of a building and all such locations is ensured. For this purpose, control boxes are installed at individual floor/location throughout the building. The control boxes have provision to monitor pressure, possibility to close the flow, alarm for out-of-limit pressures, and emergency supply inlet.

**Monitoring:** Modern medical gas systems incorporate computerized network-based monitoring system. The system provides real-time information to the maintenance personnel on the status of all essential medical gas devices. The monitoring system continuously scans every device in the system and displays it on a PC monitor screen. If there is an alarm condition in any of the devices, it is displayed continuously, and the scanning of all other devices gets terminated.

**Safety features:** The gas supply system is designed to ensure that medical gases reach the patient safely, without interruption and in accordance with applicable requirements, rules, and standards regarding quality. The safety valves are usually set at 1.5 times the working pressure. Each pipeline, cylinders, and outlet are colour-coded specific to the gas. There are non-interchangeable adaptors for each type of cylinder and outlet. The pressure regulators are provided with locknut for controlling their misuse. The pipeline pressure is continuously monitored and issue alerts for pressure getting out of the set limit.

## Specifications

**Bed head panel:** A horizontal bed head panel with provision of all the gas outlets and electrical 5/15 A switches, sockets, nurse-call cut-out as per requirement on each bed

**Alarm panel:** Area alarm panel/master alarm panel for all medical gases

**Terminal outlets:** Fitted with quick release mechanism, leak proof, identifiable with colour for specific gas/vacuum

**Flow meter:** Needle valve type fitted with inlet filter – 100  $\mu\text{m}$ , flow rate range between 0 and 15 l/min, minimum inlet pressure 60 psi

**Alarm system for gases:** Audio visual alarm for high and low level gas pressures

**Manifold:** Nominal flow rate – 120  $\text{m}^3/\text{h}$ , operating pressure – 3.5–5.5 bar

## Applications

Medical gases form the very backbone of a hospital and most other healthcare facilities. They are the life-supporting element that has direct influence in maintaining the life of a patient. It would be impossible to run a hospital effectively without these gases. Central medical gas system plays an essential role in the functioning of critical care units and key operational areas like operating rooms, intensive care units (ICUs), and high-risk procedural areas. Most of the ventilators are run by medical air in the hospital. In ICU, the patients receive oxygen, and in operating rooms, gases like nitrous oxide and carbon dioxide are utilized frequently.

## 77

**Centrifugal Analyser: Automated****Purpose**

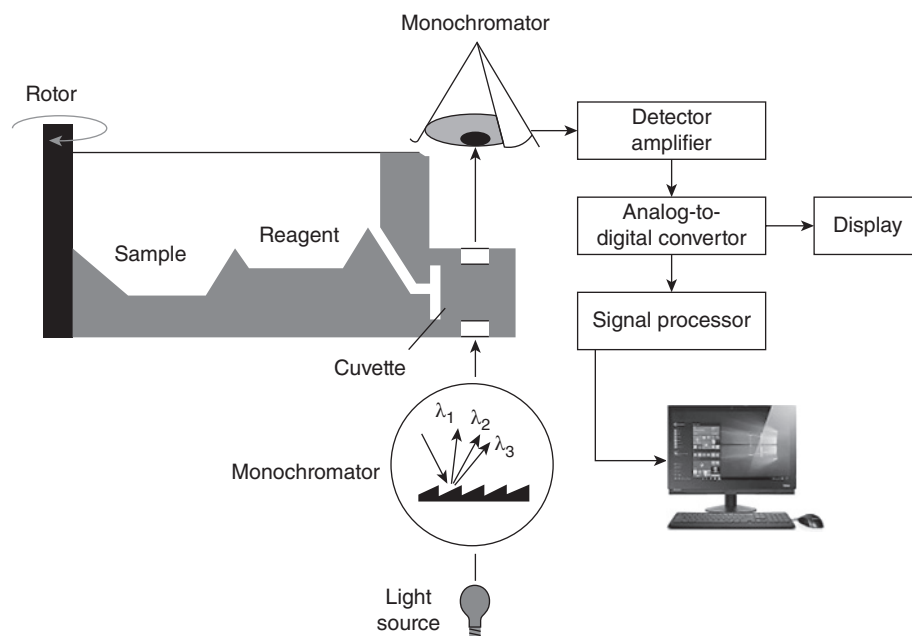
Centrifugal automated analyser falls under the category of automated clinical analysers, which are used to carry out analysis of a number of biological constituents of clinical interest that are considered necessary for diagnosis and monitoring of therapy. They are particularly deployed where well-established methods are not suitable or particular difficulties are encountered in their analysis. These analysers are specifically used for studies of rapid reactions having half-lives of seconds or for routine enzyme analysis in clinical laboratories. They use relatively small volumes of sample and reagents, and hence they have become popular instruments for measuring enzyme activities.

**Principle*****Automated Analysers***

Automatic analytical systems generally fall into two categories: *continuous flow analysers* and *discrete analysers*. The distinction is based on how transport of the specimen is achieved. In a discrete instrument, each sample is maintained as separate entity and kept in a separate vessel throughout each unit operation when it is transported through the analyser. Discrete analysers are of several types; prominent among them are centrifugal and in situ. In continuous flow systems, all specimens go through the same continuous path and the sample becomes a part of the flowing stream. Several operations take place on the flowing sample as it moves from the sample carousel to the flow-through measuring system and then to the waste container. The samples are separated only by the time between them as they pass through each point of operation in the analyser. Continuous flow systems are usually based on two technique, namely, segmented flow analysis system and flow injection analysis system, although the former has been more popular among the users.

***Centrifugal Analyser***

In centrifugal analysers, the reagents and the sample are added into separate specially designed centrifugal type cuvettes. The centrifugal force is then used to mix the sample and the reagents together, and the mixture is then propelled into the corresponding cuvette that is in the outer rim of the rotor. It is here that the contents of the reaction are measured. The principle of working of an automated centrifugal analyser is shown in Figure 77.1. It consists of a rotor that carries multicuvette assembly for samples, reagents, and the detector for measurement. The cuvette has three compartments, which are oriented radially around a circular transfer disc. Samples and reagents are delivered either automatically or manually in specially designed wells of a Teflon or plastic transfer disc. Samples are then kept in an autosampler in the sample cups from which they are added to the sample compartment of the centrifugal cuvette. Similarly, the reagent



**Figure 77.1** Block diagram of centrifugal clinical chemistry analyser. It shows cross sections through a centrifugal analyser showing the wells holding the sample and the reagents, the mixing of the sample and the reagents, and the configuration of the spectrophotometric detector.

is added to the reagent compartment of the centrifugal cuvette by the reagent probe that may be one or two. Both sample and reagents are maintained at the reaction temperature. Control and monitoring of the temperature of each of the solutions are achieved by means of thermistors (sensors) and heated air, circulating water baths, or electrically heated cuvette spacers.

The sample and the reagent are pulled into the outermost cuvette (microcell) by the centrifugal force where mixing of sample and reagent takes place when the rotor holding the cuvette is spun at high speed (4000 rpm) and then suddenly stops. Thus, the sample and reagent get added due to the spinning action while the mixing occurs due to the turbulence caused by sudden stop. The transfer and mixing process may take from 2 to 25 seconds to result in a series of completely homogeneous reaction mixtures. The reaction mixture then settles at the bottom of the cuvette. After mixing, the rotor is spun at 1000 rpm.

The outer edge of the transfer disc has clear transparent sides for spectrophotometric measurement. The final reaction product is passed through the flow cell (10–500  $\mu\text{l}$ ) of the photometer. The flow speed is maintained at 0.5–5 ml/min. A single fixed optical source and detector are used to measure the absorbance, every time the cuvette passes through the optical beam path. Wavelength isolation is achieved by incorporating interference filters or a diffraction grating into the light path. The detector output is connected to amplification circuits and analog-to-digital converter and a microcontroller. An LCD display allows visual observation of the 'real-time' pulsed signals and alphanumeric values from each cuvette. The test results and data are also available on a printer-generated hard copy. The operation of the rotor and the accumulation, processing, and storage of data are all accomplished by the microcomputer.



The system requires a very small sample size, which could be as small as 2  $\mu\text{l}$ . The requirement of reagent volume is also quite small of the order of 250  $\mu\text{l}$ . The only disadvantage is that only one test type can be performed each time. This type of analyser allows many samples to be assayed both simultaneously and rapidly and is sometimes referred to as a parallel-fast analyser. The analysers are all computer controlled, and the results are monitored by a computer, which calculates concentrations and averages results that become available in 30–180 seconds after the start of the rotor. Most analysers are equipped with an automatic wash cycle that takes place at the end of each analytical run. In this way, the transfer disc and cuvette assembly areas get cleaned and dried to be ready for the next run. Some analysers also include ion-specific electrodes (ISEs) module that allows the determination of chloride, sodium, and potassium in serum, plasma, and urine samples. Batch analysis is a major advantage of centrifuge analysers because reactions in all cuvettes are read virtually simultaneously.

## Specifications

*Number of samples:* 144 samples/h

*Parameters:* 40–60 analytes

## Applications

These instruments are ideally suited for monitoring the rates of chemical reactions, as they attain rapid temperature, which is accurately and precisely maintained that is necessary when using kinetic methods of analysis. These instruments are comparatively flexible, allowing the user to choose a methodology, to some extent, one may like to use. Centrifugal analysers are utilized for analysis of a large number of metabolites.

# 78

## Centrifuge: Blood Bank

### Purpose

Centrifuges are used in blood banks to centrifuge the ‘whole blood’ received from the donors. The blood bank centrifuges are usually big and heavy. They are mostly refrigerated and stationary and are mostly employed in hospitals. They are also widely used in pharmaceutical industry, research centres, vaccine manufacturing industry, and university laboratories. Thus, large capacity centrifuges are critical components in both blood banking and bioprocessing applications.



## Principle

The function of blood banks is to collect, process, store, and distribute blood and blood products. An important piece of equipment in the blood banking workflow is the centrifuge machine, which is required to separate whole blood into red blood cells (RBCs), platelets, and plasma. These machines are large in size as they are designed to carry 16 ml × 500 ml blood bags. Blood bank centrifuges usually spin with a speed of 4000–6000 rpm. The heavy-duty steel fabricated centrifuge is provided with stainless steel inner chamber and effectively insulated to provide sufficient cooling of the chamber. A typical blood bank centrifuge is shown in Figure 78.1.

The blood bag liners are held in position in rotor buckets. Rotor buckets are generally nickel coated that provide protection against corrosion due to moisture, chemicals, or alkaline solutions. The blood bag liner enables easy transportation and stabilization of blood bags for processing. The liner stand simplifies the bucket loading and unloading process, resulting in improving the quality of the blood separation. The separation is closely impacted by the physical properties of blood and the physical principles of centrifugation. Therefore, it is necessary to determine the appropriate centrifuge parameters such as time and speed and the optimal acceleration and deceleration profile for the optimal centrifugation for blood component production.

## Rotor

A number of designs of rotors are available for a broad range of applications. For example, in the swinging bucket rotor design, four hermetically sealed round buckets for 1000 ml each or rectangular buckets that can accept up to 120 ml × 15 ml tubes can be accommodated. In another design, six different types of buckets are used. Four buckets



**Figure 78.1** A typical blood bank centrifuge from M/s Thermo Fisher Scientific, USA.

are specially designed for centrifuging blood and producing thrombocyte concentrations. Two other buckets used in combination with various adaptors allow all tubes with nominal volumes between 1.5 and 1000 ml to be centrifuged. The nominal speed of the rotor is kept around 5000 rpm. The speed may be selected in 10 and 500 rpm increments. The rotor is driven by a powerful brushless induction motor with low level of vibration and noise with smooth acceleration and deceleration. The rotor is situated in the centre of a centrifugation bowl.

In most of the machines, different rotors can be fitted to the drive to match the sample containers and achieve the required performance. The maximum speed and consequently the centrifugal force is a function of the rotor in use. The rotor speed, acceleration and braking rates, runtime, and temperature are all monitored from the control unit. The control unit is microprocessor controlled and allows automatic rotor recognition and digital control of speed. It incorporates radius correction features that permit g-value calculation with compensation for varying tube sizes and adapters. The braking power can be adjusted to any of the available intensity levels. The microprocessor controls the centrifuge with temperature controller, speed controller, and LED display for efficient performance.

### ***Time***

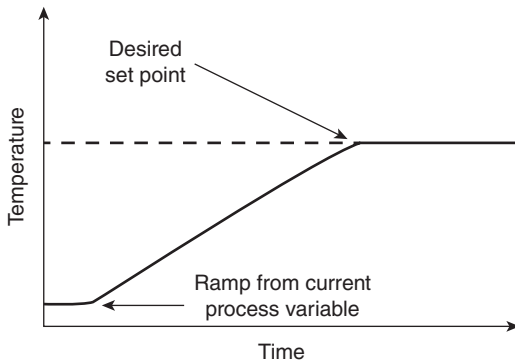
Operation time may be set from 1 to 60 minutes or continuous operation. The amount of time remaining to complete the run is displayed on the control panel. The centrifuging time is controlled by a programmable timer, which applies power to the motor for the time entered by the operator on the panel.

### ***Temperature***

The temperature can be set from  $-10$  up to  $+40^{\circ}\text{C}$ . The temperature indicator indicates preset and actual sample temperature. Different types of temperature controllers are used to control the chamber temperature. Some machines use 'ramp and dwell' type of temperature controllers that have the facility to ramp their effective set point towards the final target value at a predefined rate. When the set point reaches the top of the ramp, a 'dwell period' begins where the set point is maintained at this value. Ramping provides protection to a process from rapid changes in the set point that may otherwise result in thermal shock as the controller may try to force the process variable to follow. This feature is particularly useful when there is a frequent power cut, because it guides the rise back to the target set point when power is restored. The principle of ramp and dwell type temperature controller is shown in Figure 78.2.

### ***Display***

The front panel displays on LED either rotor speed (in rpm) or g-force. In case of selection of speed exceeding the maximum rating of the installed rotor, the centrifuge will automatically correct the setting to the maximum speed of the rotor without terminating the run. This important safety feature eliminates the possibility of overspeed.



**Figure 78.2** Principle of ramp and dwell type of temperature controller used in blood bank refrigerated centrifuge.

### Refrigeration System

The function of the refrigeration system is to allow the rotor chamber temperature to be controlled at a lower level than the ambient temperature. The cooling unit has either an air-cooled condenser or a water-cooled condenser. For the cooling system, the chlorofluorocarbon (CFC)-free refrigerant R 404A is commonly used. The refrigerant fluid circulates around the bowl to achieve maximum efficiency. The rotor and rotor chamber can be pre-cooled to the required working temperature prior to a centrifuge run. The blood bank refrigerated centrifuge range is useful for temperature sensitive samples.

### Safety Features

At any time, the centrifuge detects a fault condition, the screen will display a special message indicating the nature of the fault. The fault condition could be imbalance of the inserts requiring redistribution of the samples to produce an equal weight on diametrically opposite sides of the rotor. The imbalance detector automatically stops in case there is any imbalance. The other fault conditions include improper shutting of the lid, motor over temperature, overspeed, and chamber over temperature. Safety features also include a lid latch safety switch that automatically shuts off power to the centrifuge motor and brakes the centrifuge when the lid is opened. The lid cannot be opened while the rotor is spinning. Similarly, the motor cannot spin while the lid is open. If there is a power failure, a fail-safe system can be used to open the lid.

### Specifications

*Maximum speed:* 4900 rpm

*Speed range:* 500–4900 rpm

*Speed accuracy:*  $\pm 10$  rpm

*RCF (gravitational acceleration 'g'):*  $7300 \times g$

*Maximum capacity:* 4 ml  $\times$  1600 ml, 6 ml  $\times$  1000 ml

*Timer range:* 0–99 hours 59 minutes 59 seconds

*Temperature range:*  $-20$  to  $+40^{\circ}\text{C}$

*Accuracy:*  $\pm 1.5^{\circ}\text{C}$

## Applications

Blood bank centrifuges find applications in blood banks, biochemistry, biotechnology, and pharmaceutical industry, where large volumes are required to be centrifuged at high speeds and constant temperatures.

# 79

## Centrifuge: Cell Washing

### Purpose

Cell washing centrifuges are special-purpose machines that support specific applications in the clinical and medical industry such as washing away cellular debris, extraneous proteins, and other constituents from red blood cells of donor blood. The washed red blood cells are used for tests such as cross-matching prior to blood transfusion, and thus cell washing centrifuge is a vital equipment for use in blood banking and other laboratory procedures.

### Principle

A cell washing centrifuge is generally a benchtop machine that is designed to separate and wash the sample with saline in multiple washing cycles using saline solution. The cell washer provides blood cells after sample separation, which can be used for further blood testing such as antiglobulin test, ABO compatibility, Rh testing, cross-matching, and antibody screening.

In construction, a metal cabinet supports a centrifugation chamber, which is a removable plastic guard bowl. The drive assembly comprising brushless induction motor having permanently sealed self-lubricating ball bearings is mounted to the cabinet base. The motor shaft projects through the centre of the guard bowl. A solenoid plunger and a rotor are set on the motor shaft. A cover assembly forms the top section of the chamber. An aluminium cover assembly includes a feed-dispensing nozzle for inserting saline solution into the tubes in the rotor and a cylindrical splash guard for directing the decanted waste into the drain hole in the chamber. The machine is microprocessor

controlled and employs a peristaltic pump for dispensing saline solution. A typical cell washing centrifuge machine is shown in Figure 79.1.

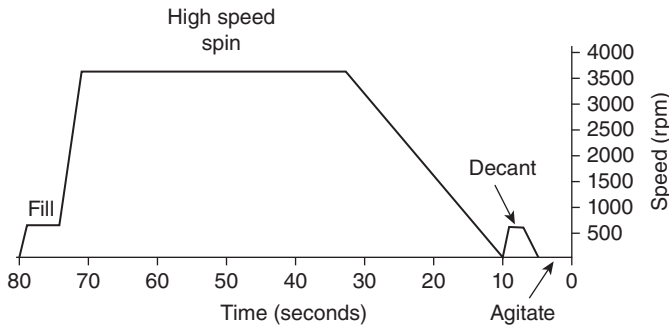
All electrical and electronic components, along with the peristaltic pump and the rotor drive assembly, are mounted on the base section of the machine. The cell washer operates on the gravity principle for drainage purpose. Therefore, the drain tubing should flow downward without any restriction. If the drain line becomes kinked or restricted, there is a possibility of the drained liquid backing up the drain hose and into the motor compartment causing motor failure. When the cover is closed and latched, an interlock prevents the cover from opening when the rotor is in motion. The interlock also prevents operation when the cover is not closed.

The cell washing centrifuge machines usually accommodate either twelve 12 mm × 75 mm tubes or twelve 10 mm × 75 mm tubes. The appropriate quantity of saline solution is filled equally into 12 or 24 tubes, depending on the rotor and mixed with a previously pipetted drop of blood. During the washing process, which consists of several wash cycles, the physiological saline solution is added successively, the erythrocytes are sedimented by the centrifugation process, and finally the physiological saline solution is decanted again. The machine can be programmed to run up to four or more wash cycles. Each basic wash cycle run is for 80 seconds, which is stored in the system memory. The required number of wash cycles is programmed by the user. Each wash cycle involves four phases as illustrated in Figure 79.2 and described as follows:

*Fill (low speed):* In this phase, saline wash solution is drawn from the reservoir by the peristaltic pump. The saline moves up through the flow control valve, the flow switch, and the saline dispensing nozzle. The nozzle feeds the saline into the inlet porthole in



**Figure 79.1** Typical cell washing centrifuge machine with different rotors.



**Figure 79.2** Wash cycle in a cell washing centrifuge.

the rotor distributor. From there, the filler tubes supply the saline into the test tubes in a well-directed stream.

**Spin (high speed):** During this phase, the system rapidly accelerates to full speed. Automatic dynamic braking at the end of this phase results in providing rapid deceleration.

**Decant (low speed):** In this step, the tubes are held by the rotor at a slight negative angle and the spent saline is expelled from the test tubes by low centrifugal force. Here, almost all residual saline is effectively removed while retaining virtually all cells in the tubes. Decanted waste solution is then driven into the waste container through the drain tubing.

**Agitate:** In this step, rapid 'stepping' motion of the rotor results in breaking up the cell pellets for resuspension of the cells during subsequent wash cycles. The system automatically eliminates the 'agitate' step from a single, or the final, wash cycle so that the clean pellet is well defined at the completion of the run. If desired, the agitation sequence may be manually added at the end of the run.

The four-step wash cycle is fully automated so that all the necessary steps for precise and thorough cell washing process are taken care of. Cell washers spin at relative centrifugal forces (RCFs) at or below  $1500\times g$  and support 3 and 5 ml culture tubes. The machine includes all safety features typical of a centrifuge machine.

## Specifications

**Capacity:** 12/24 tubes – 12 mm  $\times$  75 mm or 10 mm  $\times$  75 mm tubes

**RCF (gravitational acceleration 'g'):**  $1200\times g$

**Maximum tube size:** 10/12 mm  $\times$  75 mm

**Cycle time:** 80 seconds.

**Spin speed:** 3500 rpm

## Applications

Cross-matching tests are a part of the routine work in transfusion centres. These tests are used to establish whether the donor blood is compatible with the blood of the recipient. The cell washing centrifuge provides support for this task, by performing the onerous steps to be automated.

## 80

### Centrifuge: Haematocrit

#### Purpose

Haematocrit centrifuge is an equipment that uses centrifugation to measure the ratio of the volume of compact red blood cells to the total given volume of blood. Haematocrit, also termed as packed cell volume, is expressed as a percentage in relation to the volume of whole blood. Interpretation of the resulting packed cell volume may be used to detect the presence of anaemia or polycythaemia.

#### Principle

The working principle of haematocrit centrifuge is the same as that of laboratory centrifuge, but the sample sizes are much smaller. Thin capillary tubes contain only a small amount of blood, so that the required forces are kept relatively low. At the end of a centrifugation, the capillary tubes display the results and no further analysis is necessary. The speed of haematocrit centrifuges ranges from 7000 to 15 000 rpm.

The haematocrit centrifuge can hold up to 24 capillary tubes of size 1.2 mm (or 1.5 mm)  $\times$  75 mm. Centrifugation of anticoagulated whole blood results in the packing of red blood cells. The haematocrit reading is the percentage of the volume of packed red cells in relation to the total volume of whole blood. The haematocrit tube is filled with anticoagulated whole blood, one end sealed by heat or insertion into a sealing clay and then centrifuged. A typical haematocrit centrifuge machine such as that shown in Figure 80.1 features a digital timer, up to 99 minutes, fixed speed, brake control, and reading scale. The machine has a thermal cutout switch to prevent overheated operating temperature.

The microhematocrit centrifuge is a special-purpose version of a fixed-head centrifuge machine that can quickly attain speeds of 11 000 rpm and relative centrifugal forces (RCFs) of up to 15 000 g to spin microcapillary tube samples. Only a small quantity of blood sample is adequate for these small tubes. The components of a microhematocrit centrifuge are usual and comprise of a motor that supplies power to the shaft and rotor,

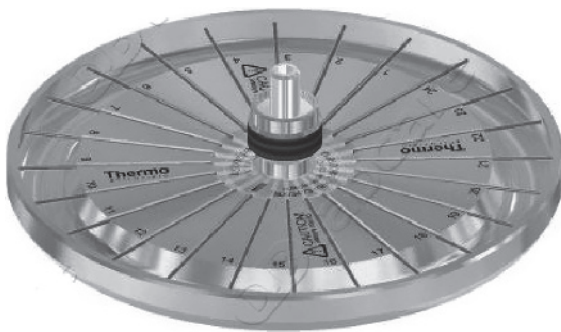


**Figure 80.1** Typical haematocrit centrifuge.

centrifuge carriers (heads) that spin on the rotor, and lid latch. The rotor with the tube fixed for centrifugation is shown in Figure 80.2. The motor used is brushless induction motor that is capable of accelerating the rotor to its maximum speed in a very short time. The motor is protected against overheating. The lid also serves as an evaluation disc allowing determination of haematocrit values without having to remove the capillaries and disturbing the sedimentation. The centrifuge head contains the cups or shields that cover the rotor and turns on a spindle. A safety shield in the chamber surrounds the rotor.

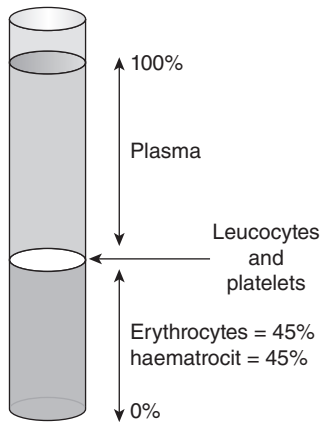
Some microhematocrit centrifuges include a reading scale, a capillary tube reader, a timer, a braking system, a tachometer, and a potentiometer. Some models are equipped with LED display and a small keyboard, enabling the user to program a specific speed or view device status.

The time and speed of the machine are controlled by a microprocessor control system. The performance parameters such as speed and time can be programmed from the front panel keyboard. The rise in sample temperature is minimized by means of the



**Figure 80.2** Haematocrit rotor carrying capillary tubes.





**Figure 80.3** Various components of blood after centrifugation.

continuous air flow system through the air channels in the lid. As in other centrifuge machines, the lid locking system ensures that the lid cannot be opened while the rotor is spinning and the program cannot be started if the lid is open or not closed well. The rotor is made of polypropylene, which is resistant to a wide range of chemicals and can be autoclaved.

The measurement of haematocrit is done by filling a heparinated capillary tube about three-fourths with blood and sealing the unused end of the tube by holding it near the tip and pushing it into a tray of sealing clay at a 90° angle with a twisting motion. The tube is then placed in one of the grooves of a microhematocrit centrifuge with the sealed end facing the perimeter of the centrifuge tray. After closing the lid, the centrifuge is run for four minutes. The tube is then removed from the centrifuge. The fractions of plasma, a thin lightly coloured buffy coat, and red blood cells are clearly seen in the tube as shown in Figure 80.3. The red blood cell fraction can be read from the tube in percentage on the graduated tube.

## Specifications

*Maximum capacity:* 24 capillaries

*Rotor speed:* 200–14 000 rpm, 10 rpm increments

*Capillary tube size:* 1.1–1.2 mm × 75 mm (length)

*Maximum RCF:* 14 490 × *g*

*Timer:* 30 seconds to 99 minutes

## Applications

The haematocrit centrifuge is intended to provide laboratory tests for haematocrit values in the fields of biochemistry, microbic immunity genetics, and blood separation, as well as general clinic tests.

## 81

## Centrifuge, Laboratory

### Purpose

A laboratory centrifuge is a piece of equipment, used mainly in the clinical laboratories to separate the components of body fluids such as blood and urine through centrifugal force. Like all other centrifuges, laboratory centrifuges work by the sedimentation principle, where the centripetal acceleration is used to separate substances of greater and lesser density. In hospital clinical laboratories, benchtop laboratory centrifuges are mostly used. These are commonly referred to as general purpose centrifuges as they offer versatility and convenience and can be equipped in many ways to meet a broad range of clinical requirements, making them a cost-effective solution for many laboratories.

### Principle

The examination of the components of body fluids such as blood and urine are important diagnostic tests. But before particles of body fluids can be analysed, they must be extracted from the supporting fluid. This is precisely accomplished by a centrifuge machine. The liquid samples are put in the test tubes and spun around at high speed in a centrifuge machine, which exerts large centrifugation forces on the sample. In effect, the substances get separated due to their differing densities. The particles with a higher density than that of the solvent sink or sediment, whereas the particles that are lighter float to the top. The separation of particles from a sample by a centrifuge takes place according to their size, shape, density, viscosity of the medium, and the machine rotor speed.

A centrifuge is driven by a motor, which spins liquid samples at high speed. There are various types of centrifuges that depend on the size and the sample capacity. Benchtop or table-top platform is the most common type of centrifuge as this type of machines offer versatility and convenience and can accommodate most applications, though they have smaller throughputs. Tabletop models include general purpose low speed clinical centrifuges used for diagnostics; high speed instruments for whole-cell harvesting; and cell washers, which are highly specialized for washing red blood cells. Floor model centrifuges, on the other hand, are generally chosen for either high speed or high-capacity sample processing. The floor models include superspeed centrifuges, ultracentrifuges, and low speed centrifuges.

Centrifuges depend on the principle of applying centrifugal force to separate suspended particles from a liquid or to separate liquids of different densities. By creating forces many times greater than gravity, centrifuges can greatly accelerate separations that occur naturally as a result of density differences. The relative centrifugal force (RCF or g-force) that the samples undergo depends on the speed of rotation in rpm and the rotating radius. The rotating radius is measured from the centre axis of the rotor to the extreme ends of the centrifuge tubes. RCF is a unitless numerical value, which is normally used to compare the separation or sedimentation capacity of various centrifuges, since it is independent of the type of device.

The parameters such as speed, RCF, and the rotor radius are interrelated as per the following formula:

$$\text{RCF} = 11.18 \times 10^{-6} \times r \times n^2$$

$r$  = radius in cm

$n$  = speed in rpm

If two values are given, the third value can be determined by the equation. If the speed or the rotation radius is changed, the resulting RCF will be recalculated. If the RCF is altered, the speed will get accordingly altered.

The laboratory centrifuge machines generally operate on AC mains supply and operate at low or medium speeds, typically up to 6000 or 12 000 rpm. The major parts of the machine are an electric motor, a vertical shaft, a horizontal rotor attached to the upper end, and control electronics. The motor chosen is asynchronous three phase induction motor. The asynchronous direct-drive motor used is brushless for quiet operation. The small bench top centrifuge machines can also operate on a single-phase universal motor. The motor is called universal motor because it can run on both AC and DC.

Three different types of rotors are mostly used in the centrifuge machines:

*Swing-out rotor:* A metal arm holds four or six buckets, which swing outwards to a horizontal position during centrifugation. The sample tubes are held in these buckets by means of adapters. The buckets are designed to carry several tubes. Swing-out centrifuges are generally used for low speed applications.

*Fixed angle rotor:* The sample tubes are held in a solid rotor at a fixed angle, usually between 20° and 45°. The fixed angle centrifuges are faster and less expensive than swing-out types and are mostly general purpose machines.

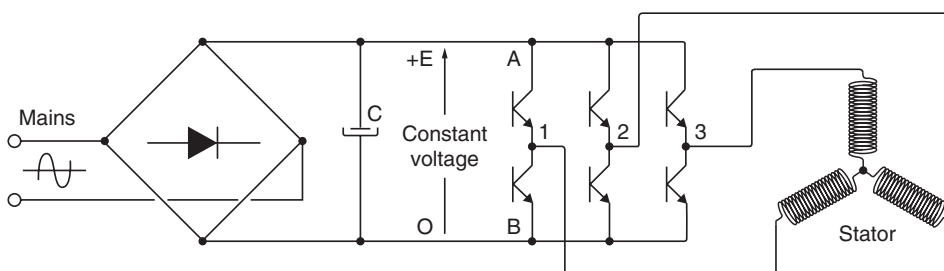
*Vertical rotor:* Here also the tubes are held in a solid rotor but in the vertical position. The machines with vertical rotors are used in ultra-high speed centrifuges.

The modern laboratory centrifuges are microprocessor controlled in which the centrifuge management program is embedded in the EPROM. The control electronics generate sinusoidal three phase voltages, which can be varied in amplitude and frequency. The rotor is connected directly to the motor shaft and there is no gear or other mechanism in between. Most of these centrifuges spin at RCFs at or below 3000×g. The volume of sample required ranges from 3 ml up to 15 ml tubes, with throughput ranging from 4 to 28 tubes per run, depending on the tube size and machine selected. Centrifuge tubes are precision-made, high-strength tubes of glass or plastic made to fit exactly in rotor cavities. Figure 81.1 shows a typical laboratory centrifuge along with the details of the rotor construction.

Figure 81.2 shows the circuit diagram of power control system for the motor. Three voltages, variable in amplitude and frequency, de-phased by  $2\pi/3$ , is supplied from a 50 Hz single phase mains supply. The voltage is rectified by a bridge circuit followed by a capacitor filter to supply the constant voltage +E. The six transistors act as switches (open or closed). These transistor commute at a fixed frequency (8 kHz). The transistors are given opposite commands, e.g. A = closed and B = open. By changing the cycle ratio (closed/open), it is possible to vary the amplitude and frequency of the sinusoidal waveform. The laboratory centrifuges incorporate several safety features.



**Figure 81.1** A typical laboratory centrifuge along with the details of the rotor.



**Figure 81.2** Speed control circuit in a centrifuge machine.

A number of sensors are used for sensing abnormal conditions. These sensors operate under the control unit as shown in Figure 81.3. The various sensors are as follows:

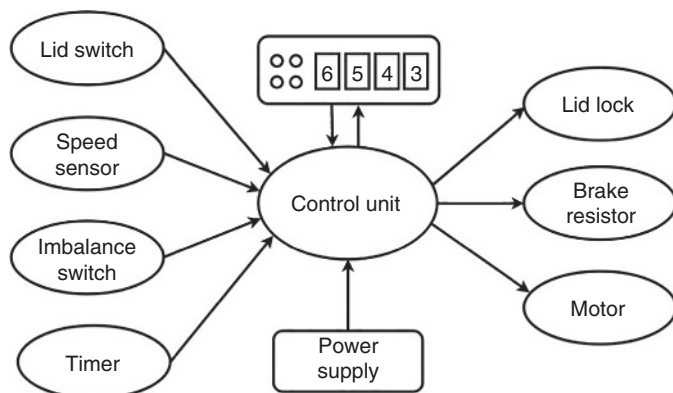
**Speed sensor:** The speed sensor is usually a Hall effect sensor, which uses a magnet mounted on the motor shaft. The Hall effect sensor responds to the magnetic field of this magnet. The output is a square wave signal with a frequency of pulsed output signal that depends on the speed of the motor. The higher the speed, the higher the frequency. Photoelectric sensors are also employed in some machines as speed sensors.

The speed control circuit compares the square wave signal from the sensor with the set speed from the control panel and adjusts the voltage for the motor until the actual speed reaches the set value. The speed signal also activates the safety lock.

**Brake:** The function of the brake is to decelerate the motor. The brake is just a resistor that bypasses the rotating motor. The rotating motor acts as a generator and produces energy, which is absorbed by the resistor resulting in heating. The 'generator' thus runs under heavy load and slows down.

**Imbalance detector:** An imbalance sensor is basically a microswitch, which is mounted on the motor close to the shaft. In case of an imbalance due to the rotor loading, the shaft starts to wobble and finally activates the microswitch, thereby sending a signal to the control circuit, which stops the motor.

**Lid sensor:** This sensor ensures that the centrifuge should not be started when the lid is open. The sensor is a microswitch mounted at the lock mechanism that detects an open lid and passes this information to the control circuit.



**Figure 81.3** Various types of sensors in a centrifuge machine that operate under the control of a control unit.

**Lid lock:** This provision keeps the lid locked during centrifugation by preventing the lid from opening while the rotor is spinning. This is achieved by using a solenoid that is activated by the control unit. Only when the speed sensor detects a standstill, the solenoid is activated and releases the lid.

**Temperature sensor:** A thermistor in the rotor chamber continuously monitors chamber temperature. A temperature control system allows to set the run temperature between  $-20$  and  $+40^{\circ}\text{C}$ . The microprocessor calculates the required chamber temperature to maintain the selected rotor temperature.

**Timer:** The machines are provided with an electromechanical timer, although modern machines include an electronic timer.

The current machines are microprocessor controlled that manages all the sensors including those for speed, lid lock, imbalance, timer function, motor, and the brake.

## Specifications

*Maximum speed:* 13 000 rpm

*Timer:* At least 60 minutes

*Rotors:* Both fixe angle and horizontal (swinging bucket) rotor fittings

*Number of samples:* 6 samples at one time

*Sample tube:* 5–15 ml

*Electronics:* Microprocessor control with digital display

## Applications

A laboratory centrifuge finds applications in clinical laboratory, histology, haematology, immunology, microbiology, pathology, serology, and toxicology in most laboratories from academic to clinical to research fields.

## 82

## Microcentrifuge

### Purpose

The microcentrifuge is normally used in research laboratories where small samples are required to be subjected to high relative centrifugal force (RCF) (g-force) for relatively short time intervals. They are available both as non-refrigerated and refrigerated bench-top centrifuge used in research and routine laboratories in the biosciences and clinical and analytical laboratories.

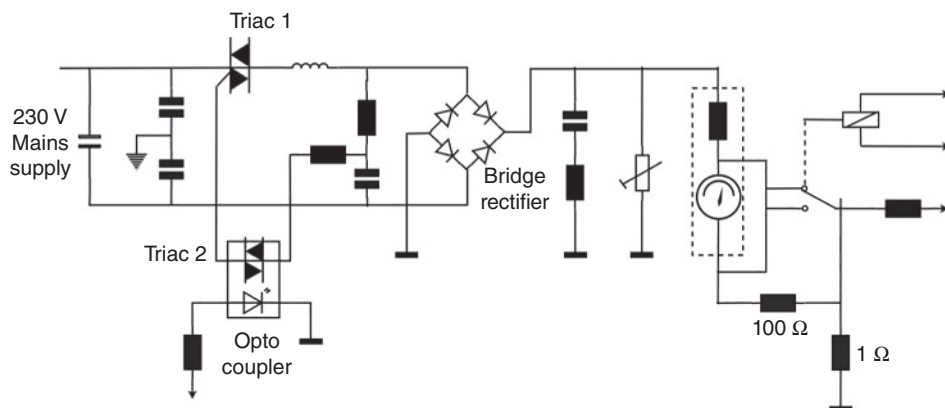
### Principle

The microcentrifuge is a small compact benchtop centrifuge designed for micro tubes of 0.2–2.0 ml in size. The speed of a typical microcentrifuge ranges between 13 000 and 15 000 rpm, which corresponds to a gravitational force (g-force) of 16 000–20 000×g. Microcentrifuges designed for high speed operation can reach up to 35 000 rpm, giving RCF up to 30 000×g, and are appropriately called high speed microcentrifuges. The machine has a compact design and small footprint. It can accommodate up to 96 well plates. The rotor of microcentrifuges provides an aerosol-tight containment for safe centrifugation of hazardous samples that include viruses, pathogen bacteria, blood samples, or radioactive probes.

A typical microcentrifuge as shown in Figure 82.1 has a brushless DC motor, which does not require routine maintenance. It can reach speeds of up to 14 000 rpm/16 000×g.



**Figure 82.1** Typical microcentrifuge Model 5418. *Source:* Reproduced with permission of M/s Eppendorf, Germany.



**Figure 82.2** Circuit diagram of motor drive and brake mechanism.

The maximum load of the rotor and the maximum speed are established by the manufacturers and the same should not be exceeded. The machine is supplied with an 18 ml × 1.5 ml rotor for microsamples. Tubes smaller than 1.5 ml can also be used by using adapters. The microcentrifuge can also be converted into a haematocrit centrifuge when a special rotor is mounted to hold the required capillary tubes.

Figure 82.2 illustrates the speed control circuit of a typical microcentrifuge. The machine operates on 230V AC mains supply, which is regulated and then rectified. The TRIAC controls the AC voltage to the motor. The control signal is received from the microprocessor via an optocoupler. The optocoupler decouples the mains potential of the TRIAC from the potential-free low voltage of the control unit. The regulated AC is then rectified by the four diodes before it is given to the motor. The brake circuit consists of a brake relay, which gets activated when the centrifuge does not brake. When on standby mode, the brake resistor (100 Ω) is connected across the motor. In case of power failure, the relay would release, and the resistor bypasses the motor and slows down the centrifuge. When the centrifuge starts, the relay is activated, the contact switches over, and the motor gets connected via the 1 Ω resistor (vertical) to the regulated power supply, bypassing the brake resistor. The resistance creates a small voltage drop depending on the motor current passing through it. In case of fault, the motor current may become too large, increasing the voltage drop across this resistor, resulting in switching off the centrifuge or slowing it down.

The centrifuge safety features are usual and include an electromechanical *door-locking mechanism* that prevents operator contact with spinning rotor. When the door is closed, it locks automatically and can be unlocked only by pressing the door key. The lid can be opened only when the power is on and the rotor is at rest. The *imbalance detector* monitors the rotor during the run, causing automatic shutdown if rotor loads are severely out of balance. A thermistor in the rotor chamber continuously monitors chamber temperature. In the unlikely event of a complete cooling system failure, the drive will switch off if the chamber temperature reaches 50 °C. Restarting the centrifuge will not be possible until the chamber is cooled. An EEPROM allows to store current operating parameters, such as rotational speed, duration of the last run, and operating hours. This data is not lost even if the centrifuge is switched off and can be called up again after the centrifuge is switched on again.

## Specifications

*Speed:* Up to 14 000 rpm

*Max. RCF:* 16 873×g

*Capacity:* 18 micro test tubes

*Sample size:* 0.2–2 ml

*Max. load:* 18 ml × 2.0 ml micro test tubes

*Permissible density of material to be centrifuged:* 1.2 g/ml

## Applications

Microcentrifuges find applications in biosciences, medicine, clinical diagnostics, industry, and the chemical field.

# 83

## Centrifuge, Refrigerated

### Purpose

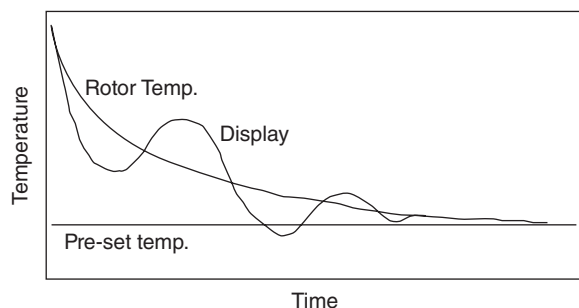
Refrigerated centrifuges are basically used in analysis of human and animal biological samples for scientific and medical purposes. This type of centrifuge is one of the most popular variant of laboratory centrifuges. The refrigerating feature of these machines is very useful in the analysis of DNA, polymerase chain reaction (PCR), RNA, and antibodies. Refrigerated microcentrifuges are also available and can be used for spinning liquid samples below 2 ml in quantity.

### Principle

A refrigerated laboratory centrifuge is usually a high speed machine that can obtain rotational speeds of over 30 000 rpm and a relative centrifugal force (RCF) of over 65 000×g. When a centrifuge spins at extremely high speeds, heat is generated due to the friction with the surrounding air. The heat results in warming up the samples that may have adverse effect on the samples. This can be avoided by providing refrigeration facility in high speed centrifuges.

The basic components of the refrigerated centrifuge consist of an electric motor, a shaft and rotor heads on which the centrifuge head turns, and a motor drive assembly with control electronics. The refrigerated centrifuge, in addition, has a compressor and associated components. A refrigeration compressor circulates chlorofluorocarbons (CFC)-free refrigerant through copper tubing wrapped around the chamber bowl, which is insulated to increase refrigeration efficiency. The entire system is contained





**Figure 83.1** Chamber temperature stabilization curve.

within a chamber. The cabinet protects the operator should a tube break or any metal parts fail while the centrifuge is running. The centrifuge head carries the cups or shields that cover the rotor and turns on a spindle. The rotor is surrounded by a safety shield in the chamber. Most modern models of refrigerated centrifuges use brushless motors that are noiseless. The drive motor has permanently lubricated, sealed bearings. They have digital displays with an LCD/LED and a keyboard that allows the user to program a specific speed and time.

Refrigerated laboratory centrifuges have a wide temperature range from  $-20$  to  $+40^{\circ}\text{C}$ . A thermistor is used as a sensor for measurement and control of temperature to  $\pm 2^{\circ}\text{C}$  of set temperature. The temperature adjustment with sensor, refrigeration system, and processor control is so designed that the set temperature is reached within the shortest possible time. During this adjustment period, it is possible that the temperature varies above or below the set temperature. A typical chamber temperature stabilization curve is shown in Figure 83.1. The temperature variations depend on rotor speed and set temperature. In case you want to process samples that are very temperature sensitive, the rotor, buckets, and tube racks must be pre-cooled, to the required temperature.

Refrigerated centrifuges are available in a number of rotor configurations, including swing bucket or fixed angle types, or both. They utilize centrifuge tips and tubes or well plates depending upon the application, with capacities reaching  $4\text{ ml} \times 500\text{ ml}$ . These machines have automated conversion capability from refrigerated to normal temperature operation. Most centrifuges have an electrical brake system to bring the rotor to a standstill shortly after the run is finished. All these machines include standard safety features such as imbalance detector and electromechanical door-locking mechanism. A typical refrigerator centrifuge from M/s Beckman Coulter is shown in Figure 83.2.

The refrigerated centrifuges are of two types:

*Large capacity refrigerated centrifuges:* These machines can go up to maximum speed of 6000 rpm and produce a maximum RCF nearing  $6500\times g$ . They are mostly used to sediment the substances that sediment rapidly like erythrocytes, yeast cell, nuclei, and chloroplast.

*High speed refrigerated centrifuges:* These centrifuges are capable of operating at 25 000 rpm or above and can generate RCF of about  $60\,000\times g$ . They are mostly used to collect microorganism, cellular debris, larger cellular organelles, and proteins precipitated by ammonium sulfate.



**Figure 83.2** A typical refrigerated benchtop centrifuge model Allegra X15R. *Source:* Image courtesy of Beckman Coulter.

## Specifications

*Speed:* 15 000 in 10 rpm increments

*Time:* 99 hours 59 minutes

*Temperature:*  $-10$  to  $+40^{\circ}\text{C}$  in  $1^{\circ}$  increments

## Applications

Refrigerated centrifuges find applications when it is desired to spin a large number of tubes at higher RCF in less time. They are ideal for applications from clinical biology to molecular biology.

# 84

## Centrifuge, Ultra (High Speed)

### Purpose

Ultracentrifuges are commonly used in molecular biology, biochemistry, and cell biology research. Their applications include the separation of small particles such as viruses, viral particles, proteins and/or protein complexes, lipoproteins, RNA, and plasmid DNA.

### Principle

Ultracentrifuge is a type of centrifuge that is designed to rotate samples at ‘ultra-high’ speeds, which are much higher than conventional centrifuges. Some of these machines

have a rotational speed of up to 150 000 rpm, producing a centrifugal force up to more than 1 million  $\times g$ . This speed can only be attained when the rotor spins in a vacuum and the centrifuge is also cooled. All such machines are microprocessor controlled. They incorporate a variable-frequency induction drive, thermoelectric temperature control system, self-purging vacuum system, rotor overspeed detection system, program memory containing operating protocols, and a choice of acceleration and deceleration rate. A programmed operation feature in the machine stores run conditions that allows the operator to recall those conditions whenever required, thus saving time in setting. The stored run conditions remain intact even after the power switch is turned off. Digital displays on the control panel generally display rotor speed, run time, and rotor temperature.

### Types

Ultracentrifuge machines are available in floor models that are usually large. There are also smaller, compact benchtop models that save on lab floor space. A typical floor model of an ultracentrifuge from M/s Beckman Coulter is shown in Figure 84.1. The choice of the model partly depends on particular protocol, available lab space, or other features. There are two types of ultracentrifuges:

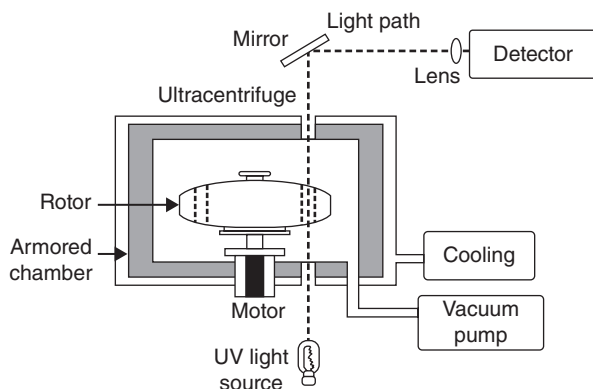
- Analytical ultracentrifuge
- Preparative ultracentrifuge

The difference between analytical and preparative ultracentrifuge lies in the way they are used in the laboratory. Analytical centrifuges provide useful information about molecules in the sample, such as their overall shape and conformational changes, while preparative ultracentrifuges are mostly used for separating particles according to their densities, isolating and/or harvesting denser particles, and clarifying suspensions containing particles.

**Analytical Ultracentrifuge** Analytical ultracentrifuges allow real-time monitoring of the sample's progress during a centrifugal spin. In this way, it is possible to watch the



**Figure 84.1** Ultracentrifuge Model Proteome Lab XL-A/XL-I.  
Source: Image courtesy of Beckman Coulter.



**Figure 84.2** Schematic diagram of the optical system of an analytical ultracentrifuge.

sedimentation process and observe the sample concentrate as the centrifugal force increases. Two types of experiments are generally performed on analytical centrifuges: sedimentation velocity experiments and sedimentation equilibrium experiments. The sedimentation velocity experiments yield information about the shape, mass, and size of the molecules, whereas sedimentation equilibrium type of analysis gives information about mass and chemical equilibrium constants.

The real-time monitoring is done by using a scanning ultraviolet light-based optical detection system. A detector collects light absorption data, which a computer digitizes and records for further mathematical analysis. Figure 84.2 shows the optical system used in an analytical ultracentrifuge. A high intensity xenon flash lamp is used to obtain ultraviolet light in the wavelength range between 190 and 800 nm. The lamp is fired in a pulsed manner as the selected sector passes the detector. Cells and individual sectors can be examined in turn, taking the timing information from a reference magnet mounted on the base of the rotor. A slit below the sample moves to allow sampling of different radial positions. Multiple readings at a single position are taken and averaged to minimize the effect of noise. The variation in lamp output is compensated by sampling a reflected small fraction of the incident light. A wavelength scan may also be made at a specific radial position in the cell, resulting in an absorbance spectrum of the sample at that point, thereby allowing discrimination between different solutes.

An additional detection system consisting of Rayleigh interference optics, which measures changes in the refractive index that occur when the sample concentration changes is also added in some machines. This additional detection system allows to study a broader range of sample concentrations. Rotors for analytical ultracentrifugation should be able to withstand tremendous gravitational stresses, which are generated at extremely high speeds. Also, the rotor should be so designed that it allows the passage of light through the spinning sample. The rotor has four holes, out of which three positions are available for sample cells and one for the counterbalance.

**Preparative Ultracentrifuges** These machines do not have any optical readout arrangement as they directly collect fractions and analyse them after the run. They can be used on larger sample sizes and are generally employed to separate organelles and molecules.

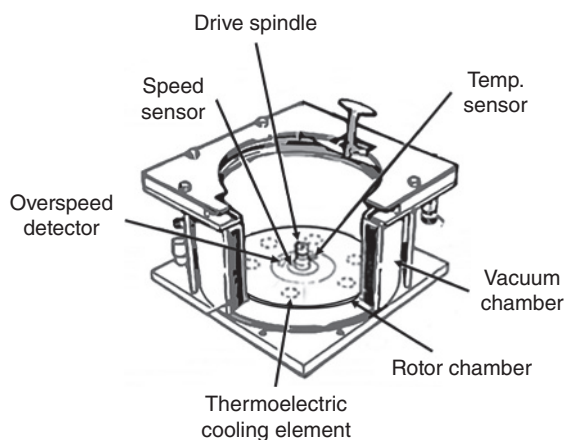
Most centrifugation work is commonly done using preparative ultracentrifuge. They are available with a wide variety of rotors suitable for a great range of experiments, which can spin samples of different numbers, at different angles, and at different speeds. In most preparative ultracentrifuges, the rotors can be swapped out and replaced it with another type. The type of rotor you use depends on your particular samples and experiments.

### **Drive**

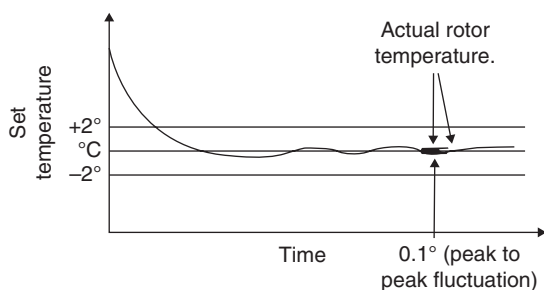
The ultracentrifuge utilizes air-cooled direct-drive induction motor, which is frequency controlled, and requires no gears or brushes. In addition, the drive does not require an oil vacuum seal or external oil reservoir or continuously operating damper. Externally cooled by forced air and internally cooled by oil, the drive delivers ultra-smooth, quiet performance with high tolerance of rotor imbalance. In order to avoid overspeeding, the system includes photoelectric sensors in the rotor chamber next to the drive spindle and an overspeed disk on the bottom of the rotor. As the rotor spins, the photoelectric device generates a series of pulses whose rate is dependent on the speed of the rotor. If the speed exceeds a set limit, the overspeed diagnostic message will light up and the rotor will automatically come to a stop. The location of various controls and sensors in the ultracentrifuge is shown in Figure 84.3.

### **Vacuum System**

In order to minimize frictional heating and aerodynamic turbulence, the rotor usually operates in an evacuated chamber. A diffusion pump, in series with a mechanical vacuum pump, reduces chamber pressure to below  $10\mu\text{m}$  ( $1.34\text{ Pa}$ ). The vacuum pump starts automatically when the power is turned on and the door is closed. The diffusion pump is automatically activated when chamber pressure reaches about  $500\mu\text{m}$ . When the instrument is on and the door closed, a self-purging system continuously removes moisture from the vacuum system. The level of the chamber pressure is indicated in microns on the front panel in discreet steps.



**Figure 84.3** Location of various components in the rotor chamber.



**Figure 84.4** Temperature control curve in an ultracentrifuge.

### ***Temperature Sensing and Control***

Rotor temperature is measured by a radiometer that is mounted in the bottom of the rotor chamber when the chamber pressure is below 100  $\mu\text{m}$ . In case the pressure is above 100  $\mu\text{m}$ , or if the radiometer fails, the chamber temperature is measured by a thermistor mounted in the chamber. For control of temperature, a solid state thermoelectric refrigeration and heating system is used. The system uses only forced air from a cooling fan and no other coolant is required. After the power is turned on, the temperature control system is activated when the door is closed and the vacuum system is turned on. A sensor in the rotor chamber continuously monitors chamber temperature and the microprocessor calculates the required chamber temperature to maintain the selected rotor temperature. The rotor temperature is controlled to  $\pm 0.5^\circ\text{C}$  of the set value as shown in Figure 84.4.

### ***Defrost Function***

If the chamber door is left open between low temperature runs, moisture from the ambient air humidity can condense and even freeze on the cold evaporator chamber walls. If the machine is operated with a significant amount of moisture in the evaporator chamber, the time required to reach a high level of vacuum will increase. For such situations, a defrost function is provided in the machine as a convenient means to melt ice build-up so that the moisture can be easily removed.

### ***Cells***

The cells used with ultracentrifuge must be able to withstand the stresses caused by the extremely high gravitational fields. They must not leak or distort, and yet must allow the passage of light through the sample so that the concentration distribution can be measured. To achieve these ends, the sample is usually contained within a sector-shaped cavity sandwiched between two thick windows of optical-grade quartz or sapphire.

### ***Sample Size***

Most ultracentrifuges use standard sizes of centrifuge tubes, with typical sample volumes that range from 0.2 to 30 ml.

## Specifications

*Speed:* 100 000 rpm in 1000 rpm increments

*Maximum RCF:* 802 000×g

*Maximum capacity:* 6 × 250 ml

*Drive:* Imbalance tolerant direct drive

*Speed control accuracy:* ±10 rpm

*Temperature set range:* 0 to +40°C

*Temperature accuracy:* ±0.5°C

*Vacuum system:* Oil rotary vacuum pump with moisture removal function and oil diffusion pump; vacuum of 0.13 Pa

## Applications

Ultracentrifuges are used both for analytical and for preparative applications. An analytical ultracentrifuge is mostly used for studying the properties of macromolecules as well as for analysing complex mixtures of macromolecules. Preparative ultracentrifuges are used to purify macromolecules such as proteins and nucleic acids based on their physical properties such as size, molecular weight, density, and mobility. Their range of applications include cellular biology, genomics/molecular biology, proteomics, microbiology, biochemistry, drug discovery, nanotechnology, and food processing.

# 85

## Cervical Cancer Screening System, Automated

### Purpose

Automated cervical cancer screening system is a device that uses computer imaging technology to assist in primary cervical cancer screening of Pap test slides. Cervical cancer is considered as the second most common cancer disease in women worldwide. The Pap test is the basic screening test for the disease involving the microscopic examination of cells sampled from in and around the cervix. Precancerous changes can be treated before they have a chance to progress to cancer. In most countries, the screening test is still done by visual examination of the Pap test slides, but automated computerized cell image analysers have considerably improved screening accuracy and has offered a low-cost and robust screening solution.

### Principle

The Pap smear test is the most effective cancer prevention measure developed so far. The basis for the Pap smear screening is that cancerous or precancerous

abnormal cells have larger nuclei and more irregular shape and structure than normal cells. However, the task is not as simple as stated due to the fact that cells in the specimen are often folded, overlapped, covered by blood cells or other artefacts, and clustered. Also when the screening of the smears is done visually, it is time consuming, and in practice, it is the most demanding function of the human eye–brain axis, exhaustive and fatigue producing.

To address the above problems, automated Pap smear test screening and analysis devices have been developed that use computer imaging technology that aids physicians in identifying whether a slide contains cancerous cells. These systems use advanced image acquisition, processing, and classification techniques coupled with better slide preparation technique. These devices have offered a solution, which can be adopted for mass screening of cervical cancer. All automated screening systems employ algorithms directing the cytologist's attention to abnormal cellular morphology, which in turn requires visual confirmation.

### ***The System***

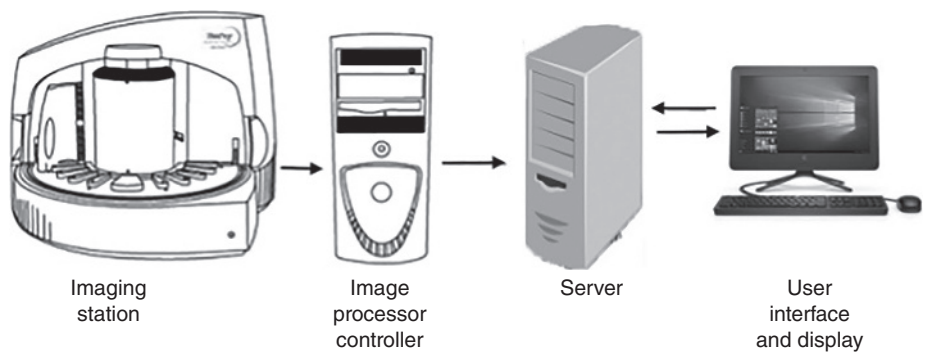
The system is based on static image analysis and comprises a cell scanner linked to an independent review system, which presents selected images to the cytologist. The scanner captures the images through a digital camera mounted on a microscope, which has a motorized stage. The camera is linked to a high performance computer, which is programmed to record and analyse the images captured by the camera as it scans the smear. The optical images acquired by the camera are converted into digital images inside the camera and stored on a storage media. The camera with the digital microscope produces RGB images with a spatial resolution of  $3264 \times 2448$  pixels and sensor pixel size of  $2.7 \mu\text{m}$ . The complete complementary metal-oxide semiconductor (CMOS) sensor is very small, with physical dimension of  $8.81 \text{ mm} \times 6.61 \text{ mm}$  only. To capture the maximum possible area in a field of view (FOV), a demagnifier of  $0.63\times$  magnification is used, resulting in an effective pixel size of  $0.1 \mu\text{m}$ . The computer is programmed to analyse and classify the images as per the built-in algorithm. The computer selects images/smears that most probably contain abnormal cells and presents them to the cytotechnologist for further confirmation under the microscope.

Figure 85.1 shows various subsystems of an automated cervical cancer screening system. The system has three main components: (i) an imager system, (ii) a PC-based computer, and (iii) a review microscope with a motorized mechanical stage. The imager system comprises the following:

- *Imaging station:* Its function is to image the slides.
- *Image processor controller:* The image processor subsystem is a computer-controlled microscopic imaging device that determines the cells of greatest abnormality and stores their locations in a database for future access. Besides capturing the images, it controls the electromechanical components of the system.
- *Server:* It stores the slide identity and relevant image data.
- *User interface:* It consists of a monitor, keyboard, and mouse that the operator uses to interact with the instrument via a graphic menu-driven interface.

Specimens are prepared on glass slides, loaded into slide cassettes, and placed into the imaging station. The slides are processed in a batch, one slide at a time, by the imaging

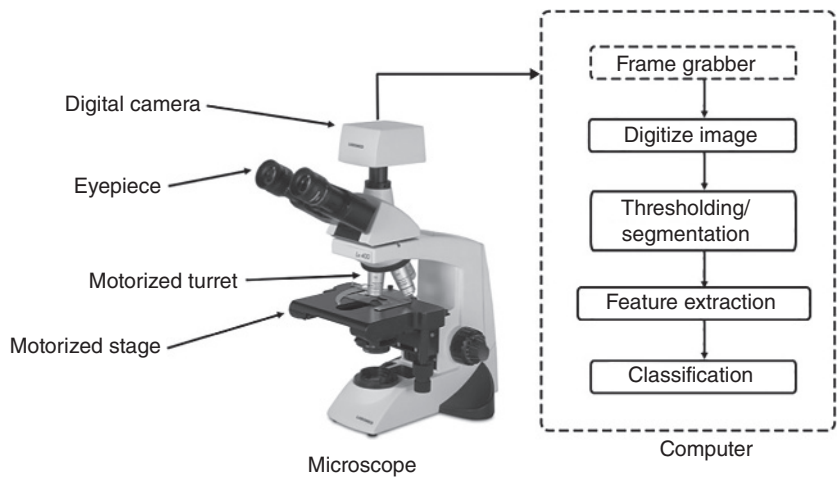




**Figure 85.1** Various components of an automated cytology system. The system consists of imaging station, image processor controller, server, and user interface model.

station, which reads the slide accession ID number and images the cell spot of the slide. The system identifies objects of interest observed on the slide, based on integrated optical density. The coordinates of 22 of those objects are recorded and the slide is returned to its cassette. The image processor controller contains the processors used to image and analyse the slide data. In the image processing station, each image undergoes a series of processing and analysis steps to finally classify the specimen as either normal or suspicious. The slide ID data and associated data record are sent to the system server for storage. The server acts as the central data manager for the imaging system and maintains the database and communicates to the review scope. The user interface is a menu-driven graphical display used by the operator for operating the equipment.

The slides are generally magnified through a 40× lens to accurately quantify nuclear chromatin distribution. The system uses algorithms to select 22 fields of view that are most likely to be diagnostically relevant. A cytotechnologist then uses the review scope, which consists of elements of a standard microscope with a camera as shown in Figure 85.2, augmented with automated capabilities for viewing and marking the



**Figure 85.2** Review station set-up and software flow chart for final cervical cancer screening.

microscope slides to identify any abnormal cells in these 22 fields. If there are none, the slide is considered negative and no further review is necessary. If abnormal cells are found, the cytotechnologist reviews the entire slide. During slide imaging, the alphanumeric slide accession identifier is recorded and the  $x$  and  $y$  coordinates of 22 fields of interest are stored in the computer database.

Feature extraction is the heart of the quantification and automation task that determines what is to be measured and how it should be measured. Over the last five decades, a large set of features have been tried and tested for various applications, out of which around 40 mathematical features that can accurately determine morphology, texture, and densitometry of cervical epithelial cells have been identified heuristically. A hierarchical multistage classification approach is followed for classifying normal smears from suspicious smears. The preprocessing, segmentation, feature extraction, and classification modules are all integrated with a graphical user interface (GUI) application.

Although examination of the conventional cervical smears has been the practice for years for manually screening for cervical cancer, liquid-based cytology and automation systems have steadily grown.

## Specifications

*Slide processor*

*Throughput:* 3 batches of 80 slides, up to 60 000 samples/y

*Capacity:* 80 sample vials (two 40-vial trays) per batch, 2 cartridges of 100 microscope slides, 4 slide staining racks of 20 slides each

*Microscope review station objectives:* 4 $\times$ , 10 $\times$ , and 40 $\times$

## Applications

The Pap test is currently the most widely used screening test for the early detection of cervical cancer throughout the world. The device is used for automated screening for cervical cancer with a high throughput and can be used for all patients who are advised to undergo a Pap test.

86

## Chloride Meter

### Purpose

A chloride meter is a noninvasive in vitro diagnostic device used for measuring the chloride concentration in serum, urine, sweat, and other body fluids. Chloride

monitoring is essential for determining and managing the patient's electrolyte status through intravenous therapy or other forms of fluid therapy as well as indicating other disease processes.

## Principle

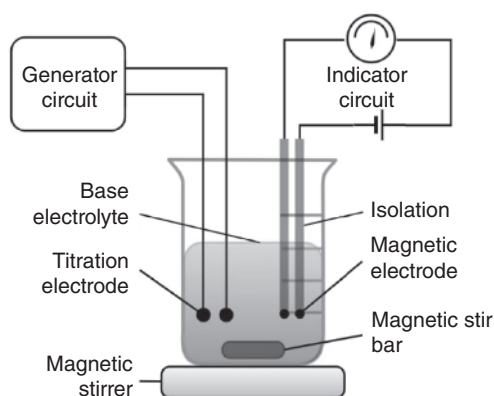
There are several methods for determination of chloride in a fluid. The following methods are commonly employed in clinical laboratories.

### *Coulometric Method*

This measurement method is based on the principle of coulometric impulse titration by using an end point, which is determined by measuring the current between two silver electrodes. Figure 86.1 illustrates the set-up for making chloride measurement. Two silver electrodes (anode and cathode), termed as generator electrodes, are dipped into a working solution contained in a measuring vessel. The working solution comprises an acid buffer and a colloid stabilizer that keeps the silver chloride, which forms later on in suspension.

Initially, the buffer does not contain any silver ions. However, when a constant current from the current generator is passed between the two silver electrodes, silver ions are released at the anode. The measuring electrodes dipped in the solution maintain the silver ion concentration. When a sample containing chloride ions is added to the solution, the free silver ions from a non-soluble silver chloride precipitate together with the free chloride ions of the sample, resulting in drop of the indicator current. By controlling the generator current, silver ions are released until all chloride ions are precipitated as silver chloride. When all the chloride has combined with generated silver, free silver ions become available in the solution and original silver ion concentration is restored, indicating the end of the titration process.

At this stage, the conductivity of the solution changes and this change is sensed by the detector electrodes. The digital readout is stopped, displaying the results directly in milliequivalents of chloride per litre. The digital display is held until automatically reset by



**Figure 86.1** Coulometric principle of measurement of chloride.



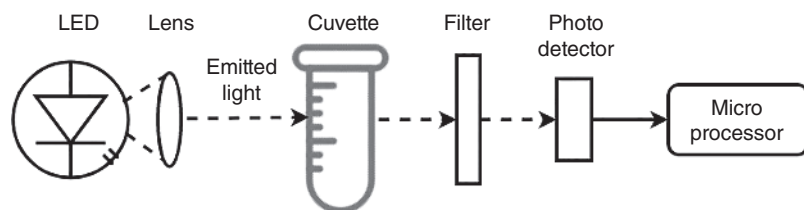
**Figure 86.2** Chloride meter based on optical absorption. *Source:* With permission of M/s Hanna Instruments.

the start of another measurement. The period of flow of the generator current is measured during the titration process and is proportional to the chloride concentration. The operations of modern chloride meters are automated under microprocessor control. The sample recognition, titration, and the measurement process proceed fully automatically after the sample is inserted without the need for manual intervention by the user.

### ***Photoelectric Method***

This method is based on the absorption of light when it is made to pass through a solution containing a substance of interest. A commercial instrument shown in Figure 86.2, the HI96753 from M/s Hanna Instruments uses an adaptation of the mercury (II) thiocyanate ( $\text{Hg}(\text{SCN})_2$ ) method to measure chloride concentrations of less than 20.0 mg/l (ppm). When both the mercury (II) thiocyanate and iron-based reagents are added to samples containing chloride, the sample colour will become orange. The greater the concentration, the deeper the colour. A standard photoelectric colorimeter is used to measure the colour changes and determine the concentration according to the Beer–Lambert law, which states that light is absorbed by a complementary colour and the emitted radiation is dependent upon concentration. For determination of chloride, a narrow band interference filter at 466 nm (blue) allows only blue light to be detected by the silicon photodetector and omits all other visible light emitted from the light source.

The portable instrument used for the measurement of chloride use standard optical system consisting of a light emitting diode (LED), a narrow band interference filter, and silicon photodetector as illustrated in Figure 86.3. The instrument is microprocessor controlled. The LED emits radiation, which is first optically conditioned and is made to pass through the sample contained in the cuvette. The optical path is fixed by the diameter of the cuvette. Then the light is spectrally filtered to a narrow spectral bandwidth with the help of an interference filter. The photoelectric detector collects the radiation that is not absorbed by the sample and converts it into an electric current, producing a potential in the mV range. The microprocessor uses this potential to convert the incoming value into the desired measuring unit and to display it on the LCD. There is a cuvette locking system that ensures that the cuvette is inserted into the measurement cell in the same position every time to maintain a consistent path length.



**Figure 86.3** Principle of measurement of chloride by optical absorption method.

### ***Use of Ion-Specific Electrodes (ISE)***

An ion-specific electrode (ISE), also known as a selective ion electrode, converts the activity of a specific ion dissolved in a solution into an electrical potential. An ion specific electrode generates a difference in electrical potential between itself and a reference electrode. The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation. As in other ion-specific electrodes, the chloride electrode consists of a sensing element bonded into an epoxy body. When the sensing element is placed in contact with a solution containing chloride ions, an electrode potential develops across the sensing element. This potential depends on the level of free chloride ions in solution and is measured against a constant reference potential with a digital pH/mV meter or specific ion meter. The measured potential corresponding to the level of chloride ion in solution is governed by the Nernst equation as follows:

$$E = E_0 + S \log(A)$$

where

$E$  = measured electrode potential

$E_0$  = reference potential (a constant)

$A$  = chloride ion activity level in solution

$S$  = electrode slope (about 57 mV/decade)

The level of chloride ion,  $A$ , is the activity or 'effective concentration' of free chloride ion in solution. If the background ionic strength is high and constant relative to the sensed ion concentration, the activity coefficient is constant and activity is directly proportional to concentration.

The use of specific ion electrode allows a quick measurement of the concentration of the chloride ion in a sample. In construction, the chloride ISE has a combination-style, non-refillable, gel-filled electrode. It has a solid state membrane that does not need to be replaced. A solid state electrode employs relatively insoluble inorganic salts in a membrane. The sensor is built with a silver chloride pellet used for the detection of free chloride ions in samples. The reference and sensing electrodes are built into one electrode, which requires less amount of solution and reduces waste. The built-in reference junction prevents electrode clogging and provides fast and stable readings. Its double junction design contains an Ag/AgCl, gel-filled reference chamber. The polyetherimide (PEI) electrode body is suitable for a wide range of applications and most suitable for field measurements due to its ruggedness and durability. The shielding around the spherical glass tip minimizes breakage due to accidental bumping or dropping of the electrode. The PEI



**Figure 86.4** Chloride ion-specific electrode. *Source:* With permission of M/s Hanna Instruments.

plastic is a high-quality plastic that is chemically resistant to many harsh chemicals. A typical chloride ion electrode from M/s Hanna Instruments is shown in Figure 86.4.

## Specifications

*Photometric principle*

*Light source:* LED

*Light detector:* Silicon photodiode

*Filter:* 466 nm, interference type

*Range:* 0.0–20.0 mg/l (ppm)

*Resolution:* 0.1 mg/l (ppm)

*Accuracy:*  $\pm 0.5$  mg/l

## Applications

Chloride meter is used in medical laboratories for chloride determination in serum, urine, sweat, or other body fluids for diagnostic purposes. The chloride measurement is also useful for examination of food products for quality control purposes and water analysis.

# 87

## Clinical Chemistry Analyser, Dry

### Purpose

A dry chemistry analyser is a medical laboratory instrument designed to measure different chemicals and other characteristics in biological samples such as blood and

other fluids, which may be considered useful in the diagnosis of a disease. The dry chemistry technology is quite convenient as it eliminates the use of liquid reagents and there is no need for water, plumbing, vents, or drains. As a result, the instruments are generally of compact design and are very easy to use. Such type of instruments is ideal for use in blood banks, physician offices, and hospital labs and is quite suitable for point of care testing.

## Principle

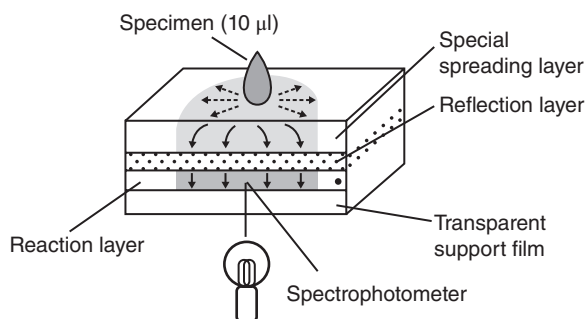
There are two types of testing approaches in biochemistry for clinical testing: those utilizing liquid reagents and those in which the tests are based on dry reagents. The tests based on dry reagent chemistry are easier to handle and depend upon simple analysers for measurement. The key component in this technique is a slide composed of dry film layers. All the reagents necessary to perform a specific bioassay and to remove substances that might interfere with the analyte are contained on the slide. The only liquid required is 10  $\mu\text{l}$  sample. The diagnostic format is a test pad that is bonded to a support structure and impregnated with an analyte that will change colour or some other physical property that can easily be seen or measured when exposed to a test sample. This quantitative analysis of the chemical reactions is usually done by desktop analysers. One of the most well-known applications of dry chemistry technology is urine testing. Numerous clinical evaluations have validated the dry chemistry technology against conventional wet chemistry analysis.

### *Dry Chemistry Film*

M/s FUJI Films announced for the first time in 1980 a dry chemistry analyser based on a multilayered film method. The initial product was a dry chemistry slide and an analyser for measuring glucose concentration by spotting a 6  $\mu\text{l}$  sample of whole blood. The slide had a special spreading layer made of cloth, which enabled the use of whole blood samples. Modern instruments using dry film technology work on whole blood, serum, or plasma samples, making it an extremely simple and flexible system for point-of-care diagnostic applications. Being highly reliable and requiring almost no regular maintenance or servicing, the technology is very useful for remote and rural healthcare settings.

The dry chemistry-based systems are now widely used in international markets as automatic clinical chemistry analysers that fulfil the increasing needs of emergency testing. Correspondingly, a range of peripheral items have also been developed. For instance, special pipette tips, now called 'Fuji Clean Tip', were introduced to enable automatic spotting. Because the tips do not require wiping, there is little danger of operator contamination from blood samples. Manual pipetting can be also performed when less sample is available. Dilution, which is generally a time-consuming process, is automated in modern instruments. Plasma filter is used to generate plasma sample by aspirating and separating the whole blood inside the filter within 1 minute.

The dry film slides allow to perform complex sequential reactions that are otherwise not possible to run in solutions. The multilayer coatings with physical and chemical



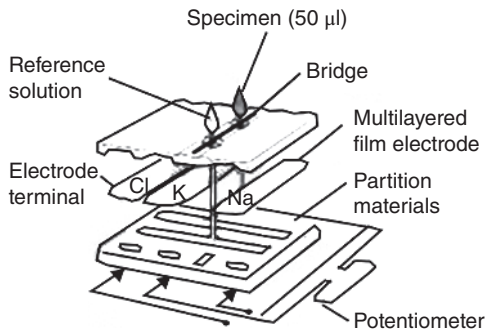
**Figure 87.1** Dry chemistry-based glucose concentration analyser by colorimetric technique.

properties such as filtration, selective adsorption, or kinetic optimization offer a base for multiple reactions within a single slide. In the slide, the multilayered analytical elements are coated on polyester supports. There can be three or more layers: (i) a spreading layer, which receives the sample; (ii) one or more central layers, which alter the aliquot; and (iii) an indicator layer, where the analyte of interest can be quantified. The number of layers could vary depending on the assay to be performed. A small amount of patient sample is put onto the slide that gets evenly distributed to all of the layers. The spreading layer contains the appropriate substrate and other reagents required for the reaction. The reagent layer contains enzymes, dye precursor, and buffers necessary for the analysis of a specific component. The slides are of two types: colorimetric or potentiometric.

**Colorimetric Slide** A typical example of a dry chemistry analyser is that of glucose slide, wherein the actual measurement is conducted as follows. Ten microlitres of plasma or serum are spotted on a dry chemistry slide as illustrated in Figure 87.1. After spotting, the sample spreads uniformly on the spreading layer and diffuses into the underlying layer. As the process proceeds, large molecular weight components such as proteins or dye components are filtrated, and only small molecular weight components are able to permeate and diffuse into the reagent layer. Glucose oxidase catalyses the oxidization of sample glucose to generate hydrogen peroxide. Hydrogen peroxide reacts with dye precursors and finally forms red dye. The slide is incubated at 37°C for a specified number of minutes in the analyser and the optical reflection density is measured at 505 nm. The optical reflection density is then converted into the glucose concentration using a calibration curve preinstalled in the analyser.

**Potentiometric Slide** This type of slides is designed for electrolyte analysis. The analysis is based on measurement of the generated voltage difference between ion-selective electrodes applied to a reference solution and to the sample. For example, ion-selective electrodes for sodium (Na), potassium (K), and chloride (Cl) are combined into one slide. A drop of reference sample and a drop of patient sample are spotted on the slide, each on its respective electrode. When the samples interact with coated reagent layers, a pair of electrochemical half-cells are generated. The drops spread towards one another across the paper bridge, meeting at the centre and forming a stable liquid junction. A voltmeter measures the potential difference of the





**Figure 87.2** Dry chemistry-based electrolyte measurement by potentiometric technique.

two half-cells. This difference potential is sent to a microprocessor, which calculates and records the electrolyte concentration. Figure 87.2 shows the constructional details of a potentiometry-based slide.

### Measurement

When a specific test is required, a slide is automatically dispensed from the cartridge that holds the slides for specified tests. A small drop of the patient's blood is applied to the slide by the analyser. The analyte in the sample catalyses the reaction sequence to develop products of specific colours. The colour measurements are made at wavelengths in the visible region (340–680 nm). The basic principle of dry chemistry is based upon the reflectance spectrophotometry. A reflectance spectrophotometer is similar to a standard UV–visible spectrophotometer. Reflectance measurements are made using both diffused and specularly reflected light. In diffused reflectance, light is scattered in all directions from the sample. The scattered light can be collected onto an optical detector, and the surface reflectance is measured either at a given wavelength or by performing a scan over a range of wavelengths. Such a wavelength scan can then be used to characterize colour.

Modern dry film-based instruments are capable of analysing over 20 biochemistry parameters using single or multiparameter strips. Multiparameter strips can carry out several tests on a single sample and are available for analysing kidney, liver, heart, and many other parameters simultaneously.

### Specifications

*Sample:* Serum, plasma, and whole blood

*Parameters:* Colorimetry (28 tests), electrolyte (3 tests)

*Warm-up:* 10 minutes (25 °C)

*Processing speed:* 120 tests/h

*Data storage:* 100 measurements

*Calibration:* Calibration by magnetic card

## Applications

Applications of the dry chemistry include patient screening, use in health clinics, mobile health services, polyclinics, and hospital in-patients including point-of-care testing in critical care areas.

## 88

# Clinical Chemistry Analyser, Random Access

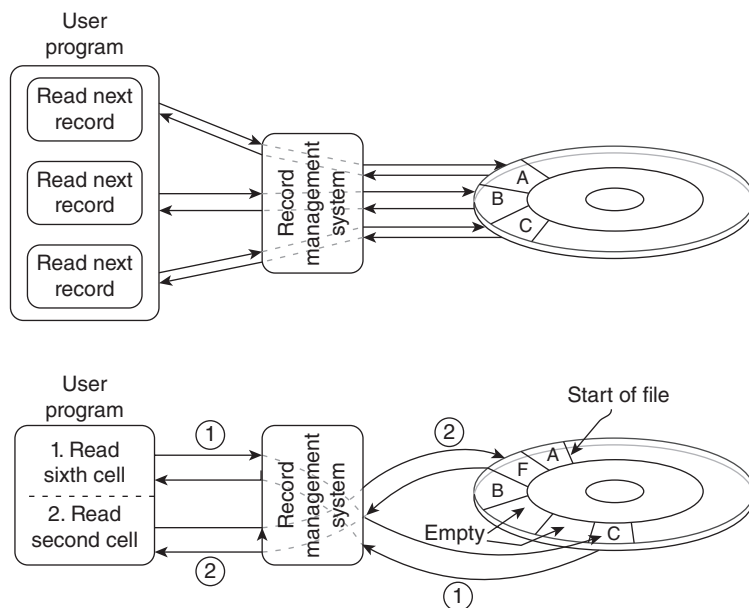
## Purpose

Random access analyser is a device used for carrying out diagnostic tests in the clinical chemistry laboratory in which the specimens can be accessed at random, i.e. out of sequence with each other. This is opposite of *sequential access* in which the sample must be accessed in the accessing order by passing through all the intervening samples. In random access analyser, the reaction vessels are available without regard to accessioning order as you can jump directly to the sample of interest. They are also known as discrete analysers.

## Principle

In automated clinical chemistry analysers, there are two ways a sample can be accessed for analysis: *sequential* or *random*. Figure 88.1 shows the conceptual difference between the two types. Unlike sequential access, random access follows no specific pattern. The instrument is programmed to directly approach any sample and carry out the necessary processing for analysis. These instruments are ideal in the laboratory set up where patient samples keep on arriving throughout the day and night. With random access instrumentation, each sample can be analysed for multiple tests, and multiple samples for one test also can be done by giving appropriate commands to computer software.

The *Roche Cobas Mira*, now discontinued by Roche, was once a preferred instrument as a random access biochemistry analyser. This system allowed for the selective analysis of chemistries in either a routine or statistical (STAT) mode. Testing sequence was by patient rather than test or batch. The optional ion specific electrode (ISE) module for sodium, potassium, and chloride determinations expanded the capabilities of the instrument. The operator could select tests, review results, and program tests, profiles, and system parameters from the control panel. The microprocessor controlled instrument could carry out 140 tests/h, with 104 test channels including 23 pre-programmed methods and the capacity to hold 2100 patient results, capacity for 72 cuvettes (six 12 cuvette segments), cuvette volume of 150–600 µl, and an analysis interval of 25 seconds. Presently, the instrument is manufactured by a number of manufacturers.



**Figure 88.1** Conceptual difference between sequential access analyser and random access analyser.

### Constructional Details

The principle of determining the concentrations of the analytes in a random access analyser is based on optical absorbance measurements. To do so, a needle draws a specific volume of the sample and the corresponding reagent through a needle, which is thermostated in the needle itself. These are then dispensed into the reactions well in the rotor where it is well shaken and the chemical reaction begins. When more than one reagent is required for a particular reaction, the reaction begins only when all the reagents have been dispensed in the same reaction well. The reactions can be biochemical or turbidimetric. The result is generation of substances that attenuate certain wavelengths, either by absorption or by dispersion that can be measured colorimetrically.

The instrument consists of three basic parts: (i) sampling unit, (ii) dispensing system, and (iii) measurement system. All these parts work under the control of an electronic system, which also allows communication with an external computer that contains the application program. All the operations of the analyser can be controlled through this program.

**Sampling Unit** The function of the sampling unit is to draw the sample and the reagents from the respective containers and provide them to the dispensing system. It consists of a three-axis XYZ Cartesian mechanism operated by three stepper motors. The motors provide horizontal movement to the dispensing needle in the X and Y axes, while the third motor moves it vertically in the Z axis. The entire cycle that takes about 24 seconds includes the following actions:

- Sucking in the reagent from the corresponding bottle with a sampling needle.
- Washing the needle externally in the washing station.
- Sucking in the sample from the corresponding tube.
- Washing it externally again.

- Dispensing the sample and the reagent into the reaction rotor.
- Finally, washing the needle internally and externally before proceeding with the next preparation.

The sampling unit operates only if the general cover of the analyser is closed. Also, the sampling arm has a system for controlling vertical movement to detect any collision with the lid or a bottle of reagent. In that case, the arm automatically restarts after verifying the straightness of the needle.

**Dispensing System** This dispensing system comprises a thermostated needle whose movements are controlled by the sampling unit and connected to a dispensing pump. The dispensing pump is a low maintenance ceramic piston pump driven by a stepper motor. The pump is capable of dispensing between 3 and 1250 ml. The waste is transported to the corresponding container by a separate membrane pump. The needle is maintained at approximately 37°C with a Peltier system and *PID* control, which can be reached in less than 15 seconds.

The level of the bottles and tubes can be detected from the capacity level to prevent the needle from penetrating too deep into the corresponding liquids. This helps to minimize contamination of the needle. If the needle is not mounted or it is too bent, the operator is informed with an automatic adjustment system. The needle is detachable to enable cleaning and replacement as and when it is found necessary.

Different machines have different capacities for sample tubes, reagent bottles, and reaction cuvettes. For example, in one machine, the sample disc can accommodate 50 samples and has 50 position reagent trays. The analyser can be configured to work with different diameter tubes, say, 13 or 15 mm of samples with a length of up to 100 mm. The samples can be patients, calibrators, or controls. The capacity of reagent bottles can be 20 or 50 ml. In addition, there are the waste and distilled water containers whose levels are continuously controlled.

The electrical signal generated by the detector is amplified and given to a high resolution A/D converter, which converts the signal into a digital value from which the analyser calculates the absorbance values. The measurements are made only when the instrument is covered.

**Control System** The control system operates under the control of a microprocessor, which carries out various functions such as needle conditioning, fluid system, rotor movement, sampling unit, and photometric measurements and calculations. The microprocessor has two external communication channels to connect the instrument to the computer containing the application program. The application program allows to control all the operations of the analyser including program parameters such as technique parameters, working out session preparation, preparing result reports, activating various test utilities, and carrying out internal quality control procedures. The control unit enables to carry out analysis of selective samples as the samples are bar coded.

## Specifications

*Halogen lamp:* 6 V, 10 W

*Measurement range:* From – 0.05 to 2.5 A

*Filters:* 340, 405, 505, 535, 560, 600, 635, and 670 nm

*Wavelength precision:*  $\pm 2$  nm  
*Temperature controller:* 4 Peltier cells  
*Working temperature:*  $37^{\circ}\text{C}$   
*Number of wells:* 120  
*Reaction volumes:* 200–800  $\mu\text{l}$   
*Light path length:* 6 mm  
*Maximum number of samples:* 72

## Applications

Clinical chemistry analysers are used in all types of biochemical laboratories, to analyse samples such as blood serum and plasma, from small point-of-care clinics to high-throughput clinical labs. Applications include monitoring diseases such as diabetes, testing for metabolic functions or cardiac markers, and drugs-of-abuse testing.

## 89

### Clinical Chemistry Analyser, Semi-automated

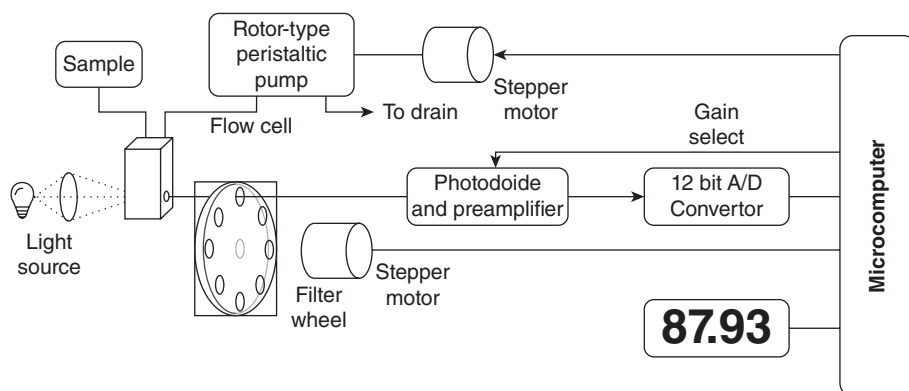
#### Purpose

Semi-automated clinical chemistry analysers are designed to meet the ever-increasing demand for laboratory investigations. These instruments are more compact as compared to fully automated analysers and are capable to perform tests on whole blood, serum, plasma, cerebrospinal fluid and urine samples. They are more suited for small-to medium-sized laboratories and as backup solutions. Therefore, it is likely that each analyser offers different features for differing requirements.

#### Principle

To meet the requirements of increasing volume of work in clinical laboratories, automated instruments have been designed in which the entire analytical process is carried out in a mechanized fashion. Their operation involves a self-regulating process, where the specimen is accurately pipetted by a mechanical probe and mixed with a particular volume of the reagent. The steps for analysis in automated devices consist of automatic sampling, preparation of protein-free filtrate, heating of the reaction solutions, detection of components of interest, and displaying and printing of the results. The automated instruments have resulted in saving labour and time and also allow reliable performance and quality control by reducing subjective errors.

In *semi-automated* (batch) discrete analysers, the initial part of the procedure involving sampling of specimen and reagent, mixing and incubation is carried out manually



**Figure 89.1** Block diagram of a typical semi-automated clinical chemistry analyser.

by the laboratory technician. All other steps in the procedure involving setting of incubation temperature (for kinetic determinations), zero setting, and photometric readings, including the calculation of the results and display, automatic printing, data management and processing are carried out by the instrument. They have brought about a revolution in the field of clinical chemistry by reducing to a minimum the work of a specialist or involvement of the laboratory staff. The semi-automated analysers are faster, more precise, cheap, and compact, compared with fully automated analysers.

Figure 89.1 shows the basic modules of a semi-automated clinical chemistry analyser, which consists of a light source, an optical module, a filter wheel, a quartz cuvette with reaction mixture, a photodetector, and signal processing circuitry based on microcontroller.

Optical module consists of a light source with reflector, condenser system, collimating objectives, flow cell, filter wheel assembly, and photodiode. Halogen lamp has been used as a light source. A constant current power supply is used to power the lamp to reduce the fluctuations in the light output. All optical components have been designed with quartz glass to have good transmission in UV region at 340 nm.

Temperature sensor LM335 and Peltier device are used to provide and maintain the required temperature for the samples in the flow cell. Peltier works in both directions for cooling and heating. This effect is used to control the temperature of the sample. Temperature sensing is achieved by a temperature sensor, mounted in a hole in the flow cell. The sensor is a three-terminal integrated temperature sensor with a duty cycle output. The output signal from the sensor is fed to a timer/counter input of the microcontroller. The microcontroller verifies, via software, if the temperature is within range of  $37 \pm 0.2^\circ\text{C}$ . If the set temperature of  $37^\circ\text{C}$  is not reached within 30 seconds, a temperature error will occur.

To get the required wavelength of light, interference filters of different wavelengths such as 340, 405, 505, 546, 578, and 630 nm, from UV region to visible region spectrum (300–700 nm), are mounted on the filter wheel. These filters are selected automatically depending on the test to be performed. When the filter of required wavelength is selected, the corresponding gain of the amplifier selected automatically. The filter wheel is driven by a stepper motor, which is interfaced with the microcontroller through driver circuit. Pulses are generated according to required sequence to rotate the motor at required angle, which brings the filter in front of photodetector. For the high wavelength range, a filter with a low transmittance is used to level out differences in energy at the low and high ends

of the spectral range. This is because the emission of the halogen lamp and the spectral response of the detector are both much higher in the visible and near-infrared range than the near-ultraviolet range. A diffraction grating can also be used in place of the filters.

Output of photodiode and preamplifier is a voltage that varies directly with the light, which is passed through the flow cell and selected wavelength filter. Preamplifier is a programmable amplifier whose gain is selected automatically through software as per the selected test parameter and filter. The output voltage from the programmable amplifier corresponds to the relative transmittance. According to Beer–Lambert law, the concentration/activity is related to the absorbance with a linear relationship. Therefore, the linear output voltage from the preamplifier must be logarithmically converted in order to obtain the required absorbance from which the significant concentration/activity can be calculated. Output of logarithmic amplifier is converted into digital value by a 12 bit analog-to-digital converter. Microcontroller performs calculations on these digital values according to the appropriate calculation algorithms developed.

A stepper motor is driven through a driver hardware that drives the roller type of peristaltic pump, which generates the required sequence of pulses for the motor driving hardware. Roller-type peristaltic pump used in the system is used for aspirating the required volume of reagents/samples and for washing the flow cell. The flow cell is made of stainless steel and has two connection pipes. The lower connection pipe is for the sipper tube (Teflon), and the upper, for the waste tube (silicone). The light path of the flow cell is 10 mm and on both sides are sealed quartz windows. This pump can be calibrated to aspirate the required quantity of water, reagent, and samples.

All functions of the analyser are under the control of a microcontroller. The program for the microcontroller is stored in flash memory with a storage capacity of 2 Mbyte. The system data memory is a nonvolatile 512 Kbytes static CMOS RAM. A lithium battery, which is used as the backup power source, will maintain the data for a period of at least four years after the instrument has been switched off. Standard communication interface is available for convenient data transmission and processing.

Semi-automated instruments allow to measure absorbance, turbidity, and end point, two point, and multipoint kinetics. *End point* method is that after mixing reagents and sample, reaction reaches the endpoint after a certain time when the colour or absorbance of reaction solution does not change any longer. The measurements of the absorbance value of reaction solution is then performed.

In *kinetics* method, after mixing reagents and sample, the absorbance values are continually measured. When the absorbance value begins to change linearly, change rate is then measured. *Two point kinetic test* method is a special case of kinetics test, which involves measurement of the difference of absorbance of two points in the linear section and obtaining the concentration of reaction solution.

## Specifications

*Light source:* Quartz halogen lamp 12 V, 20 W

*Wavelength range:* Automatic by 12 position filter wheel

- Six standard interference filters: 340, 405, 505, 546, 578, and 620 nm
- Six positions for optional filters

*Photometric range:* –0.1 to 2.3 absorbance

*Detector:* Silicon photo diode (320–1000 nm)

*Temperature control:* Peltier elements, 25, 30, and 37°C

*Flow cell system:* 32 µl flow cell with 10 mm light path

*Incubation time:* 5–999 seconds

## Applications

Semi-automated clinical chemistry analysers find applications in laboratories including the clinical, research, education, veterinary, toxicology, and pharmaceutical laboratory. They are used for performing routine biochemistry, hormonal assay, electrolytes, therapeutic drugs, and drug-enzyme investigations.

## 90

# Coagulation Analyser

## Purpose

A coagulation analyser is intended to measure blood platelet levels that serve as diagnostic information for prevention from potentially heart attack-inducing blood clots. They are also used to monitor the effect of drugs such as heparin, oral anticoagulants, and thrombolytic and antiplatelet agents on whole blood, as well as the effects of blood component therapy.

## Principle

Coagulation monitoring is essential for diagnosis of potential causes of haemorrhage, to guide haemostatic therapies, and to predict the risk of bleeding during critical surgical procedures. Blood coagulation is a complex, dynamic physiological process by which clots are formed to control bleeding at an injured site. During surgery, however, patients are treated with an anticoagulant drug such as heparin, followed by a rapid reversal to avoid excessive bleeding. This is done by maintaining a delicate balance between clotting and bleeding by monitoring the clotting time frequently until a normal clotting time is achieved. Coagulation is normally measured by recording the thickness of blood at 100 ms intervals after adding a reagent called thromboplastin, which initiates coagulation.

Two approaches are followed in modern coagulation analysers for measurement of clotting time. They are either based on (i) detection of the clot by ‘feeling’ such as mechanical or viscosity-based devices and (ii) observation of the clot formation using photo-optical or (iii) nephelometric techniques. Under these categories, the



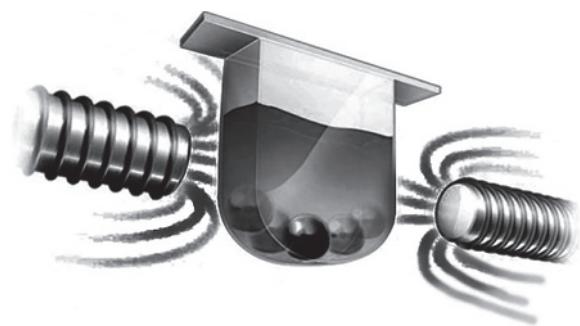
coagulometers may be automated or semi-automated. Semi-automated instruments require the involvement of a lab technician to deliver test plasma and reagents manually to the reaction cuvette. They have limitation in testing only one or two specimens at a time. Although relatively inexpensive, their use requires a trained operator. Fully automated analysers, on the other hand, have automated pipetting system to transfer reagents and test plasma to reaction vessels and measure the end point without involvement of the operator. They have the capability of testing several specimens simultaneously.

### ***Mechanical Methods***

There are two types of mechanical methods: one that is based on the movement of a metal ball between two magnets and the other depends on the movement of two probes inserted within the patient sample.

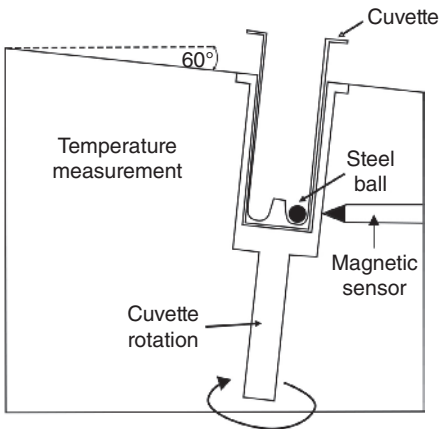
Fibrin formation impedes movement of the magnetic ball or movement of the probe in relation to each other, resulting in a finite end point, which is recorded as the clotting time. Figure 90.1 shows the principle of a moving ball based coagulation analyser. A steel ball is made to oscillate in an arc from one side of the cuvette to the other. An electromagnetic field continuously monitors the oscillation of the ball within the plasma–reagent solution. As the sample clots, fibrin strands are formed. This results in increasing viscosity, slowing the movement of the steel ball. When the oscillation decreases to a predefined rate, the timer stops, indicating the clotting time of the plasma.

Figure 90.2 illustrates another variation of a mechanical method of measuring blood clotting time. The sample is placed in a special cuvette that contains a steel ball. After the appropriate incubation period, the cuvette is placed in the measuring position. It uses a magnet in the test tube aligned with a magnetic sensor in the cuvette and remains locked in position with the detector while the test tube rotates slowly, making the cuvette turn along its longitudinal axis. This is because the cuvette is positioned at an angle, and the ball always remains at the lowest point in the cuvette due to gravity and the magnetic field. When the appropriate reagent is added, a timer is started and the



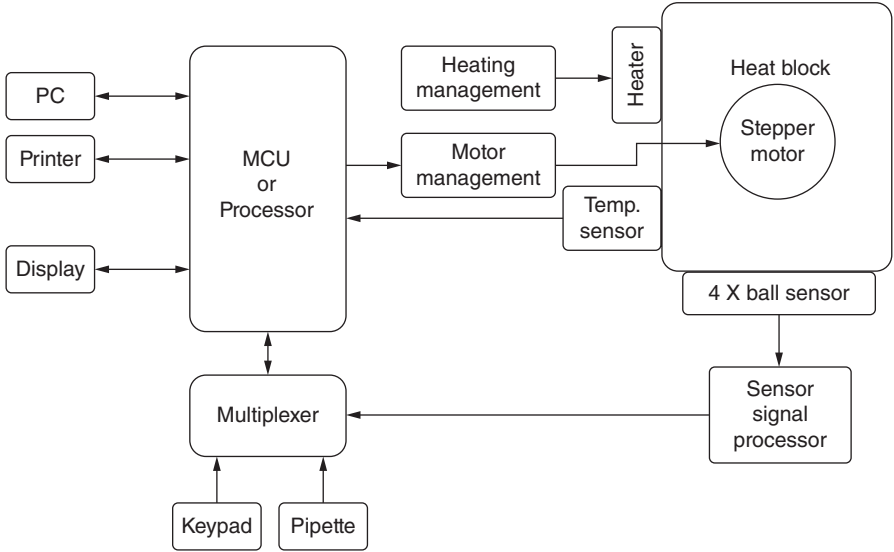
**Figure 90.1** Principle of electromagnetic clot detection method. A steel ball oscillates in an arc from one side of the cuvette to the other. Movement is monitored continuously within a magnetic field. As the sample clots, viscosity increases and movement of the steel ball is impeded. This results in variation in amplitude that stops the timer, and the interval gives the clotting time.

**Figure 90.2** Principle of coagulation analyser used by M/s Sigma Amelung, Lemgo, Germany, in their Model KC 4 Coagulation Analyser.



clotting process starts. With the formation of clot, the magnet gets entangled, thereby breaking the electromagnetic coupling. The fibrin threads pull the ball from its position and this allows the magnet to rotate with the tube, terminating the test. This change in position triggers an impulse in the magnetic sensor, which stops the timer electronically. The analysers based on this principle are available in both single channel and four channel configurations.

The analyser operates under the control of a microprocessor as shown in block diagram (Figure 90.3). The measuring station or the cuvette rotation is controlled by a stepping motor, which is driven by a 1 kHz rectangular signal generated by the microprocessor, which determines the speed of the motor. A thermistor is used to sense the temperature of the measuring module. A pulse width modulator (PWM) signal from the microprocessor is used to control the heating of the measuring station. The overheating of the



**Figure 90.3** Block diagram of four channel coagulation analyser. MCU, microcontroller.

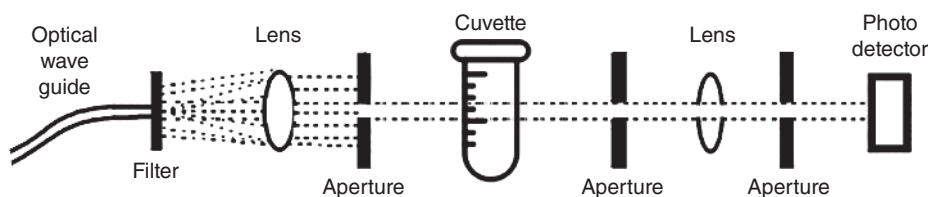
measuring module is prevented by a thermostatic switch, which interrupts the power supply to the heating transistors if the temperature exceeds 60°C. All other components are connected to the microprocessor directly or via driver stages. The display is connected directly to the microprocessor.

### ***Photo-Optical End Point Detection***

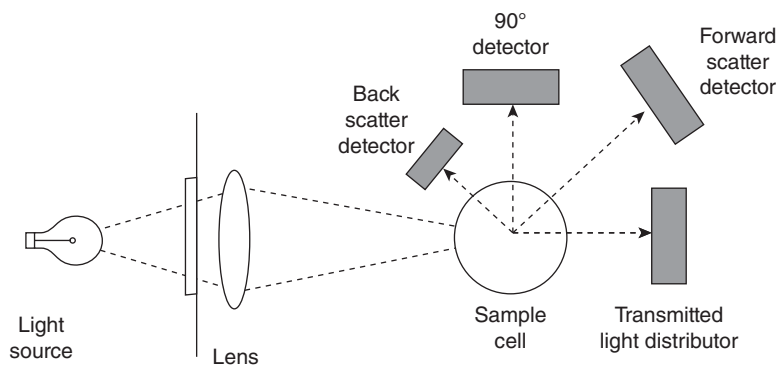
With this technique, fibrin formation is detected by the change in optical density (OD) or turbidity of the sample. After the incubation time, the cuvette is placed into the optical measuring channel. Figure 90.4 represents the basic components of the optical system for measuring coagulation time. Monochromatic light of a specified wavelength (405 nm) passes through plasma, and its intensity (OD) is measured by a photodetector. The OD depends on the colour and clarity of the sample and is established as the baseline. The timing begins with the addition of the clotting reagent. When clots start forming, the sample/reagent mixture becomes cloudy and the intensity of the light reaching the sensor reduces, thus generating an increase in OD. The time between the addition of the clotting reagent and the time when the change in the OD reaches a preset threshold, the time measurement stops. Some optical systems make use of multiple wavelengths that discriminate and filter out the effects of icterus and lipemia. Photo-optical instruments also allow to measure the rate of absorbance change at predetermined intervals. The results are usually recorded as the time to clot, and also a curve of clot formation is plotted.

### ***Nephelometric End Point Detection***

Nephelometry is again a photo-optical end point detection method in which 90° or forward-angle scatter rather than OD is measured as shown in Figure 90.5. The incident light is produced by a light-emitting diode at 600 nm and a photodetector detects variations in light scatter at 90° and near 180° (forward-angle scatter). As fibrin strands are formed, side scatter and forward-angle scatter rise. The timer stops when scatter reaches a predetermined intensity, and the time interval is recorded. This method allows to make dynamic clot measurement in which continuous readings are taken throughout clotting and measures the entire clotting sequence to produce a clot curve. Immunologic assays are also available in some coagulation laboratories that are based on antigen–antibody reactions similar to those used in nephelometry. This technology is used to measure a growing number of coagulation factors and proteins, thus expanding the diagnostic capabilities of the test.



**Figure 90.4** Optical method of measuring blood clotting time.



**Figure 90.5** Nephelometric clot detection method. Light passes from LED through the sample to the detector placed above. As fibrin polymerizes, light is deflected and detected at an angle from the original path.

Modern coagulation instruments incorporate several significant advances in terms of their capability and flexibility. They are designed to have automatic pipetting, recording, and calculation of results, thus minimizing operator expertise, intervention, and time. The present-day instruments eliminate variations in pipetting and end point detection and allow multiple analyses to be performed simultaneously on a single specimen. Some of them can handle a large number of patients, permitting the storage up to 600 patient tests. They come with built-in quality control and security lockout protocols to ensure safe and secure use and high throughput. Since 1990, many instruments have incorporated multiple detection methods into single analysers, which allow saving on cost of equipment and operator training.

## Specifications

*Operating principle:* Ball method

*Measuring channels:* 4 (mechanical)

*Display:* Liquid crystal display (LCD)

*Incubation stations:* 8

*Reagent stations:* 5

*Temperature control (measuring module):*  $37.3 \pm 0.5^{\circ}\text{C}$

*Measuring time:* 4.5 seconds (minimum) to 999.9 seconds (maximum)

## Applications

The coagulation analyser finds applications for automated clot detection for the determination of prothrombin times (PT), activated partial thromboplastin times (APTT), fibrinogen concentrations, and other clotting assays. The instruments provide capability in managing trauma and surgical patients, monitoring heparin therapy, and thrombophilia. They are used to assess the coagulation status and to predict early transfusion requirements of trauma patients.

## 91

## Coagulation Time Machine, Activated

### Purpose

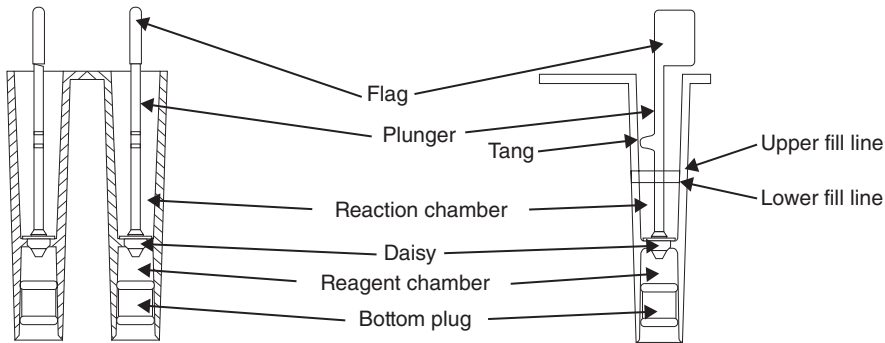
Activated clotting time (ACT) machine is a device to monitor whole blood coagulation time, which is crucial for the safe management of patients undergoing heparin therapy. The ACT test is usually performed to monitor the effect of high dose heparin before, during, and shortly after surgery that demand strong anticoagulant measures. Such situations may be cardiac or vascular surgery, interventional procedures such as cardiac angioplasty, cardiac catheterization, organ transplant, and haemodialysis that require heparin infusion. The instrument is intended for in vitro diagnostic testing in either a hospital laboratory setting or a point of care at the bedside.

### Principle

ACT machine is a workhorse for monitoring anticoagulation time during many critical situations in hospitals. During cardiopulmonary bypass, high dose heparin is used to prevent thrombosis of circuits used during extracorporeal circulation. In the traditional method, the test is done by mixing a whole blood sample with a particulate activator. When the activation is complete, it is indicated by the formation of localized clots as activated thrombin converts fibrinogen to fibrin. The clots are detected by mechanical methods. In the automated instruments, the test procedure is similar to the traditional method, except that an electrochemical sensor is used to indicate the formation of the fibrin and completion of the event.

Since it is important to rapidly monitor the degree of heparin-induced anticoagulation and its reversal, a variety of automated devices and reagents have now become available commercially, which are all designed to measure the seconds required for whole blood to clot upon exposure to an activator. The clotting time depends on a relative scale and requires a baseline value for comparison.

Modern ACT machines are microprocessor-controlled electromechanical coagulation instruments that can determine coagulation endpoints in fresh whole blood and citrated whole blood samples. Fibrin formation is the end point of the test, which is detected by measuring the rate of fall of the plunger–flag mechanism in each cartridge channel as illustrated in Figure 91.1. The machine uses a mechanical plunger–flag assembly that is dipped in and out of activated blood samples in the cartridge. The mechanism enables the plunger to mix the sample and the reagent. During testing, the unit continuously raises and drops the flag–plunger assembly until a photo-optical sensor detects impedance in the rate of fall as a clot forms. In case the sample is unclotted, the plunger assembly would fall rapidly at programmed intervals. However, the rate of fall of the plunger would be impeded during clotting due to formation of the fibrin web. The end point of the test is the time at which clot formation



**Figure 91.1** Constructional details of cartridge for automated activated clotting time machine having reagent and reaction chambers used in Medtronic ACT Plus Automated Coagulation Timer. *Source:* Reproduced with permission from Medtronic.

is detected. A photo-optical system located in the actuator assembly detects the rate of fall of the plunger. The clotting times are performed in duplicate and the results for each channel, the average of the two channels and the difference are displayed on the LCD screen. Clotting time is defined as the time at which a certain 'drop time' threshold for the plunger is reached.

A popular ACT instrument based on this principle is ACT+ from M/s Medtronic shown in Figure 91.2. The instrument can store a total of 1000 test results, any combination of patient and quality control tests. Test data may be transferred to a laboratory or hospital information system using the serial communication port with connectivity software. Test data can be transferred to a PC through USB port. Test reactions take place at  $37 \pm 0.5^\circ\text{C}$  in single-use cartridges placed in the actuator heat



**Figure 91.2** ACT Plus Automated Coagulation Timer from M/s Medtronic. *Source:* With Courtesy of M/s Medtronic, USA.

block assembly. The actuator heat block is the receptacle for test cartridges from which cartridges can be inserted into and removed. Cartridges should be pre-warmed to 37 °C for 3–5 minutes in the instrument's heating block before collecting the test sample.

The ACT+ is a dual channel instrument in which the two channels are manually filled between marked lines on the cartridge by the operator. That indicates the limit of the sample volume (0.4 ml). The cartridge is then placed in a receptacle on the actuator heat block of the machine. The test cartridge contains a liquid biological buffer, which suspends the kaolin or, less commonly, celite activator. In addition, the test cartridge contains calcium chloride to ensure adequate calcium for coagulation to occur and sodium azide to prevent bacterial growth during cartridge storage.

The cartridge consists of the reagent chamber, the reaction chamber, and the plunger assembly. The *reagent chamber* contains the activator and other reagents, which initiate and contribute to the formation of a clot. The *reaction chamber* located above the reagent chamber receives the test sample with the operation of the plunger assembly. With this action, the contents of the reagent chamber are delivered into the reaction chamber, where the mixing of the reagents takes place with the test sample.

The *plunger assembly* consists of three parts: the daisy, the plunger, and the flag. The 'daisy' serves as the upper seal for the reagent chamber and is the mechanical sensing element for the formation of a clot. When the plunger rises and falls, the 'daisy' moves up and down through the test sample/reagent mixture. The movement of the 'daisy' through the sample is impeded when there is a clot formation. The motion of the plunger through the reaction mixture is sensed by a photo-optical system with the movement of the 'flag'. When a decrease in the plunger's fall rate is detected, the timer stops and the clotting time results are displayed.

An *actuator heat block assembly* serves as the receptacle for test cartridges. It is maintained at a temperature of  $37.0 \pm 0.5^\circ\text{C}$ . This unit has two positions, open or closed, and it rotates between these positions. The cartridges are inserted into and removed from the actuator heat block when it is in the open position. When the clotting test is to be performed, the unit is moved to the closed position. On completion of the test, this unit will automatically rotate to the open position. A test can also be terminated manually and the actuator heat block rotated to the open position by depressing the appropriate control on the front panel. There is a provision for quality control, which is an interactive, mechanical, software-controlled verification device that includes both quantitative and qualitative results by mechanically emulating important functions of a test cartridge.

An instrument with extended functions is the Hepcon haemostasis management system (HMS) from M/s Medtronic, United States. It is a six-channel clot-timing instrument that automatically dispenses a blood sample from a syringe into an assay cartridge. In addition, the system can measure heparin dose response, heparin concentration, platelet function, and ACT and calculate protamine dose and patient body blood volume. The instrument is an integrated system consisting of a component for tracking clot detection and computing results, a component for sample delivery, and the single-use test cartridges for actual performance of the tests. Handheld, battery-operated, single-channel units capable of performing several coagulation tests on whole blood are also available. Unlike the other systems, which rely on mechanical detection of a clot, these machines employ an electrochemical sensor to detect the conversion of a thrombin substrate for the determination of the ACT.

## Specifications

*Number of channels:* 2

*Blood sample:* 0.4 ml

*Timing range:* 0–999 seconds

*Actuator heat block temperature range:*  $37.0 \pm 2^\circ\text{C}$

*Resolution:*  $0.1^\circ\text{C}$

*Accuracy:*  $0.1^\circ\text{C}$

## Applications

Activated coagulation timer machine is designed for in vitro diagnostic testing applications in a hospital laboratory setting or a point-of-care situations such as in the operating room, cardiac catheterization lab, cardiovascular and vascular surgery, intensive care unit, haemodialysis units or clinic, etc.

# 92

## Cobalt-60 Machine for Radiotherapy

### Purpose

Cobalt-60 machine is intended to deliver precise radiation treatment to the patient suffering from a cancerous growth. The machine provides high dose of radiation to the tumour under treatment and is designed to cause minimum damage to the surrounding healthy tissue or organs. Cobalt-60 therapy can be used anywhere on the body but is particularly useful in brain tumour patients because of its preciseness. Cobalt machines have the advantage of producing a completely predictable, steady, reliable beam of radiation energy. Because of its effectiveness and simple design, doctors have used cobalt-60 therapy to treat cancer for almost 60 years.

### Principle

Cancer is one of the leading causes of death in the world. It is presently managed using one or a combination of three methods of treatment: surgery, chemotherapy, and radiation therapy. More than half of all cancer patients receive radiation therapy either as a primary or adjunctive treatment. Radiation therapy is a cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumours. Radiation therapy may be given from outside by applying external beam of radiation or inside the body, which is known as brachytherapy. In external beam radiation therapy, a machine directs radiation at the cancer and surrounding tissue. In internal radiation therapy, a radioactive



material is put in thin tubes and placed inside the body near the cancer. Radiotherapy with a good success rate and lower total cost of treatment is considered as a preferred method in cancer management among patients.

There are two types of sources that are used for radiation therapy. These are  $\gamma$  rays, which are emitted by radioactive material, and X-rays that are generated by a particle accelerator. For brachytherapy, a radioactive material is mostly used, whereas for external beam treatment, where a device delivers radiation into the body from outside, a cobalt-60 machine producing gamma rays or linear accelerator machine generating X-rays or electrons is most often used. Treatment machines incorporating  $\gamma$  ray sources for use in external beam radiotherapy are also called teletherapy machines.

### **Cobalt-60**

In the early 1950s, the cobalt unit was introduced into medical use. Prior to that, the radiation therapy treatment was carried out only by high energy X-ray machines. An X-ray machine operating at 400kV could provide an average energy of 133keV. The introduction of the cobalt-60 machine was a great step forward as it provided an average photon energy of 1.25MeV, which is almost 10 times of the X-ray machine and consequently had more penetrating power.

Cobalt is a hard metallic substance and has an atomic number of 27. Its atomic weight is 58.933 and its mass density is  $8900\text{kgm}^{-3}$  and it melts at about  $1500^{\circ}\text{C}$ . For radiotherapy, a pellet of radioactive cobalt isotope is used as a source of radiation. However, the radioactive isotope  $^{60}\text{Co}$  does not exist in nature and has to be produced by bombarding the stable isotope of cobalt,  $^{59}\text{Co}$ , by neutrons in a nuclear reactor. The isotope has a half-life of 5.26 years, which is relatively quite long. When the isotope decays, it yields two  $\gamma$  (gamma) rays with energies of 1.17 and 1.33MeV respectively. Since these are produced in equal number, their average would be 1.25 MeV. These properties make  $^{60}\text{Co}$  unique as a source of radiation for cancer treatment. A simple radiation treatment typically involves an absorbed dose at the tumour of 2.0 Gy (200 rad).

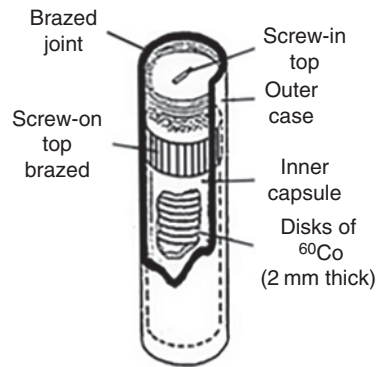
Cobalt sources are usually made up into a capsule on demand from stocks or pellets. The pellets are about 1 mm in diameter and have been pre-irradiated to a selection of specific activities in a nuclear reactor. To produce a source, the pellets are loaded in a stainless steel container. They are held in place by spacers, which hold them in position. Finally, this cylinder, when capped, is inserted into another cylinder and sealed by cold welding. Finally, the source is shipped in a well-protected and shielded container and sent to the place where it is to be loaded into a cobalt unit.

### **Constructional Details**

A cobalt machine consists of the following major subsystems:

- Cobalt source head comprising a radioactive source and its housing.
- Head mounts for source movement mechanism (gantry and stand).
- Beam collimator.
- Treatment table or patient support assembly.
- Control console and safety interlocks.

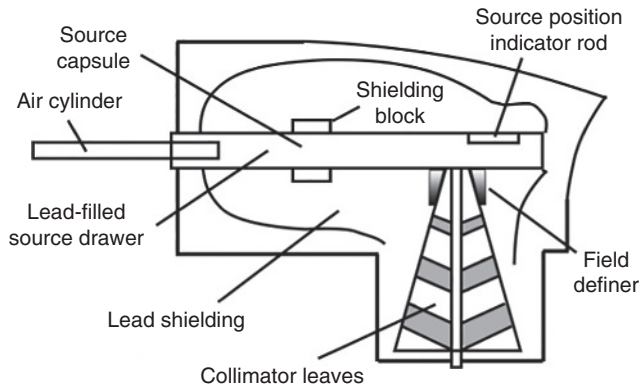
**Figure 92.1** Design of the cobalt source capsule. The container is cylindrical double-welded stainless steel capsule with pellets of 1–2 cm in diameter.



**Cobalt Source Head** The heart of the system is the cobalt source. The typical diameter of the cylindrical source is between 1 and 2 cm; the height of the cylinder is about 2.5 cm. Usually, a diameter of 1.5 cm is chosen as a compromise between the cost and penumbra. The head assembly of the machine is a cast shell with lead and tungsten shield. Maximum capacity is 15 000 Ci of cobalt-60 equivalent to a unit output of approximately 390 cGy/min. The lead-filled container is 25 cm thick in all directions from the source. Its design should ensure that the leakage radiation coming through its thickness would not cause an overexposure to anyone staying at its surface for prolonged periods of time.

The source is placed near the centre of a large, lead-filled steel container as illustrated in Figure 92.1. A number of methods have been devised for moving the source from the 'off' to the 'on' position. In one method, the source is mounted in a heavy metal like tungsten wheel that is rotated through 180° to carry it from the 'off' position to the 'on' position. The transfer between 'on' and 'off' positions takes place in less than two seconds for pinpoint exposure accuracy. The motor drive acts against a heavy-duty torque spring that instantly returns the source to the 'off' position for normal exposure termination and in the event of an electrical power failure. In another method, the source is mounted in a sliding plug or drawer, which carries the source from the 'off' to the 'on' position. This method has become the most commonly used one in commercial machines. All machines must be arranged so that they are fail 'safe,' that is, the source must be held in the 'on' position by the continuous application of a force so that if the power fails, it must return quickly to the 'off' position. In one machine, the safety facility is in the form of total closure of the diaphragms electrically (0 cm × 0 cm field size) during source stuck position using a safety interlock.

**Mounts (Gantry)** There are two types of arrangements of mounting radiation treatment units. In the earlier designs, the head of the unit was held in a yoke which can be moved up and down, or back and forth, and can be rotated about the axis. In this case, the head mount is suspended from a set of rails attached to the ceiling. In the later models, the unit was mounted on a column with vertical motion and a pivot for head rotation. The distance from the source to the skin of the patient source to skin distance (SSD) is usually fixed at 80 cm, and the focus of the set-up is the surface of the patient. The alternative mount is the so-called isocentric or fixed source–axis distance (SAD) mount. The isocentre is defined as the point where the collimator and gantry rotational



**Figure 92.2** Various components of source head in a cobalt machine.

axes intersect. This point lies within a sphere of 1 mm radius as the gantry rotates through  $360^\circ$ .

The head is encased in a streamlined plastic cover and is mounted on a gantry that can rotate about a horizontal axis. The gantry supports the source head at one end and the radiation barrier or counterweight at the opposite end. It accurately maintains an 80–100 cm distance from the source to the axis of rotation located 120 cm above floor. The drive consists of a DC motor with microprocessor control and dynamic braking circuits that allow uniform rotation and accurate control of the gantry motion.

The gantry consists of a rugged heavy-gauge steel frame with 2.5 cm thick base and anchoring plates. The base plate is fixed to the floor with two heavy duty anchoring bolts. The carriage and hanger assembly provide vibration-free movement along with the vertical guide rails. Control of the vertical movement can be done through a pendant switch. The gantry rotates in both clockwise and counterclockwise directions. Gantry rotation can be under variable speed control to facilitate treatment set-up. The range of gantry rotation is  $\pm 360^\circ$ . The system automatically determines and controls the appropriate gantry speed for a single pass-defined arc. The range of gantry speed is variable between 0.01 and 1.0 rpm. The layout of the various components in the gantry is shown in Figure 92.2.

**Collimators** A symmetrical/asymmetrical collimator assembly defines the  $X$  and  $Y$  axes relative to the collimator axis. The collimator consists of a set of bars that can produce a radiation beam with a square or rectangular cross section. The collimator can rotate at an angle of  $360^\circ$  about its beam axis, and rotary knobs lock the bars at the desired position. The position of the collimator bars is indicated on an indicator scale that is calibrated in  $1^\circ$  increments. The field size can be continuously varied to define the shaping of square or rectangular fields whose size can be adjusted from  $3\text{ cm} \times 3\text{ cm}$  to  $35\text{ cm} \times 35\text{ cm}$  at 80 cm from the source. The adjustment of the field size is done by a moving the collimator vanes, which are motor driven. The geometric penumbra, which results from a finite source diameter, is minimized by using small diameter sources and by using penumbra trimmers as close as possible to the patient's skin.

The collimator is constructed of four sets of flat, interleaved lead vanes with angulated inner tungsten trees for continuously variable field sizes. As the vanes move, the

beam defining tungsten trees automatically angulate to follow the divergence of the beam. The built-in system projects light field on the patient's skin to indicate precisely the radiation field at the 50% geometric penumbra line. A built-in optical device projects an easy-to-read scale on the patient's skin to facilitate a direct readout. It indicates 60–100 cm in 1 cm increments. When the desired number is superimposed on cross hairs, the patient's skin is at the desired distance from the source.

The collimators are generally designed to be asymmetrical that allows the jaws to move independently, providing freedom in treatment planning. For example, arc therapy can be provided simply by entering the arc angle and time, and the control system automatically determines the gantry speed to complete the arc. The motorized wedge allows to treat with the required wedge angle between  $1^\circ$  and  $60^\circ$ . The collimator may be rotated  $\pm 180^\circ$  from its central position at variable speed, up to a maximum speed of 6° per second. An optical device projects a scale on the patient's skin to facilitate the adjustment of the field size and shape.

**Treatment Table** The patient to be treated is made to lie on a table whose position can be adjusted upwards or lowered. It can also be moved sideways so that for any angle of the gantry, the beam will pass through the tumour. The axis of rotation is a fixed distance from the source, and the size of the beam is specified by its size at the axis. The arrangement is called isocentric because the axis of rotation of the gantry intersects with the central axis of the beam (axis of rotation of the collimator) so that they both rotate about the same centre. In addition, the treatment table can usually be rotated about a vertical axis so that it also passes through the isocentre. Longitudinal and transverse tabletop travels are usually manually controlled, while the vertical movement is motor driven. In addition, the entire table can be rotated  $180^\circ$  about the vertical beam axis.

The various movements of the table are controlled by an aluminium casting carriage assembly mounted directly below the tabletop. It comprises bearing assemblies and positioning controls. The longitudinal movement is achieved through ball bearings, which ride in hardened steel tracks, while the linear ball bearings move on hardened steel shafts for transverse travel. The patient table is provided with multiple safeguards to protect the patient and the therapist. The table can be moved using the remote control or by using the table controls located on each side of the table.

**Control Console and Safety Interlocks** The computerized control console is always placed outside the treatment room that facilitates control of various functions. The machine is controlled by an advanced software control system, which monitors treatment parameters continuously. It permits the selection of treatment techniques such as rotation, oscillation, skip scanning, or multi-portal indexing. The X and Y leaf positions of the collimator are displayed on the in-room display monitor. The direction selector establishes clockwise or counterclockwise rotation of the gantry. An exposure timer counts down as treatment time diminishes and is displayed by a four-digit LED readout. Similarly, the count-up exposure time is displayed with the progress of the treatment. An emergency button interrupts source-drive current for torque-spring return to 'beam off' condition with momentary actuation. Similarly, an entrance door interlock permits interconnection to the safety switch at the entrance door. Exposure automatically terminates if the entrance door is opened while the source is 'on'. A

'safety key switch' controls the source transfer mechanism to prevent unauthorized use. The design of the cobalt head must meet the international standards for source shielding, radiation transmission, and radiation leakage. The dual computer control system monitors the source position and automatically retracts the source if a problem with source travel or position is detected.

The use of cobalt-60 machines is regulated by national regulatory authorities in the respective countries that provide clearance for the concrete rooms, issue license for the procurement, and use of these equipment, conduct periodic surveys, and document radiation levels for such installations.

### **Field Light System**

The field light system consists of an external parabolic mirror projector assembly, which is designed to allow for quick and easy replacement of the quartz halogen lamp. An automatic timer turns off the light field at the start of the treatment and is generally configured for a preset time between 1 and 3 minutes, extending the usage of the light field.

### **Timer**

The prescribed target dose is delivered under the control of two treatment timers: primary and secondary. The primary timer actually controls the treatment time, while the secondary timer serves as a backup timer in case of failure of the primary timer.

The cobalt unit is mechanically simple, and its output is totally predictable and reliable. The beam characteristics are well known and relatively easy to measure. It is also easy to make special filters and beam modifiers for individual treatment needs. Because of the source decay, sources must be renewed at intervals of around 2–3 years, but this procedure is quite straightforward. The expense of periodically changing the source is more than offset by the low maintenance cost of the machine. Also, less infrastructure requirements, low power demands, and simple quality assurance of the beam parameters make the cobalt-60 machine useful for highly populated developing countries. However, cobalt machines are now being gradually replaced by linear accelerators, which produce X-rays and electrons having higher energy outputs and greater penetration capability resulting in shorter treatment time.

## **Specifications**

*SAD:* 100 cm or 80 cm configuration

*Source:* High activity sources 1.5 or 2 cm diameter

*Dose rate:* 390 cGy/min at 80 cm and 250 cGy/min at 100 cm

*Collimators:* Asymmetric, auto set-up

*Field size:* From 1 cm × 1 cm to 35 cm × 35 cm at 80 cm

*Physical wedges:* 15°, 30°, 45°, and 60°; motorized wedge at 1°–60°

*Beam type:* Fixed beam and arc treatment

*Gantry speed:* Between 0.01 and 1.0 rpm

*Safety:* Collision detection ring

*Display:* Graphical data entry interface, service diagnostics

## Applications

Cobalt-60 machine has been a workhorse in radiotherapy departments ever since they were introduced in the 1950s. Although newer facilities have gone for linear accelerators, some facilities still continue to have these machines in operation. Cobalt systems cannot deliver the higher power radiation that is possible with a linear accelerator and thus may not be as effective at destroying certain types of cancerous tumour. Also, the radiation produced by a linear accelerator can be turned on and off, whereas the cobalt system consists of a radioactive source material that is always on.

## 93

## Cochlear Prostheses

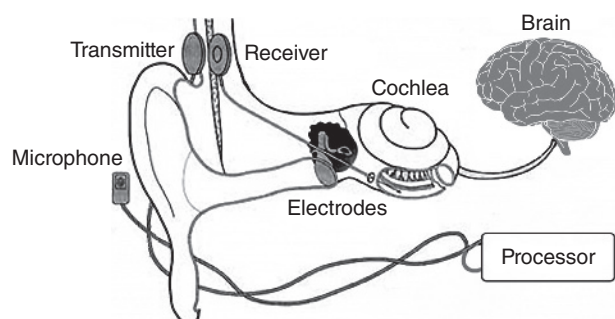
### Purpose

A cochlear implant is a device that is surgically implanted to help persons overcome problems of hearing in the inner ear, or cochlea. The cochlea is a snail-shaped, curled tube located in the area of the ear where nerves are contained. Its function is to acquire electrical signals from sound vibrations and transmit them to the auditory nerve or hearing nerve. The hearing nerve then sends these signals to the brain, where they are translated into recognizable or perceptible sounds. However, it is important to understand that these devices do not restore normal hearing and are only tools that allow sound and speech signals to be processed and sent to the brain.

### Principle

Sensorineural deafness affects a large number of people throughout the world. This type of deafness can be caused either by cochlear damage or by damage within the auditory nerve or to the neurons of the central auditory system. The hair cells are the sensory cells that transduce mechanical motion into electrical signals that can be recognized by auditory neurons. The auditory neurons carry information from the hair cells to the cochlear nucleus in the brainstem and, via the cochlear nucleus, to higher nuclei in the brain.

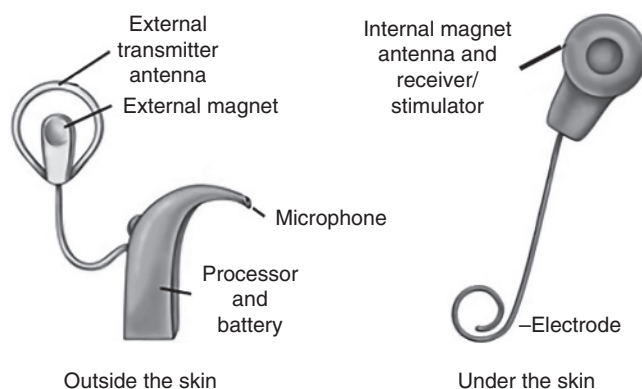
The normal cochlea and the associated neurons of the central auditory system provide information about both the frequency content and intensity of the auditory signal. Auditory information is decomposed into its fundamental frequencies by the mechanically tuned properties of the basilar membrane. The location of hair cells along the cochlea determines their optimal response to frequency: hair cells at the apex are responsive to low frequencies, while hair cells at the base are responsive to high frequencies. Around 30 000 fibres of the auditory nerve have an auditory threshold function that is sensitive to a small range of frequencies. So, specific fibres are driven by frequencies in particular regions of the audio spectrum.



**Figure 93.1** Cochlear implant system in position.

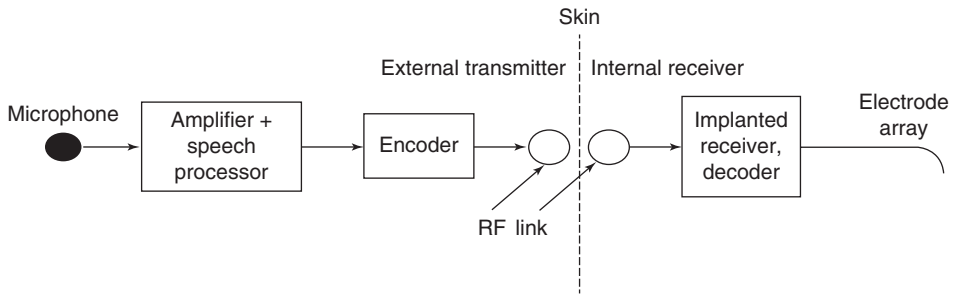
The treatment of choice for the sensorineural deaf is the cochlear prosthesis or cochlear implant as shown in Figure 93.1. A cochlear implant is a prosthetic inner-ear replacement that provides direct electrical stimulation to the inner ear's auditory nerve, allowing for perception of the sensation of sound. By completely bypassing the damaged part of the cochlea, the cochlear implant uses its own electrical signals to stimulate the auditory nerve, allowing the person to hear. The device is used for patients with severe-to-profound hearing sensorineural loss who cannot be helped with hearing aids. In the general design of a cochlear implant, the sound is decomposed into useful frequency bands for transmission and reception of speech, and critical features of the signals within those frequency bands are delivered to auditory neurons via an array of electrodes.

Figure 93.2 shows a cochlear implant device that consists of a *microphone* that picks up the sound and a *speech processor* to analyse the sound and convert it into an electrical signal. The signal processor sends the signals to a *transmission system* that transmits the electrical signals to the implanted electrode or an *electrode array* (multiple electrodes) that is inserted into the cochlea by a surgeon. A block diagram of a transcutaneous link, most often in generic cochlear implant, is shown in Figure 93.3. The microphone converts acoustic signals into electrical signals. The electrical signals are amplified and sent to the sound and speech processor. The main function of the signal processor is to decompose the input signal into its frequency components, much like a healthy cochlea analyses the input signal into its frequency components. It is then



**Figure 93.2** Various parts of a cochlear implant.





**Figure 93.3** Schematic of a cochlear implant with a transcutaneous link. RF, radiofrequency link.

encoded in various ways in the block called stimulus encoder. In the vast majority of implants, the stimulus encoder is worn outside the head, producing a serially coded signal that is transmitted across the skin.

The link sends both data and power to an internal circuit that decodes the serial data stream and decomposes it into signals that are delivered to the current sources that drive the electrodes of the cochlear electrode array. Each electrode of the array is driven with either a pulsatile or an analog electrical signal. The signals traverse the tissues of the inner ear, usually the fluids of the scala tympani, and excite the auditory neurons. The excitation depends upon the number of intact neurons that remain, the proximity of the electrode array to the neurons, and the spatial and temporal characteristics of the current–density fields that affect the neurons.

The implant package determines the amount of electric current, which should be sent to the electrodes. The amount of current determines loudness, while the position of the electrodes determines the pitch of the sound. The electrical signals stimulate the nerve endings in the cochlea (the area where the hair cells are located) resulting in sending the message to the brain along the hearing nerve. The brain interprets the sound allowing the person to hear the same.

In single channel implants, only one electrode is used. In multichannel cochlear implants, an electrode array is inserted in the cochlear so that different auditory nerve fibres can be stimulated at different places, thereby exploiting the place mechanism for coding frequencies. Different electrodes are stimulated, depending on the frequency of the signal. Electrodes near the base of the cochlea are stimulated with high frequency signals, while electrodes near the apex are stimulated with low frequency signals. The loudness of the sound can be controlled by varying the amplitude of the stimulus current.

Different types of cochlear implants are available, which differ in the following characteristics:

- *Electrode design:* Number of electrodes and their configurations, monopolar or bipolar. Bipolar electrodes produce more localized stimulation.
- *Type of stimulation:* Analog or pulsatile; pulsatile pulses are preferred as there are lesser channel interactions.
- *Transmission link:* Transcutaneous or percutaneous. In transcutaneous system, there is an implanted receiver, which receives stimulating pulses from outside and delivers them to the electrodes. In percutaneous system, there is no implanted part other than the electrodes that receive stimulating pulses from external unit.
- *Signal processing:* Waveform representation or feature extraction.



Cochlear implant is a remarkable development in the field of biomedical engineering. It has provided patients with the last measure to overcome the dreadful problem of deafness by partially restoring the hearing inability. The users are able to recognize the environmental sounds such as automobile horns, knocks at the door, and sirens. The cochlear prostheses are under continuous development with a focus on new designs of electrode arrays, signal processing, and direct stimulation of the nervous system.

## Specifications

### *Transmitter*

*Microphone:* Omnidimensional

*Weight:* Up to 5 g

*Frequency range:* 100 Hz–10 KHz

*Stimulation:* Monopolar, bipolar mode, and biphasic current pulses

*Stimulation rate:* 30 KHz or higher

*Pulse width:* 12–400  $\mu$ s per phase

### *Receiver stimulator*

*Weight:* ~10 g

*Housing:* ~50 mm  $\times$  30 mm (flexible silicon)

*Electrodes:* ~20 no.

*Material:* Platinum moulded in a perimodiolar shape

*Electrode contacts:* Arranged a non-uniform spacing from 0.4 to 0.8 mm and spaced over 15 mm active array

*Electrode diameter at apical end:* ~0.5 mm

## Applications

Cochlear implants are designed to be used by deaf people to receive and process sounds and speech. They are used both by children and adults. A cochlear implant is particularly useful for those who do not benefit from powerful hearing aids.

## Colonoscope

### Purpose

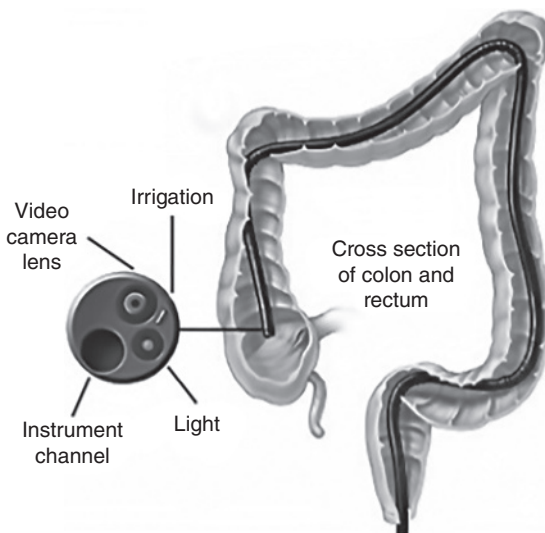
Colonoscope is intended to examine the inside of the colon using long, flexible fibre optics-based camera. The device helps to diagnose various diseases including intestinal cancer, source of bleeding, ulceration, and polyps. It is also used for the removal of

foreign bodies, excision of tumours or colorectal polyps (polypectomy), and control of haemorrhage. These colonoscopy procedures reduce the need for invasive surgical diagnostic and therapeutic procedures.

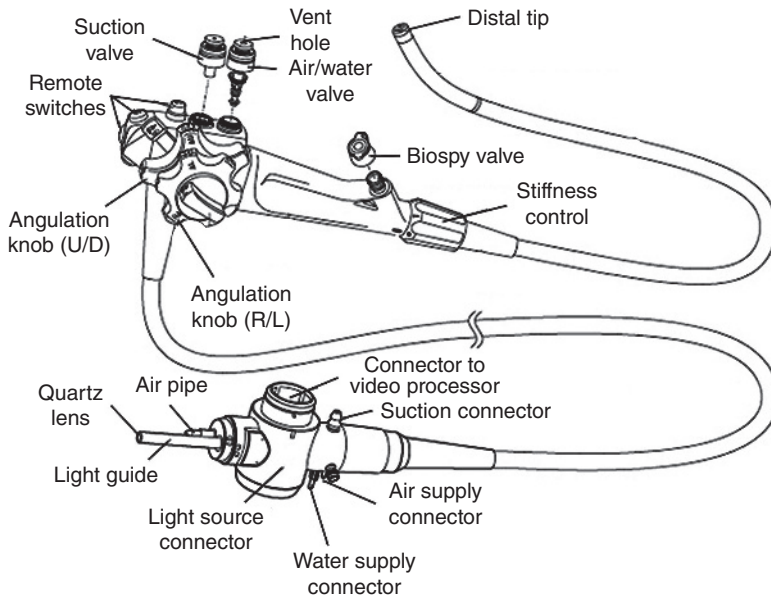
## Principle

Colonoscopy is an extension of the endoscopic examination of the large bowel and the distal part of the small bowel for diagnostic and screening purposes. Though the system is intended for diagnostic visualization of the digestive tract, the system also provides access for therapeutic interventions using standard endoscopy tools. The procedure is done with a charge-coupled device (CCD) camera or a fibre optic camera on a flexible tube that is passed through the anus as shown in Figure 94.1. It provides a visual image of the area under examination leading to the diagnosis of, say, ulceration, polyps, etc. It also provides the opportunity for biopsy or removal of suspected colorectal cancer lesions, which can be subsequently studied with the aid of a microscope. Images from the camera in the colonoscope are displayed on a video screen in the examination room. Still images can also be taken to allow the physician for a closer examination and for comparing them with previously taken or future colonoscopy images.

A modern video colonoscope is a combination of sophisticated electronic imaging technology and precision mechanical engineering. Its main components are illumination optical fibres, angulation cables, and suction and air/water channels. These are all packed within a water-tight tube, which is just about 10–12 mm in diameter and about 150 cm long. The total assembly should be strong enough to permit the physician to push it through the 1.8 m long colon. It should be sufficiently flexible so that it can be bent around the sharp turns and at the same time elastic enough to return to its original



**Figure 94.1** Colonoscope in position in the body.



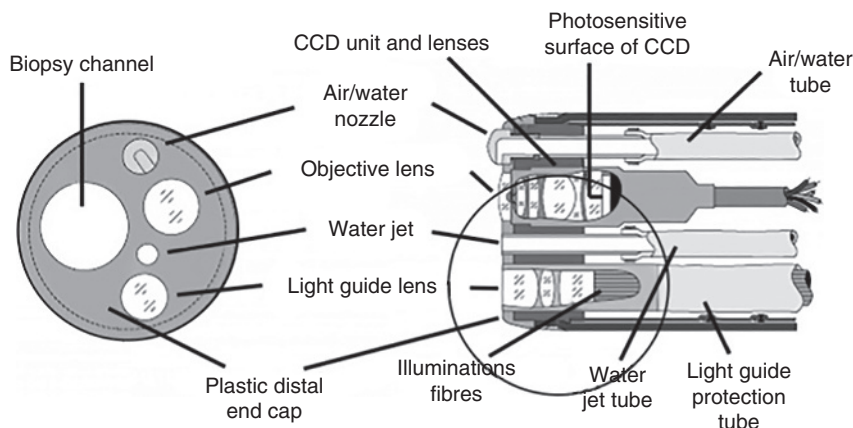
**Figure 94.2** Constructional details of a colonoscope.

shape when it is pulled back. It should be capable of transmitting the hand actions of the operator from the proximal shaft down to the distal tip.

The colonoscope comprises the following sections as illustrated in Figure 94.2:

- (i) *Colonoscope head*: This carries an illumination port, which is connected to a cord that also has connectivity to the video processor, the suction, and the air/water supplies. The head also carries switches and valves that can be operated by the physician for controlling various functions.
- (ii) *Insertion tube*: This is a long, straight tube that is designed to intubate the colon. The insertion tube carries three hollow tubes for suction/biopsy, air and water for washing the lens, and water for the forward-directed jet. The distal tip of the tube shown in Figure 94.3 contains the channel openings, the air–water nozzle that allows insufflation and lens cleaning, the objective lens, and the light guide lens. The insertion tube is more flexible in the distal 40 cm end than the proximal part. This facilitates the distal part to move around the complex convolutions of the colon without stressing the proximal portion to form loops. Insertion tubes in some instruments have a variable stiffness property that can be activated by a ring on the proximal end of the insertion tube. The stiffness of the insertion tube is determined primarily by the formulation of the outer polymeric layer and an outer wire mesh.

At the distal end of the insertion tube is a 10 cm bending section, which is controlled by the angulation wires through control wheels. Four angulation cables are used for right/left and up/down controls. They are positioned at 3, 6, 9, and 12 o'clock. The tip deflection provided in most colonoscopes is 180° up/down and 160° right/left. The insertion tube transmits the torque from the external shaft of the instrument, through

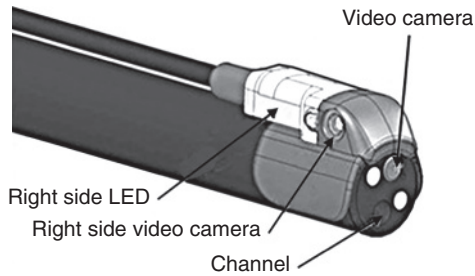


**Figure 94.3** Cross-sectional view of distal end of the colonoscope. Source: <https://www.quora.com/What-is-colonoscopy>.

the bends in the colon and to the tip of the instrument. This is achieved by using oppositely spiralled flat metal bands that run along the entire length of the instrument. The bands are so arranged that a twist of the scope in one direction will tighten one set of bands, while a twist in the opposite direction will tighten the other spiral bands.

- (iii) *Light source*: The light source is a xenon lamp, which is connected to the distal end through thousands of hairlike,  $30\text{ }\mu\text{m}$  wide, glass fibres contained in the insertion tube. The glass fibres transmit the light from and to the distal end of the instrument from the colonoscope head. The glass fibres coated with glass causing internal reflections that allow light transmission through the fibre even when it is flexed. The light is used to illuminate the field of view in the patient's colon.
- (iv) *Camera*: The distal tip of video colonoscopes includes a CCD that serves as a small camera and electronically transmits the image from the CCD to an external video processing unit. The small chip camera is located behind the objective lens. Most modern instruments incorporate high resolution camera, which allows to resolve two lines or points located only fractions of a millimetre apart. The cameras have high definition image sensors, which can feed to densely pixilated monitors. Video images can be transmitted to the display monitor or a recording device. The angle of view of most colonoscopes is  $140^\circ$ , while some instruments do provide a viewing angle of  $170^\circ$ .

For many years, colonoscopes have been forward-looking devices that provided a single view of the intestinal lumen. However, some instruments such as shown in Figure 94.4 are now available that makes use of three small cameras at the tip of the insertion tube, as compared with one at the tip of a standard, forward-viewing endoscope. This provides a wider viewing angle of  $330^\circ$  that allows nearly twice the surface area and anatomy of the colon. It is possible to monitor the position of the scope inside the colon at all times via a 3D reconstruction on the monitor. Some instruments provide two-stage optical system that allows the user to switch between two focus settings. The 'near mode' features high resolving power for close mucosal observation and 'normal mode' for normal observation.



**Figure 94.4** The camera system in a colonoscope.

- (v) *Control section:* In the proximal housing, this contains the angulation dials and locks for up/down and right/left tip deflection, the air–water and suction valves, and the remote switches that control photography, illumination light type (e.g. white light versus narrow band), and zoom functions.

It may be noted that with a colonoscopy and a sigmoidoscopy, the tube enters the colon through the anus of the patient, while in the case of upper endoscopy, it is put through the mouth. During a colonoscopy, a flexible tube with a camera at the end is guided through the colon and possibly the very end of the small intestines. In case of sigmoidoscopy, the tube only goes through the sigmoid colon and is used to screen for problems in the lower part of the large bowel (colon) only. The colonoscope, however, is long enough to inspect all of the large bowel and even the lower part of the small intestine. The upper endoscopy allows viewing of the oesophagus, stomach, and the very beginning of the small intestines.

## Specifications

*Diameter of distal end:* 13.8 mm

*Diameter of insertion tube:* 13.5 mm

*Working length:* 1300 mm

*Total length:* 1650 mm

*Diameter of instrument channel:* 3.2 mm

*Field of view:* 170°, forward viewing

*Depth of field:* Normal, 3–100 mm; Near field, 2–6 mm

*Angulations:* 180° up/down, 160° right/left

*Water flow:* ≥40 ml/min

*Air flow:* ≥800 ml/min

*Suction flow:* ≥400 ml/min

*Light source:* Xenon lamp

## Applications

Colonoscopy is performed in the hospital, the ambulatory surgical centre, or the physician office to diagnose colorectal cancer. The instrument can be used to remove polyps

from the entire length of the colon, which reduces the incidence of colorectal cancer. Furthermore, colonoscopy allows to obtain biopsy samples, which screen for patients that are at a higher risk of developing cancers in future. Colonoscopy is also useful and an effective method to evaluate problems such as blood loss, abdominal or rectal pain, and changes in bowel habits, such as chronic diarrhoea.

## 95

# Colony Counter, Automated

## Purpose

A colony counter is an instrument that is commonly used to count colonies of bacteria or other microorganisms on a plate containing a gelled growth medium.

Biological procedures often depend upon an accurate count of bacterial colonies and cells. Typical applications include Ames testing, bacterial mutation assays, and *Escherichia coli* bacterial colonies.

## Principle

Bacterial colony is defined as a cluster of bacteria derived from one common bacterium. An accurate measure of the bacterial colonies and other organisms is considered essential for many biological procedures. The counting of bacterial colony is usually done manually by well-trained technicians.

The principle of manual counting is very simple, though tedious. In one model, a pencil-like probe with a metal tip, which is connected by an electrical connection to the gelled growth medium, is used. When the probe is touched to a colony on the plate, the electrical circuit gets completed, causing an increment of 1 unit on the readout of the colony counter. Sometimes, colonies are very small and too much crowded, which make them difficult to count. Counting can be made convenient by dividing the plate into several square divisions and magnifying the colonies by a magnifying glass, which makes counting easy. A magnifier mounted on a flexible arm is usually provided as an accessory. Multiple adapters for various sizes of plates are available from 60 to 150 mm. A typical manual colony counter is shown in Figure 95.1.

The manual counting process allows a very low throughput and is time consuming, tedious, and labour intensive in practice. Also, when counts are made by more than one technician, wide variations are often observed. Alternatively, semi-automatic or fully automatic systems have been developed to ensure reliability and minimize operational problems. The semi-automatic methods are based on the use of software alone, whereas automatic methods use both hardware and software solutions. An increased area of focus in microbiology is the automation of counting methods. The challenge in automated counting systems



**Figure 95.1** Typical manual colony counter.

includes handling of colonies that touch or overlap other colonies and identifying each colony as a unit in spite of differing shapes, sizes, textures, colours, light intensities, and others.

However, a more popular method consists of simply placing the illuminated Petri dish on the electronic pressure pad and touching the dish with a felt tip pen to mark each colony. The touch pressure causes a count to be registered on the digital display, which is confirmed by an audible tone advancing one digit on an LED display. Marking the dish with a felt tip pen avoids missing colonies or double counting. The pressure required to register a count can be adjusted on the instrument panel. The instrument is supplied complete with one Wolffhuegel graticule, segmentation disc, and centring adapters for 50–90 mm dishes. A built-in averaging facility allows multiple plates to be counted and then average colony count calculated by the software. Optimum viewing of colonies is necessary that is assisted by peripheral, glare-free illumination. There is also a dark background facility for difficult translucent cultures. The background can be selected dark or bright field by operating a toggle switch. A USB connectivity allows the results to be sent to a computer to ensure traceability or be printed.

### ***Automated Systems***

A fully automated system would essentially consist of collecting images using any one of the digital image capturing devices such as document scanner/charge coupled device (CCD) digital camera/webcam or video equipment. Colonies can be counted from pictures of plates using software tools. A picture of each plate is taken and subsequently all the pictures are analysed. It just takes less than 10 seconds to take a single picture, as opposed to several minutes to count colonies manually, thus saving considerable time.

The captured images are then digitized on a computer utilizing an image processing software package that has programming capabilities. The digitized picture is processed using single/multi-threshold segmentation procedures to separate and detect the colonies present. The digital images of a plate collected in small laboratories not having a colony counter can be sent via the Internet for an accurate colony count from a remote laboratory that has an appropriate counting software.



**Figure 95.2** Advanced version of a typical colony counter.



In automated systems, the objects and their backgrounds can be varied widely. Usually, one of the three methods of illumination can be selected to enhance visibility and increase accuracy. These are the following:

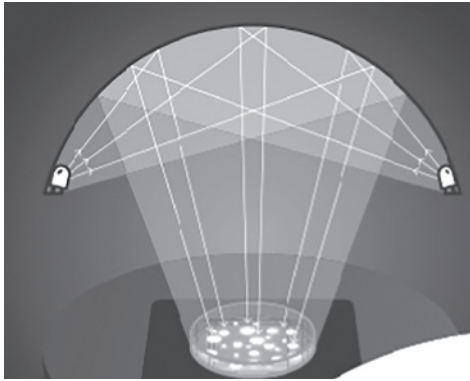
- > *Transmission method*: Used for routine objects of high contrast with relatively transparent backgrounds
- > *Reflection method*: For objects with high contrast with opaque backgrounds
- > *Dark field method*: For objects with low contrast and relatively transparent backgrounds

Modern instruments offer high definition colour images taken with a 1.4 megapixel CCD camera, which can capture and detect colonies as small as 0.43 mm and zones to an accuracy of 0.1 mm. A typical automated colony counter is shown in Figure 95.2. The illumination system used in this device consists of red, green, and blue long-life LEDs that give good colour images with excellent contrast. The illumination exposes the plate to rapid bursts of red, green, and blue lights, resulting in a colour composite image that has excellent definition and clarity with no chromatic aberrations.

The background of the sample platform can be selected from black, white, or clear for effective bright field and dark field exposure. The round plate size can be 55–150 mm. Square plates up to 150 mm× 150 mm can also be used. The instrument can count colonies as small as 43 µm (0.043 mm) or measure zones accurately to 0.1 mm. The system can be used with 1D and 2D bar codes.

Illumination of Petri dishes, which are reflection and shadow free, is quite difficult as they are transparent and reflective. Heterogeneous lighting produces artefacts on the edges of the agar and on the sides of the dish. These artefacts are likely to be counted as colonies and can lead to inaccurate counting. M/s INTERSCIENCE for Microbiology, France, has designed a white diffusing dome for 360° lighting without reflections or shadows as shown in Figure 95.3. The lighting is spread evenly everywhere on the plate and allows the operator to count the colonies on the entire surface. This arrangement is incorporated in their Scan® 4000 model, which is equipped with ultra-high resolution 5 megapixels CCD camera.





**Figure 95.3** 360° spread of light on Petri dish used in Scan 4000 model of M/s INTERSCIENCE for Microbiology, France. The arrangement gives lighting without reflections or shadows, and the lighting is spread evenly everywhere on the plate and allows the operator to count the colonies on the entire surface.

## Specifications

### *Manual method*

*Digital display:* 3-digit LED

*Light source:* White LED

*Count:* 0–999

*Dish size:* Up to 90 mm

### *Automated method*

*Camera:* Minimum 1.4 megapixel CCD camera

*Resolution:* 43  $\mu\text{m}$

*Image lighting:* 3 LED systems

## Applications

The colony counter is used for microbiology applications for fast and accurate counting of bacterial and mould colonies. Modern instruments are used for counting colony and zone and a range of other applications.

## 96

## Colorimeter, Photoelectric

### Purpose

A colorimeter is a device used for the quantitative analysis of a particular substance, usually in an aqueous sample by measuring the intensity of the colour that develops

upon introducing a specific reagent into the solution. In biochemistry, a photoelectric colorimeter is commonly employed for measurement of different substances in the blood like glucose, blood urea, blood enzymes, and others.

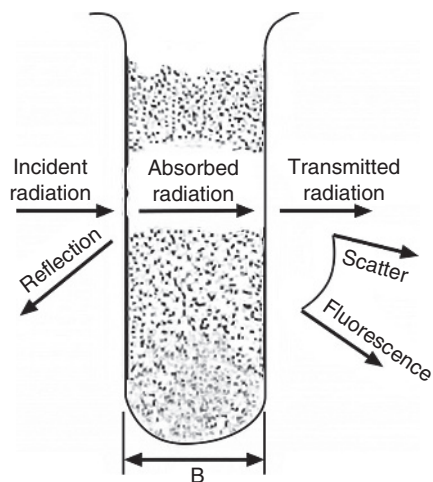
## Principle

A photoelectric colorimeter is a device used for measuring the transmittance and absorbance of light passing through a liquid sample. The device measures the intensity or concentration of the colour that develops upon introducing a specific reagent into a solution. The colour of a solution may be inherent or derived by adding another reagent to it. The device is based on the interaction of radiation (light) with matter. When a beam of radiant energy strikes the surface of a substance, the radiation interacts with the atoms and molecules of the substance. As shown in Figure 96.1, the radiation may be transmitted, absorbed, scattered, diffracted, or reflected, or it can excite fluorescence depending upon the properties of the substance. However, in photocolourimetry, we are usually concerned with absorption and transmission of radiation. Generally, the conditions under which the sample is examined are selected to keep reflection and scattering to a minimum. The amount of absorption that occurs is dependent on the number of molecules present in the absorbing material. Therefore, the intensity of the radiation leaving the substance may be used as an indication of the concentration of the material.

### Laws Relating to Absorption of Radiation

The colorimeter is based on two important laws for its working: Lambert's law and Beer's law.

**Lambert's Law** It states that when a monochromatic ray of light passes through a colour solution, its intensity decreases with respect to the length of the solution. The proportion of incident light absorbed by a given thickness of the absorbing medium is independent



Figures 96.1 Interaction of radiation with matter.

of the intensity of the incident light, provided that there is no other physical or chemical change to the medium.

Let us suppose  $I_o$  is the incident radiant energy and  $I$  is the energy that is transmitted. The ratio of the radiant power transmitted by a sample to the radiant power incident on the sample is known as the transmittance ( $T$ ). Lambert's law is expressed as follows:

$$T = I/I_o$$

It is customary to express transmittance as a percentage:

$$\%T = I/I_o \times 100$$

The logarithm to the base of the reciprocal of the transmittance is known as absorbance.

$$\text{Absorbance} = \log_{10}(1/T) = \log_{10}(I_o/I)$$

$$\text{Optical density} = \log_{10}(100/T)$$

The concentration of an unknown sample can be determined from the graph plotted from percentage transmittance of a series of solutions of known concentration or 'standards'.

**Beer's Law** It states that when a monochromatic ray of light passes through a colour solution, its intensity decreases with respect to the concentration of the solution, i.e. the higher colour concentration, the lower the intensity.

**The Beer-Lambert Law** When the two laws are combined, known jointly as the Beer-Lambert law, it defines the relationship between absorbance ( $A$ ) and transmittance ( $T$ ). It states that the concentration of a substance in solution is directly proportional to the 'absorbance',  $A$ , of the solution:

$$A = \epsilon c b$$

where

$A$  = absorbance (no unit of measurement)

$\epsilon$  = molar absorptivity ( $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ )

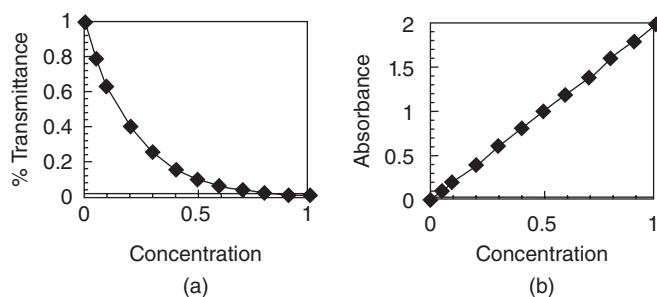
$c$  = molar concentration ( $\text{mol dm}^{-3}$ )

$b$  = path length (cm)

It may be noted that  $\epsilon$  is a function of wavelength. So, the Beer-Lambert law is true only for light of a single wavelength or monochromatic light. Absorptivity is a constant, depending upon the wavelength of the radiation and nature of the absorbing material. Absorptivity is also sometimes referred to as specific extinction and absorbance as 'optical density'. Absorbance is the property of a sample, whereas absorptivity is the property of a substance and is a constant.

Mathematically, absorbance is related to percentage transmittance  $T$  by the expression:

$$A = \log_{10}(I_o/I) = \log_{10}(100/T) = \epsilon b c$$



**Figure 96.2** (a) Transmittance plotted against concentration. (b) Absorbance plotted against concentration.

If we plot the concentration against transmission of radiation through a sample, it is found that the resultant graph is exponential as illustrated in Figure 96.2a. However, by plotting the absorbance against concentration, it will be seen that the plot is linear as shown in Figure 96.2b. It is, therefore, more convenient to express results in absorbance rather than transmission when measuring unknown concentrations since linear calibration plots are easier to read and interpret.

### Instrumentation

The colorimetric method usually involves measurement of colour in the visual region of the electromagnetic spectrum (400–700 nm) and ultraviolet region. For making measurements in a colorimeter, a sample compartment is provided with a holder to contain the cuvette, which carries the liquid sample under examination. Usually this holder is mounted on a slide with positions for at least two cuvettes so that sample and reference cuvettes can be placed in them. The reference sample is measured first and the sample is then moved into the beam, and the light passing through it is measured as a percentage to the reference value.

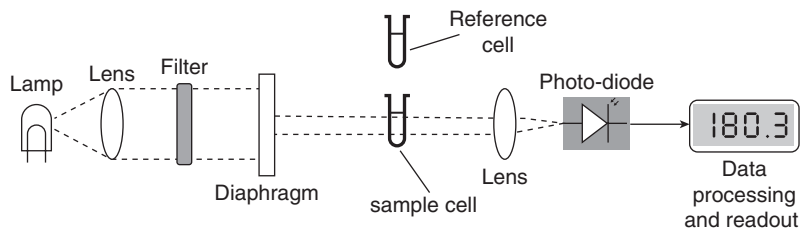
$$\text{Sample concentration} = \frac{\text{Standard concentration} \times \text{Sample reading}}{\text{Reference reading}}$$

### Types of Colorimeters

A colorimeter uses a light source and a filter to get monochromatic light of specific wavelength. When this monochromatic light passes through the solution sample inside the test tube, the intensity of light decreases due to its absorption by the sample. The light then falls on the photodetector, which is in turn connected to an analog meter or digital display. The display is designed to read transmittance or/and absorbance. The instrument can also directly display concentration units by calibrating it with a standard solution. The different types of colorimeters are as follows:

**Single Beam Filter Photometers** Figure 96.3 illustrates the basic components of a single beam filter photometer. The essential parts of the device are as follows:

- A light source that is often an ordinary low voltage tungsten filament lamp or tungsten halogen lamp. In modern colorimeters, the filament lamp has been replaced by light-emitting diodes (LEDs) of different colours.



**Figure 96.3** Block diagram of single beam colorimeter. The reference cell is first placed in the light path and later replaced by the sample cell.

- > An adjustable aperture.
- > A set of coloured filters, which may be either absorption or interference type. Changeable optical filters are used to select the wavelength of light that the solute absorbs the most, in order to maximize accuracy.
- > A sample holder, which may be a cuvette or a test tube. In most colorimeters, the cuvettes are inserted and removed by hand. Some colorimeters are fitted with a flow cell through which solution flows continuously.
- > A detector is usually a photodetector that is a silicon photodiode to measure the transmitted light.
- > An analog or digital meter to indicate the output from the detector. The output shows either as transmittance (a linear scale of 0–100%) or as absorbance (a logarithmic scale from zero to infinity). The useful range of the absorbance scale is 0–2, but it is desirable to keep within the range 0–1 because, above 1, the results become unreliable due to scattering of light. In addition, the output may be sent to a chart recorder, data logger, or computer.
- > In addition, there may be a voltage regulator, to protect the instrument from fluctuations in the mains voltage. The lamp is energized from a highly stabilized DC source or by the output of a constant voltage transformer.

The advantages of single beam photometers are its low cost and ease of operation. The limitations of single beam photometers are errors in %  $T$  due to variation in light intensity and light beam not being monochromatic.

**Double Beam Filter Photometer** A double beam photometer allows the instrument to make automatic corrections for variations in light intensity. To do so, the light path is split into two segments by using mirrors. One segment is used as a reference, and the other acts as the working path. Referring to Figure 96.4, a filter is used that provides single wavelength light that is divided, one part passing through the solution in the sample cuvette before falling on the photodetector. The other part is deflected to the reference cell. The light transmitted from both the sample and reference cells falls on the same photodetector, which alternately receives the two light beams. A comparison of transmittance of sample and reference values is made and the resultant signal is amplified and displayed. Modern instruments no longer use mirrors for beam splitting; instead, they use fibre optic arrangement to carry light for the two beams. This method allows to make measurements on flowing liquids through the flow cells.

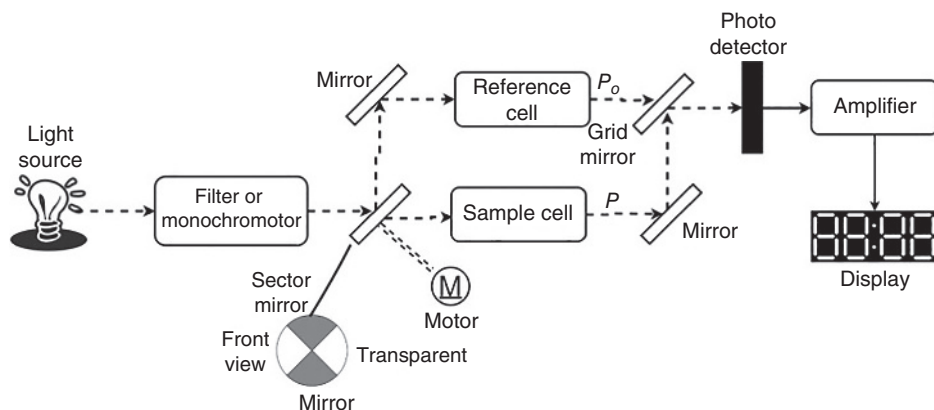


Figure 96.4 Block diagram of double beam colorimeter.

### Probe-Type Photometer

Probe-type colorimeters use optical fibre to transmit light from the source to the solution. The light from a tungsten lamp travels down a fibre optic cable, which is dipped into the solution of interest (sample). The light then passes through the solution and a mirror reflects the light back to a return fibre optic cable. The arrangement is shown in Figure 96.5. Manufactured by STH, the instrument is useful for measuring the optical transmittance, absorbance, and/or concentration of liquids. It is designed for use in the visible/near-infrared photometric range. The instrument comprises a precisely controlled light source (lamp), fibre optic probe, interface filter(s), and photodiode measurement cell to determine the amount of light that passes through a liquid.

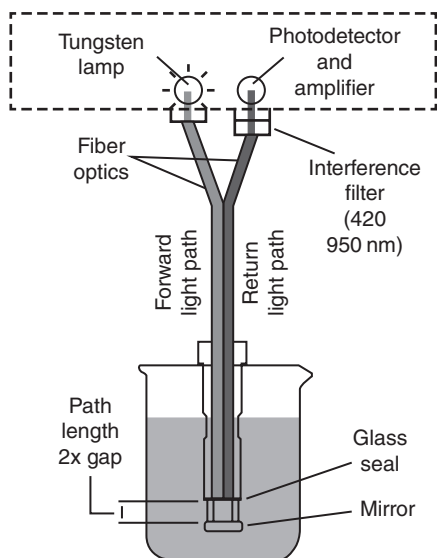


Figure 96.5 Principle of probe-type photometer from M/s STH, USA. Source: <http://www.sthcompany.com/>.

The instrument has the advantage that extraneous ambient light does not affect measurements, and readings can be taken at any level of illumination, whether artificial or natural. For measurements, the fibre optic probe tip is dipped directly into the sample container with a sample as small as in a 0.5 ml test tube. The instrument operates in the 420–950 nm range and the wavelength is selected by interference filters. The reflected light is then passed through a photodiode with an amplifier and an electronic chopper, which is synchronized with the lamp. This results in the detector not responding to extraneous light.

### ***Multi-channel Photometer***

An increasing number of chemical analyses are carried out in the laboratories of hospitals, and in most of these cases, the final measurement is performed by a photometer. One of the limitations for rapid analyses is the speed at which the samples can be transferred in the light path. Obviously, it is felt necessary to increase the capacity of the laboratory by using photometers, which have a large measuring capacity.

In a multi-channel photometer, instead of introducing one sample at a time into a single light path, a batch of samples is introduced and measurements carried out simultaneously, using a multiplicity of fibre optic light paths and detectors, and then scanned electronically. A separate channel serves as a reference beam and eliminates possible source of noise such as ambient light and detector drifts. The light source is a powerful 50 W tungsten halogen lamp, driven from a precisely controlled voltage source. The light is chopped by means of a mechanical rotating chopper. A lens focuses the light on the end of a bundle of fibre optic elements. The output of the detectors is amplified and displayed on a digital voltmeter. The whole operation is synchronized with digital logic circuits.

### ***Portable Colorimeter***

A portable photometer is a lightweight, battery-operated waterproof device that has been designed for field work. It has accuracy comparable to a lab instrument, yet it remains simple to use. It operates on fixed wavelengths 420, 450, 476, 500, 550, 580, 600, and 650 nm with bandwidth of 15 nm. They use a silicon detector, fixed bandwidth of  $\pm 2$  nm, absorbance range of 0–2.5 Abs, and sample cell path lengths of 1 cm and/or 22 mm.

The portable colorimeter is usually factory programmed for one or two of more than 35 possible parameters. No manual calibration is ever required. The operation of the instrument is very simple. Just zero the instrument with a blank, insert the reacted sample, and read the result. Wavelength-specific generic models without factory calibration are also available for programming custom methods. The use of multi-LED photometers allows a wide range of the electromagnetic spectrum to be covered simultaneously or individually without manually changing the LEDs. For example, the portable pHotoFlex<sup>®</sup> Colorimeter from M/s Xylem uses energy-efficient LED optics equipped with six wavelengths and a foldable adapter for various applications with 16 and 28 mm cuvettes. The photometer shown in Figure 96.6 features a data logging function that allows users to store and recall the most recent data points, eliminating the need to manually record data. A list of favourites for the most commonly used tests, sample ID numbers, and more than 3000 measurements per battery set facilitate field



**Figure 96.6** Typical portable photoelectric colorimeter. *Source:* Courtesy of M/s Xylem Analytics GmbH & Co. Germany.

measurements. The accuracy and reproducibility of the instrument is comparable to more expensive lab instruments and is designed for a long working life under harsh conditions. The LEDs used as the light source have low power requirements that ensure long battery life.

Colorimeters are simple in construction and operation. They are used for a great deal of analytical work, where very high accuracy is not required. The disadvantage is that a range of filters is required to cover different wavelength regions. Also the spectral bandwidth of these filters is large in comparison with that of the absorption band being measured.

## Specifications

*Wavelength range:* 400–800 nm

*Light source:* LED

*Detector:* Silicon photodiode

*Filter:* Interchangeable filters, 420, 460, 510, 540, 600 nm

*Cuvette:* Round, with length of 105 mm, 10 mm ID, 12 mm OD; Square, 10 mm × 10 mm × 45 mm

*Transmittance:* 0–100% *T*

*Absorbance:* 0–1.999 Abs

## Applications

The photoelectric colorimeter is widely used in biochemical laboratories for quantitative analysis of specific substances in human body fluids (blood and urine) that have capability to absorb light in visible region for analysis of different constituents.



## 97

## Colposcope

### Purpose

A colposcope is a device used for examining the cervix and surrounding tissue of female patients. The instrument magnifies the cervix, vagina, and vulvar surface and allows the clinician to examine the area for any abnormalities. When an abnormality is detected, a biopsy or tissue sample is taken, for better accuracy of diagnosis.

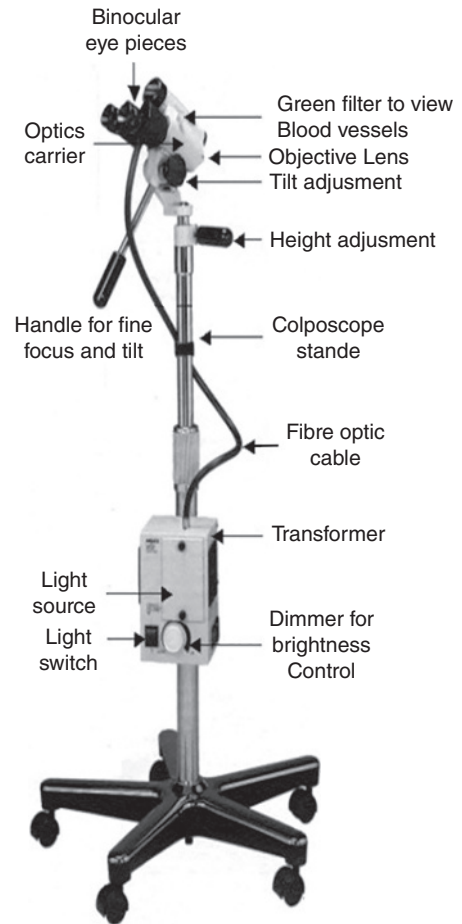
### Principle

A colposcope is a low power, stereoscopic, binocular field microscope and a variable intensity light source that illuminates the area under examination. A typical colposcope is shown in Figure 97.1. Modern colposcopes usually permit adjustable magnification, generally in the range of  $6\times$  to  $40\times$  although most of the investigations can be done in the magnification range of  $6\times$  to  $15\times$ . The adjustment can be made usually in steps such as  $9\times$ ,  $15\times$ , and  $22\times$ . The magnification can also be altered using electrical zoom capability provided in some sophisticated instruments. Lower magnification ( $2\times$  to  $6\times$ ) provides a general impression of the surface architecture, while the wider view and greater depth of field are required for examination of the cervix. However, higher magnifications ( $8\times$  to  $25\times$ ) are used to evaluate the vagina and cervix to define finer features such as abnormal blood vessels. This helps to identify certain vascular patterns that may indicate the presence of more advanced pre-cancerous or cancerous lesions.

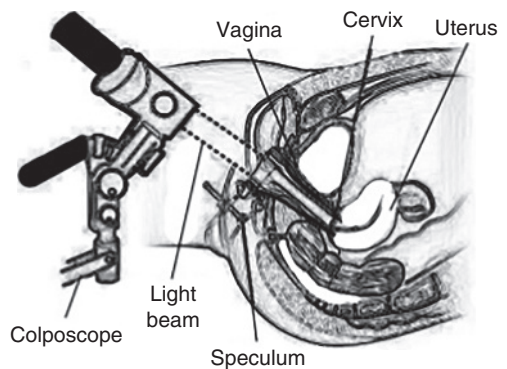
The microscope is binocular and consists of an objective lens positioned nearest to the area being examined and two eyepieces that provide stereoscopic vision, a light source, and green and/or blue filters that can be interposed between the light source and the objective lens. The instrument lens has a focal length ranging between 200 and 300 mm, which allows a comfortable working distance for the observer. Sometimes, the objective can be of lesser focal length, say, 125 mm for special colposcopy techniques. A controlling knob introduces the filter, and another knob changes the magnification of the objective lens. The filter helps to remove red light that allows the visualization of blood vessels by making them appear dark. The entire optical head assembly can be tilted up and down to facilitate examination at various positions. The height of the head from the floor can also be adjusted by using the height adjustment control. On most machines, there is a tilting mechanism and a side arm that allows either a still or video camera to be attached to the microscope. Figure 97.2 illustrates the colposcope in use.

The light source in a colposcope may be halogen, xenon, tungsten, or incandescent bulbs. Halogen bulbs are usually preferred, as they produce powerful white light. The intensity of the light source is usually adjustable. The light source is mounted either in the head of the instrument or somewhere on the stand from where light is carried via a fibre optic cable to the head of the colposcope. Focusing the colposcope is achieved by

**Figure 97.1** Various controls on a typical colposcope.



**Figure 97.2** Colposcope in use.



adjusting the distance between the objective lens and the patient by positioning the instrument at the appropriate working distance. A fine focus control allows fine focus adjustments. By changing the power of the objective lenses, the magnification and working distance can be altered.

A basic colposcope may have the following accessories:

- > *Monocular teaching side tube:* Useful for real-time teaching and discussion of findings.
- > *Photographic camera:* For documentation of colposcopic findings and quality control.
- > *Charge coupled device (CCD) video camera:* To create high resolution digital images of the colposcopic images.

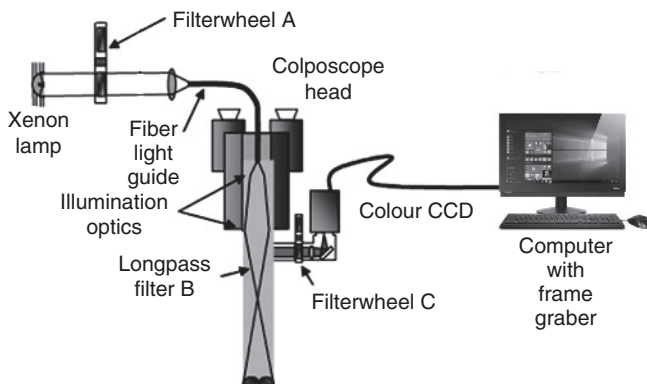
For all these accessories, a beam splitter is used in most colposcopes. It splits the light beam in parts and sends the same image to the viewing port and the other ports. The colposcopes are generally quite heavy and are either mounted on floor pedestals with wheels or suspended from a fixed ceiling mount.

### Digital Video Colposcope

The digital video colposcope imaging system optimizes the investigation process by combining video and image recording, image annotation, pathological report management, data summarization and analysis, information sharing, and patient case management. The report can be printed to provide textual information. The system comprises of high resolution colour camera and image management workstation. The area under investigation is magnified and viewed directly on the 17 in. colour monitor attached to the image workstation. The colposcope has a magnification up to 28 $\times$ , working distances in the range of 150–350 mm, and a green filtered light source mounted on a floor stand.

A system diagram of the digital colposcope is illustrated in Figure 97.3. Most of the components are common with the conventional tilt-stand colposcope. The system comprises of three subsystems:

- (i) A *light source*, usually a xenon lamp, with a parabolic reflector to produce collimated monochromatic and broadband illumination and a fibre optic probe that directs the excitation light to the tissue. Bandpass filters mounted in a motorized filter wheel provide fluorescence excitation light. A filter wheel also includes filters to block UV light and near-infrared light when the device is required to be used in reflectance mode. A combination of lenses is attached to the distal end of the illumination probe



**Figure 97.3** System diagram of the digital colposcope.

that produces a 3.5 cm diameter illumination spot at a working distance of 30 cm. A filter with the lowest cutoff wavelength is attached in front of the objective lens in order to prevent UV light from reaching the collection optics, thereby preventing the optics from autofluorescing. Another manual filter wheel containing a filter with the highest cutoff wavelength allows acquisition of broadband illumination images.

- (ii) A *colposcope* with integrated video camera adaptor and a selection of filters.
- (iii) A *colour CCD camera* with A/D frame grabber used to spectrally resolve the fluorescence and reflectance images from the tissue. The camera is connected to a computer via frame grabber. A specially designed software is used to acquire, save, process, and display the images.

There are a number of reasons to recommend colposcopy, but its main goal is to prevent cervical cancer by early detection of precancerous lesions and treating them. The technique also supports tracking of disease dynamics by comparing pre-/post-treatment images, as well as images from similar patient cases and reference libraries.

## Specifications

*Focal length:* 300 mm

*Magnification:* 4–36

*Field of view:* 10–150 mm

*Depth of field:* 5–120 mm

*Filter:* 3-range built-in green

*Filter:* 3-range built-in green

*Light source:* Ultra white light diodes, illumination > 2200 lux

*Camera:* HD colour digital CCD

## Applications

The colposcope is intended to be used in hospitals and clinics. The digital video colposcope provides excellent visualization of genital tissue, thus enabling identification of unusual changes in cellular tone and colour to help detect and analyse abnormal tissue and identify lesions due to the presence of certain abnormal medical conditions.

# 98

## Compression Machine, Intermittent Pneumatic

### Purpose

Intermittent pneumatic compression (IPC) machine is used to increase venous blood flow in at-risk patients in order to help prevent deep vein thrombosis (DVT) and

pulmonary embolism. The inflation–deflation cycle of IPC therapy simulates the thigh, calf, and foot's normal ambulatory pump action, increasing both the volume and rate of blood flow, eliminating venous stasis, and replicating the effects of the natural muscle pump.

## Principle

Arteries in the cardiovascular system are the blood vessels that carry oxygen-rich blood and nutrients to the various parts of the body. Veins, on the other hand, are the blood vessels that bring oxygen-poor blood and waste products back to the heart. A DVT is a blood clot that is formed in a vein deep inside the body, usually inside one of the deep veins of the thigh or lower leg.

DVT is a common condition, especially in the elderly people, and can happen in both males and females of any age. It is a serious medical condition that can cause swelling, pain, and tenderness in the leg. In some cases, a clot in a leg vein may break free and reach the vessel in the lung, thereby causing a blockage in the lung vessel, commonly known as a pulmonary embolism. Pulmonary embolism generally results in severe shortness of breath and even sudden death. A range of potential prophylactic measures have been developed for reducing the risk of DVT including pharmacological interventions.

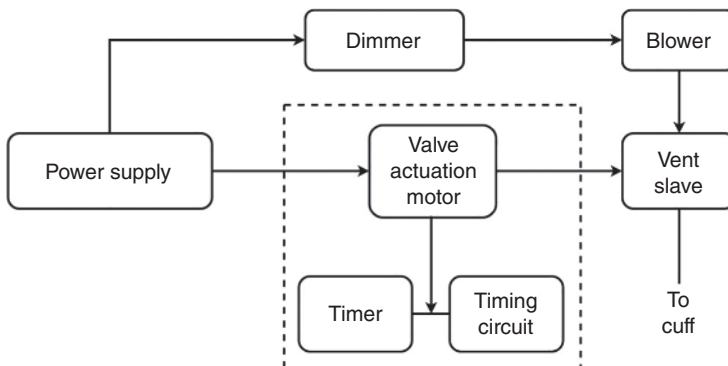
There are mechanical techniques to counteract venous stasis including graduated compression stockings and IPC devices. The IPC device works in a similar way as the blood pressure measuring method. The calf or whole leg of the patient is enclosed in a cuff. While the cuff is allowed to be filled with air, it squeezes the leg, similar to a blood pressure cuff. Then the cuff is allowed to deflate and relax. The process is made to repeat over and over again. The compression produced by the pressurized cuff helps in moving the blood through the veins towards the heart. Between compressions, when the cuff of the device deflates and relaxes, the oxygen-rich blood continues to flow in the arteries of the leg.

### *The Device*

Figure 98.1 shows a typical commercial IPC device. The complete system consists of an air pump, a controller, the tubing sets, and single-patient-use inflatable garments. Basically, the IPC device depends upon the use of inflatable garments, both leg sleeves and foot cuffs that are wrapped around the respective limbs and are connected between the jacket and the air pump. These garments are inflated by the pneumatic pump, which provides intermittent cycles of compressed air, thereby forcing fluids, such as blood and lymph, out of the pressurized area. A short time later, the pressure is reduced, allowing increased blood flow back into the limb. Thus, the garment chamber is alternately inflated and deflated, which assists in enhancing venous return and ensures the movement of venous blood. The controller usually incorporates a compliance meter, to monitor the amount of time a patient receives compression therapy either by shift, by day, or during an entire hospital stay. Generally, the pump operates on a three-minute automatically timed cycle with 90seconds of compression followed by 90seconds of decompression.



**Figure 98.1** Various controls on an antiembolism compression unit.



**Figure 98.2** Block diagram of the control electronics.

Figure 98.2 shows a block diagram of the controller electronics. When the garment is connected to the controller, the system verifies the type of the garment selected by the user. After garment selection and verification has completed, an inflation cycle is initiated, releasing air through the set of valves, mounted to a manifold. A pressure transducer monitors the pressure in the garment. The pressure reading from the transducer provides feedback to the controller that is used in adjusting the pump's motor speed to deliver the proper pressure to the garment in the appropriate amount of time. The IPC device is a prescription device for use in a clinical setting or in the home.

## Specifications

*Pressure range:* 20–250 mmHg

*Set pressure:* Leg sleeves, 45 mmHg; foot cuffs, 130 mmHg

*Compression type:* Leg sleeves, sequential, gradient, and circumferential; foot cuffs, uniform

*Compression cycle:* Leg sleeves, 11 seconds compression; foot cuffs, 5 seconds compression

*Maximum time display:* 999 hours

*Alarms:* Low pressure, high pressure, and electronics malfunction

## Applications

Intermittent compression devices are used on patients suffering from venous insufficiency, venous stasis ulcers, and oedema following trauma or surgery.

# 99

## Computed Tomography

### Purpose

Computed tomography (CT) is one of the important diagnostic imaging modalities used to generate detailed images of internal organs, bones, soft tissues, and blood vessels. The images created during a CT scan cross-sectional imaging can be reformatted in multiple planes, and even three-dimensional (3D) images can be generated, which can be viewed on a computer monitor, printed on film, or transferred to electronic media. CT scanning is most often the method of preference for detecting many different cancers since the doctor can confirm the presence of a tumour and determine its size and location from the images. In emergency cases, the internal injuries and bleeding can be quickly determined to help save lives, as the CT is fast, painless, noninvasive, and accurate. CT scans are frequently used to evaluate the brain, neck, spine, chest, abdomen, pelvis, and sinuses. CT has in fact revolutionized medicine because it allows doctors to see diseases that, in the past, could often only be found by autopsy. It is also called computerized tomography and computerized axial tomography (CAT).

### Principles

When conventional X-rays are used to examine internal structures of the body, the image so obtained has two limitations. Firstly, the X-ray image is a shadow of all organs and structures in the path of the X-rays. That means the 3D information is superimposed onto a single plane, which may make diagnosis confusing and often difficult. Secondly, the photographic film usually has a limited dynamic range, and, therefore, only objects having large differences in X-ray attenuation with respect to their surroundings will cause sufficient contrast differences on the film to be distinguished by the eye. Thus,



while details of bony structures can be clearly seen, it is difficult to discern the shape and composition of soft tissue organs accurately, especially in case of carrying out studies of the brain as there is overall shielding of the soft tissue by the dense bone of the skull. These limitations were overcome with the development of CT machine, the EMI brain scanner, by G.N. Hounsfield at the Central Research Laboratories of EMI Ltd., United Kingdom, and was produced on a commercial scale in 1972. For this development of the CT scanner, Hounsfield was awarded the Nobel Prize for Medicine in 1979.

CT has overcome the limitations of the conventional medical radiography by completely eliminating the superimposition of images of structures outside the area of interest. In addition, CT produces images with a high contrast resolution, which makes it convenient to differentiate between soft tissues that differ in physical density even by less than 1%. CT differs from conventional X-ray techniques in that the images displayed are not photographs but are reconstructed from a large number of absorption profiles taken at regular angular intervals around a slice of the body. In CT, the quality of the reconstructed image depends upon the difference between  $\mu$ -X-ray attenuation coefficient, which is well correlated with the specific gravity of the tissue. Thus, the reconstructed CT image can be considered as the mapping of densities of various tissues with respect to that of water.

### **Contrast Scale**

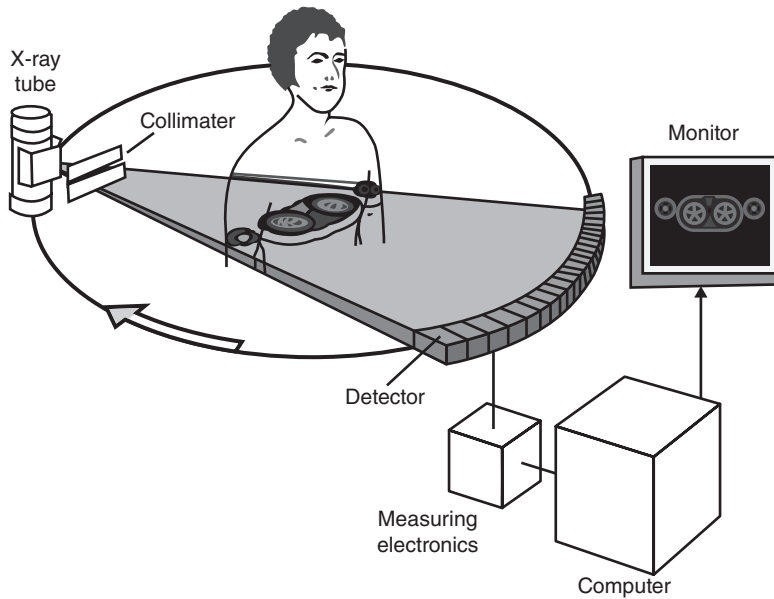
The reconstruction of an image determines a number related to the linear attenuation coefficient value of tissue represented by the scanner computer as integers that usually range in values from -1000 to +1000. These integers have been given the name 'Hounsfield units' and are abbreviated as H. They are also denoted by CT numbers. The values are normalized to the value for water as a reference, and accordingly 0 is assigned to water as the CT number. The CT scale also assigns -1000 to air and the value +1000 represents highly dense materials. The CT numbers are generally stored in the computer as 12 bit integers covering a CT number range of -1023 to 3072.

Since the human vision is limited in its ability to differentiate all the 2000 steps in this scale nor can the television display system show all the shades of grey, the CT display or viewing systems have both window level and window width controls. These controls determine where and over what range of CT numbers will the video greyscale possibly lie. The window level is indicative of the CT value that will be displayed as the middle value, whereas the window width is the range of CT numbers that will have grey values from white to black. With these controls, it is possible to see very small changes in tissue density more clearly, since the greyscale is spread over a smaller range and any given change in tissue density shows an increased contrast.

### **The System**

Figure 99.1 illustrates a block diagram of the principle of working of a CT scanning system. It consists of an X-ray subsystem, a gantry, a patient table, and a controlling computer. A high voltage X-ray generator supplies electric power to the X-ray tube, which usually has a rotating anode and is capable of withstanding the high heat loads generated during rapid multiple-slice acquisition. The gantry houses the X-ray tube, X-ray generator, detector system, collimators, and rotational frame. The X-ray source and detectors are mounted opposite each other in the rigid gantry with the patient





**Figure 99.1** The basic schematic diagram of producing CT images.

lying in between and by moving one or both of these around and across the relevant sections, which is how the measurements are made. The patient lies on a motorized couch and is moved into the aperture of the gantry, with the location to be accurately determined by means of a narrow strip of light that falls on the body from the gantry and illuminates the section to be examined. From the keyboard mounted on the operating console, details such as the patient's code, the name of the hospital, and so on are encoded into the system, and settings for X-ray parameters for the scan are made.

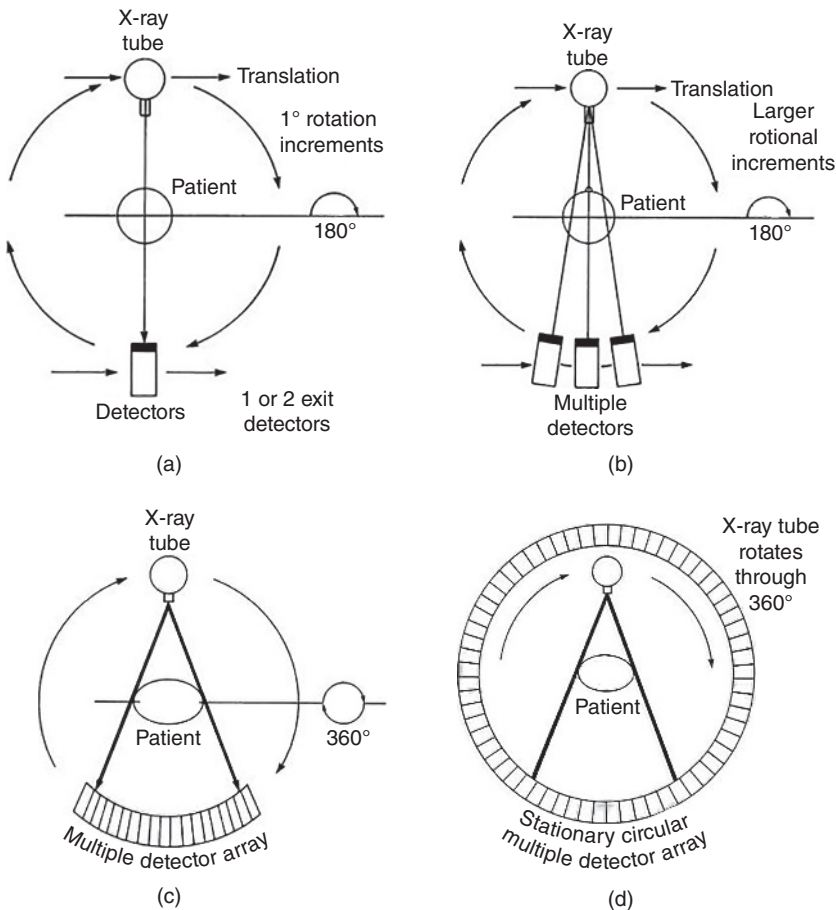
All computer tomography systems consist of the following four major subsystems:

- (i) *Scanning system*: Takes suitable readings for a picture to be reconstructed and includes X-ray source and detectors.
- (ii) *Processing unit*: Converts these readings into intelligible picture information.
- (iii) *Display part*: Presents this information in visual form and includes other manipulative aids to assist in diagnosis.
- (iv) *Storage unit*: Enables the information to be stored for subsequent analysis.

**Scanning System** The purpose of the scanning system is to collect enough X-ray attenuation information to reconstruct an image for an accurate diagnosis. It is desirable to acquire a sufficient number of independent readings so as to get the final image of required spatial resolution and density discrimination. The readings are taken in the form of 'profiles', which represent a plot of the total absorption that takes place along each of the parallel X-ray beams. It is thus obvious that the higher the number of profiles obtained, the better the resulting image. In practice, 180 such profiles each taken at  $1^\circ$  intervals are normally required to reconstruct a diagnostically useful image.

**Scanning Arrangements** There are several designs of scanning arrangements that have been commercially developed. They used different mechanical configurations for mounting X-ray source and detectors.

*First-generation scanners:* The first-generation CT scanners were based on the 'translate and rotate' principle and were used in the earliest commercial system, the EMI MKI brain scanner. The system shown in Figure 99.2a used a narrow pencil beam generated by finely collimated X-ray source that passes through the body, and its attenuation is detected by a detector on the other side of the patient. The detector moves on a gantry along with the X-ray tube. The tube and detector move in a straight line and



**Figure 99.2** (a) Scanning arrangement of the early CT machines. They made a linear traverse before taking a 1° rotation. The system employed a single-source and single-detector system. (b) Second generation machines employed a fan-shaped beam and a small array of detectors. This arrangement allowed larger steps reducing the scanning time. (c) If the fan beam is large, no traverse motion is required. Only rotational movement of the scanning frame is needed, thus offering considerable improvement in scanning time. (d) The X-ray tube rotates while the all detectors are stationary, giving much faster speed of scanning.

sample the data 180 times. After reaching the end position of the scan, the scanner gantry moves to the next position with a  $1^\circ$  tilt for the next translation across the patient. This assembly travels  $180^\circ$  around the patient's position. Obviously, this is a fairly slow procedure and requires a typical scan time of five minutes. It is thus essential that the patient remains still during the scan period, and for this reason, the earlier scanners were limited in their use to only brain studies.

*Second-generation scanners:* The design of the second generation CT scanners is shown in Figure 99.2b. This system employed a fan beam of X-rays and a bank of detectors. The motion of the X-ray source and detector bank was similar to first-generation systems but showed great improvement in speed of scanning over the traverse–index arrangement. This system effectively takes several profiles with each traverse and thus permits greater index angles. For example, by using a  $20^\circ$  fan beam, it is possible to take 20 profiles, at  $1^\circ$  intervals, with each traverse and then index through  $20^\circ$  before taking the next set of profiles. Therefore, a full set of 180 profiles can be obtained with 9 traverses. In this way, scan times could be considerably reduced to about 10–30 seconds range.

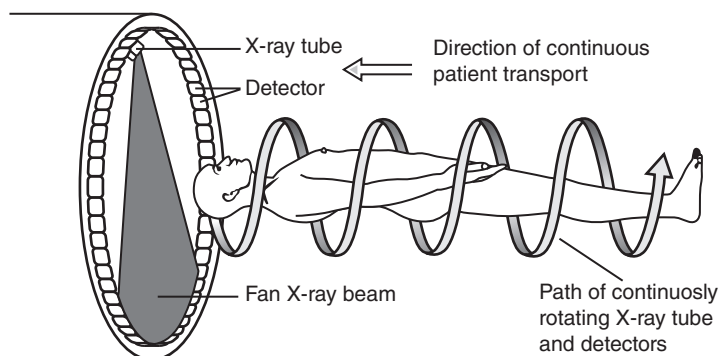
*Third-generation scanners:* The third-generation scanners avoided the mechanical multiple alterations between translational and rotational movements of the linear scanning arrangement. The system used a sufficiently wide fan-shaped X-ray beam, which encompasses the whole object cross section and a multiple detector system mechanically fixed to the X-ray tube, which permits a simultaneous measurement of the whole absorption profile in one projection direction. The arrangement is shown in Figure 99.2c. Here, the rotational movement is not stepwise but continuous. The system gives a wide fan beam, typically between  $30^\circ$  and  $50^\circ$  and rotates usually through  $360^\circ$ . Since the translational movement has been eliminated, the frame can be made to travel quite fast, and exposure time may be reduced to only a few seconds.

*Fourth-generation scanners:* In this type of machines, the detectors are placed in a  $360^\circ$  ring around the patient, and it is only the X-ray source that rotates around the patient. The system employs as many as 2000 detectors to maintain a good spatial resolution. The individual detectors are lined up practically without gaps so that the radiation that has penetrated the patient is optimally used as shown in Figure 99.2d. The scan times in this arrangement are a few seconds or even less.

Higher scanning rates are now available that permit whole body scanning. The patient is required only to hold his or her breath and lie completely still for a few seconds in which the entire scanning process gets completed. The scanning procedure can also be synchronized with electrocardiogram (ECG), which makes it possible to reconstruct slices of the heart in various phases of the cardiac cycle.

### ***Spiral/Helical Scanning***

This is a scanning technique in which the source and detector travel along a helical path relative to the object. In a typical arrangement, the patient couch is moved through the bore of the scanner, while the gantry rotates. This operation is often referred to as helix, spiral, volume, or 3D CT scanning. Spiral CT can achieve improved image resolution for a given radiation dose, compared to individual slice acquisition, and allows a scan to be performed in a single hold of breath. Figure 99.3 illustrates the



**Figure 99.3** Principle of spiral CT scanning system.

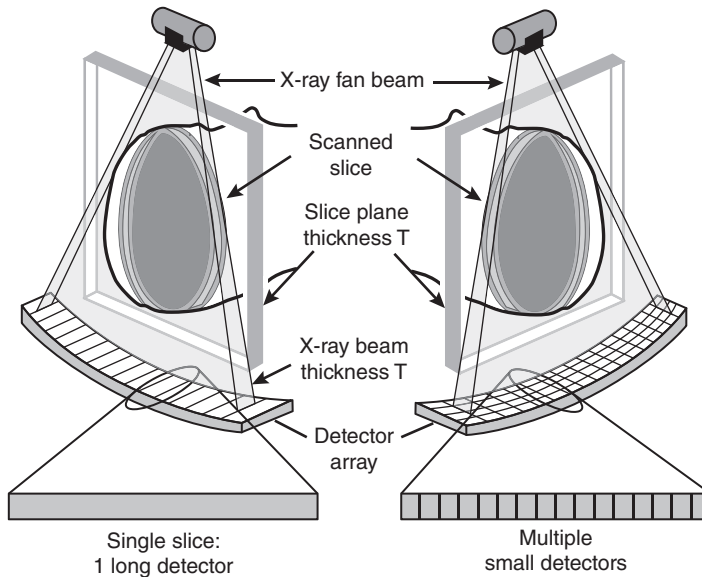
principle of spiral scanning technique, which shows that the focal spot follows a spiral path around the patient. The technique allows multiple images to be acquired while the patient is moved through the gantry in a smooth continuous motion rather than stopping for each image. Projection data are obtained, which allows the reconstruction of multiple contiguous images. This technique allows acquiring of images with faster scan times and obtaining multiple scans for 3D imaging to obtain and evaluate 'volume' at different locations.

In helical scanning, the patient table speed of 1–10 mm/s and complete 360° rotations are achieved in half a second or less with the fan beam collimated to 1–10 mm thick slice. This technique has introduced a new scanning parameter called the *pitch*, which defines the ratio of the table movement distance in a single rotation to the slice thickness. A table movement of 10 mm and a slice thickness of 10 mm, therefore, generates a pitch of unity. Pitch values of 0.5–2 are used depending upon the desired spatial resolution along the z-axis.

### **Multislice Computed Tomography**

A revolution occurred in 1998 in CT scanner technology when all major CT manufacturers introduced multislice computed tomography (MSCT) systems, which typically offered simultaneous acquisition of data for four slices. This provided considerable improvement towards the goal of 3D imaging and reconstructing the images at any position along the patient axis. The ability to acquire volume data formed the very basis for newer applications, such as computed tomography angiography (CTA), which has revolutionized noninvasive evaluation of vascular disease and development of 3D image processing techniques.

Figure 99.4 shows the basic difference between single slice computed tomography (SSCT) and MSCT detector arrangement. In the SSCT, the detector arrays are one-dimensional and consist of a large number (typically 750 or more) of detector elements in a single row across the irradiated slice to receive the X-ray fan beam. In the MSCT, each of the individual, monolithic SSCT detector elements in the z-direction is divided into several smaller detector elements, forming a two-dimensional array. Rather than a single row detector encompassing the fan beam, there are now multiple parallel rows of detectors.



**Figure 99.4** Principle of multislice CT. (a) Single slice detector array containing single, long elements. (b) Multislice detector array with several rows of small detector elements. Source: Adapted from Goldman, L.W. (2008). Principles of CT-Multislice CT. *Journal of Nuclear Medicine Technology* 36 (2): 25.

With the advancement of data acquisition technology, 64-slice scanners were developed and announced by 2005. The approach used by most manufacturers for 64-slice detector array designs was to lengthen the arrays in the  $z$ -direction and provide all sub-millimetre detector elements. 256-slice MSCT scanners with a 128 mm  $z$ -axis field of view has also been introduced. The introduction of area detectors large enough to cover entire organs, such as the heart, the kidneys, the brain, or a substantial part of a lung, in one axial scan (120 mm scan range) has brought a new quality to medical CT, with a whole spectrum of new applications, such as functional or volume perfusion studies. With the help of modern CT, it is possible to visualize anatomy as small as  $150\mu\text{m}$ , providing CT image quality with resolution typically seen only in cath labs. This has become possible with the use very thin detectors having size of the order of  $0.25\text{ mm/slice}$ . This allows visualization of more detail in coronary plaques, in-stent restenosis and the ability to clearly see individual stent struts. A typical CT machine from M/s Siemens is shown in Figure 99.5.

### X-ray Source

In CT scanners, the highest image quality, free from disturbing blurring effects, is obtained with the aid of pulsed X-ray radiation. The number of pulses, the pulse duration, and tube current determine the dose of the patient. These factors can be selected by the operator in the same way that they are selected in conventional X-ray systems. The X-ray tubes used in the CT scanners is the rotating anode air-cooled type. These tubes have a higher power capability for exposure times in the 2–20 second range. The power requirements of these tubes are generally variable within 100–160 kV. Typical



**Figure 99.5** CT scanner model Somatom Force. *Source:* Courtesy M/s Siemens.

power requirements of these tubes are 120 kV at 200–500 mA, producing X-rays with an energy spectrum ranging from approximately 30–120 keV. Most systems have two possible focal spot sizes, approximately  $0.5 \text{ mm} \times 1.5 \text{ mm}$  and  $1.0 \text{ mm} \times 2.5 \text{ mm}$ . A collimator assembly is used to control the width of the fan beam between 1.0 and 10 mm, which, in turn, controls the width of the imaged slice. The important parameters for X-ray tube used in CT systems are its focal spot size, the heat capacity, and the cooling rate of the anode.

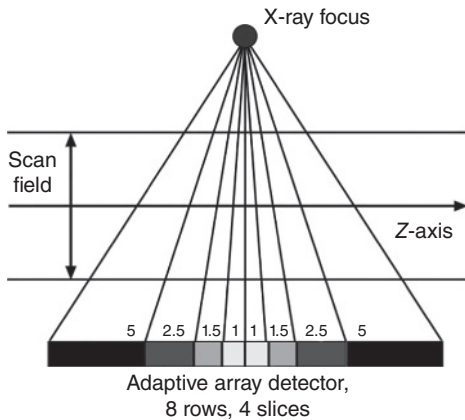
The X-ray generator has a high voltage transformer, which generates necessary high voltage for production of X-rays. All modern systems use high frequency X-ray generators, typically operating between 10 and 50 kHz. A heat exchanger on the rotating gantry is used to cool the tube. Spiral scanning especially places heavy demands on the heat storage capacity and cooling rate of the X-ray tube. A new X-ray tube based on liquid-metal-filled, spiral-groove bearings, which allow very high continuous power, has been developed to meet this requirement. In such systems, a low voltage is transferred to the rotating part of the gantry through an electrical slip ring arrangement. New applications such as CTA have become possible with these developments.

### ***Beam Collimation***

For producing a fan beam, a collimator consisting of tungsten or lead plates is incorporated between an X-ray tube and the patient. The thickness of the slice can be selected by varying the width of the fan beam. The CT scanner beams are required to be filtered to reduce the patient dose and beam hardening artefacts. A filter inside the collimator housing shapes the beam intensity. In body scanners, two types of filters are used, one for the body scanning and the other for the head. These are automatically selected by the computer based on the application. These filters produce intensity variation, which significantly reduces the dynamic range requirements on the electronics.

### ***Detectors***

The earliest X-ray detectors were scintillation detectors with photomultiplier tubes excited typically by sodium or caesium iodide crystals. The scintillator photomultiplier detectors suffer from the disadvantage that the smallest commercially available



**Figure 99.6** Principle of adaptive array. The spacing between the detectors in the centre is much less than at the edges.

photomultiplier tube has a diameter of 12 mm. Caesium iodide was later replaced during the 1980s by ion chambers containing high pressure xenon gas and then with scintillation systems based on photodiodes instead of photomultipliers.

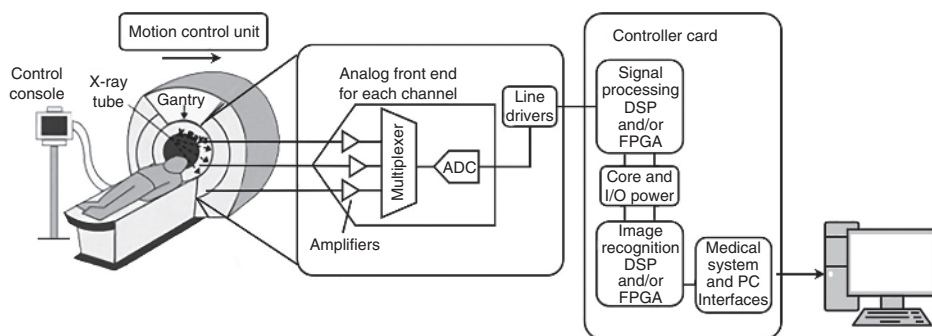
Modern systems employ rare earth garnet or rare earth oxide ceramics as scintillation materials with more desirable characteristics. These are solid state detectors such as single crystal cadmium tungstate ( $\text{CdWO}_4$ ), ceramic gadolinium oxysulfide ( $\text{Gd}_2\text{O}_2\text{S}$ ), gadolinium oxide, or yttrium gadolinium oxide, with photodiodes that have some inherent advantages such as a higher efficiency in detecting X-ray photons. One of the recent developments is the use of multi-array detectors, i.e. a number of parallel rings of solid state detectors that will allow faster volume scanning.

For MSCT systems, two types of arrangements are used for detectors: the matrix detector, which has elements of a fixed size, or the adaptive array arrangement of detectors. The latter provides a more flexible design as shown in Figure 99.6. Instead of columns of equal detector widths, this array uses columns of detectors of variable width, such that the width in the two central columns is relatively narrow, with the column width increasing towards the periphery. This gives the capability of collecting data simultaneously both for thick and thin slices. This design of the adaptive array detector takes into account the cone beam constraints for optimal image quality, optimizes the dose efficiency, and provides a flexible selection of slice widths. With narrow detector elements close to the centre, the width of the detector rows increases with distance from the centre, and, thus, unnecessary dead spaces are avoided.

### Processing System

**Data Acquisition System** A typical CT data acquisition system (DAS) consists of precision pre-amplifiers, current-to-voltage converters, analog integrators, multiplexers, and analog-to-digital converters (ADCs), and computer system. Modern systems make use of optical or wireless transmitters on the rotating gantry to send data to fixed optical receivers. Data transfer rates of the order of 10 MB/s are generally required. Although good detector properties are a prerequisite for obtaining optimal image quality, the





**Figure 99.7** Simplified block diagram of electronics of a CT system.

measuring electronics must have a large dynamic range to back up the detector. The dynamic range in a typical CT system is 1 : 400 000, which implies that with such systems, an optimal image will always be obtained irrespective of whether the patient is obese or thin or whether we are concerned with bones or soft tissues.

Figure 99.7 shows a block diagram of the typical electronics system used in CT systems. The configuration is designed to generate 3D images of internal body structures. The tomographic images are generated by exposing the patient to a fan-shaped X-ray beam and detecting the attenuated X-rays on a thin semicircular digital X-ray detector. Photodetector arrays used in CT imaging have as many as 1000 detectors in the semicircular detector arch. The patient lies between the source and detector. The geometric centre of the detector is so configured to be located at the X-ray source. The data collected at the detectors corresponds to the X-ray projection of a very thin transverse slice of the body. To collect and store the data from multitude X-ray projections necessary to generate a tomographic CT image, both the X-ray source and detector are rotated about the patient within a supporting gantry. As in conventional X-ray machines, the signal levels in the image slice represent the relative radiation density along a line from the X-ray source to the corresponding pixel location.

After amplification, ADCs convert the analog signals to their corresponding digital signals. The sampling speed of the ADCs determines the level of multiplexing and, hence, the number of converters and amplifiers in the system. The ADCs must have high dynamic range with at least 32 bit resolution or greater that are commonly used. The outputs of the ADCs then go to an image signal processor over a high speed link for further signal processing and image reconstruction.

The image reconstruction card is connected to the host computer where the CT images are reconstructed by combining the digital data by the selected mathematical procedure of tomographic reconstruction. Control cards include digital signal processors (DSPs) and field programmable gate arrays (FPGAs), power supplies, clocks and clock distribution circuitry, and interface blocks. DSPs can be used to provide accurate control of the gantry rotation, the movement of the table (up/down and in/out), the tilting of the gantry for angled images, and other functions such as turning the X-ray beam on and off. Another important DSP control functionality is ECG gating used to reduce motion artefacts caused by heart movement. Here, the data acquisition is carefully synchronized with the heartbeat.



An image processor, which is typically a very high speed computer, performs the massive calculations required for the tomographic image reconstruction on the digital image data. The resulting image will have a very large dynamic range with 16 bit grey-scale images, which are subsequently converted into the limited visible display range. To improve image capture times and resolution, MSCT imaging techniques are employed. Instead of a single 2D detector array, which provides only a single image slice, multislice imaging uses a 3D array. From the multislice image data, 3D images are constructed using edge detection image processing algorithms and displayed on screen.

**Processing Unit** Earlier models of CT scanners used filtered back projection as the algorithmic technique for reconstruction of the image. The technique is well established, conceptually simple, and computationally undemanding. However, the technique assumes a highly simplified physics, which leads to a number of artefacts, high noise, and impaired image resolution. Some systems make use of iterative technique in which by adopting more and more iterations, the image matrix matches more and more closely with the object matrix, thereby generating the image of the object with the help of a computer. This technique provides images with improved resolution, reduced noise and fewer artefacts, and reduced radiation dose in certain circumstances. Although there are very high computational requirements, advances in computer technology and high-performance computing techniques have helped to use it in practice. Modern commercial systems use a mathematical technique, known as convolution or filtering along with back-projection. This technique employs a spatial filter to remove the blurring artefacts in the final image, gives faster reconstructions, and permits processing the data as projection views are obtained.

The information received by the computer from the scanning gantry needs to be processed for reconstructing the pictures. The data from the gantry contains information on the following parameters:

- > Positional information, such as which traverse is being performed and how far the scanning frame is along its traverse.
- > Absorption information including the values of attenuation coefficient from the detectors.
- > Reference information that is obtained from the reference detector that monitors the X-ray output.
- > Calibration information that is obtained at the end of each traverse.

The first stage of computation is to analyse and convert all the collected data into a set of profiles, normally 180 or more. However, the main part consists of processing the profiles to convert the information, which can be displayed as a picture and then be used for diagnosis.

**Computer System** The computer system is uniquely important in a CT scanner because without it, there would be no image computation and formation. The computer controls X-ray generation, gantry and table motion, data acquisition, image formation, display, and storage. Usually, the CT computer system includes a powerful microcomputer for control functions, an array processor, and video memory to enable viewing of the reconstructed images. The image can be viewed on a console and a hard copy can be made on a multi-format camera. A multiple array processor is used to achieve the computational speed of

200 Mflops (million floating-point operations per second). The reconstruction time from such a configuration is approximately five seconds to produce an image on a  $1024 \times 1024$  pixel display. By using faster computers, the reconstruction time is significantly reduced.

**Viewing, Storage, and Documentation System** In most of the CT systems, the final picture is available on a computer monitor. The picture is constructed by a number of elements in a square matrix wherein each element has a value representative of the absorption value of the point in the body that it represents. This technique facilitates a much larger dynamic range than the eye can possibly have. The absorption values are displayed alongside a linear scale corresponding to air through tissue to dense bone. In the CT scanners that are presently being manufactured, the picture points are divided into 2000 steps. These two parameters can be varied at will within the range of the absorption.

The commonly used calculations that are displayed on the monitor are the area, mean value, and standard deviation in CT numbers, which may well show an identifiable difference between healthy and diseased tissue. It is also possible to subtract one picture from another to demonstrate differences that have occurred during treatment. Sophisticated post-processing techniques are typically used on an independent 3D workstation or a picture archival and communication system (PACS) station with 3D capability. These images can be generated by a trained radiologist and sent to PACS for reviewing and archiving.

The CT images are usually printed on a large  $356 \text{ mm} \times 531 \text{ mm}$  transparent film, which can be viewed on an illuminated X-ray view box. For photography, one can choose between the multiple-format camera and the 100 mm cut film camera. Hard copy printouts can be made in the greyscale or in colour shades. In the greyscale picture, the shades of grey are restricted to 8 or 10. The CT picture in colour can be made by using 32 colour shades using the ink-writing system, the image resolution being  $256 \times 256$  points. However, the modern multislice scanners generate thousands of images for a single procedure. In such situations, it is not possible to print a large number of hard copies. PACS systems are preferred. They are useful both for storage of images and for documentation purposes.

**Gantry Geometry** Gantry is the most prominent part of a CT scanner. It looks like a 'doughnut' and contains X-ray tube, filters, collimator, detectors, X-ray tube heat exchanger (oil cooler), high voltage generator, direct drive gantry motor, rotation control mechanism, DAS, slip rings, detector temperature controller, high voltage generator (75–150 kV), power unit to convert AC to DC, and line noise filter. The gantry is a heavy structure and may typically weigh about 1750 kg.

The display on the front panel of the gantry (external view) includes X-ray exposure indicator light, gantry controls, emergency stop buttons, ECG gating monitor, patient guide lights, sagittal laser alignment light, external laser alignment lights, and a microphone. Most gantries can be tilted  $+20^\circ$  in order to obtain oblique slices. A narrow visible light field is used to indicate where the CT slice will be taken. An intercom system is generally available near the inside of the gantry opening to enable verbal communication with the patient. The patient support table or couch allows for bringing the patient into the doughnut hole, which is approximately 60–72 cm in diameter. The top of the table on which the patient is made to lie is made of carbon fibre for maximum strength and radio transparency. The table provides longitudinal movement over a range of 150 cm, which enables uninterrupted scanning without repositioning the patient.

## Specifications

*Number of slices:* 64

*Capability:* Integrating with any PACS/HIS/Dicom system

*Gantry:* Aperture, 75 cm or more; field of view, 50 cm or more; tilt,  $\pm 300^\circ$  adjustable, 3D laser lights for positioning

*X-ray generator:* High frequency type, power output of 80 kW or higher, mA range, 700 mA; kV range, 80–130 or more

*X-ray tube:* Tube voltage, 80–130 kV or more

*Spiral acquisition:* Scan time of 0.35 seconds or less for full  $360^\circ$  rotation, slice thickness of 0.625 mm or less, pitch factor that is manually variable between 0.5 and 1.5 or more

*Image resolution:* High contrast resolution at least 15 lp/cm for axial and spiral scan at 0%, 10 mm slice thickness

*Data acquisition system:* Detector, capable of acquiring 64 or more slices per  $360^\circ$  of rotation; at least 64 rows of independent detectors with z-axis coverage of 38 mm or more

*Processing:* Iterative reconstruction technique

*Operator console:* Colour monitors of 19 in. or more with image area matrix dimension of  $1024 \times 1024$  or more, hard disk having image storing capacity of 500 000 or more in  $512 \times 512$  format

*Workstation:* Speed of 3.0 GHz or better, independent hard disk 512 GB or more

*Software:* Standard post processing software and image evaluation tools

## Applications

Since its introduction in the 1970s, CT has become an indispensable tool in medical imaging practice. It is used to image a head or brain to evaluate the various structures of the brain to look for a mass, stroke, area of bleeding, or blood vessel abnormality. CT of the chest is useful to further study an abnormality observed on a plain chest X-ray. Imaging of abdominal and pelvic with CT helps to look for the abdominal and pelvic organs such as the liver, spleen, kidneys, pancreas, adrenal glands, and the gastrointestinal tract. A spine CT test is generally used to detect a herniated disc or narrowing of the spinal canal in people with neck, arm, back, and/or leg pain.

## 100

## Computed Tomography, Single Photon

### Purpose

Single photon emission computed tomography (SPECT) camera is an imaging device, which detects the  $\gamma$  radiation that is emitted from patients after administration of a

radiopharmaceutical. The technique allows the study of organ function, cell metabolism, and other functional parameters in the human body that helps to detect pathological changes at the molecular level before the changes in the anatomical structure become visible with computed tomography (CT).

## Principle

The clinical use of radionuclide ( $\gamma$ -emitting radioisotopes) imaging depends on obtaining a map of distribution of the radionuclide in the patient. The radionuclide is labelled to a compound that is taken up or metabolized in some way by the human tissue, which is intended to be studied. The patient receives the material (radiopharmaceutical), usually by intravenous injection into the bloodstream, and after some delay, its uptake takes place in the target tissues when the imaging process is commenced. In this way useful static images, each taking 2–10 minutes, can be produced of the bone, brain, thyroid, lung, and so on. Dynamic studies can be performed with SPECT starting at the moment of injection and capturing frames of the data digitally. Numerical analysis of such data can produce useful information on organ function, blood flow, clearance rates, and so on.

Emission CT provides in vivo three-dimensional (3D) maps of a pharmaceutical labelled with a  $\gamma$  ray emitting radionuclide. The 3D distribution of radionuclide concentrations are estimated from a set of two-dimensional (2D) projectional images acquired at many different angles about the patient. Several of the reconstruction algorithms are derived from the mathematical approaches used for transmission CT. However, appropriate modifications have to be made to account for attenuation and photon scatter within the patient.

### *Types of Emission Systems*

Emission CT has developed in two complementary directions based on the type of radiation that is detected. One approach, positron emission tomography (PET), consists of the detection of two annihilation photons per event. When a positron – a positively charged electron – is emitted from the nucleus within tissue, it annihilates and rapidly loses its kinetic energy with a negatively charged electron, resulting in the emission of two 511 keV photons at  $180^\circ$  from each other. The distance that the positron travels from the emission site depends on its initial energy and typically has a range between 1 and 3 mm. Typically, one or more rings of discrete scintillators are used to detect the two photons and to reconstruct cross-sectional representation of the distribution of the positron emitter.

The second approach to emission computed tomography (SPECT) involves the detection of single photon per event. SPECT uses conventional radionuclides such as Tc-99m (140 keV  $\gamma$  photon) and TI-201 that are routinely used in all nuclear medicine departments. SPECT scans, however, are significantly less expensive than PET scans, because they are able to use longer-lived, more easily obtained radioisotopes than PET.

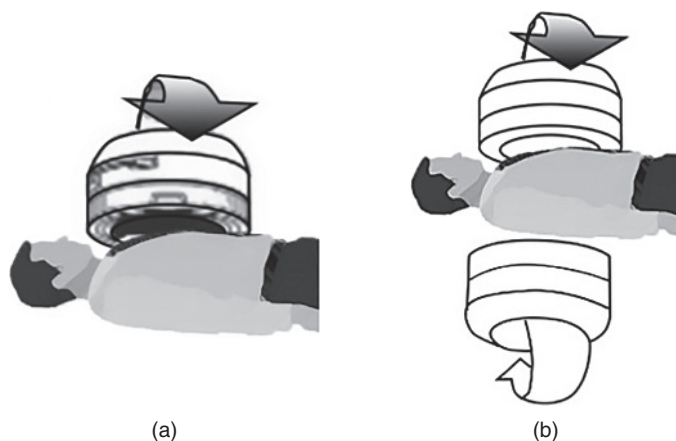
When a radiotracer containing a  $\gamma$ -ray emitting radioisotope such as Tc-99 or I-123 is injected into a patient's bloodstream, a  $\gamma$ -ray photon is released due to decay of short-lived excited nucleus. Thereafter, once the  $\gamma$ -ray photon exits the patient's body, its interaction with a collimator takes place. The location of the original de-excitation event is

determined by scanning at specific fixed angles. Collimators consist of a base of high density and high atomic number elements like lead or tungsten. They have a set arrangement of perforations for photons to enter the detector. Photons reaching the collimator with the appropriate angle of incidence go to the detector for optimum image resolution, while the photons at the wrong angle are absorbed by the collimator and do not reach the detector.

### Instrumentation

SPECT instruments fall into two categories: non-camera-based and camera-based systems, although the latter dominate both academic and commercial development. Both single-head and multi-head  $\gamma$ -camera-based systems are vastly used, primarily because they can produce both head and body SPECT images.

**Camera-Based Systems** In camera-based systems, the SPECT is very similar to conventional nuclear medicine planar imaging technique using a  $\gamma$  camera can provide true 3D information. Although the information is typically presented as cross-sectional slices through the patient, it can be easily reformatted or manipulated as per requirement. The largest category of SPECT systems uses a single  $\gamma$  camera mounted on a specialized mechanical gantry that automatically rotates the camera 360° around the patient. SPECT systems acquire data in a series of multiple projections at increments of two or more degrees. From the sequence of projections, an image is reconstructed by filtered back-projection algorithm, which comprises the multi-angled, 2D views and projects them onto a computer monitor. The projection data are combined to produce transverse (also called axial or trans-axial) slices. Sagittal and coronal image slices can also be produced through mathematical manipulation of the data. Figure 100.1 illustrates the principle of camera-based SPECT system. It uses a  $\gamma$  camera that rotates about the patient to obtain a set of projectional views over 360°. These views are then used to reconstruct the regional radiopharmaceutical concentrations within the body. Since the  $\gamma$  camera obtains



**Figure 100.1** Principle of camera based SPECT. (a) Single camera. (b) Double camera.



**Figure 100.2** Dual camera SPECT scanner for performing a total body scan. The patient lies on a table that slides through the machine, while a pair of  $\gamma$  cameras rotate around the patient. *Source:* Reproduced with permission of M/s DDD-Diagnostic, A/s Denmark.

2D images, the entire organ of interest can be imaged with a single rotation of the camera about the patient.

Unfortunately, single-head systems suffer from poor sensitivity and prolonged imaging times and so high-quality brain SPECT requires either dual- or triple-headed  $\gamma$  cameras. In a dual-head system, two  $180^\circ$  opposed camera heads are used, and acquisition time is reduced by half with no loss in sensitivity. A triple-head SPECT system with  $120^\circ$  spacing further improves sensitivity. Three-head SPECT systems currently are the most sophisticated instruments for brain SPECT and offer excellent spatial resolution of the order of 6 mm. Some suppliers also offer variable-angle dual-head systems for improved positioning during cardiac, brain, and whole body imaging.

Figure 100.2 shows a typical dual camera-based SPECT. A pallet, designed to minimize  $\gamma$  ray attenuation, supports the patient between the two scintillation cameras. The camera separation is radially adjustable from 22 to 66 cm detector surface to surface. This adjustment range permits the collimators to be in close proximity to the patient for both body and brain scans. The data are collected with continuous gantry motion during a  $360^\circ$  rotation at defined points during the rotation. Acquisition times may be varied from 2 to 25 minutes. Angular samples are stored into  $2^\circ$  frames. The two NaI (TI) crystals, each having a useful field of view of 40.6 cm, are 9.5 mm thick. Each detector crystal is optically coupled to an array of 37 photomultiplier tubes. Detector electronics include the circuitry to compensate for positioning non-linearities and regional sensitivity variations.

During acquisition, each x–y pair of  $\gamma$  ray event is digitized into a 128 (perpendicular to axis of rotation [x]) by 64 (parallel to axis of rotation [y]) storage array in buffer memory, together with a detector and energy window identifying bits. Besides the primary photo-peak window, a secondary energy window is simultaneously used to record events that have undergone Compton scattering within the patient. The latter data are



used to compute the body contour that is required by the attenuation compensation algorithm.

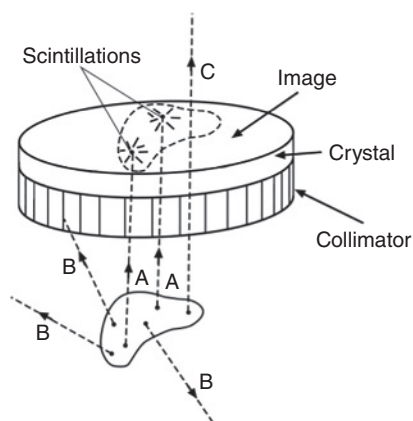
SPECT images obtained with a  $\gamma$  camera are multiple 2D images or projections, from multiple angles. A computer is then used to apply a tomographic reconstruction algorithm to the multiple projections, yielding a 3D data set. This data set is then manipulated to show thin slices along any chosen axis of the body, similar to those obtained from other tomographic techniques, such as magnetic resonance imaging (MRI) or X-ray CT. Multislice projection set conversion and angular framing are done in real time by the computer. The fast and common evaluation method for reconstruction of images is iterative reconstruction. However, an optimum number of iteration must be carried out and the computing time for the iteration must be kept as low as possible so that results are available in a time acceptable for clinical routine. Image display is accomplished on a system interfaced to a computer. A  $512 \times 512$  image format with 256 shades of grey with windowing and background subtraction is available. The image display station is a colour monitor that is directly interfaced to a film recorder. Either transparencies or rapid-process prints may be produced.

Parallel hole collimation is used for imaging organs such as the liver, lungs, and heart. For the brain, special fan beam collimators are used to increase system sensitivity. Using high resolution parallel hole collimation, system sensitivity for a Tc-99m source distributed in a 21.6 cm diameter water-filled cylinder is 54 000 (cps)/( $\mu$ Ci/m) using all axial slices. In order to determine the volume sensitivity per slice, this quantity would be divided by the number of slices that were reconstructed from a single revolution about the patient.

The system's software allows for a variety of image processing protocols, many of which are user defined. Some of the more popular general software applications provided by manufacturers are image smoothing, normalization, and interpolation; image addition or subtraction; background subtraction; contrast enhancement; cyclic display of sequential images (cine) region-of-interest construction and display; curve or histogram construction and display; and creation of alphanumeric overlays. Cardiac applications include first-pass acquisition; multi-gated acquisition; automatic edge detection; and determination of end systolic and end diastolic volumes, stroke volume, cardiac output, global ejection fraction, and regional ejection fraction. An electrocardiogram ECG gate is interfaced to the system. Thus, it is possible to acquire multi-gated end-diastolic and end-systolic SPECT images of the heart. Coronal and sagittal sectional images are generated from the set of contiguous transverse slices using a data reorganization algorithm.

The radioisotopes typically used in SPECT to label tracers are iodine-123, technetium-99m, xenon-133, thallium-201, and fluorine-18. These radioactive forms of natural elements will pass safely through the body and be detected by the scanner. Various drugs and other chemicals can be labelled with these isotopes.

**Non-camera-Based Systems** Imaging times can be decreased by using another SPECT configuration – a ring of detectors completely surrounding the patient. Although multiple camera heads reduce acquisition time, they do not significantly shorten procedure/exam time because of factors such as patient preparation and data processing. The sensitivity of a SPECT system is mainly determined by the total area of the detector



**Figure 100.3** Arrangement of ring detector and collimator in a non-camera-based SPECT.

surface that is viewing the organ of interest. Of course, there is trade-off of sensitivity versus spatial resolution.

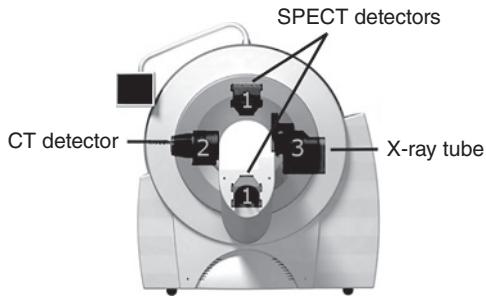
Most widely available non-camera-based system is a fixed-ring system, which uses fixed sodium iodide annulus/rotating collimator machine that yields 8–10 mm resolution images. Modern systems however use semiconductor detectors. This is a slice-based tomograph built with very thick crystals that operate much like pinhole cameras as they traverse through space to obtain tomographic data. A schematic of a high sensitivity system is illustrated in Figure 100.3, which consists of an annular crystal combined with a rotation collimator. However, this device is limited to brain imaging, whereas the triangular system is suitable for both brain and body imaging.

Some systems such as G-SPECT, from MILabs – a spin-off from the University Medical Centre Utrecht (Netherland) – have been designed as a full-ring SPECT system that has <3 mm isotropic resolution as against 7 mm in conventional systems and is suitable for imaging a wide range of isotopes including Tc (99m) and  $^{123}\text{I}$ . With its potential for both high resolution and extremely fast dynamic imaging, it is likely to find applications in brain, bone, and paediatric imaging. A larger bore collimator can also permit high resolution cardiac imaging. Another advantage of the G-SPECT is its scanning speed. Conventional SPECT machines are equipped with heavy, rotating detectors and can take 10–30 minutes to acquire a 3D image. G-SPECT, on the other hand, is a full-ring system that works without requiring any rotation of the detectors, resulting in total imaging time of about half a minute in the brain, and in some other cases, less than one second. This ultrafast dynamic imaging allows visualization of fast processes, such as changes in blood flow.

### **SPECT/CT**

SPECT/CT are tomographic imaging systems that combine the functional imaging capabilities of SPECT with the precise overlay of CT images acquired sequentially as a part of a single examination. SPECT produces computer-generated images of local radiotracer uptake, while CT produces 3D anatomic images of X-ray density of the human body. SPECT/CT systems use a low-dose single slice or multislice CT where both the





**Figure 100.4** An integrated SPECT/CT system showing the location of two SPECT detectors, a CT detector and an X-ray tube, all rotating on the same gantry.

SPECT and CT detector are mounted on the same rotating platform. SPECT/CT is characterized by high spatial resolution and faster scanning time. Each one of the both tomographic imaging procedures has separately proven good diagnostic performance. Improved sensitivity and specificity provided by the SPECT/CT combination help in achieving accurate dosimetric estimates as well as in guiding interventional procedures or in better defining the target volume for external beam radiation therapy. The arrangement of various subsystems in a typical SPECT/CT integrated imaging system is shown in Figure 100.4.

## Specifications

Dual-head variable angle SPECT (CT) capable of acquiring multislices  
Digital imaging and communications in medicine (DICOM) compatible

*Patient opening:* Max 66 cm and minimum 12 cm

*Gantry:* Axis of rotation 100–104 cm; rotation precision, 0.1°; rotation speed, 003–3.0 rpm

*Detectors:* Size: 40 cm to 60 cm × 40 cm to 50 cm or more

*CT:* Standard CT specifications with clinical processing software and comprehensive protocols

## Applications

A SPECT scan is mostly used to view how blood flows through arteries and veins in the brain. It is found that SPECT scan might be more sensitive to brain injury than either MRI or CT scanning because it can detect reduced blood flow to injured sites. Brain SPECT is commonly used in diagnosis, prognosis assessment, therapy response evaluation, and detection of benign or malignant tissue. SPECT is used many times to complement any  $\gamma$  imaging study, where a true 3D representation can be helpful. Combination of SPECT and CT scans can facilitate the precise extraction and deep integration of medically relevant information due to its ability for differentiating tissue boundaries in bone imaging.

## 101

## Continuous Flow Analyser: Automated

### Purpose

Automated continuous flow analysers have been used mainly for routine repetitive medical laboratory analyses for determining various biochemical parameters in blood serum or other bodily samples in clinical laboratories. They automate the analysis steps, which are otherwise done manually by a laboratory technician. This allows analysis of hundreds of samples every day with a single operating technician. They can be used for testing multiple samples sequentially for individual analytes or for multiple analytes simultaneously in the sample. The technique enables up to 16 determinations simultaneously at speeds of up to 120 samples/h. The AutoAnalyzer is a legacy instrument in the category of continuous flow analysers and is still used for a few clinical applications. They have been mostly replaced by discrete analysers because of the lower consumption of reagents. Today, majority of such systems are employed for industrial and environmental work.

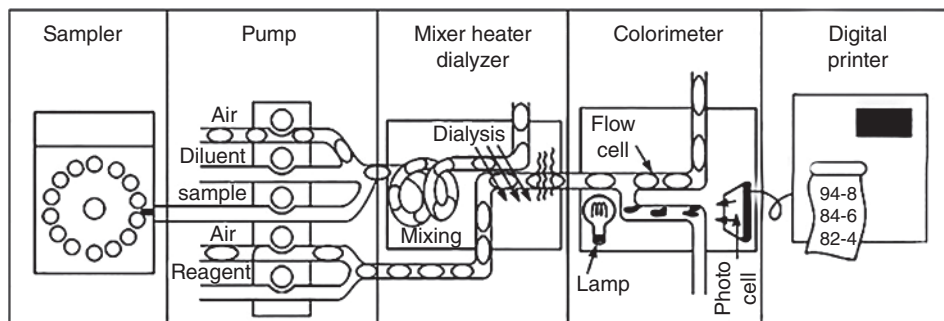
### Principle

The first automated analyser based on continuous flow analysis technique for clinical analysis was invented in 1957 by Leonard Skeggs and commercialized by the Technicon Corporation. This was followed by the introduction of Technicon AutoAnalyzer II, which profoundly changed the way the biochemical analysis work is carried out in the chemical testing laboratory by facilitating significant increases in the number of samples that can be processed per day, which could be hundreds or even thousands per day. Basically, there are two types of automatic analysis techniques: (i) segmented flow analysis and (ii) flow injection analysis.

#### *Segmented Flow Analysis (SFA) System*

The principle of segmented flow analysis (SFA) system is illustrated in Figure 101.1. The continuous streams of material consisting of sample and reagents are combined and are transported in tubing and mixing coils. They are divided by air bubbles into discrete segments in which chemical reactions take place. The samples are passed from one apparatus to the other through the tubing, with each apparatus performing different functions, such as dialysis, heating, incubation, distillation, and finally measuring and recording the results. The core of the technique is the introduction of air bubbles to separate the samples by acting as a barrier between packets to prevent cross-contamination as they travel down the length of the tubing. The air bubbles also aid in mixing by generating turbulent flow in the reaction coils.

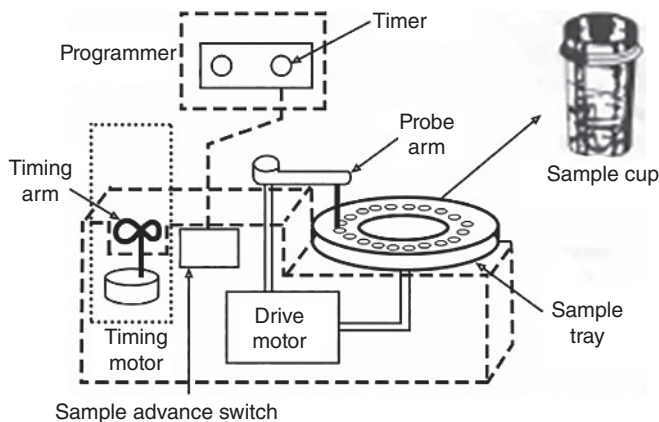
The system basically consists of an autosampler, a peristaltic pump, a chemistry manifold, a detector, and a data acquisition software. Samples and reagents are pumped



**Figure 101.1** Principle of continuous segmented flow analyser.

continuously through the chemistry manifold. Air bubbles are introduced at regular intervals forming unique reaction segments, which are mixed using glass coils. Glass is ideal, as it is inert, stays clean, and enables easy visual checks. Sufficient reaction time is provided to achieve mixing and chemical equilibrium, within the individual segments of liquid, before the debubbled stream is passed through a colorimeter, or fluorescence or other detector. A dialyser with a cellophane dialysis membrane is used to remove high molecular weight components contained in samples that interfere with chemical reactions.

**Sampling Unit** The sampling unit allows to introduce unmeasured samples and standards into the analyser system. The main components of the automatic sampler are a carousel turntable, a stainless steel probe, a wash solution, and a timing control mechanism. The circular turntable as shown in Figure 101.2 carries around its rim 40 disposable polystyrene cups of 2ml capacity. The sample plate carrying these cups rotates at a predetermined speed under the control of timing mechanism. The movement of the turntable is synchronized with the movements of a sampling crook. The hinged tubular crook is fitted at a carrier fixed with the base. The crook carries a thin flexible polythene tube, which can dip into a cup and allow the contents – water, standard, or



**Figure 101.2** Principle of working of an autosampler.

test solution – to be aspirated. At regular intervals, the crook is raised, so that the end of the sample tube is lifted clear of the cup. The process results in continuous aspiration, with the specimen flowing through the probe to the next stage.

Between each sampling, the crook is washed with water or other wash fluids to prevent cross-contamination of one sample with another. The ratio of sampling time to wash time is normally 2 : 1. The sampling rate can be adjusted to 20, 40, or 60 h<sup>-1</sup>. The volume of liquid taken up in most cases ranges from about 0.2–1.0 ml.

Mechanical cams were used in the earlier modules of analysers for timing control and to initiate and control sample aspiration and wash cycles. Modern systems are micro-processor based and use electronic timers to do the same function. These samplers provide greater flexibility in controlling sample-to-wash ratios, which in turn allows better control in setting up parameters for analysis. The samplers are usually designed to complement the automatic dilutor and standards preparation unit, which automatically creates a range of standards from a single working standard as well as creating all drift and blank controls.

**The Proportioning Pump** The heart of the continuous flow analyser is the proportionating pump. It is to continuously and simultaneously push fluids, air, and gases through the analytical chain while varying their ratio over a large range. Here, all the sample and reagent streams, in any particular analysis, are driven by a single peristaltic pump, which consists of two parallel stainless steel roller chains with finely spaced roller thwarts that press continuously against a spring-loaded platen. A series of flexible plastic tubes, one from the sampler and the others from reagent bottles or simply drawing in air, is placed lengthwise along the platform. The roller-head assembly is driven by a constant-speed gear motor. When the rollers are pressed down and the motor switched on, they compress the tubes containing the liquid streams (sample, standard, and reagents) against the platen. As the rollers advance across the platen, they drive the liquid before them.

The roller head rotates at a constant speed. The different flow rates required in the several streams (0.15–4 ml/min) are achieved by selecting tubes of appropriate internal diameter, but of constant wall thickness. Since the proportions of the various reagents are fixed by the tube sizes, no measurements are needed. The plastic tubes are held taut between two plastic blocks having locating holes, which fit on to pegs at each end of the platen. Before beginning a run, the tubes are stretched. With use and time, the tubes lose elasticity and pumping efficiency is reduced. Therefore, each block has three sets of holes, so that the tubes can be increasingly stretched and the tension thus maintained.

**Segmentation** At each point in the system, the sample or reaction stream is separated by air bubbles into a large number of distinct segments. The air bubbles completely fill the lumen of the tubing conducting the flow, thereby maintaining the integrity of each individual sample. In addition, the pressure of the air bubble against the inner wall of the tubing wipes the surface free of droplets, which might contaminate the samples which follow. The proportioning system includes an air bar device, which adds air bubbles to the flowing streams in a precise and timed sequence. The air bar is actually a pinch valve connected to the pump rollers that occlude or open the air pump tubes at a timed interval. The release of air into the system is carefully controlled, thereby ensuring exactly reproducible proportioning by the peristaltic pump.

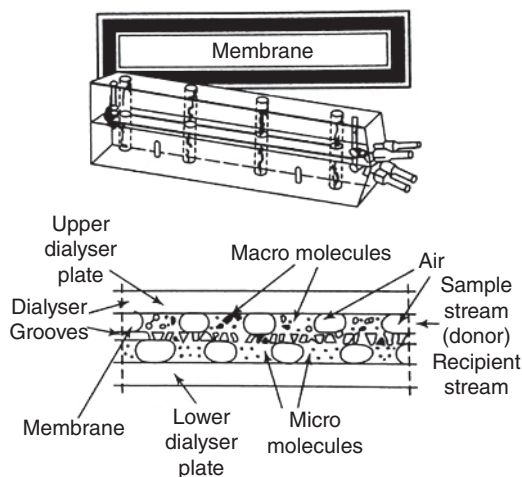
**Chemistry Manifolds** A variety of chemistry manifold types and combinations is usually available in the automatic analysis systems. A manifold mainly consists of a platter, pump tubes, coils, transmission tubing, fittings, and connections. Each test requires a separate manifold for which the changes can be done within a short time. The pump tubing and the connected coils are mounted on a manifold platter, which keeps them in proper order for each test. The constant and correct tension on the tubes provides the continual delivery of a constant volume. The inside diameter of the pump tubing determines the flow rate per minute. To ensure that the correct proportions of the reagents will be mixed, the cross-sectional areas of the tubing are made in the ratios of whole numbers to each other. This means that if correct concentration of the reagent and the tubing of appropriate cross section are used, the right amount of reagent gets mixed with the sample.

Three types of coils are used in the system—mixing coils, delay coils, and phasing coils. At each point in the system where two liquids (sample and/or reagents) come together, a *mixing coil* of sufficient length is provided where the liquids remain for the required mixing time. Mixing coils are glass spirals of critical dimensions, in which the mixing liquids are inverted several times, so that complete mixing can result. As the mixture rotates through the coil, the air bubble along with the rise and fall motion produces a completely homogeneous mixture. The mixing coils are placed in a horizontal position so that proper mixing can take place.

The *delay coils* are employed when a specimen must be delayed for completion of a chemical reaction before reaching the colorimeter. These coils are selected in length according to the requirements. In order to ensure proper sequencing for presentation of the results, a number of devices have been provided to make this adjustment an extremely simple operation.

*Phasing coils* are used to permit the channels to enter the detector system in the proper sequence. This produces a series of bubbles at regular intervals in the liquid stream. A uniform bubble pattern is very essential for accurate analysis. Electronically controlled air valves are used to provide precise air bubble injection. This allows each liquid segment to be of the same volume and contains the same proportion of sample and reagents, thus improving reproducibility.

**Dialyser** In the analytical work, it is often necessary to remove large molecules such as proteins and albumin that can result in inaccurate results in the determination of smaller molecules. In order to obtain an interference-free analysis, the analysers accomplish it by using dialysis process. The constructional details of a dialyser are shown in Figure 101.3. It consists of a pair of Perspex plates, the mating surfaces of which are mirror grooved in a continuous channel, which goes in towards the centre of itself and returns to the outside. A semipermeable cellophane membrane is placed between the two plates, and the assembly is clamped together, similar to the kidney dialyser. The continuous groove channel thus gets divided into two halves, and the dialysis occurs across the membrane. Sample solution is passed through the channel on one side of the membrane, and the recipient solution is passed on the other side of the membrane. The substance to be separated from the sample stream will diffuse through the semipermeable membrane by osmotic pressure into the recipient stream, and the non-diffusible particles will be left behind.



**Figure 101.3** Simplified diagram of dialysis process in a segmented flow analyser.

The cellophane membrane usually used in the dialyser has a pore size of 4–6 nm. The rate of dialysis is dependent upon temperature, area of contact, and concentration gradient across the membrane. For this reason, the dialyser unit is usually immersed in a water bath maintained at a constant temperature ( $37 \pm 0.1$  °C). The temperature is kept constant with a thermostatically controlled heater and a motorized stirrer.

**Heating Bath** The completeness of a reaction is often a function of both incubation time and temperature. It is therefore necessary that the temperature of the reaction mixture is tightly controlled. The reaction mixture, after passing through the mixing coils, moves into another larger coil that is immersed in mineral oil in a heating bath, which is a double-walled insulated vessel. A thermostatically controlled immersion heater maintains a constant temperature within  $\pm 0.1$  °C. Inside the bath, the stream passes along a helical glass coil about 40 ft long and 1.6 mm I.D., immersed in oil, which is constantly stirred. The heating bath may have fixed temperature, as 95 or 37 °C or an adjustable value. Some systems have dry heating bath that operate at temperatures up to 165 °C controlled to  $\pm 0.1$  °C. The dry bath heater uses a standard glass coil, approximately 6 ml volume, with preset digital temperature control adjustable from 37 °C. The heating bath is not used in all the tests performed by the analyser.

**Measurement Techniques** Automated analysers are mostly using absorption UV–visible spectrophotometry as the major measurement technique. The photometers used in the automated systems continuously monitor the amount of light transmitted through the sample. In addition to photometric detection, a wide range of other detectors can be connected to the analyser such as fluorometer (for cases requiring high sensitivity and selectivity), flame photometer (for  $\text{Na}^+$  and  $\text{K}^+$ ) or ion selective electrodes (ISEs), and amperometric detectors for special applications. In all such measurements, flow cells whose size may vary from 6 to 15 mm are employed. The latest designs of flow cells are all of tubular construction, and they require a much smaller volume of fluid, so that a smaller volume of sample can be used.

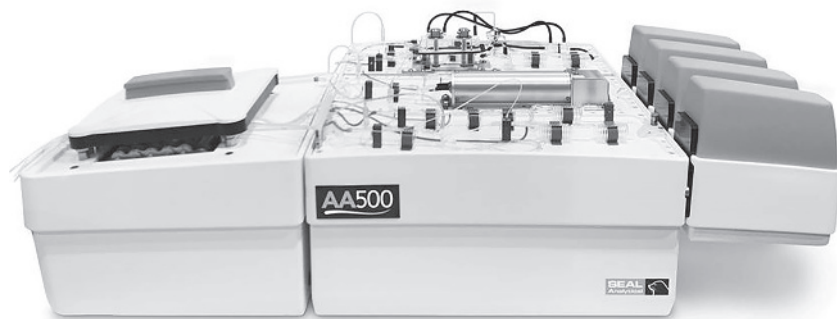


**Signal Processing and Data Handling** The use of microcontrollers had a major impact on the signal processing and data handling of analytical procedures in automated systems. Real-time acquisition and processing of data, by means of specific algorithms, so that the output is immediately useful and meaningful, has become possible. Transformation of complex, non-linear standard responses into linear calibration curves have allowed automation of procedures, such as spectrophotometry.

Specifically, microcomputers are now being used in automated methods for the complete control of the electromechanical operation of the analyser in relation to transfer of solutions, selection, and placement of proper filters and continuous monitoring of operation. This ensures that all functions are performed uniformly, repeatedly and in correct sequence. In addition, they allow acquisition assessment, processing, and storing of operational data from the analyser, monitor the equipment function, and give out message describing the site and type of problem in a malfunctioning equipment.

Previously, a chart recorder was used to record the detector output as a function of time so that each sample output appears as a peak whose height depends on the analyte level in the sample. Modern automatic analysis systems make use of PC as multi-tasking data processor and system controller. These systems have comprehensive software support that includes method development, special functions, interfacing requirements, and system control of power values, pump, colorimeters, etc. The software package also controls the complete analyser, with auto start-up and shutdown, hardware functions control, detector auto-scaling, pre- and post-run sample dilutions, result calculation, and statistics.

The SEAL AutoAnalyzer 3 (AA3) consists of all usual components consisting of an autosampler, a peristaltic pump, a chemistry manifold, a detector, and a data acquisition software. The AA3 is a MacroFlow system in which the internal diameter of all glassware is 2 mm. This enables more complex and non-homogeneous sample matrices to be run without clogging. The system allows for long reaction times as well as the automation of inline distillation, UV digestion, and other complex procedures. Most methods run at 60–70 samples/h. In the microflow system, the internal diameter of all glassware is 1 mm. This reduces reagent consumption and increases throughput, with most methods running at 100–120 samples/h. There are still hundreds of Technicon AutoAnalyzers in use around the world, and they are still well supported by SEAL Analytical. The newer version of system is AutoAnalyzer Model AA500 (Figure 101.4), which has the



**Figure 101.4** AutoAnalyzer model AA500. Source: Courtesy M/s SEAL Analytical, Inc., USA.

advantages over other technologies in terms of the high throughput, often over 600 tests/h, high reproducibility, and extremely low detection limits – even in complicated matrices. The advanced optical detection systems, light emitting diode (LED) as light sources, and software allow analysis at lower method detection limits. The system has more automation – with automatic start-up and shutdown with pump platen engage and release and reagent/wash valves.

Automated SFA methods are generally preferred over manual methods because they are more precise, are independent of timed reactions, avoid tedious repetitive steps, and are relatively faster. They also consume less sample, and in multichannel systems, several parameters can be analysed simultaneously from one sample cup. Analysis quality improves by eliminating human errors that can occur during manual tests.

## Specifications

*Number of samples:* 40 (up to 270)

*Sample cup volume:* 0.5, 2, 4, or 5 ml

*Photometer type:* Dual beam

*Wavelength range:* 420–900 nm, standard 340–900 nm option

*Flow cell design:* Glass barrel with sapphire light pipes

*Flow cell path length:* 10, 30, or 50 mm

*Flow cell internal diameter:* 0.5, 0.7, or 1.0 mm

*Light source:* Krypton lamp or LED

*Pump:* Number of pump tubes: 28; number of air lines: 8

*Chemistry module:* Number of manifolds: 1–4, depending on methods

*Heating baths:* 25–120°C

## Applications

The main applications of continuous flow automated analysers have been in the large clinical laboratories mainly for routine repetitive analysis work. Although they are still being used, they have been largely replaced during the last few years more and more by discrete analyser systems that allow lower reagent consumption and faster operations.

# 102

## Continuous Passive Motion Machine (CPMM)

### Purpose

Continuous passive motion machine, generally called CPMM, is a device that is used as a postoperative procedure designed to aid in recovery after joint surgery. After joint surgery, if a patient fails to move their joint tissue around conveniently, the joint is likely



to become stiff resulting in formation of scar tissue with limited range of motion of the joint. CPMM is used for restoration of the range of motion of the knee, hand, leg, arm, elbow, hip joint, shoulder joint, wrist, fingers, and feet joints. The machine is also used for stimulation of the muscles around the mouth and the lower jaw by moving the effected joint through a controlled range of motion.

## Principle

Continuous passive motion (CPM) devices are usually used during the first phase of rehabilitation following a surgical procedure or trauma. The purpose is to control post-operative pain, reduce inflammation, and provide passive motion in a specific plane of movement. The device can be used both in the hospital and in the home. The CPM device constantly moves the joint through a controlled range of motion. Generally, the exact range of motion depends upon the joint, and in most cases, the range of motion is increased over time. The device is designed to gradually move the affected joint through a prescribed arc of motion. The treatment is carried out under prescription by a physician who will provide usage instructions, including the speed of the machine, the duration of usage, the amount of motion, and the rate of motion increase.

### Types of CPM Devices

Passive motion is movement generated through an outside source and does not require the activation of muscles. Repetitive passive motion for rehabilitation can be done by either a physical therapist or a CPM device. The CPM devices can be manual or motorized. The manually operated devices mimic the approach taken by a physiotherapist when manipulating the limb manually for the purpose of flexing and extending a joint. The limb is held and supported on both sides of the affected joint and pushed, pulled, and torqued to create the required movement. CPM devices that try to follow this approach are called *free linkage machines*. A typical example of a manually operated machine is shown in Figure 102.1.

### Motorized Machine

The CPM technique refers to the use of a stationary electronically controlled motorized machine to apply continuous range of motion that the doctor prescribes for a particular joint. In these devices, the limb is cradled in a frame that has adjustments to accommodate a range of limb sizes. It is designed to provide desired movement of the limb relative to the frame.

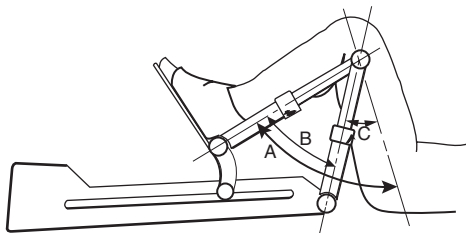
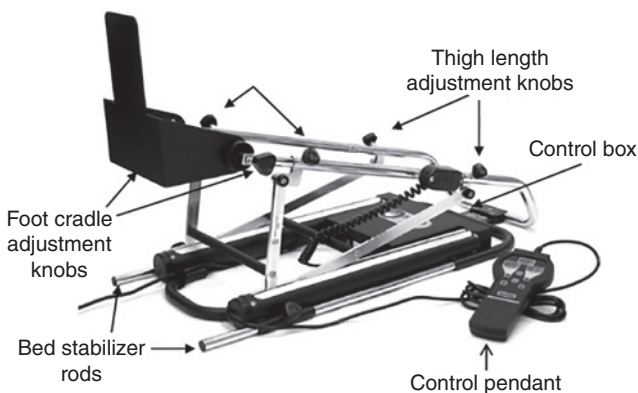


Figure 102.1 Schematic of a manually operated motion machine for knee joint.

The linkages in the machine are hinged at locations roughly coinciding with the joints of the body. The frame is driven by a motor drive to produce articulated back and forth movement of the hinges and, concurrently, similar movement of the joints, through a range of motion without the patient needing to use his or her muscles to move the joint. There are several different protocols that a physician may advise for using the machine. The most typical protocol is to have the machine start with a predefined amount of joint flexion and then increase this amount on a regular basis.

The structure of the CPM machine differs depending on their intended use. For example, a knee CPM machine has a cradle to hold the leg in which the machine slowly bends and straightens the knee. There are differently designed machines for the elbow, knee, shoulder, etc. Currently there are a large number of different solutions, and their structures may vary from each other depending on the manufacturer providing the device. They can be adjusted to suit the individual biophysical characteristics of the patient. Most of the CPM machines use the four-bar linkage mechanism to enhance the stability and rigidity of movement in the mechanical structure. The elements of the mechanism are usually made of durable aluminium alloys, tubes, or flats. In addition, the devices are provided with components that increase comfort level of the limb support, as well as fixing and stabilizing strips that are useful in the rehabilitation process.

The various essential parts of a motorized machine are illustrated in Figure 102.2. Typically, the motion of joints of the motorized CPM machine is provided by an electric linear actuator or by a rotary drive system with a direct current (DC) motor. The *linear actuator* is basically a push–pull mechanism that is generally attached to extreme ends of a linkage to provide maximum leverage with a minimum drive force creating maximum torque at the hinge point. The second method is direct *rotary drive* to the hinge. A rotary drive gives better functional performance in safety, range, and consistency of motion. However, a linear actuator is preferred where force and torque requirements are high such as in the case of a leg. Therefore, most of the commercial machines use rotary drive. For smaller joints such as for the hand, torque requirements are small and hence both types of drives are feasible. Medium-sized joints such as the elbow are more easily driven with linear drives, but rotary drives can also be used without any problem. Rotational speed and smoothness of motion are much better with a rotary drive due to direct coupling through gearing of the motor to the joint. However, a linear drive



**Figure 102.2** Various components of a motorized continuous passive motion machine.

operating at a constant motor speed delivers a variable rotary speed, which depends on the angle of movement.

In some special cases, it is desired for a CPM machine to provide joint movement through its entire physiologic range of motion. Most joints in the body move through more than one axis and some, like the shoulder and hip, even move in three axes. A device built to move in two axes is quite difficult, and the same is realized usually taken to couple the secondary axis to the movement in the primary axis, requiring only one motor and drive system. Commercial machines to move all three axes of the shoulder have not been feasible. The machines providing movements of a joint in three planes just move one or two axes at a time.

Modern CPM machines usually employ conventional high-quality brush-type DC motors as the power source. These motors are usually used with reduction gears to reduce their speed. They are operated at less than 50% of their rated speed and load capacity to increase their life and reduce noise. Although stepper motors, brushless DC or alternating current (AC) motors can also be used, but they are not preferred because of less power to weight capability and lower electrical efficiency. The angle of motion varies from  $-10^{\circ}$  to  $125^{\circ}$ . The measurement of the angle of deflection is made using a potentiometric system, which is located in the rotary joint mechanism. Systems are also capable of increasing/decreasing the velocity of movement and the amount of force exerted on the limb taking into account the individual post-operative pain tolerance. A patient compliance meter monitors patient usage and tracks in tenths of an hour readings. A handheld programming unit (pendant) allows for precise adjustments of patient-specific therapy parameters. They have graphical representation facility to indicate overall treatment cycle.

Some researchers feel that the CPM has not evolved much from a very basic means of movement as the model designed during the advent of knee replacement surgery is still the same today. A modification of the CPM has however been introduced known as *pressure modulated knee rehabilitation* (PMKR) technique. This is a computerized machine that works in a different way than a traditional CPM machine. Rather than having the knee move back and forth between two fixed points at a constant pressure as in the case of the traditional CPM machine, the PMKR machine uses *variable pressure technology*. This technology puts control over the amount of pressure exerted on the leg into the hands of the patient. The machine employs pressure sensors, adjustable exercise arc, and strengthening modules.

The patient can set the maximum pressure he/she is comfortable with and then can focus on making rapid gains in range of motion without fear of sharp or excessive pain. The machine continuously reads and reacts to your body so you won't push too far during your therapy. As the patient achieves increases in range of motion, he/she adjusts the pressure as frequently as needed to continue to work within her own unique pain threshold, thus making each session highly productive. Large arcs of motion, working at terminal limits, greatly enhance the pumping action eliminating blood and periarticular fluid while gently stretching and realigning the muscle fibres. The machine provides wireless connectivity to allow patient results to be made digitally available to therapists and surgeons for timely action, if required. It does this by training patients to control critical aspects of their recovery, supported by telemedicine coaching and in-person therapist visits. The machine is specifically designed to provide and strengthen leg muscles via isometric, concentric, and eccentric exercises.

## Specifications

*Knee flexion:* 120°

*Knee extension:* -10° to 105°

*Speed:* 1°s<sup>-1</sup> at lowest setting, 3°s<sup>-1</sup> at highest setting

*Pauses:* 0 – 30 seconds

*Knee joint to foot sole length:* 25–57 cm

*Hip joint to knee joint length:* 31–49 cm

*Maximum patient weight:* 160 kg

## Applications

CPMM is commonly used in rehabilitation medicine in the hospitals. The machine is employed in both training and active or passive exercise therapy. CPM is used to improve range of motion during the post-operative rehabilitation period and to promote cartilage growth and enhance cartilage healing during the non-weight-bearing period.

# 103

## Continuous Positive Airway Pressure Machine

### Purpose

Continuous positive airway pressure (CPAP) machine is a device that gives a constant flow of oxygen/air to the patient at a preselected pressure, thereby producing a small overpressure within the lungs that helps in the gas exchange.

This function is usually provided in advanced ventilators, but this generic device, when available as a separate device, can be used in a number of treatment settings, typically in the intensive care unit. CPAP system is the most common type of device used to treat obstructive sleep apnoea in adults. It is also useful in providing ventilation for newborns and anyone suffering respiratory failure.

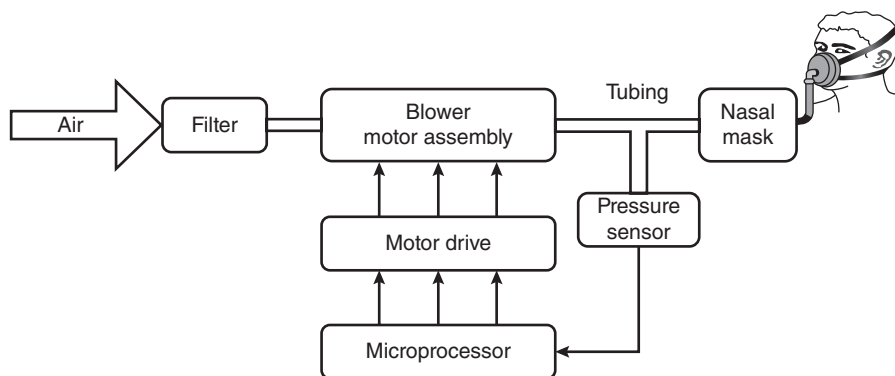
### Principle

A CPAP machine provides breathing assistance to patients with obstructive sleep apnoea syndrome by keeping the airway open during the night by gently providing a constant stream of air through a mask, which the person wears while asleep. The person is able to sleep through the night without waking up from lack of oxygen. They are also used as a preventive and support device for patients with other diseases, such as acute asthma, congestive heart failure, cardiogenic pulmonary aedema, and chronic lung disease.

Technically, the device is very simple. Figure 103.1 shows a block diagram of the CPAP system. It consists of a microprocessor or a digital signal processing (DSP), a pressure sensor, a brushless DC motor integrated with a blower, a motor controller, a flexible tubing, and a nasal mask. When operated, ambient air is drawn through the air filter by the blower and is then pressurized. The pressurized air is directed to the patient airway via the flexible tubing and a nasal mask. A pressure sensor near the nasal mask detects the pressure signal and gives it to the microprocessor. The microprocessor calculates the error between the desired pressure and the measured pressure and regulates the rotational speed of the motor by varying the input voltage to the motor driver. This adjusts and controls blower output pressure to keep pressure variations within allowable errors. For patient comfort, some CPAP devices include algorithms that decrease the air pressure during exhale and increase during inhale.

A typical CPAP machine such as shown in Figure 103.2 has three main parts:

**Control unit:** A control unit includes an air pump that blows air into the tube and control electronics. The air pump works as a small compressor. The device is designed to optimize the air pump parameters such as noise, response time, air volume, power



**Figure 103.1** Block diagram of continuous positive airway pressure (CPAP) machine.



**Figure 103.2** Typical CPAP machine.

consumption, size, and cost. To meet these requirements, system designers use motors that are extremely quiet and do not make sound beyond a whisper, which can be controlled with flexible integrated motor control integrated circuits ICs. The air at room temperature is drawn through a replaceable filter that filters out particulates and impurities. It is then gently pressurized so as to deliver the desired amount of air pressure required to clear the obstruction. Machines having built-in humidifiers have a small water tank that, when turned on, heats up the water to provide moisture to the air sent to the patient. Besides logic circuitry, CPAP machines also use a number of sensors to collect physical data during operation. Pressure sensors monitor the pressure of the air being delivered; the data is conditioned with analog circuitry and routed to the analog-to-digital converter on to the microprocessor. Likewise, air temperature and humidity can be measured and adjusted to make the therapy comfortable for the patient.

*Mask:* A mask that fits over the nose or nose and mouth of the patient is kept in place by a strap. CPAP masks come in all shapes, sizes, and materials to suit individual requirements for wearing comfort. Typically three types of masks are available: nasal pillows, nasal masks, and full face masks. Choosing the right mask comfortable to the patient is the most important part of CPAP compliance. The mask must fit properly, not only for comfort but also to keep air from leaking out.

*Hose:* Hose is a tube that connects the mask to the machine's motor. It is simply a delivery device that transports the pressurized air from the blower to the wearer's mask. While most hoses are 6 ft in length, their diameter can be different depending on the machine that one uses. Most hoses are now heated to reduce water condensation accumulation caused by the humidifiers.

The heated humidifiers used in the CPAP machines can help reduce side effects from the treatment and make it easier for the person to breathe through the mask. Some people may have nasal irritation or drainage from using CPAP, which can be avoided by providing cool or heated moisture to the air coming from the CPAP unit machine. The humidity level can be adjusted by the patient. The CPAP machines are small, lightweight, and fairly quiet.

The air pressure delivered to most patients with sleep apnoea ranges between 6 and 14 cmH<sub>2</sub>O. A typical CPAP machine can deliver pressures between 4 and 20 cmH<sub>2</sub>O. More specialized units can deliver pressures up to 25 or 30 cmH<sub>2</sub>O. The machines are powered either from an electrical wall outlet or from a battery. Switchover to battery operation is usually automatic and is signalled by an alarm. The controls commonly provided on the panel are used to set inspiratory time and pressure, expiratory time and pressure, rate, trigger sensitivity, and panel lock.

There are two types of pumps that are used in CPAP machines: (i) those that deliver a fixed pressure and (ii) those that automatically adjust the pressure. *Fixed pressure pumps* operate at a pressure that has been set by the doctor according to the specific need of the patient. The pressure in these machines increases slowly in a ramp function to the desired level after it is switched on. *Auto-adjusting devices* monitor airflow and continuously adjust pressure overnight to keep the throat open. They are useful for those patients whose pressure requirements significantly vary during sleep and are high at times. The CPAP machine is generally placed near the patient during sleep. Therefore, it must be noise free and should not require any operational action that might disturb the patient's sleep.

## Specifications

*Pressure support:* 4–30 mmHg

*Pressure waveform:* Ramp function

*Flow range:* 4–40 l/m

*Alarms for:* Lack of water; sensor failure; high/low temperature

*Air temperature precision:*  $\pm 1^\circ\text{C}$

*Displays:* Tidal volume, inspiratory pressure, inspiratory time, expiratory time, IE ratio,  $\text{FiO}_2$ , feedback control of the warming, temperature

*Patient alarms:* Power failure, low battery, overheating, mask/tube fault inlet

## Applications

A CPAP machine was initially used mainly by patients for the treatment of sleep apnoea at home as it is the best treatment for obstructive sleep apnoea. Over the years, it finds applications in intensive care units as a form of ventilation support.

# 104

## Crash Cart: Resuscitation

### Purpose

A resuscitation or emergency crash cart is a mobile cart equipped with emergency medical equipment, essential supplies, and drugs to resuscitate a patient experiencing cardiac emergency. The storage of disposable and non-disposable medical equipment and accessories is made available in the cart in adequate quantity so that the cart can meet the requirements of emergency management of patients with critical and urgent conditions. Usually, a properly organized crash cart contains supplies and equipment that are vital to treat life-threatening situations.

### Principle

The function of a crash cart is to provide a mobile station within the hospital that contains almost everything that is considered necessary to manage a life-threatening situation. The cart stores life-saving equipment and drugs in a hospital emergency room, intensive care unit, clinics, and other areas. A mobile station allows the treatment to be provided to the patient whenever and wherever required in the hospital. In some parts of the world, the crash cart is also called emergency trolley. The essential equipment for resuscitation includes more than 100 items such as drugs, syringes, electrodes, cardiac monitor and defibrillator, power source, and easy access to electrical power. A standard



checklist of compulsory equipment and drugs is usually available in the cart that can assist in daily systematic, visual, and functional verification. The Resuscitation cart is specially designed for the purpose of cardiopulmonary resuscitation and management of other similar emergencies in the hospital. The cart must be easily accessible in the emergency room/intensive care units and able to be moved to any area within the medical facility as and when required.

A well-organized crash cart can save a lot of time and confusion during an emergency, which in turn proves helpful in saving a life. It serves ready for situations that demand prompt action for recovering consciousness or restoring the vital signs of the patient. Therefore, the crash cart is kept in an accessible place and routinely monitored by staff nurse to ensure that all supplies are replaced in time. All the equipment must be kept in working condition and stock of emergency life-saving drugs are up to date. The nurses and doctors on duty must be aware of the placement of the emergency cart and the contents of each drawer.

### ***Contents of the Emergency Crash Carts***

A crash cart is basically a set of trays/drawers/shelves housed in a chest that is mounted on the wheels as shown in Figure 104.1. The contents of a crash cart vary from hospital to hospital, but it typically contains instruments for cardiopulmonary resuscitation, supplies, essential tools, and drugs needed to treat a person in emergency. The number of drawers present in a cart can vary from 3 to 7. Drawers are organized and arranged from top to bottom in the following order: medications, airway, circulations, IV solution and tubing, and miscellaneous. These include but are not limited to the following:

*Cardiac monitor/defibrillator:* This vital life-saving equipment is placed on top of the crash cart or placed on a shelf provided in one side of the top of the cart. The

**Figure 104.1** Typical emergency cart with defibrillator and IV facility.





shelf features a swing arm that moves the monitor/defibrillator without moving the cart. A hook and loop closure strap can be adjusted to fit monitors/defibrillators from different manufacturers. The swing arm shelf attaches to most carts with four screws. The defibrillator is essential for administering an electric shock of a high voltage to the heart so as to restore its normal rhythm in the event of a cardiac emergency. Other items that are placed on the shelf, and containers include defibrillator pads, latex gloves, stethoscope, bag valve masks (BVMs), sharps container, suction devices, oxygen, inventory checklist/code Blue sheets, etc.

*First drawer:* It contains emergency or advanced cardiac life support (ACLS) first-line, rapid sequence drugs.

*Second drawer:* Carries paediatric medication and IV solutions.

*Third drawer:* Breathing equipment including adult intubation supplies, endotracheal tubes, tracheostomy tube, Ambu bag, oral and nasal airways, oxygen masks and nasal cannulas, pressure cuffs, carbon dioxide detector, suction catheters, nasal cannulas, laryngoscope, forceps, guidewire, bulbs, blades, batteries, straight and curved blade, syringe, lubricant, adhesive tape, exam gloves, IV cannulas, disposable syringes, etc. are placed in this drawer.

*Fourth drawer:* This drawer has infant and paediatric intubation supplies and paediatric doses of emergency drugs and small-sized endotracheal tubes, blood pressure cuffs, oxygen masks, cannulas, etc.

*Fifth drawer:* This drawer contains IV supplies (cannulas, drip sets, fluids) and blood draw supplies. It usually contains catheters, tourniquets, syringes, tubes, and tape.

*Last drawer:* It has intravenous solutions, tubing, and different types of surgical kits.

The IV (intravenous) pole provides two storage hooks for IV bags and thus eliminates the need for a doctor or nurse to hold bags when they could be assisting in another area. The IV pole can be adjusted to different heights. Attachments like holders and brackets can be affixed to a crash cart to accommodate larger items such as oxygen cylinders and resuscitating devices. Though Ambu bags can be hung from IV poles, they are not well secured. A special Ambu bag holder offers a convenient and secure way to store the bag. The various drawers of a crash cart are properly labelled to avoid any confusion in accessing the right item.

### **Construction**

The cart body is constructed from blow moulded high-density polyethylene body panels. The cart frame is epoxy coated 14 gauge, cold rolled steel. The top of the body is given antimicrobial protection that helps maintain a cleaner cart and provide better infection control. One-side panel also provides integrated pivot pockets for tilt out bins, which could be locking or non-locking. Strapless defibrillator platform is adjustable to accommodate various defibrillators and has adjustment mechanism with 360° rotation. Swing arm is 18 gauge tubular steel, epoxy coated with tensioning knob. It can swing 90° from work surface and allows the defibrillator to be brought closer to the patient that also helps to clear the top work area. A typical crash cart with a defibrillator is shown in Figure 104.1.

Full extension drawers have self-closing ball bearing slides to provide easy access to medications and supplies. The drawer body is acrylonitrile butadiene styrene (ABS) injection moulded, blow moulded high-density polyethylene (HDPE) with Microban antimicrobial drawer front, ABS and Microban antimicrobial injection moulded coloured drawer pull and full extension, self-closing, and ball bearing drawer slides. Convenience features include an extendable IV pole, O<sub>2</sub> tank storage, suction pump shelf, glove box holder, lockable sharps container, hospital grade outlet strip, cord management, and trays and dividers. In one design, the steering mechanism includes a fifth wheel that is actuated by squeezing a polymer trigger mounted to the cart handle. When activated, the fifth wheel is locked perpendicular to the handle providing positive control when cart is pushed. When trigger is released, all five wheels swivel allowing manoeuvrability in any direction. The four corner castors are of 5 in. (127 mm) diameter stem casters with polyurethane tread and polymer horn.

Most of the crash cart manufacturers produce carts of modular design. That means that sizes are universal and that drawers and accessories are interchangeable. This type of design offers a flexible and adaptable solution that allows the user to expand storage and transport capabilities. By adopting a specific combination of interior components and accessories, the user can recreate new functionality or styles by exchanging components. Standard cart sizes are 20 and 24 in. wide and 36, 42, and 72 in. high, thus giving options for targeted functions or high-capacity storage.

Crash cart boxes are used to organize medications and supplies in the drawers. They are available in full and half drawer sizes and are provided with handles that make for easy placement and removal. The modular construction allows for easy removal and easy access during an emergency situation as well as during the replenishing of stock. These crash cart boxes are usually sized to fit the majority of the crash carts used in the hospitals. For shallow and deep cart boxes, plastic dividers are also available. The dividers are suitably grooved so that they can be interlocked to provide a stable and secure fit. Alternatively, a more customized solution can be achieved by using foam inserts. These inserts are available in both full and half crash cart box sizes and can also be cut to accommodate any size or shape medication container. The foam inserts are usually thick foamed blue polyurethane.

It is essential that the crash cart is ergonomically designed and is user friendly. Such a design includes rounded corners and a softer surface material than metal. The edges and pulls must be smooth and sturdy. The cart should be of lighter weight. The casters should be smooth and sturdy and provide ease of mobility and movement over doors and elevator thresholds, especially when quick response is essential. Carts are available with lockable doors to ensure security of supplies.

The crash cart program needs to be appropriately designed so that all elements of control, security, and accountability are ensured so that all types of emergency situations can be dealt with efficiently and quickly. Different hospitals have different and varying needs for the composition of drug products on a crash cart, and also differences can exist throughout the various departments within the same hospital. For example, the crash cart for a paediatric unit will differ from that which is on a general medical and surgical unit versus that which is in labour and delivery department. Such factors are important considerations in planning the design and procurement of a crash cart.

## Specifications

*Overall size:* More than length: 900 mm × width: 500 mm × height: 1500 mm

*Material of construction:* 25.4 mm × 18 G stainless steel grade SS 304 tubular frame work and SS sheet of grade 304

*Electronic equipment:* Electrocardiogram (ECG) monitor/defibrillator

*Castor wheels:* Mounted on 12.5 cm dia swivelling castor wheels; oxygen cylinder stand: SS 304 grade, on one side

## Applications

Crash cart is needed in any facility that treats patients who have the potential to have a sudden deterioration in their condition. This includes hospitals, outpatient surgery centres, urgent care centres, and all centres where conscious sedation is performed. Nursing homes that provide treatment for patients in cardiac field also require a crash cart. In addition, laboratories where diagnostic testing such as cardiac stress testing or stress ECG/echocardiogram is performed must have a readily available crash cart.

# 105

## Critical Care Analyser

### Purpose

Critical care analyser is an analytical instrument that is used for the measurement of blood gases (hydrogen ion concentration [pH], carbon dioxide partial pressure [pCO<sub>2</sub>], oxygen partial pressure [pO<sub>2</sub>]); electrolytes (sodium [Na<sup>+</sup>], potassium [K<sup>+</sup>], ionized calcium [Ca<sup>2+</sup>], chloride [Cl<sup>2-</sup>], and certain metabolites (glucose, blood urea nitrogen [BUN/urea], lactate [Lac]); total haemoglobin concentration (tHb); and haemoglobin oxygen saturation (SO<sub>2</sub>). These tests can be carried out in samples of whole blood or in serum and plasma. Traditionally, these analytes are determined using large benchtop analysers in clinical laboratories or point-of-care situations.

### Principle

For management of critical care patients, it is essential to continuously carry out analysis of some of the important quickly-changing blood analytes. Ideally, the clinical decisions should be made on the basis of trends observed with continuous, online monitoring of such parameters. However, it is not always found practical and sufficiently reliable to perform continuous intravascular measurements routinely on such patients. The next-best clinical alternative is to perform in vitro discrete

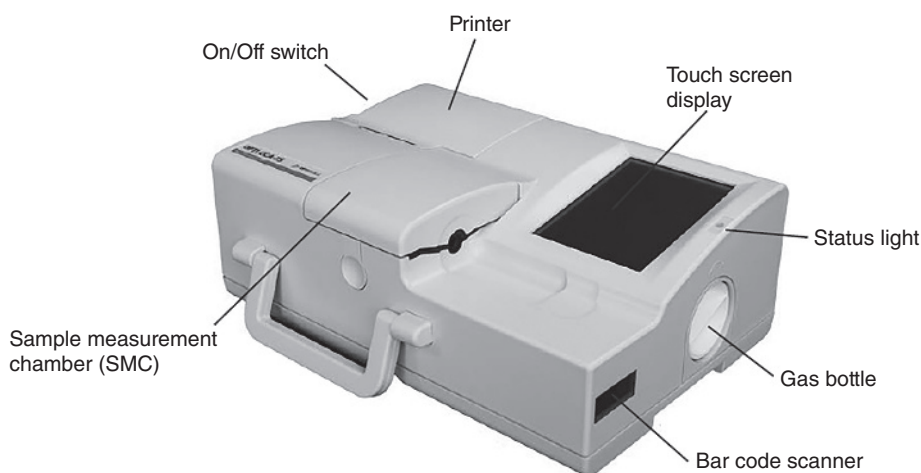
measurements frequently, preferably near the patient's bedside, in the emergency room, or in the intensive care unit. This can result in minimizing the decision time for therapeutic interventions, thereby improving patient recovery. Critical care analysers have been designed to fulfil this requirement with technological innovations of sensing and processing of analytical measurement data by using specially designed sensors called 'optodes'.

A critical care analyser is based on the use of solid state sensors with fluorescence optode technology or thin-film electrodes. The analyser utilizes single-use cassettes providing different parameter configurations, allowing the users to select the cassette as per their need. The cassette contains the microchip, reagents, sampling device, and calibrators and does not require any external reagent. The analyser comprises of standard components that include a bar code reader to identify the type of test to be performed, a sample delivery system, reaction cell, sensors specific to parameters under test, calibration, data management, storage, and display. The optical sensors are much less complex than their electrochemical equivalents, having fewer macroscopic components. They do not require any reference sensors, and there is no surface fouling by biologic proteins. Calibration verification is done with each cassette immediately prior to use. The analyser is designed to be operated either by its on-board rechargeable battery for up to eight hours or directly from AC mains power.

Two types of optodes have been developed for medical applications. For in vitro applications, the sensor chemistry is placed on a flat, rigid, and optically transparent support material. This type of optode is known as a planar optode.

### Instrumentation

Critical care analyser Model CCA-TS2 Analyzer from M/s OPTI Medical Systems, Inc. as shown in Figure 105.1 is a typical example of a microprocessor-controlled instrument based on measurement of optical fluorescence by optodes. The optodes essentially

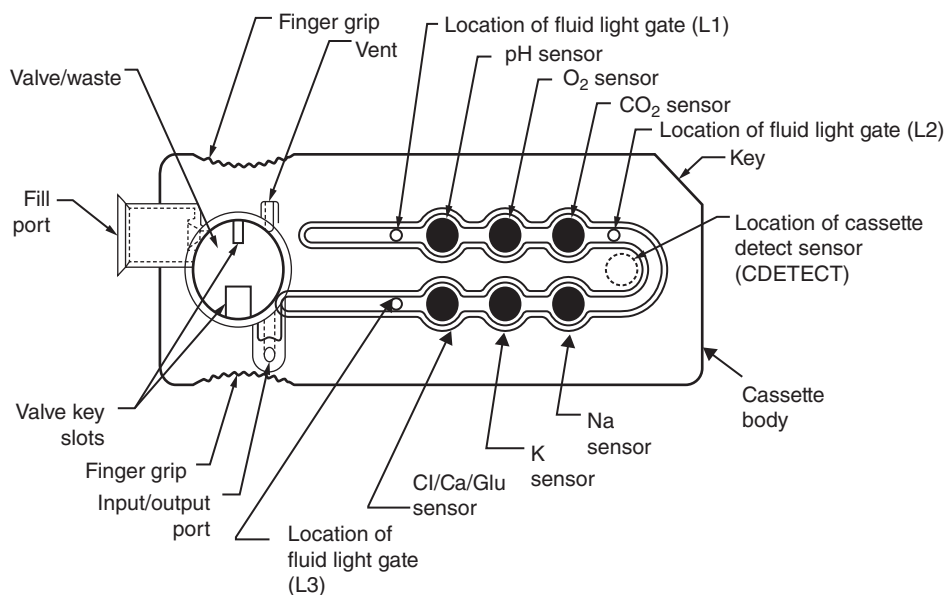


**Figure 105.1** Critical care analyser Model CCA-TS2 Analyzer. Source: Courtesy of M/s OPTI Medical Systems, Inc., USA.

measure the intensity of light emitted from fluorescent dyes. The measurement system has light emitting diodes (LEDs) that supply excitation energy to the optodes, while laser diodes are employed for the reflectance-based oximetry measurements. The LED light is directed to the sensors via a dichroic beam splitter. The fluorescence emission from the sensor is directed back through the dichroic beam splitter and filters to isolate specific wavelengths. The emitted light is separated from excitation light by means of optical filters then to the photodiode detector, which converts the light photons into a measurable electrical current. Since the excitation light energy is kept constant, the small amount of light that is emitted changes only by the concentration of the analyte and is measured by the analyser after passing through lenses and additional optical components. The concentration of the analyte is determined from the calibration curve. The measurement cycle takes approximately 150 seconds. The equipment works on a minimum sample size of 125  $\mu\text{l}$ .

### The Cassette

The disposable, single-use cassette contains all of the essential subsystems required for sample measurement, waste containment, and calibration. Figure 105.2 shows a typical layout of a cassette. It is equipped with six optodes for measurement of pH,  $\text{pCO}_2$ ,  $\text{pO}_2$ ,  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$ , all by fluorescence. Additional cassettes are available with optodes to measure  $\text{Cl}^{2-}$ , glucose, urea, and other parameters. The calibration information from the cassette can be scanned into the analyser by using a bar code scanner. The cassette is then placed into the measurement chamber. The tests are



**Figure 105.2** Cassette used for analysis in the critical care analyser Model CCA-TS2 Analyzer.  
Source: Courtesy of M/s OPTI Medical Systems, Inc., USA.

performed at 37 °C and for that the cassette is warmed to this temperature. The calibration verification on the  $p\text{CO}_2$  and  $p\text{O}_2$  sensors is done by passing a precision calibration gas mixture across the optode sensors. The calibration of the pH and electrolyte channels is performed with precision buffer solutions contained in the cassette. The total Hb and  $\text{SO}_2$  channels are factory calibrated. The syringe adapter shown at the right side of the cassette allows the automatic aspiration of a sample directly from a syringe. Removing the adapter allows for direct sample aspiration from a capillary or microasampler.

After the calibration is verified, the blood sample is aspirated by the instrument into the cassette and across the optode sensors. Fluorescence emission as a result of various reactions is then measured and displayed. The cassette, after a single test containing the blood sample, is removed from the analyser and discarded. The machine is again ready for accepting another cassette. No internal cleaning is required, and the waste is contained in the anaerobically sealed valve compartment of the cassette. The principles of measurement of various blood analytes are described in the following text:

### ***pH Measurement***

For pH measurement, the hydrogen ions in the blood bind to a pH-sensitive fluorescent indicator dye, which is immobilized in the sensing layer of the optode. The measurement principle is based upon pH-dependent changes of the luminescence of the fluorescent dye. The relationship of luminescence to pH is quantified as to how the fluorescence emission intensity increases as the blood pH is increased. pH optodes do not require a reference electrode to measure pH, but they do show a small sensitivity to the ionic strength of the sample being measured.

### ***pCO<sub>2</sub> Measurement***

The  $p\text{CO}_2$  optode is a modified pH optode and uses the same indicator dye but with ion-permeable membrane covering the sensing layer. The optode is similar to the conventional  $p\text{CO}_2$  blood gas electrodes. The membrane blocks the passage of  $\text{H}^+$  and other ions into the sensor but allows  $\text{CO}_2$  through it, where it forms carbonic acid. This results in increase in the local  $\text{H}^+$  ion concentration (reducing the pH) and reducing the fluorescence. Thus, increased  $p\text{CO}_2$  is associated with low fluorescence and decreased  $p\text{CO}_2$  with high fluorescence.

### ***pO<sub>2</sub> Measurement***

In the  $\text{O}_2$  optode, oxygen from the blood rapidly diffuses down into the sensor and interacts with an immobilized dye that is specific for oxygen. The oxygen quenches or reduces the fluorescence of the dye and the luminescence forms the basis of measurement. The relationship between the partial pressure of oxygen ( $p\text{O}_2$ ) and fluorescence intensity defines as to how the fluorescence emission intensity is reduced as the  $p\text{O}_2$  is increased. The relationship is an inverse one, leading to reduced fluorescence intensity with higher  $p\text{O}_2$ .

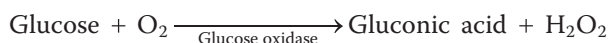
### **Electrolytes**

The measurement of  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$  is based on the use of optodes that work on the principle of ion selective electrodes (ISEs) or ion selective recognition elements, known as ionophores. The ionophores are linked to fluorescent dyes instead of conventional electrodes and are accordingly termed as fluoro-ionophores. These types of dyes are commonly used in fluorescence microscopy and cell counters. Increasing ion concentration results in binding larger amounts of ions and causes the fluorescence intensity to increase or decrease, depending on the particular ion. There is no need for a reference electrode with the ion optode, but a small pH sensitivity is exhibited by them that is automatically compensated in the device using the measured pH.

For measurement of chloride, the optode is constructed by photoactivated immobilization of a proprietary chloride sensitive indicator. Chloride from the blood diffuses down into the sensor and quenches or reduces the fluorescence intensity of the dye. The relationship is an inverse one, leading to reduced fluorescence intensity with higher concentration of chloride.

### **Glucose**

The metabolites are measured using biosensors employing enzymes, typically immobilized onto an electrode capable of measuring a product or reactant of the enzyme reaction, such as hydrogen peroxide. The glucose optode measurement is based on the well-known enzymatic oxidation of glucose, as per the reaction given as follows:

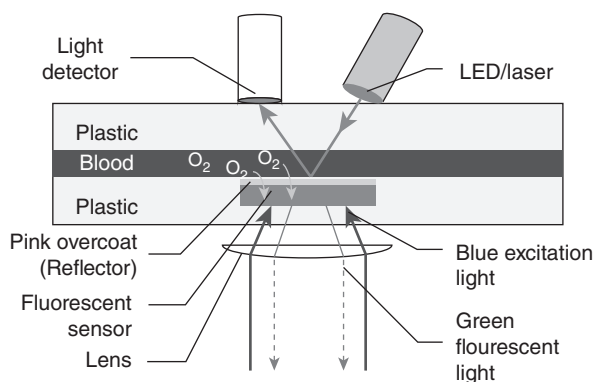


The glucose sensor is constructed by putting an enzyme layer over an oxygen sensor. As a sample containing glucose contacts the sensor, this oxidation of the glucose consumes the oxygen locally present in the sensor. This results in decrease in oxygen that is detected by the  $\text{pO}_2$  optode. The amount of glucose will be proportional to the rate at which the oxygen is consumed.

### **Total Haemoglobin**

The measurement of total haemoglobin (Hb) and oxygen saturation ( $\text{SO}_2$ ) is based on the principle of optical reflectance spectrophotometry. A key component of the measurement system is a pink or reflective overcoat that lies on the top of the  $\text{pO}_2$  optode, which acts as a reflector for the photometric measurements as shown in Figure 105.3. The method uses three wavelengths in the red and near-infrared range to measure the two haemoglobin derivatives. Red and infrared light from one LED and two laser diodes is directed at whole, non-haemolysed blood that lies within the precisely defined part of the cassette over  $\text{pO}_2$  optode. The light is partially absorbed and reflected by the erythrocytes in proportion to the haemoglobin concentration. A portion of the reflected light exits the top of the cassette and is measured by the detector in the instrument. From a combination of readings at the two infrared wavelengths and the red wavelength, it is possible to obtain optimum measurements of the oxy and deoxyhaemoglobin.





**Figure 105.3**  $pO_2$  sensor that can also measure total Hb and  $SO_2$ .

The sum of these is equivalent to the total haemoglobin, and the proportion of oxyhaemoglobin as a percentage of the both oxy- and deoxyhaemoglobin is  $SO_2$ . The infrared wavelengths are selected for the haemoglobin measurement because they are largely independent of  $SO_2$ , that is, the predominate forms of adult and foetal haemoglobin absorb similarly within the 750–850 nm wavelength range. The red wavelength is used for the  $SO_2$  measurement because it is much more strongly absorbed by deoxyhaemoglobin than all other haemoglobins, and is also close to the isosbestic point for oxy- and carboxyhaemoglobin.

With the development of fibre optic based blood gas sensors, routine replacement of electrode membrane and maintenance have become history. Continuous self-monitoring provides clear and immediate information of instrument performance. The keyboard-based user interface provides advanced analytical performance and data processing capabilities.

## Specifications

### Operating parameters

*Sample type:* Heparinized whole blood, plasma/serum

*Sample input device:* Syringe, capillary, micro sampler

*Sample size:* 125  $\mu$ l

*Sample input:* Automatic aspiration

*Analysis time:* <2 minutes

*Type of measurement:* Optical fluorescence method (pH,  $pCO_2$ ,  $pO_2$ ,  $Na^+$ ,  $K^+$ ,  $Ca^{2+}$ ,  $Cl^-$ , Glu, urea, lactate) and reflectance method (tHb,  $SO_2$ )

### Typical range

*pH:* 6.6–7.8 pH units

*$pCO_2$ :* 10–200 mmHg

*$pO_2$ :* 10–700 mmHg

*$Na^+$  (sodium):* 100–180 mmol/l

*$K^+$  (potassium):* 0.8–10.0 mmol/l

*$Ca^{2+}$  (ionized calcium):* 0.2–3.0 mmol/l

$Cl^-$  (chloride): 50.0–160.0 mmol/l  
 Glu (glucose): 30–400 mg/dl, 1.7–22 mmol/l  
 BUN (urea): 2.8–112.0 mg/dl, 1–40 mmol/l  
 ctHb (total haemoglobin concentration): 5–25 g/dl  
 $SO_2$  (haemoglobin oxygen saturation): 60–100%  
 Lactate: 0.3–17.5 mmol/l

## Applications

Critical care analyser finds applications in intensive care units, operating room, emergency department, clinical laboratories, and point-of-care locations.

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## Cryostat

### Purpose

A cryostat is a device intended to maintain low temperatures of samples or devices mounted within them. The device is used in routine as well as research applications in biology, medicine, and industry. They are also used for rapid freezing and demanding needs of cryosectioning systems in the field of biomedical, neuroanatomical, and pharmaceutical research.

### Principle

A cryostat is nothing but advanced thermostat that is used to maintain extremely low cryogenic temperatures. Cryogenic is a system that operates at temperatures of 77 K (boiling point of nitrogen) and below, but usually systems operating below 4.2 K (boiling point of Helium) and above 1 K.

There are two methods of reaching low temperatures. These are by using liquid cryogens or using mechanical coolers. With *liquid cryogens*, evaporation of the liquid maintains the temperature at the boiling point and the cooling is attained in the following way. Heat is used in evaporating the liquid wherein it absorbs latent heat. It is then used in warming the gas from the boiling point to room temperature. The heat required to achieve this is given by the *enthalpy* change. The working of a liquid cryogen-based cryostat is similar to a Dewar flask, which has a two-layer container. Both the layers join at their necks, and the area between the two layers is kept at almost vacuum so as to avoid heat transfer by conduction or convection.

If an experiment requires cooling only to 77 K, liquid nitrogen is usually employed. However, if the system requires cooling down to 4 K, the cooling is done first by 77 K with liquid nitrogen and then by helium. This offers a cost-effective solution as liquid nitrogen is extremely cheap as compared with helium.

The *mechanical coolers* are mechanical refrigerators that comprise of a compressor and an expansion chamber inside the cryostat. They generate low temperature due to compression and expansion of gas. The helium gas is compressed at room temperature in the compressor and then transferred to the cryostat where it is expanded to produce cooling. There are two types of mechanical coolers, as follows:

- > *Gifford–McMahon (GM) coolers*
- > *Pulse tube refrigerators (PTRs)*

Both the systems use similar compression/expansion cycle, but PTR system does not have the moving regenerator found in GM cryocoolers. The GM cooler employs a piston in the expansion chamber, whereas a PTR uses acoustic pulses in the helium gas in place of a moving piston. The advantages of PTR include reduced vibration and reduced maintenance cost. No liquid cryogens are used in these coolers.

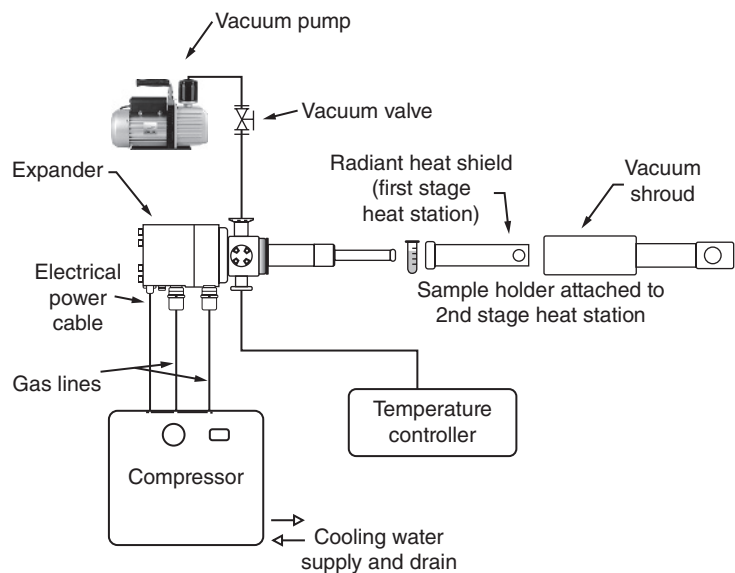
### **Types of Cooling Systems**

There are four main types of cooling systems that are used in cryostats: closed-cycle, continuous flow, bath, and multistage.

**Closed-Cycle Cryostats** Closed-cycle cryostats pump cryogenic vapour (cold helium) through a chamber. An external mechanical refrigerator extracts the warmer helium exhaust vapour, which is cooled and recycled. Closed circuit cryostats consume a relatively significant amount of power, but they do not need to be refilled with helium – making them suitable for continuous-duty applications for indefinite period. The device consists of a chamber through which cold helium vapour is pumped. Closed-cycle cryostats consume a relatively large amount of electrical power, but need not be refilled with helium, and can run continuously for an indefinite period. Objects can be cooled by attaching them to a metallic cold plate kept inside the vacuum chamber, which is in thermal contact with the helium vapour chamber.

Figure 106.1 shows the major components of the closed-cycle cryostat. They include the expander, compressor, vacuum shroud, and radiation shield. In addition, there is a temperature controller to measure and adjust the sample temperature, provision for cooling water for the compressor, and a vacuum pump for the sample space. The GM refrigeration cycle takes place in the expander. The expander is connected to a compressor by two gas lines, wherein one gas line supplies high pressure helium gas to the expander, and the other gas line returns low pressure helium gas from the expander. The compressor provides the required helium gas flow rate at the high and low pressure for the expander to achieve the desired refrigeration capacity. The cold end of the expander is surrounded by the vacuum shroud limiting the heat load on the expander, which may be caused by conduction and convection. The first stage of the expander actively cools the radiation shield, and the second stage is insulated from the room temperature thermal radiation emitted from the vacuum shroud.

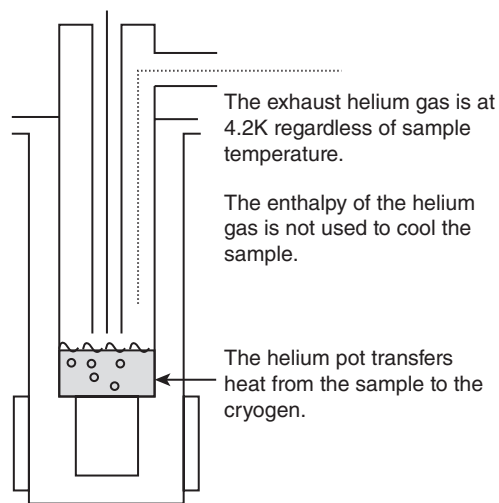
**Continuous Flow Cryostats** Continuous flow cryostats are cooled by liquid cryogens, typically liquid helium or nitrogen. As the cryogen boils within the cryostat, it is continuously replenished by a steady flow from the storage vessel. Temperature control of the sample within the cryostat is typically achieved by controlling the flow rate of



**Figure 106.1** Main components of a closed cycle cryostat.

cryogen into the cryostat along with a heating coil placed in a proportional-integral-derivative (PID) temperature control loop. These devices obviously expend large quantities of liquid cryogens when operating.

Continuous flow systems consist of a cold finger, radiation shield, sample holder, lightweight aluminium vacuum shroud, and high efficiency flexible cryogen transfer line. Figure 106.2 shows a simplified conventional helium flow cryostat. The liquid helium is contained in a reservoir similar to a copper cup over the sample mount. As the



**Figure 106.2** Schematic diagram of continuous flow cryostat.

helium boils and evaporates, only the latent heat of vaporization is used to cool the sample mount. The boil-off rate is minimized by shielding the bath with either cold helium vapour or vacuum shield with walls constructed from some super insulator material. The helium vapour that boils away from the bath very effectively cools thermal shields around the outside of the bath. There is no provision to capture the enthalpy of the gas, as it escapes from the cryostat at 4.2 K regardless of the sample temperature. The cooling power of the gas is wasted.

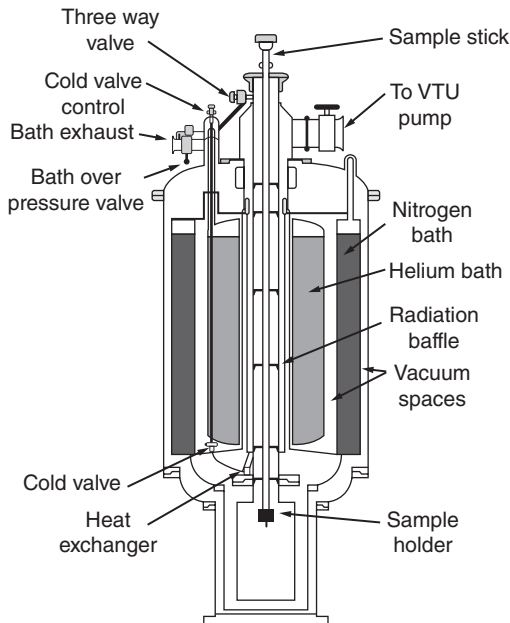
The Helitran<sup>®</sup> from M/s Advanced Research Center, USA, incorporates an extended surface heat exchanger, matrix heat exchanger, at the cold tip that provides efficient heat transfer between the helium and the sample mount. The liquid helium flows through this heat exchanger and as the latent heat of vaporization cools the sample mount, the liquid evaporates. The gas continues to flow through the heat exchanger and provides additional cooling to the sample mount. Coarse temperature control is maintained by adjusting the liquid He flow. Fine temperature control is maintained by means of a heater at the cryostat heat exchanger, the current to which is proportionally controlled by means of a rhodium sensor on the heat exchanger and a set point on the temperature controller in the device. If the flow is optimized, the helium gas will exit the matrix heat exchanger at a temperature equal to the sample temperature. A high efficiency superinsulated, vacuum-jacketed transfer line, equipped with evacuation and safety pressure relief valves, connects the cryostat head to a storage dewar.

Continuous flow cryostat systems provide fast cooling action, 15 minutes or less to 4.2 K with liquid helium cool down. Standard systems produce sample temperatures of 77–325 K (LN<sub>2</sub>) and 4.2–325 K (LHe) with precise temperature control capability.

**Bath Cryostats** Bath cryostats are similar in construction to vacuum flasks but are filled with liquid helium. Figure 106.3 shows a schematic diagram of a bath type cryostat. A cold plate is placed in thermal contact with the liquid helium bath. Bath cryostats contain large enough supplies of cryogens for a convenient period of operation. They are typically designed to give operating periods between up to about four months. However, the replenishment of liquid helium may be required as it boils away, depending on the volume and construction of the cryostat. The boil-off rate is minimized by shielding the bath with either cold helium vapour or vacuum shield with walls constructed from super insulator material. The liquid helium reservoirs are always shielded from room temperature radiation by a cooled shield. The helium vapour that boils away from the bath very effectively cools thermal shields around the outside of the bath. Liquid nitrogen bath cryostats (Dewar flasks) are made from DURAN borosilicate glass 3.3. They are used either as a single cryostat or as a liquid nitrogen cooling shield for liquid-helium cryostats.

**Multistage Cryostats** Multistage cryostats are used to achieve temperatures lower than liquid helium. This is done by adding additional cooling stages. Temperatures down to 1 K can be reached by attaching the cold plate to 1-K pot, which is a container of He-4 isotope, which is connected to vacuum pump. Temperatures down to 1 mK can be reached by employing dilution refrigerator or dry dilution refrigerator typically in addition to the main stage and 1 K pot. Temperatures below that can be reached using magnetic refrigeration.

**Peltier Effect Coolers** The devices based on Peltier effect for cooling depend on the thermoelectric principle. The Peltier elements are thermodynamically reversible and



**Figure 106.3** Schematic diagram of a bath type cryostat.

are low impedance devices that operate on high current DC supply. With a single stage Peltier cooler, a temperature of  $-40^{\circ}\text{C}$  can be attained. Several stages are required to achieve lower temperatures. The advantage is their small size and vibration-free operation. However, they have small cooling range and limited cooling power.

Each type of cryostat has advantages and disadvantages and is selected based on the application. When the cryostat has to be very large, for example, to contain a superconducting magnet, a 'bath' cryostat is preferred. A suitable continuous flow insert can be fitted within the bath cryostat to achieve the sample temperature range required for a particular experiment. However, if the cryostat must be fitted into a small space or has to be thermally cycled rapidly and often, a 'continuous flow' cryostat is preferred.

## Specifications

*Temperature range:*  $<2-325\text{ K}$

*Initial cool down time:* 15 minutes

*Nominal temperature stability:* 50 mK or less

*Cryogen:* Liquid nitrogen and liquid helium

## Applications

The applications of cryostats include infrared detector assemblies, thermal imaging systems, and optoelectronic instrumentation. In magnetic resonance imaging (MRI) machines, cryostats maintain the magnet's superconductivity. In histology, they are used to cut or slice tissue under cryogenic conditions.

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## Cryosurgical Unit

### Purpose

A cryosurgical unit is a device that employs extreme cold or freezing temperature in surgery to treat diseased or abnormal tissue by involving surgical application of cryoablation technique. Cryosurgery has been historically used to treat a number of diseases and disorders, especially a variety of benign and malignant skin conditions. Other areas where cryosurgery has been found useful include oral surgery, gynaecology, urology, otolaryngology, etc. Ophthalmic cryosurgery has been used for cataract removal in some countries, but its use has mostly decreased over the past decade.

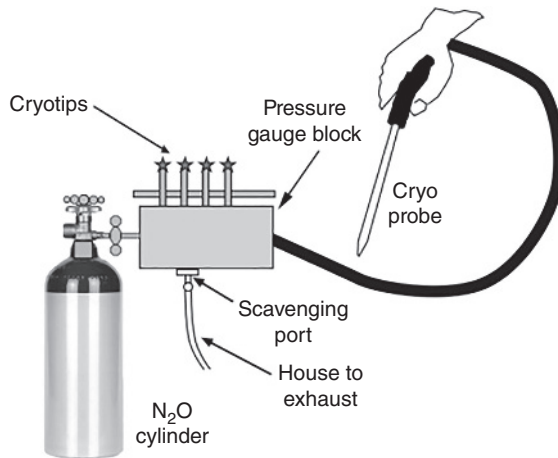
### Principle

Cryosurgery, also referred to as cryoablation, is a surgical technique that employs extreme freezing temperatures to destroy diseased tissue due to the destructive force of freezing temperatures on cells. Cryosurgery units apply a cryogen to withdraw heat from target tissue either through direct application or indirectly through contact with a cryogen-cooled probe. When the temperature of the cells is cooled below a certain level, ice crystals begin to form inside the cells and, because of their lower density, eventually tear apart those cells. Further damage to malignant growth will result once the blood vessels supplying the affected tissue begin to freeze and the related deleterious effects and vascular stasis are caused by microcirculatory failure. The main advantage of cryosurgery is that cell destruction is localized, which minimizes damage to surrounding healthy tissue. The cryosurgery is conducted by means of a cryoprobe by placing its continuously cooled tip either on or into the tissue to be treated.

### Freezing Methods

Two main methods are used to cool the cryoprobe. It is either based on the expansion of a compressed gas through a nozzle, causing cooling by the Joule–Thomson effect, or the use of cryogenic liquids such as liquid nitrogen. The most common method is by the use of liquid nitrogen as the cooling solution. This  $-196^{\circ}\text{C}$  ( $-321^{\circ}\text{F}$ ) cold liquid may be sprayed on the diseased tissue, circulated through a tube called a cryoprobe, or simply dabbed on with a cotton or foam swab. Carbon dioxide ( $-78.5^{\circ}\text{C}$ ) is also commonly used as a spray and is used to treat a variety of benign spots. Less frequently, doctors use carbon dioxide ‘snow’ formed into a cylinder or mixed with acetone to form a slush that is applied directly to the treated tissue. Recently, technology has been developed to use argon gas ( $-187^{\circ}\text{C}$ ) to drive ice formation again based on the Joule–Thomson effect. This allows physicians excellent control of the ice, and minimizing complications using ultra-thin 17 gauge cryoneedles. In addition, a mixture of dimethyl ether and propane is used in some ‘freeze spray’ preparations.





**Figure 107.1** Schematic diagram of a cryosurgical system using  $N_2O$  as a cooling agent.

Compressed gases such as nitrous oxide ( $N_2O$ ) are also often used to obtain the cold temperatures necessary for cryosurgery. These systems are designed to allow the gas to expand through a valve inside the metal tip of the cryosurgical probe, causing the tip to reach extremely low temperatures. Figure 107.1 shows a simple arrangement based on the use of compressed nitrous oxide. The exhaust gas from the probe must be properly vented so as to maintain  $N_2O$  concentrations in air during a cryosurgical procedure. Most modern  $N_2O$  cryosurgical units are therefore equipped with a scavenging port where the gas is exhausted. A plastic tubing is connected directly to this port, with the other end connected to a discharge location. It should be ensured that the discharge location is not an area where people are normally present or in close proximity to an outside air intake or window where  $N_2O$  could re-enter the building. Alternatively, if scavenging is not possible, carbon dioxide ( $CO_2$ ) can be used as a cryogenic gas on many of the cryosurgical units.  $CO_2$  is considered less hazardous and has a much higher airborne exposure limit than  $N_2O$ . However, since it does not cool as low as  $N_2O$  ( $-79^\circ C$  for  $CO_2$  versus  $-89^\circ C$  for  $N_2O$ ), it is likely to require longer freeze times.

The cryosurgery units employ either a closed or an open system. In a closed system unit, the cryogen flows through an insulated shaft in the hollow probe, cools the tip, and is exhausted back through the probe. Open-system units use cryogen directly to the target tissue. The units based on the use of  $N_2O$  or  $CO_2$  are not usually considered suitable for use as open systems as cryogen 'snow' would build up on the target tissue and result in insulation of the lesion from the cryogen spray. Liquid nitrogen based systems, however, can be either open or closed systems.

### Cryosurgical Systems

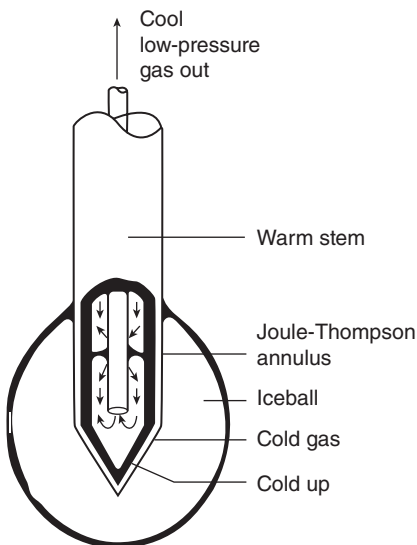
A number of companies have developed cryogen delivery systems for cryosurgery. Most are based on the use of liquid nitrogen, although some employ the use of proprietary mixtures of gases that combine to form the cryogen. These devices are available as consoles or as stand-alone or handheld units. The *console* based units typically contain

cryogen gas cylinders, pressure regulators, indicators, and operating controls. They are usually battery powered and can be equipped with a probe-tip fibre optic light source for transillumination of tissue. The *stand-alone* units consist of a tank, a pressure regulator, and a probe attached by tubing to the tank. The *handheld units* are lightweight, portable units that typically use liquid nitrogen as the cryogen and are either reusable or disposable, with individual gas cartridges.

Cryosurgery procedure is monitored by two methods: (i) *Local monitoring*: This is done by thermometry or impedancemetry. The thermometry makes use of thermocouples that are inserted inside the tissue to be frozen, and direct measurement of local temperature can be made. The impedancemetry consists in using electrode needles that are placed inside the target tissue to detect freezing-induced changes in local impedance. Both the techniques are invasive and give only localized information. (ii) *Imaging monitoring technique*: Here, the freezing process is monitored with the help of medical imaging by ultrasound or magnetic resonance imaging (MRI) to adjust the cooling power of the individual cryoprobe so as to maximize the cell death and minimize the destruction of surrounding normal tissue or organ. Freezing interfaces can be conveniently monitored with conventional ultrasound because there is a large difference in acoustic impedance between ice and water. Ice essentially reflects all the acoustic energy, therefore entire freezing area looks dark. MRI produces a precise three-dimensional image of freezing interface; therefore it can be used to calculate the temperature distribution in the frozen region.

### Cryoprobes

Cryosurgical units consist of a handheld unit with a probe, known as the cryoprobe, and a switch to control the temperature of the probe. At the distal end of the probe, there is a 'cryotip', which can be placed in contact with the lesion. Figure 107.2 shows the



**Figure 107.2** Constructional details of a cryoprobe based on Joule–Thomson effect.

constructional details of a cryoprobe, which is a hollow cannula that contains a smaller inner cannula. A pressurized cryogen gas at approximately 800 psi travels down the outer cannula and is released into the distal cannula tip. The rapid expansion of the gas at the cannula tip extracts surrounding heat, because of the Joule–Thompson effect. As a result of the temperature drop, an ice ball forms at the tip of the probe. The gas is then vented through the inner cannula. In this way, the closed-end cannulas ensure that no gas is injected into the body. Spray type cryoprobe are considered more efficient than traditional contact type probes. Most cryoprobe have an integrated thermistor to measure tip temperature. The size and length of the probe vary, depending on the intended use. Cryoprobe may be either reusable or disposable.

### Console

In the console-based devices, the cryoprobe is connected to the console and cryogen tank by a long flexible tube. The reusable probe and tubing can be steam or gas sterilized. The console systems usually include a sensory and motor stimulation component that allows for more precise sensory nerve localization in the awake patient, as well as confirmation of intended or unintended motor stimulation. The probes for these systems are usually large (12–16 gauge), though smaller systems (20–25 gauge) have also been developed.

The efficiency of the cryoprobe is determined by the gas flow in the probe. The volume of gas flowing through the probe is usually measured by the flow meter. Flow is the most important parameter that indicates if the cryoprobe is in good condition. If the flow value is small, the cryoprobe may be partly closed with dirt or moisture or cryogen pressure in the cylinder is too low.

After the cylinder valve is opened, internal circuit of the apparatus is filled with gas under pressure, which is also monitored with a pressure gauge. In addition, a timer mechanism is used to measure the procedure duration in the range from 0 to 10 minutes. The device includes provision for automatic cleaning of the probe that can be performed using foot switch or touch panel so that the site of a lesion remains sterile. Blocking of the cooling gas feed within the cryoprobe may occur during freezing, which may prevent the probe cooling to the required temperatures. The use of medical grade gases greatly reduces this risk.

The modern machines with single use and reusable cryoprobe designed for specific applications are fully automatic in which the machine autoconfigures to probe characteristics based on the optimal operating parameters. Temperature of the probe, pressure, gas flow, and time of the treatment are displayed during freezing. They employ open type cryoprobe with fluent, adjustable freezing power that is more efficient in comparison with traditional contact probes.

## Specifications

- Cooling medium
  - $\text{CO}_2$  – 78°C or  $\text{N}_2\text{O}$  – 89°C
  - *Maximum pressure:* 70 bars ( $\text{CO}_2$ ) and 55 bars ( $\text{N}_2\text{O}$ )
  - *Working pressure:* 48–65 bars ( $\text{CO}_2$ ), 38–53 bars ( $\text{N}_2\text{O}$ )

- Voice information system about key figures during procedure
- Automatic control of flow rate parameters, gas pressure, and freezing temperature

## Applications

Cryosurgery is an accepted treatment modality within the fields of dermatology, oral surgery, gynaecology, urology, otolaryngology, proctology, and ophthalmology.

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## Cryotherapy Machine

### Purpose

Cryotherapy machine is a device that employs extremely cold temperatures to freeze and destroy abnormal skin cells that require removal. Cryotherapy also offers a pain treatment modality that utilizes localized freezing temperatures to treat abnormal skin cells in dermatology and cosmetics for the elimination of aging and pigmentation spots, as well as the elimination of warts, bulging acne, etc. Cryotherapy is widely used to relieve muscle pain, sprains, and swelling either via soft tissue damage or via postoperative swelling.

### Principle

Cryotherapy is the local or general use of low temperatures in providing medical therapy and to treat a variety of benign and malignant tissue damage, generally called lesions. The treatment involves a range of techniques from the ordinary technique of applying ice packs or immersion in ice baths to the use of cold chambers in case of whole body or partial body cryotherapy and or face masks or body cuffs with controlled temperature, often called Hilotherm.

Cryotherapy involves the use of imaging guidance, a needle-like applicator called a cryoprobe, and liquid nitrogen or argon gas to create intense cold to freeze and destroy diseased tissue. In modern devices, the cryoprobe is inserted into the tissue next to the affected nerve. The temperature of the probe drops to then effectively freeze the nerve. The freezing inactivates the nerve and, as a result, painful nerve irritation is relieved.

The use of cryotherapy for cosmetic applications has opened up a wide new field for safe and reliable treatment, known as CryoCosmetics. Until recently, methods generally used involved cooling the applicator to a very low temperature using various cryogens in order to treat patients. They had a high operating cost and did not give reproducible results. It was also observed that at excessive dosages of cold, operating at temperatures as low as  $-190^{\circ}$  could result in scarring the tissue. The new Cryocare system from M/s gbo Medizintechnik AG, Germany, is a specially designed apparatus for such applications in

which the cold temperature is generated electronically by a microprocessor-driven high-capacity Peltier element and kept at a constant level of  $-32^{\circ}\text{C}$  on the applicator tip.

The device works without a cooling agent, and without fluorocarbon and supply of water. The generated waste heat is dissipated through an internal cooling circuit. The main advantages of this are the reproducibility of the treatment results and the patient safety. The device operates with a temperature of  $-32^{\circ}\text{C}$ , which is considerably more moderate. The treatment time is just 8–15 seconds and is considerably safe with regard to dosing. The tip of the cryo pistol is the most frequently used applicator for many indications. Nevertheless, spread and form of the skin appearance may also require other applicators. The device is usually provided with five applicator types differing in form and size. Individual applicators have been designed for rope-shaped punctiform and rectangular forms of skin appearances.

### ***Whole Body Cryotherapy***

Whole body cryotherapy consists in exposing the body to vapours at ultra-low temperatures ranging from  $-200^{\circ}\text{F}$  to  $-250^{\circ}\text{F}$ . The persons who are to be given whole body cryotherapy treatment are enclosed in relatively confined spaces, typically for two to four minutes. The person stands alone in an individual-size can-like enclosure that is open at the top. A person's torso and legs are enclosed in the device and exposed to low temperatures, while the head remains above the enclosure at room temperature. Alternately, several people sit or stand in a totally enclosed chamber for two to four minutes. The entire body including the head is subject to freezing temperatures, generated by liquid nitrogen. Once the person is inside the chamber, several short bursts of nitrogen gas are delivered every 30 seconds.

Some systems operate by using refrigerated cold air, which circulates in a circuit. During these exposures, individuals wear minimal clothing. Partial body cryotherapy devices are cylindrical chambers, typically having an aperture at the top, with the patient's head remaining outside and not subjected to the cold stimulus as shown in Figure 108.1. Some units are equipped with an electric lift that is used to adjust a patient's height in the chamber so that the body is submerged in the hypercooled air up to the neck, while the head remains above. This improves the patient's overall comfort.

Cryotherapy has been used as an adjunct treatment for reducing symptoms of pain and inflammation associated with a number of chronic conditions. Furthermore, cryotherapy significantly improves recovery time for athletes, treats skin conditions, and aids in weight loss. However, there are potential hazards that include asphyxiation, especially when liquid nitrogen is used for cooling. Moreover, subjects may run the risk of frostbite, burns, and eye injury from the extreme temperatures. As a matter of safety, the Cryo Chamber is provided with a non-locking pivoting door that can be opened at any time. The unit has a heated ventilating system to minimize moisture residues and to vent out used nitrogen gasiform air.

## **Specifications**

### *Cosmetic unit*

*Operating temperature:*  $-32^{\circ}\text{C}$  to  $-60^{\circ}\text{C}$

*Timer:* 0–99 seconds

*Air flow:* 350–1500 l/min



**Figure 108.1** Whole body Cryo Chamber in use.

*Whole body cryotherapy chamber*

*Temperature range:*  $-166^{\circ}\text{F}$  to  $-320^{\circ}\text{F}$

*Technology:* Continuous flow for stable temperature

*Session time:* 2–3 minutes

*Nitrogen usage during session:* Average of 6l/session

Electric lift with push button control

## Applications

Cryotherapy devices are used in medical practices, clinics, and spas especially for CryoCosmetic applications. They are also used in the sports sector, for the treatment of rheumatic diseases and several other sports connected injuries.

## 109

## Cutaneous Blood Flow Monitor: Laser Doppler

### Purpose

Laser Doppler cutaneous blood flow monitor is a device that is used to measure the total local microcirculatory blood perfusion in capillaries, arterioles, venules, and shunting vessels. This noninvasive technique of measuring microvascular blood flow in tissue often provides a good indicator of peripheral vascular disease. The device is

found useful in many situations in routine clinical medicine where such measurements of the blood flow are considered important.

## Principle

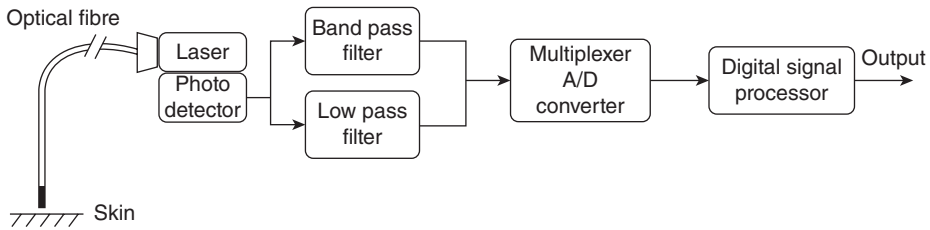
The cutaneous blood flow monitor based on the laser Doppler technique is the most common technique for measuring skin blood flow. Like ultrasound, it depends on Doppler effect, i.e. the change in frequency between an applied laser beam and the returning beam of light to determine the speed of blood cells in the sample volume. When a laser beam is directed towards the tissue under study, absorption and scattering of laser light take place. Laser light scattered by movable structures, such as red cells, is shifted in frequency due to the Doppler effect, while there is no shift in frequency of the light scattered in non-moving soft tissue. The mixing of these two different light frequencies produces a beat frequency. This beat frequency can be detected by the laser Doppler machine and then analysed to provide a skin blood flow measurement. The blood cells move through the capillaries at about 1 mm/s, which in tissue is approximately  $2 \times 10^{11}$  mm/s. The effective radiation penetration depth is approximately 1 mm in soft tissue, and scattering and absorption take place mostly in the papilla region and the underlying corium – two dermal layers containing the capillary network of the skin.

There are two types of laser Doppler flowmetry devices. One type is a single-point laser probe, which evaluates the microvascular blood flow at one point of the skin. The other type is a real-time laser scanner, which evaluates the blood flow in an area of skin. A wide range of probes designed to measure flow from almost any type of tissue is available. These include skin probes, needle probes, and endoscopic probes. The measuring depth depends on tissue properties such as the structure and density of the capillary beds, pigmentation, oxygenation, etc. It also depends on the wavelength of the laser light and on the distance between the sending and receiving fibres in the laser Doppler probe. In normal skin, a probe with standard fibre separation (0.25 mm) and a 780 nm wavelength laser, the measuring depth will be of the order of 0.5–1 mm.

In principle, light from a low power laser is coupled into a quartz fibre and transmitted to the skin. The light is reflected from both the non-moving tissues (reference beam) and moving red blood cells (Doppler-shifted beam). The two beams are received by a plastic fibre and transmitted back to a photodiode where optical heterodyning takes place. The heterodyned output signal that is proportional to the Doppler shift frequency is amplified, and both RMS and DC values are calculated. The RMS value is weighted against the back-scattered light intensity using the measured DC value as an index of total received power. This gives a measure of the output flow velocity.

As shown in Figure 109.1 (laser Doppler imaging), red or near-infrared light from a low power laser (He–Ne laser operating at 632.8 nm or laser diode at 785 nm wavelength) is directed via an optical fibre using a converging lens to the tissue, which results in an increased power density at the skin surface and thus enables the detection of flow in the more deeply seated veins and arteries. The light scattered back from the tissue is coupled to the photodetector through a laser line filter. The photodetector converts the





**Figure 109.1** Block diagram of laser Doppler cutaneous blood flow monitor.

optical signal into an electrical signal. The photodetector functions as a square law device and gives out current, which is proportional to the intensity of the incident light and, therefore, to the frequency of beating of the shifted and unshifted signals. The light falling on the photodetector is an optically mixed signal involving a Doppler-shifted signal back scattered from the moving red blood cells with the 'reference' signal reflected from the non-moving skin surface. The diode is connected in a configuration so that it gives wideband performance (DC–100 kHz).

A bandpass filter is used to remove noise outside the bandwidth and extract blood flow related AC components. A low-pass filter is also connected to the output of the photodetector and is used to extract DC components proportional to the intensity of the collected light. Outputs of the bandpass and low-pass filter are converted into digital form by a multiplexer and A/D. Spectral analysis of the digitized Doppler signal, blood flow calculation, and movement artefact detection and removal is performed by a digital signal processor (DSP) device in real time. It may be noted that the instrument measures an averaged red blood cell speed and not true flow, as both the cross-sectional area of flow and the angle the incident light beam makes with each capillary are not precisely known.

Figure 109.2 shows a typical laser Doppler blood flowmeter from M/s Moor Instruments, UK.

The laser probe can be designed to suit different applications. Its main part of the probe, i.e. the core, is a thin piece of stainless steel tubing (diameter 1.5 mm and length



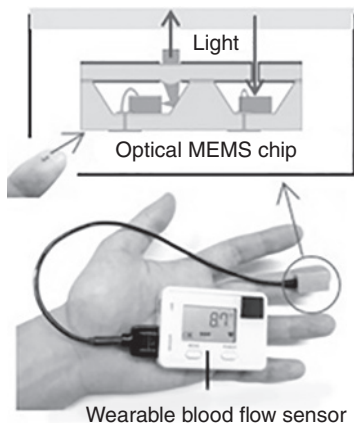
**Figure 109.2** Cutaneous blood flow laser Doppler monitor. MEMS, micro-electro-mechanical systems. Source: Reproduced with permission of M/s Moor Instruments, UK.

10–80 mm), in which the terminating ends of the two fibres – one efferent and one afferent – are moulded together. For easier handling, the core can be inserted into a tight fitting plastic sleeve. It can also be inserted into a thermostat head where the core-end forms the centre of a 15 mm diameter contact surface, the temperature of which can be set from 25 to 40°C. Evaluation of the laser Doppler flowmeter has shown that a linear relationship exists between the flowmeter response and the flux of red cells, with red cell velocities and volume fractions within the normal physiologic range of the microcirculatory network of the skin. It has also been found that different degrees of oxygenation influenced the Doppler signal only to a minor extent.

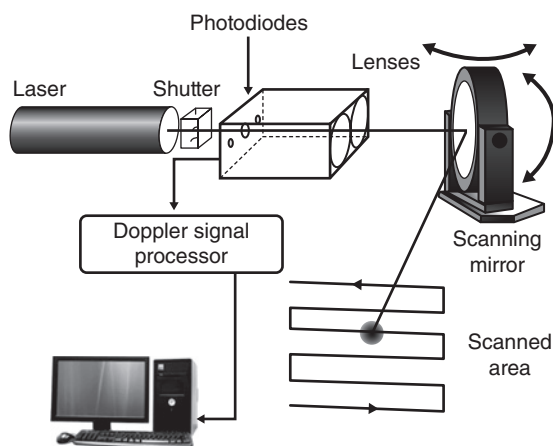
The laser diode, photodiode, and optical waveguide can be integrated onto a single chip, and the entire laser blood flowmeter can be made into a tiny device that can be worn on the wrist as illustrated in Figure 109.3. The sensor head, which is placed in contact with a fingertip, contains optical elements that are precisely mounted on a chip with 1 µm accuracy using advanced micromachining and surface mounting technologies. Measurement data can be sent wirelessly and displayed or recorded.

Laser Doppler flowmetry being a noninvasive technique offers several clinical and research advantages, i.e. high sensitivity, no injectable traces, and ease of use. However, because the technique samples from a very discrete volume, long-term assessments can be difficult unless experimental care is taken, or a laser Doppler imager used to sample spatial (as well as temporal) variation.

Single-point dynamic measurements can also be made with the laser beam directed towards any position within the image area. A block diagram of such a system from M/s Moor Instruments, UK, is shown in Figure 109.4. The scanning is done by laser beam in a raster pattern over skin or other tissue surfaces. Moving blood in the microvasculature causes a Doppler shift, which is processed to build up a colour-coded image of blood flow. The measurement is non-contact and can register chronic changes or measure repetitively in quick succession. Perfusion of each image position is recorded at resolutions of 0.2–2.0 cm for further analysis.



**Figure 109.3** Wearable laser Doppler blood flow monitor. *Source:* Iwasaki, W., Nogami, H., Takeuchi, S. et al. (2015). Detection of site-specific blood flow variation in humans during running by a wearable laser Doppler flowmeter. *Sensors* 15: 25507.



**Figure 109.4** Principle of single-point measurement by scanning a low power laser beam across the tissue. *Source:* Reproduced with permission of M/s Moor Instruments, UK.

## Specifications

*Laser:* Diode

*Wavelength:* 780 nm

*Energy output:* 2 mW

*Angular spread of laser light at tissue:* 26°

*Tissue measurement area:* Approximately 1 mm<sup>2</sup>

## Applications

Laser Doppler flowmetry is a widely used technique currently used for assessing blood flow in the skin microcirculation as it has several clinical applications underlying pathologic skin disorders.

## 110

## CyberKnife

### Purpose

The CyberKnife is a robotic radiosurgery system that offers a noninvasive alternative to surgery for the treatment of both cancerous and non-cancerous tumours anywhere in the body. The treatment involves delivery of beams of high-dose radiation to tumours with pinpoint submillimetre accuracy from virtually any direction, thus minimizing damage to the surrounding healthy tissue and nearby critical structures. Contrary to its

name, the CyberKnife treatment involves no cutting. It is a pain-free, non-surgical option for patients suffering from inoperable or surgically complex tumours.

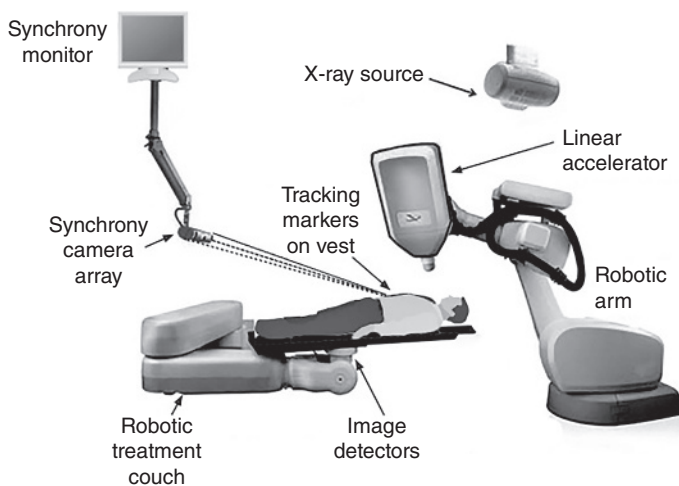
## Principle

The low tolerance of radiosensitive structures such as the optic nerve or spinal cord to conventional external beam radiotherapy treatment limits the treatment dose to a level that is far below the optimal therapeutic dose. The CyberKnife provides the appropriate radiation dose that is confined precisely to the treatment volume and at the same time minimizes the risk of spinal cord injury.

The CyberKnife is an image-guided stereotactic radiotherapy treatment, in which high doses of focused radiation beams from a linear accelerator (LINAC) are delivered using image-guided robotics from multiple locations outside of the body to destroy a tumour or lesion within the body. This flexibility of the robotic arm allows for treatment of areas of the body that cannot be treated by other radiosurgery techniques. The CyberKnife uses real-time X-rays to establish the position of the lesion during treatment and then dynamically brings the radiation beam into alignment with the observed position of the treatment target. Each beam is aimed independently – without a fixed isocentre. When the target moves, the process detects the change and corrects the beam pointing in near real time. Figure 110.1 shows a schematic diagram of the CyberKnife system, which consists of the following subsystems.

### Linear Accelerator

The LINAC is that part of the CyberKnife that delivers beams of high energy radiation to the tumour with submillimetre accuracy. The LINAC structure is mounted on a robotic arm. Generally, the LINAC produces 6 MeV X-ray radiation. The LINAC has a



**Figure 110.1** Essential parts of the CyberKnife. Source: <http://www.multicare.org/files/library/70e03625b5b85f9d.png> – Online (accessed 7 November 2016).

compact design that does not require a bending magnet. The LINAC uses an X-band cavity magnetron and a standing wave, side-coupled accelerating waveguide, to produce a beam with a dose rate of 1000 cGy/min. There is no beam flattening filter. Secondary collimation is achieved using 12 fixed circular collimators with diameters ranging from 0.5 to 6 cm. The radiation beam is collimated using fixed tungsten collimator, which produces circular radiation fields, with sizes varying from 5 to 60 mm. Variable aperture collimators are also available.

### ***Robotic Manipulator***

The radiosurgery treatment delivery device is a frameless robotic system. The LINAC is mounted on a robotic manipulator that has a position repeatability of better than 0.12 mm and has 6° of freedom. This allows it to position the LINAC within a large three-dimensional (3D) workspace around the patient with high precision. The high precision robotic manipulator positions the LINAC in almost any direction providing extremely accurate radiation delivery. Mounting the radiation source on the robot allows near complete freedom to deliver radiation from many different directions without the need to move both the patient and source. With a LINAC mounted on the flexible robotic arm, it is possible to select from thousands of different angles from which to deliver radiation treatments. Image acquisition, target localization, and alignment corrections are checked repeatedly and continually during treatment delivery, typically every 30–60 seconds. The robotic manipulator compensates for changes in target position based on the corrections obtained from the most recently acquired image pair. It orients itself during treatment by adjusting the beam position and orientation rather than by moving the patient. The purpose is to adjust the beam aim to the target rather than bringing the target in line with the beam.

### ***X-Ray***

During a CyberKnife treatment, low energy X-ray images are constantly taken to track the tumour position and to adjust the position of the LINAC with a view to spare healthy tissue surrounding the tumour. Near real-time image allows for patient movement tracking within 1 mm spatial accuracy. It helps establishing the position of the lesion during treatment and then dynamically bringing the radiation beam into alignment with the observed position of the treatment target. Two diagnostic X-ray sources are mounted to the ceiling that illuminates two X-ray detectors by projecting square X-ray fields at 45° from vertical. In the point where the central axes of these beams intersect, the X-ray field size is approximately 15 cm × 15 cm. The flat panel X-ray detectors are mounted flush with the floor. The CyberKnife aims each beam independently, without a fixed isocentre. If the target moves, the process detects the change and corrects the beam pointing in near real time.

### ***Floor Image Detectors***

The detectors consist of cesium-iodide scintillator deposited directly on amorphous silicon photodiodes that generate high resolution digital images having 1024 × 1024 pixels with 16-bit resolution. They are floor mounted and capture high resolution anatomical images from the X-ray throughout the treatment. These live images are continually

compared with previous images to determine real-time patient positioning and target location. Based on this information, the robotic manipulator instantly adjusts for any detected movement. The imaging system allows the CyberKnife to deliver radiation with an accuracy of 0.5 mm. The use of image guided technique is referred to as 6D because corrections are made for the three translational motions (X, Y, and Z) and three rotational motions. The X-ray sources and detectors are rigidly fixed, and their projection geometry is calibrated and known in the treatment room coordinate system.

### ***Synchrony***

The CyberKnife System incorporates a synchrony system that is utilized primarily for tumours that are in motion while being treated, such as lung tumours. The Synchrony Systems creates a correlation model between the patient's breathing pattern that is monitored in real time and the precise location of the target from the imaging system at various points in the respiration cycle. The Synchrony Systems uses a combination of surgically placed internal fiducials and light-emitting optical fibres (markers) mounted on the patient skin. A computer algorithm creates a correlation model that represents how the internal fiducial markers are moving compared with the external markers. The system automatically determines the best correlation model for the treatment, which minimizes overall correlation error. The light from the markers can be tracked continuously using a charge coupled device (CCD) camera and is placed so that their motion is correlated with the motion of tumour.

### ***Patient Table***

The CyberKnife has a special patient treatment couch that is mounted on a second robotic arm. This positioning system is called RoboCouch, which has six-axes movement. During treatment with the CyberKnife, the RoboCouch moves the patient slightly to allow the CyberKnife the best angle to treat the tumour. The patient table has 6 degrees of freedom (five rotational axes and one linear axis) that provides the capability for significantly improving patient positioning options for treatment. During patient set-up, the table is adjusted to align the patient with the treatment plan. During the delivery of the treatment, the system automatically corrects the LINAC position for any calculated offsets within a specified tolerance. The table is available with a flat carbon fibre couch top.

### ***Software***

The working of the CyberKnife System depends upon sophisticated software and advanced imaging to track tumour and patient movement and adjust the beams of high-dose radiation for treatment with a high degree of accuracy. Treatment planning starts with acquiring one or more 3D images from volumetric computed tomography (CT) images that allows visualization of the target volume and nearby organs at risk. The 3D images are then transferred to the Treatment Planning System. The imaging software tracks and continually adjusts treatment for any movement of the patient or tumour. Because of this precision tracking ability, the CyberKnife System eliminates the need for patients to have stabilizing frames bolted to their head or limit their breathing during treatment to minimize movement of the tumour. The robotic manipulator is programmed to move in a fixed and

predetermined workspace. The treatment paths adopted by the robotic manipulator are dependent on the location of the target and patient anatomy being treated.

### ***Treatment Procedure***

Prior to treatment with the CyberKnife, the patient undergoes scanning procedures to determine the size, shape, and location of the tumour. The imaging is usually done with a standard high resolution CT scan, or in certain cases, magnetic resonance imaging (MRI), angiography, or positron emission tomography (PET) may also be used. The image data is then digitally transferred to CyberKnife's treatment planning workstation, where the treating physician identifies the exact size, shape, and location of the tumour. This is followed by generation of a treatment plan using the CyberKnife software to provide the desired radiation doses to the identified tumour location while avoiding damage to the surrounding healthy tissue. During the procedure, the patient lies comfortably on the treatment table, which automatically positions the patient. The treatment generally lasts between 30 and 60 minutes and is typically completed in one to five visits.

The CyberKnife gives maximum flexibility in its use to treat any lesion in any part of the body noninvasively. However, it also has limitations. One of the major limitations is the prolonged treatment time, though this does not alter the accuracy because of repeated verifications before each beam delivery.

## **Specifications**

### *X-ray generator*

*Radiographic kVp range:* 40–150  $\pm$  (5% + 1 kVp)

*mA range:* 0.1–640 mAs

### *X-ray detector*

*Detector:* Amorphous silicon with total area – 40  $\times$  40 cm<sup>2</sup>

*Number of pixels:* 1024  $\times$  1024

### *Linear accelerator*

*X-ray energy:* 6 MV

*Depth of maximum dose:* 15 mm  $\pm$  2 mm

*Dose rate:* 1000 MU/min  $\pm$  10%

*Source to axis (SAD) distance:* 800 mm

### *Robot*

6-axis robotic manipulator

*Maximum reach:* 2500 mm (98 in.)

### *Monitor*

*Resolution:* 1920  $\times$  1200

## **Applications**

The CyberKnife Robotic Radiosurgery System is used for the treatment of both cancerous and non-cancerous tumours anywhere in the body, including the prostate, lung, brain, spine, liver, pancreas, and kidney.



## 111

## Cystoscope

### Purpose

A cystoscope is a medical device that allows a surgeon to visually examine the body organs and passages of the urinary system for diagnosis and treat of abnormal medical conditions. They are particularly used to diagnose, monitor, and treat problems affecting the bladder and urethra. Cystoscopy is one of the most commonly performed procedures in the urology departments and is an invaluable tool in diagnosing lower urinary tract pathology. With a large variety of accessories, many lesions can be treated with the help of a cystoscope.

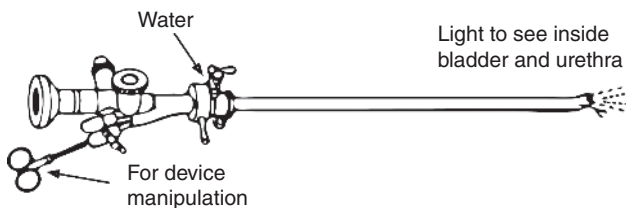
### Principle

Cystoscopy is a procedure that allows the doctor to examine the lining of the bladder and the tube (urethra) that carries urine out of the body. The procedure is carried out by an instrument called 'cystoscope', which is a long, thin, optical instrument having lenses like a telescope or microscope with an eyepiece at one end, a rigid or flexible tube in the middle, and a tiny lens and light at the other end of the tube. The lenses allow the physician to focus on the inner surfaces of the urinary tract. By looking through the cystoscope, the urologist can see detailed images of the urethra and bladder, which are part of the urinary tract. Magnified images from the camera can also be displayed on a monitor screen for viewing.

There are two main types of cystoscopes: rigid and flexible. They differ in the flexibility of the instrument in reaching the area of interest.

#### *Rigid Cystoscope*

A rigid cystoscope as shown in Figure 111.1 is a thin, solid, straight telescope as thin as a pencil. They range from paediatric to adult sizes, with diameters approximately from 6 to 9 mm. It is composed of three parts: telescope, bridge, and sheath. The *telescope* transmits the light into the urinary bladder and the image to the urologist. Telescopes are complex precision optical systems and contain multiple finely ground optical lenses



**Figure 111.1** Parts of a rigid cystoscope. Water can be poured down side channels to fill and flush the bladder. Also, various devices can be passed down the side channels. These can be manipulated by the doctor to take out specimens.

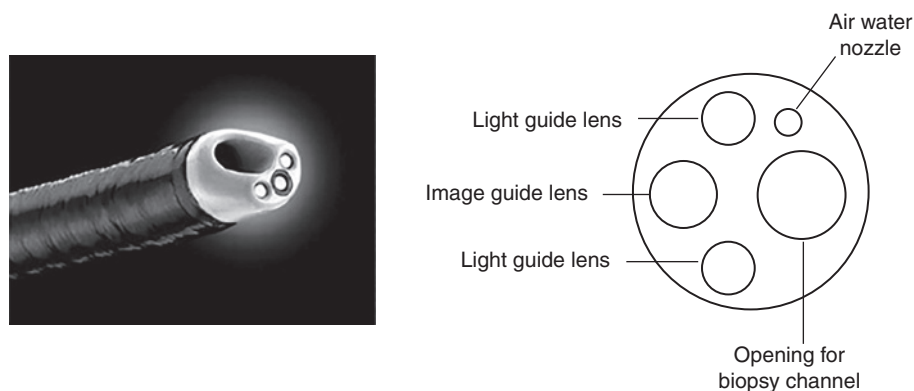
that transmit the image from the distal end inside the bladder or urethra to the eyepiece used by the urologist to view internal structures. Additional rod-shaped elements (i.e. field lenses) are located between each pair of lenses. Properly spaced throughout the length of the telescope, the lenses provide undistorted and clear vision at the desired angle and with some magnification. All telescopes are made of stainless steel.

The telescope lens couples into the light source with a fibre optic light bundle connected to the scope light source generator and provides light down the shaft of the telescope for visualization. The eyepiece can be viewed with the bare eye or attached to a camera. The camera transmits the magnified image to a monitor where still images or live video can be recorded. The telescope lens contains a rod, and mirror system is quite fragile and prone to damage if not handled with care. The telescope is designed to allow different viewing angles (e.g. 0°, 12°, 25°, 30°, 70°, or 120°), each with its own viewing capabilities and indications. The 0° and 12° devices angle downward. This helps to visualize the whole bladder.

The *sheath and obturator* are those parts of the cystoscope that are inserted through the urethra and into the bladder cavity. The hollow sheath, through which the urologic endoscope passes, may be concave, convex, or straight in configuration at the distal end. The other end has a stopcock attachment for irrigation. Sheath sizes range from 11 Fr for infants to 30 Fr for adults. The stainless steel obturator, which is inserted into the sheath, occludes the opening of the sheath and facilitates introduction into the urethra without trauma to the mucosal lining. The obturator allows direct visualization of the entire length of the urethra. The distal end of the scope, as illustrated in Figure 111.2, with its lens and instrumentation protrudes slightly beyond the tip of the sheath. It has an inflow and an outflow port for irrigation that allows the surgeon to inflate or expand the bladder to better visualize the bladder walls and urethral openings.

The *cystoscope bridge* is that part of the cystoscope into which the telescope lens slides and attaches to the sheath. The bridge is dual-lumen type with stopcock valves and seals. A cautery loop, both monopolar and bipolar types, can be attached to the resection sheath.

The cystoscopes usually have extra tubes to guide other instruments for surgical procedures to treat urinary problems. Tiny surgical tools can be put through the tube to take samples of tissue (biopsy) or samples of urine. Small bladder stones and some small



**Figure 111.2** Distal (frontal) view of insertion tube of a cystoscope.

growths can also be taken out in this way. A sterile liquid, water or saline, is injected through the cystoscope to slowly fill the bladder and stretch it to allow for a better view of the bladder wall. Rigid cystoscopy is generally performed under general anaesthesia, particularly in male subjects, due to the pain caused by the insertion of the instrument.

### Flexible Cystoscope

A flexible cystoscope is a thin, flexible, fibre optic based telescope as shown in Figure 111.3. It is the most commonly used instrument as it has several advantages. Because of its flexibility, it can easily pass along the curves of the urethra. The flexible distal tip can be moved easily, so the urologist can look all along the inside lining of the bladder. The procedure with flexible cystoscope is less painful to the patient, permits inspection of the entire bladder with a single optical instrument, and is invaluable in cases when the patient cannot be placed in the lithotomic position. Also, it allows visualization of the bladder neck area, which could not be achieved with the rigid cystoscope. Moreover, flexible cystoscopy can be carried out with local anaesthesia on both sexes. Video cystoscopes with sterile, single-use, disposable cystoscope sheaths are currently available. These sheaths reduce reprocessing time and potentially prolong the cystoscope lifespan.

Several pieces of support equipment are essential for the performance of rigid and flexible cystoscopes. These include the following:

- *Light source:* Equipment that provides the light source for the cystoscope.
- *Fibre optic light cable:* It is composed of thousands of glass fibres that are assembled to create a bundle.
- *Camera and monitor:* A three-chip camera attached to the eyepiece that can transmit the image onto a monitor. It allows the surgical team, to view the internal structures without having to look directly into the eyepiece of the instrument. Video cystoscopy provides more comfortable examination, enhancing teaching techniques and enabling patients to watch the important cystoscopic findings. Two types of typical portable video cystoscopes with monitors are shown in Figure 111.4.
- *Video printer, CD burner, memory stick:* Devices that allow the surgeon to videotape, take still pictures, or store images for future use, or for documentation purposes.

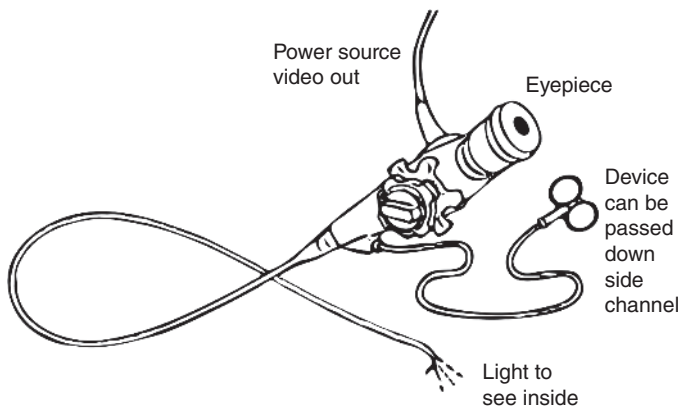


Figure 111.3 Parts of a flexible cystoscope.



**Figure 111.4** Two versions of portable flexible video cystoscopes.

- *Fluid pump or insufflator*: Used to distend the organ or body space for better visualization. The most commonly used irrigating media are sterile water and normal saline. The irrigating medium is usually warmed to body temperature before use.

The cystoscope has additional tools that include flexible biopsy forceps for taking tissue sample or a suspicious growth, cytology brush for taking cell samples, and suture removal forceps for removing stitches inside the body.

## Specifications

### *Rigid cystoscope*

*Cystoscope sheath*: 17–25 Fr

*Diameter*: 4 mm

*Rigid biopsy forceps*: 30°/70° (with double action jaws)

*Viewing system*: CCD camera

### *Flexible cystoscope*

*Optical system*: Field of view 120°

*Depth of field*: 3–50 mm

*Insertion section*: Outer diameter of distal end 11.7 Fr (4.6 mm × 2.6 mm)

*Outer diameter of insertion tube*: 16.5 Fr (5.5 mm)

*Instrument channel*: Diameter of inner channel 7.2 Fr (2.4 mm)

Minimal visible distance: 5 mm

*Angulation range*: Up 210°/down 120°

*Total length*: 700 mm

## Applications

Cystoscopy is used in the urology departments to determine the cause of many urinary system problems, remove tissue samples for testing (biopsy), and remove a foreign object. This is the most common test for diagnosing cancer of the bladder.

## 112

## Cytometer: Flow

### Purpose

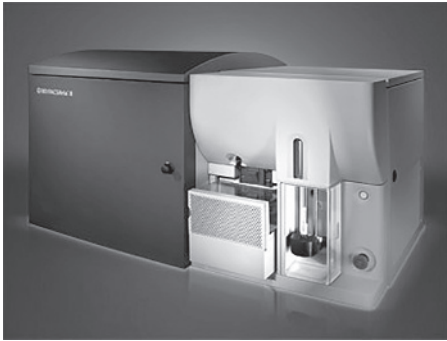
Flow cytometer is a precision analytical instrument used for rapid multi-parametric analysis of physical and/or chemical characteristics of single cells and chromosomes, the information obtained being both qualitative and quantitative. Flow cytometers were originally used for counting of blood cells, but modern instruments are designed to perform a variety of cell-based analyses in varied disciplines ranging from immunology to stem cell research. It allows to measure cell size, cytoplasmic complexity, DNA, or RNA content and a wide range of membrane-bound and intracellular proteins. Due to their cost, flow cytometers were earlier found only in larger academic centres, but advances in technology have now made it possible for modest hospitals to have these instruments.

### Principle

A cytometer is designed to simultaneously measure and then analyse multiple physical characteristics of single cells as they are made to flow in a fluid stream through a beam of light. The instrument offers a rapid, sensitive, and cost-effective method to detect, characterize, and identify cell abnormalities of various kinds and also to identify bacteria. A flow cytometer is similar to a microscope, except that, instead of producing an image of the cell, flow cytometry provides high-throughput automated quantification of desired parameters. It is a laser-based biophysical technology that involves suspending the cells in a stream of fluid flowing in single file. Fluorescent chemicals found in cells or attached to cells are analysed, as they flow through a tube and are passed in front of a light source. The light that is scattered from each cell is measured with a photodiode, and by analysing the changes in brightness at each detector, it is possible to determine various types of information about the physical and chemical structure of each individual cell.

A typical commercial high speed flow cytometer suitable for analysis and classification of cells is from M/s Becton Dickenson (BD Biosciences) shown in Figure 112.1. This instrument allows speeds up to 70 000 events/s and can identify 13 fluorescent parameters simultaneously. It uses three lasers at wave lengths: blue (488 nm, sapphire solid state), red (633 nm, helium neon air cooled), and violet (407 nm, solid state). It employs nozzles of different diameters ranging from 70 to 130  $\mu\text{m}$ . The nozzle is selected according to the size of the cells to be analysed. In general, cell size should not exceed 1/3 of the nozzle diameter. Sample temperature is controlled during analysis within a range of +4 to +42  $^{\circ}\text{C}$ . The major subsystems of the instrument are the following:

**Fluidics:** The function of the fluidics system is to transport particles in a stream to the laser beam for examination. It consists of two sources of fluid passing through it, a sheath fluid that is usually a buffered saline, and the specimen containing the cells to



**Figure 112.1** Typical flow cytometer. *Source:* Reproduced with permission of M/s Becton-Dickinson and Company, USA.

be analysed. The specimen forms a core, which is injected into the middle of the sheath fluid, and both pass through the flow chamber. Sheath fluid is injected into the flow chamber located at the heart of the instrument by pressurized lines. A pressurized airline also injects the suspended cells in the sample tube into the flow chamber. The sample pressure is always greater than the sheath fluid pressure that makes the cells to align in a single line manner through the laser beam and allows uniform illumination of a cell under hydrodynamic focusing.

The sheath and cleaning fluids are supplied from a self-contained cart that also collects waste from the cytometer. The cart also provides the air pressure and vacuum required to achieve pressure from 5 to 75 psi, to accommodate a variety of cell sorting applications. The air pressure is adjusted through software. A special quartz cuvette flow cell is used in fixed alignment with the laser and gel coupled to the collection optics. Fixed alignment configuration minimizes start-up time, improves experiment-to-experiment reproducibility, and enables automated daily quality control. A choice of nozzles lets users sort a wide range of particle sizes. Nozzles are available in four sizes: 70, 85, 100, and 130  $\mu\text{m}$ . The fluidic system must be free of air bubbles and debris and properly pressurized at all times. A bubble detector is used in the sample line to detect air bubbles from the sample tube and stops sample flow when the sample tube is empty, to avoid air bubbles from reaching the nozzle.

**Optical system:** This part consists of various filters, light detectors, and light sources. Light source is usually a laser line that produces single wavelength of specific frequency. Lasers are available for different wavelengths ranging from ultraviolet to infrared and various ranges of power levels. The types of lasers used are low-power air-cooled lasers (argon [488 nm], red-HeNe [633 nm], green-HeNe, HeCd [UV]) and diode lasers (blue, green, red, violet). Modern instruments usually have multiple lasers and fluorescence detectors.

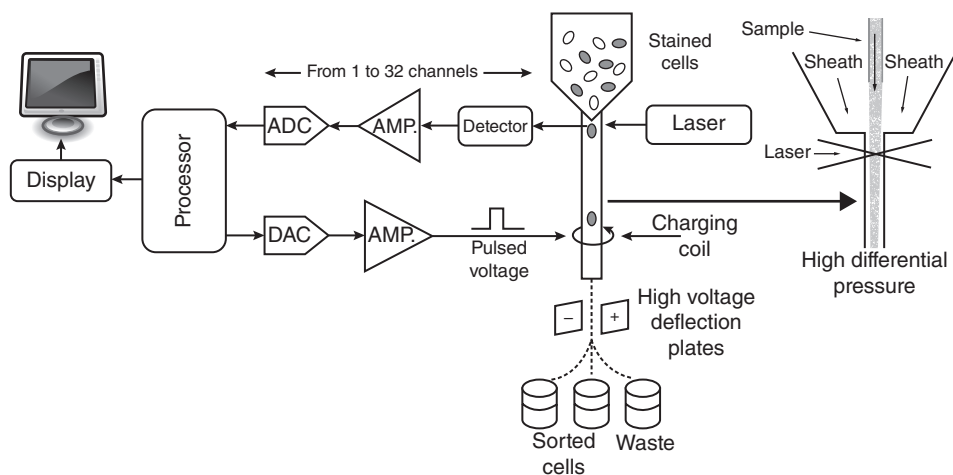
The excitation optics consist of multiple fibre coupled fixed-wavelength lasers, beam shaping optics, and achromatic focusing lenses that produce beam spots that are spatially separated and concentrated ( $9\mu\text{m} \times 65\mu\text{m}$ ). The more concentrated the beam spot, the higher the signal produced as each fluorescent labelled particle passes through the laser spot. Then, there is a group of lenses to collect light emitted from

the particle-laser beam interaction and a system of optical mirrors and filters to separate and then direct specified wavelengths of the collected light to the appropriate optical detectors. The detectors are mostly photomultiplier tubes (PMTs) or photodiodes. Fibre optics delivers emitted light from the cuvette to the detector arrays. Bandpass filters in front of each PMT allow spectral selection of the collected wavelengths. Bandpass filters allow only a narrow range of wavelengths, which is close to the emission peak of the fluorescent dye to reach the detector. In this way, filter and mirror changes within the optical array are not required to be further aligned for maximum signal strength.

**Electronics:** The electronics system converts the detected light signals by PMTs into electrical current signals that are given to an amplifier that converts it into a voltage pulse. This is followed by two types of amplifiers, which are linear and logarithmic. Dynamic range is important in choosing linear or a logarithmic amplifier. Linear amplification provides a direct visual relationship and is used if limited dynamic range (200–1000-fold) is required as in a DNA analysis. Logarithmic amplification, on the other hand, is employed if a much higher dynamic range (100–10 000) is required. The amplified analog signals are then converted into digital signals using A/D converter (ADC) for computer processing. With the help of software, operational parameters can be properly set and initial sample information displayed. The digital signals can also be displayed as plots of histogram.

**Software:** The modern instruments operate under software control that efficiently controls the set-up, acquisition, and analysis of flow cytometry data from the workstation. Log amplifiers are not used in digital systems. Instead, the logarithm of each digitized data point is computed and displayed through software. The software allows viewing the data in three dimensions in which the  $x$ - and  $y$ -axis represent parameters and the  $z$ -axis displays the number of events per channel.

Figure 112.2 shows the block diagram of a typical flow cytometer. The cells to be counted are first stained with proteins that fluoresce in response to certain wavelengths



**Figure 112.2** Block diagram of flow cytometry.



of light. These proteins are designed to attach only to certain cells. In some cases, cells are not stained, as they have native proteins that fluoresce. The cells in suspension are drawn into a tube surrounded by a sheath of isotonic fluid that creates laminar flow, allowing the cells to pass individually through a sensing point. The pore size of the tube is set to allow only a specific range of cell sizes to pass. At the sensing point, a beam of monochromatic light, usually from a laser, intersects the cells. The light emitted by the laser is in all directions, which is collected via a series of filters and dichroic mirrors so as to isolate particular wavelength bands. When passing through the laser beam, the proteins will fluoresce at a longer wavelength than the lasers. Light scattering at different angles can distinguish differences in size and internal complexity, whereas light emitted from fluorescently labelled particles can identify a wide array of cell surface and cytoplasmic antigens.

Photodetectors capture these wavelengths and measure the scattered light from the laser. The different wavelengths allow the instrument to determine the size and type of cell. The output of the photodetectors is amplified and used to drive the ADCs. Typically, there is one ADC per channel. The amplification stage requires wide bandwidth for accurate signal detection, low bias current, and low input capacitance for compatibility with the photodiode detector output, and fast settling time to ensure limited distortion and speed of the system. All of the data is processed by a digital signal processor (DSP), and histograms are generated showing the types of cells counted. Once the cells pass by the laser, they are charged by a charging ring. The amount of charge is determined by the type of cell. Deflection plates then sort the cells into different test tubes for further analysis. Up to thousands of particles per second can be analysed as they pass through the liquid stream. The resolution of flow cytometry can be enhanced by using a technique, known as *gating*. It is a method for selecting cells that are intended to be analysed in more specific detail.

Steer cell via high voltage cell sorting is a specialized type of flow cytometry where cells are sorted into different collection bins by using a set of deflection plates. These plates are kept at a high voltage potential. Uncharged cells drop straight down, while charged cells are attracted to a particular plate, effectively steering them into different collection bins. Cells can be charged individually by applying a pulsed voltage to the charging collar. It enables the pulse to the optical beam to charge each cell. It can multiply pulses of different widths to accommodate cell velocity (500 kHz–2 MHz) and has a high speed parallel interface. The resulting information usually is displayed in histogram or two-dimensional dot-plot formats.

In a flow cytometry, data about every cell that is detected is classified as a distinct event. Also, data in respect of each type of light that is detected (forward scatter, side scatter, and each wavelength of fluorescence emission) is plotted independently. The data is usually represented either as histograms or dot plots. A *histogram* measures or compares only a single parameter and typically plots the intensity detected in a single channel along one axis and the number of events detected at that intensity in a separate axis. A large number of events detected at one particular intensity will be displayed as a spike on the histogram. In a dot plot, two or three parameters are compared simultaneously on a two- or three-dimensional scatterplot.

Recently, benchtop flow cytometers have been introduced. These instruments are significantly easier to set up and run than traditional flow cytometers. They usually incorporate microcapillary flow cell technology that eliminates the need for 'sheath fluid' (the liquid used to carry cells through the laser beam), as the microcapillary allows



direct sampling by aspiration. A positive displacement syringe pump enables not only direct sampling but also adjusting of the flow rate to ensure clear data from a range of sample filters. This allows researchers to use smaller samples and results in a minimal amount of liquid waste, from litres per day to less than 50 ml/d. The optical configurations are available with single-sample loader or for a built-in multiwell to handle 96 samples. The instrument acquires up to 12 images using charge coupled device (CCD) camera simultaneously of each cell or object including bright field, scatter, and multiple fluorescent images at rates of up to 5000 objects/s. The CCD camera operates in time delay integration (TDI) mode that electronically tracks moving objects by moving pixel content from row to row down the rows of pixels in synchrony with the velocity of the cells in flow. The TDI technology combined with spectral decomposition allows the simultaneous acquisition of multiple spectral images of each cell in flow.

## Specifications

*Lasers:* Air-cooled, solid state, wavelength 405, 488, and 633 nm HeNe

*Fluorescence detectors:* PMTs

*Detector wavelength:* Violet: 450, 502, 530, 585, 670, and 780 nm

*Sample injection:* Direct into flow cell

*Max particle size:* 50  $\mu\text{m}$

*Sample flow rate, min:* 10  $\mu\text{l}/\text{min}$

*Sample flow rate, max:* 120  $\mu\text{l}/\text{min}$

*Sample acquisition rate:* 10000 events/s

## Applications

Flow cytometry is employed in life sciences laboratories for counting and sorting cells based on their individual characteristics and for assessing cell viability. The technology has applications in a number of fields, including molecular biology, pathology, stem cell research, immunology, plant biology, and marine biology. It has broad application in medicine especially in transplantation, haematology, tumour immunology and chemotherapy, prenatal diagnosis, genetics, and sperm sorting for sex preselection.

# 113

## Cytometer: Imaging

### Purpose

Imaging cytometer is used to measure multiple parameters of individual cells by adding detailed spatial context to the power of flow cytometry. It is a complimentary technique to flow cytometry in which multi-parametric data is derived by applying powerful

image segmentation and feature extraction algorithms to raw images of cells. Multiple parameters are generated by measuring the spatial distribution, intensities of markers on cells, and general morphological qualities for each cell. Imaging cytometry also allows for measuring the changes in the same cells over time and providing rich kinetic data.

## Principle

The imaging cytometer is designed to combine digital microscopy with image processing techniques that allow real-time population data analysis to produce high levels of information content with minimal investigation time. Advances in the digital imaging field over the past 30 years have led to the development of automated imaging cytometers that range from cell counters to high-content screening systems. Modern instruments usually combine the advantages of flow and image cytometry into a single system that provides flexibility and power for rapid measurements of biochemical constituents or evaluating cell morphologies. A flow cytometer enables the objective statistical analysis of high cell counts from the cells' fluorescence intensity based on the use of fluorescent markers with which the cells are labelled. Microscopes provide high resolution images in which cells can be distinguished from each other, but they lack quantitative criteria and statistical robustness. The advantages of combining flow and imaging cytometry have spurred the development of laser scanning cytometry (LSC). The LSC allows automated high-throughput image analysis to identify and measure cell properties with multiple spectra and high spatial resolution for measuring dynamic processes. These instruments offer a broad range of applications that would not be possible using either of the techniques alone as they combine the speed and sensitivity of flow cytometry with the detailed imagery of microscopy.

In LSC, the conventional flow cytometry measures forward scattered light to estimate the relative cell size, while microscopy yields the exact cell size through its bright field image. Advances in the microscopy technique have allowed both three-dimensional and higher resolutions that allow imaging of the biological structure and function beyond the diffraction limit, producing detailed fluorescent cell images. However, the process can take several minutes to produce such high-content images. Automated microscopy coupled with automated image analysis has provided with a relatively fast technique with a typical throughput of several hundreds of cells per second to identify and measure cell properties with multiple spectra and high spatial resolution.

The process of imaging cytometry involves either staining the cells to enhance contrast or staining with antibodies to directly conjugate to fluorophores. Cells are then loaded onto a slide and imaged using an imaging cytometer. The instrument simultaneously captures a series of bright field and fluorescent images (i.e. fields of view) of the sample and uses sophisticated digital image analysis algorithms to determine total and fluorescent cell counts and calculate their concentrations. Using the touch screen user interface of the instrument, one can select the number of images to capture for each experiment and gate the counts by cell size and/or fluorescence intensity. After capturing, each field of view can be selected for review, zoom in and out of the selected field of view, display channel-specific layers, and identify the cells counted through each channel.

The analysis slides are disposable slides composed of polylactic acid (PLA), which is a low-fluorescence plastic. Each slide holds the sample in two separate, enclosed chambers, allowing the analysis of two different samples or replicates of the same sample. Each chamber has a 25  $\mu\text{l}$  sample capacity and takes 10 seconds to 2 minutes for a typical assay, depending on complexity of the assay and number of fields captured.

Some companies offer instruments that function much more like a flow cytometer. The cells are actually introduced via flow stream (i.e. sheath fluid) rather than statically on a slide. The major difference in technology between an imaging cytometer and a flow cytometer lies in the fact that the former images cells as they cross in front of a light source, whereas the latter uses a photomultiplier to read fluorescence.

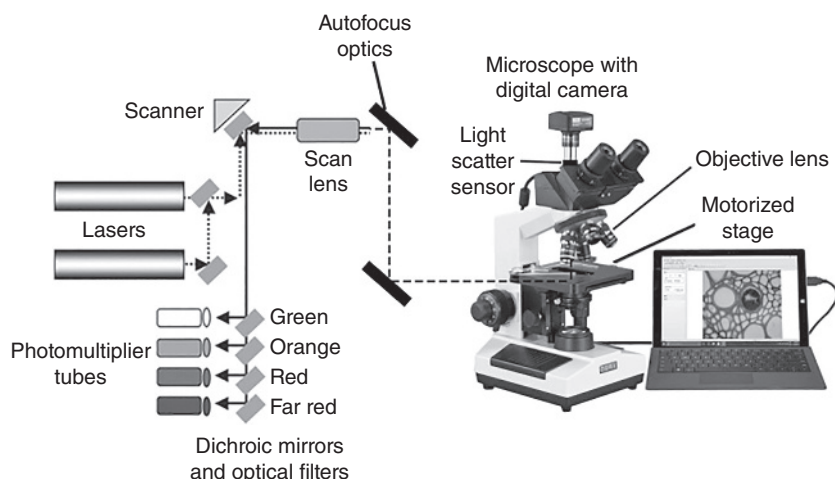
The LSC system uses four lasers that give out five different wavelengths for laser-spot scanning illumination. The detector system consists of Photomultipliers for fluorescence detection and photodiodes for absorbance and scatter detection. The operation is fully automated for analysis of cellular and tissue samples that have been stained with fluorescent or chromatic dyes. Fluorescent excitation, laser light absorbance by chromatic dyes, and scatter signals can all be acquired simultaneously.

The instrument captures up to 20 fields of view per sample with each field of view covering 0.233  $\mu\text{l}$  of the sample and presents the relevant data in terms of cell count versus cell size and cell count versus fluorescence in tables and histograms. The data from the analysis, including the image files, can be downloaded to a USB flash drive and transferred to a computer for sample comparisons. From these signals, a variety of quantitative data relating to the cells, nuclei or other subcellular structures, can be calculated such as area, integrated signal, maximum pixel, peripheral integral, circularity, perimeter,  $x$  and  $y$  coordinates, and more. The numerical values are displayed in scattergrams and histograms, which allow study of relationships among the various features and between the features and the images.

### ***System Description***

Block diagram of an LSC system comprising of essential components is shown in Figure 113.1. The system is equipped with up to four lasers chosen from a palette of five or even six possible wavelengths: 405, 488, 532, 594, 561, and 633 nm. There are four photomultiplier tubes (PMTs), which act as detectors, each detecting a specific wavelength range and collecting fluorescence from excitation by scanning lasers. As the laser light intersects the sample, scattered or transmitted light is simultaneously directed to one or more solid-state photodetectors. The photodetectors and PMT signals are converted into 14 bit pixel values that are then assembled into high resolution images.

The key component of the system is the microscope. The microscope usually has a motorized stage, autofocus motor, bright field lamp, and forward scatter detector. The fluorescence excitation laser beams from the four lasers are spatially merged by dichroic mirrors and are directed onto the computer-controlled oscillating mirror. The mirror oscillating at 350 Hz reflects the laser beams through the epi-illumination port of the microscope and images through the objective lens onto the slide. The oscillating mirror makes the laser beams scan the area of microscope slide placed under the lens. The beam spot size is dependent on the lens magnification and varies from 2.5  $\mu\text{m}$  at  $\times 40$  to 10.0  $\mu\text{m}$  at  $\times 10$ . The slide is placed on the computer-controlled motorized microscope



**Figure 113.1** Schematic representation of the laser scanning cytometer (LSC). Most recent models of LSC have an inverted format with the laser illumination originating beneath the microscope slide.

stage that moves at  $0.5\mu\text{m}$  steps per each laser scan, perpendicularly to the scan. The movement of slide is monitored for its  $XY$  position by a set of sensors.

The fluorescence emitted by the specimen is collected by the objective lens and directed to the scanning mirror from where after reflection, it passes through a series of dichroic mirrors and optical emission filters. Thereafter, it falls on one of the four photomultipliers, which record fluorescence at a specific wavelength range, depending upon the combination of filters and dichroic mirrors. An additional light is used to provide illumination to visualize the objects through an eyepiece or the charge coupled device (CCD) camera. Laser light scattered by the cells is imaged by the condenser lens, and its intensity is recorded by sensors. Variable image resolution is determined by both objective-lens magnification and stage resolution. Stage resolution can be selected from  $0.05$  to  $20\mu\text{m}$  to meet the needs of a particular assay, balancing spatial resolution, quantitative precision, and throughput.

For imaging, high speed CCD cameras are used that employ the time delay and integration technique, which is designed to image objects moving along one axis at low light levels. This type of CCD provides higher sensitivity by having multiple rows of sensors that shift their partial measurements to the adjacent row synchronously with the motion of the moving cell image across the array of sensors. This arrangement allows detecting weak fluorescence signals without motion blur caused by an increase in exposure time. The sensor arrays on CCD are divided into numerous columns to detect emission or scattered light of different spectral ranges from cells. With the use of these spectral decomposition elements, 6–12 images per cell can be acquired simultaneously. The measurement of cell fluorescence or light scatter is computer controlled and triggered by a threshold contour set above background. The instrument carries a large memory that can hold 145 GB of data, sufficient for storing numeric and graphic data files from 1000 sample runs.

The commercial instruments combine a precise method of electronically tracking moving cells with a high resolution multispectral imaging system to acquire multiple

images of each cell in different imaging modes. Usually, six images of each cell are acquired, which include a side-scatter (dark field) image, a transmitted light (bright field) image, and four fluorescence images corresponding roughly to the spectral bands of a conventional flow cytometer. The imaging objective has a numeric aperture of 0.75, and image quality is comparable with 40× to 60× microscopy. With a throughput up to 300 cells/s, this system can produce 60 000 images of 10 000 cells in about 30 seconds and 600 000 images of 100 000 cells in just over 5 minutes.

These systems employ flexible and powerful analytical software to extract the most appropriate cellular features from the data, including quantitative morphology, fluorescent signal strength, signal locations, and other image characteristics for any particular indication. One such software is the IDEA<sup>®</sup> data analysis software package that can calculate over 40 quantitative features per image, resulting in approximately 250 features per cell, which can be used to generate histograms and scatterplots much like a standard flow cytometry data analysis program.

### ***Time-Lapse Cytometer***

Time-lapse cytometry is another type of cytometry that combines time-lapse microscopy and image cytometry to understand cellular dynamics. In essence, time-lapse cytometers are imaging cytometers that monitor cells using time-lapse video recordings. The video is then processed to track cytometric parameters over a period of time.

It is an extremely powerful technique because these machines visually monitor cell morphology or state independent of the use of fluorophores. Thus, cellular damage that sometimes occurs following excitation of fluorophores does not happen. Secondly, time-lapse cytometers do not use heat-generating light sources. Therefore, the technique can be used in incubators for long-term analysis of cells, as there would not be any heat build-up inside the incubator.

## **Specifications**

*Lasers (up to 4):* Violet (405 nm), blue (488), green (532), yellow (561), and red (633)

*Detectors:* 4 photomultiplier tubes fluorescence detectors, 2 photodiodes for scatter imaging

*Emission detection:* Blue (445–485 nm), green (515–585 nm), orange (565–585 nm), red (600–635 nm), crimson (650–700 nm), near-infrared (750–800 nm)

*Microscope:* Olympus IX-51 series microscope base, variable-resolution laser scan imaging (4, 10, 20, 40, or 60 times objective lens magnification)

*Optics:* 3 channels (bright field, green fluorescence, red fluorescence)

User-selectable rate of stage motion

*Camera:* 1.3 megapixels, 4× objective, 4× or 16× digital zoom

*Display:* High resolution laser scan imaging

*Specimen carriers:* Glass or plastic microtiter plates, microscope slides, Petri Particle/  
cell diameter range: 5–60 μm

*Required sample volume:* 25 μl

Dishes and chamber slides

*Computer:* Core i7 2600k processor, 8 GB RAM, 1 TB HD, LCD monitor

## Applications

Imaging cytometry or LSC finds applications for the quantitative analysis of cells and cell systems and offer a powerful tool particularly in the fields of biology, biotechnology, and medicine. Imaging cytometry finds applications to perform automated analysis on tissue sections and microarrays, view individual events in the population data, measure and localize cellular constituents, and reanalyse the same cells under varying conditions.

## 114

## Defibrillator: External

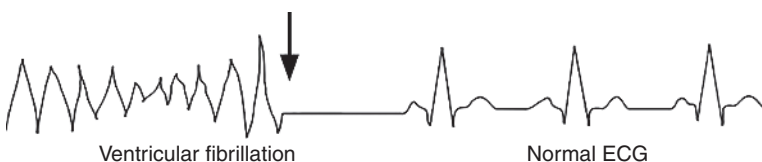
### Purpose

External defibrillators are devices intended to be used, usually under emergency conditions, on patients suffering from excessively fast and ineffective heart rhythm disorders as a result of fibrillation or tachycardia. The device delivers a strong electric shock to the patient in an effort to convert fast heart rhythm to slower rhythms that allow the heart to pump blood more effectively. External defibrillators have been in common use for many decades now for emergency treatment of life-threatening cardiac rhythms as well as for elective treatment of less threatening rapid rhythms.

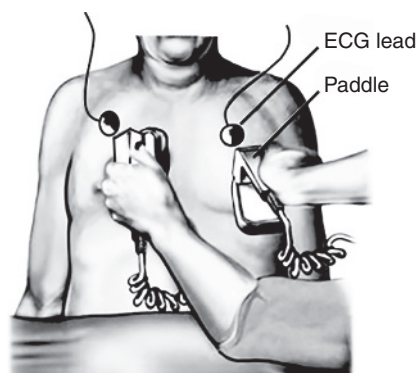
### Principle

Ventricular fibrillation is a serious cardiac emergency resulting from asynchronous contraction of the heart muscles. This uncoordinated movement of the ventricle walls of the heart may result from coronary occlusion, from electric shock, or from abnormalities of body chemistry. Because of this irregular contraction of the muscle fibres, the ventricles simply quiver rather than pumping the blood effectively. This results in a steep fall of cardiac output and can prove fatal if adequate steps are not taken promptly.

Ventricular fibrillation can be converted into a proper rhythm by applying a high energy electric shock to the heart through handheld electrodes as shown in Figure 114.1.



**Figure 114.1** ECG waveform showing ventricular fibrillation and then restored to normal rhythm in fibrillating heart as achieved by direct current shock (arrow) across the chest wall. The horizontal line after the shock shows that the cardiograph was blocked or disconnected for its protection during the period of shock.

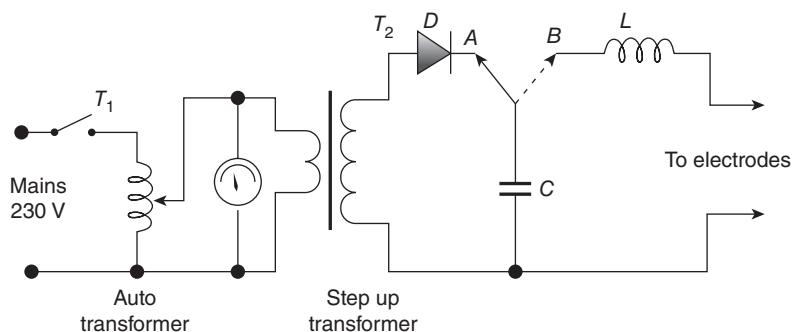


**Figure 114.2** Application of electrodes of external defibrillator on the chest of a patient.

This sudden surge across the heart causes all muscle fibres to contract simultaneously. Possibly, the fibres may then respond to normal physiological pace making pulses. The instrument for administering the shock is called a defibrillator.

In all present-day defibrillators, an energy storage capacitor is charged at a relatively slow rate (in 10 seconds) from the AC line by means of a step-up transformer and rectifier arrangement or from a battery and a DC-to-DC converter arrangement. During defibrillation, the energy stored in the capacitor is then delivered at a relatively rapid rate (within 5 ms) to the chest of the subject through appropriately placed electrodes as shown in Figure 114.2. This yields an exponential discharge typical of an RC circuit.

The basic circuit diagram of a DC defibrillator is illustrated in Figure 114.3. A high voltage step-up transformer with an auto-transformer  $T_1$  in the primary is used for adjusting the output voltage. The output voltage of the transformer goes to a diode that works as a rectifier. The output of the rectifier then goes to high voltage changeover switch. In position A, the switch is connected to one end of an oil-filled  $16\mu\text{F}$  capacitor. In this position, the capacitor charges to a voltage, set by the positioning of the auto-transformer. The required pulse duration, about 5 ms, is obtained by connecting an inductance of about 0.1 H in series. When the shock is to be delivered to the patient, a foot switch or a push button mounted on the handle of the electrode is operated. The high voltage switch changes over to position 'B', and the capacitor is discharged across the patient's heart through the electrodes.



**Figure 114.3** Basic DC defibrillator circuit.



It has been established experimentally that the success of defibrillation correlates better with the amount of energy stored in the capacitor than with the value of the voltage used for charging the capacitor. It is for this reason that the output of a DC defibrillator is always calibrated in terms of watt-seconds or joules as a measure of the electrical energy stored in the capacitor. The defibrillating shock can be delivered either externally (by applying the electrodes on the chest) or internally (electrodes placed directly on the heart muscles). For internal defibrillation, energies up to 100 Ws are usually required, whereas higher energy levels are necessary for external defibrillation. The instruments are usually designed to provide output from 0 to 400 Ws, and this range provides sufficient energy for both external and internal defibrillation.

Energy in watt seconds is equal to one half the capacitance in farads multiplied by the voltage in volts squared, i.e.  $E = 1/2 CV^2$ . If a  $16\mu\text{F}$  capacitor is used, then for the full output of 400 Ws to be available, the capacitor has to be charged to 7000 V. The DC defibrillator cannot be used for rapidly repeated shocks because it requires about 10 seconds to recharge the capacitor. In most of the instruments, a meter is that which directly indicates the amount of energy, whereas in some others, a lamp lights up the moment the adjusted energy level is reached.

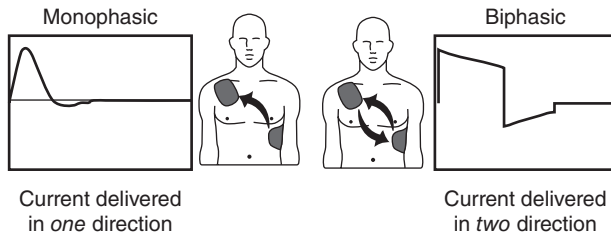
The amount of energy that the defibrillator actually delivers to the patient is the determining factor as to whether or not a defibrillation would be successful. Some of the energy indicated on the panel meter may be lost or dissipated at the skin–electrode interface. The delivered energy can be estimated by assuming the value of a load resistance that is placed between the electrodes to simulate the resistance of the patient. Usually, values of  $50\text{--}200\Omega$  are taken as patient's resistance at external defibrillation for a typical electrode size of  $80\text{ cm}^2$  and  $25\text{--}50\Omega$  at internal defibrillation. Most defibrillators will deliver between 60% and 80% of their stored energy to a  $50\Omega$  load.

The portable defibrillators such as shown in Figure 114.4 operate on rechargeable batteries and therefore make use of DC–DC converters for stepping up the voltage required for charging the storage capacitor. The maximum energy delivered by portable defibrillator is generally 300 Ws delivered into  $50\Omega$  load, which is equivalent to about 400 Ws of stored energy. When the defibrillator is charged and not fired, the instrument is a potential source for danger. In some instruments, the capacitor is automatically discharged internally through a resistance when it is not fired, say, within five minutes.

There are two general classes of waveforms that are commonly used these days for defibrillation: monophasic and biphasic as shown in Figure 114.5. Monophasic

**Figure 114.4** Typical portable external defibrillator.





**Figure 114.5** Difference between monophasic and typical biphasic, truncated exponential waveforms used in defibrillators.

waveforms use escalating high levels of energy delivered in one direction through the patient's heart, whereas a biphasic waveform delivers energy in both directions. The biphasic waveform is preferred, as it has proven in clinical studies to defibrillate more effectively than other types of waveforms.

### **Defibrillator with Synchronizer**

For the termination of ventricular fibrillation, a simple DC defibrillator can be used to restore synchronized working of the heart with the pacemaker of the body. But for termination of ventricular tachycardia, atrial fibrillation, and other arrhythmias, it is essential to use a defibrillator with *synchronizer* circuit; otherwise, there is a likelihood of the shock bringing the ventricles into fibrillation. Ventricular fibrillation is produced more spontaneously when current passes directly through the heart during a specific portion of the cardiac cycle known as the 'vulnerable period'. Vulnerable period for the ventricular muscle occurs during the upstroke of the T wave of the electrocardiogram, and even a single shock impulse lasting for less than 0.1 seconds could cause ventricular fibrillation if received during this period. There is, however, a period in the heart cycle in which the danger of applying defibrillating pulse is least, and therefore, defibrillation must take place during that period. Thus, the function of the synchroniser circuit is to permit placement of discharge at the right point on the patient's electrocardiogram (ECG). With the synchronizer unit, the shock is delivered automatically approximately 20–30 ms after the peak of the R wave of the patient's ECG. This procedure is known as *cardioversion*.

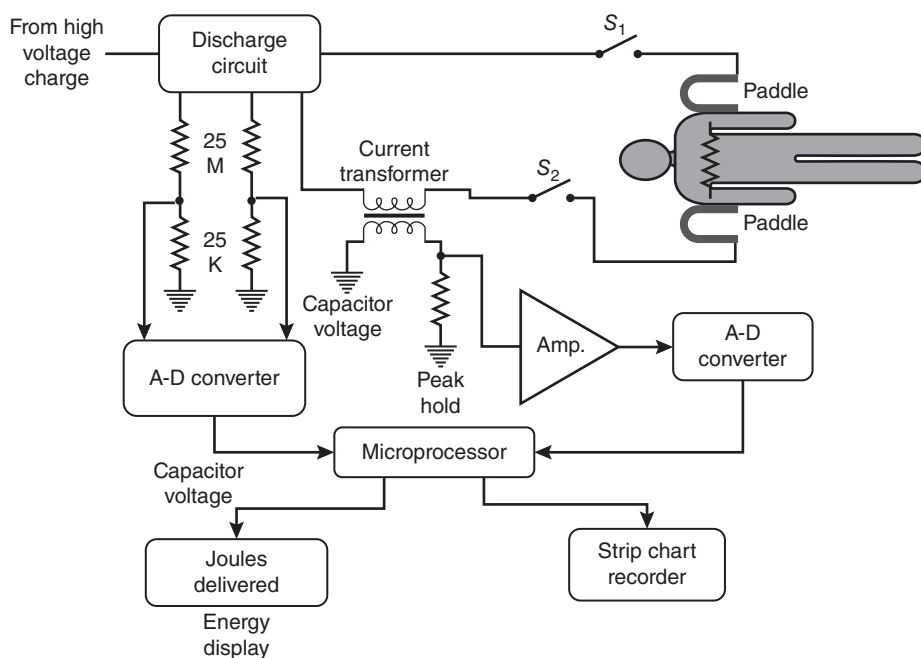
The synchronizer unit contains within it an ECG amplifier that receives the QRS complex of the ECG and uses this to trigger a time delay circuit. After an interval of the desired delay time, approximately 30 ms, the defibrillating capacitor is discharged across the chest through the electrodes. The electrocardiogram of the patient is simultaneously monitored on a display. The moment the discharge takes place, the synchroniser unit produces a marker pulse on these monitoring instruments to show the instance where the counter-shock has occurred in the ECG cycle. Most of the modern defibrillators incorporate synchronizer facility.

For effective and efficient results, the output of the defibrillating circuit is kept isolated or floating. In a floating circuit, the total energy is always contained between the two electrodes. There is no loss of energy to extraneous grounds and a high efficiency is therefore maintained. Moreover, there is no direct path to ground and the danger of shock by accidental contact with the patient during the period of defibrillation does not exist. This provides safety to the attending medical personnel.

A simplified diagram of the discharge control and recording circuitry of a defibrillator with synchroniser is shown in Figure 114.6. The instrument performs a number of functions, including the following:

- ECG signal is picked up by the electrodes and converted into a digital format that goes to the microprocessor.
- Digitized ECG signal is analysed to determine if the shock is required to be delivered.
- The internal capacitor is then discharged to a voltage high enough to defibrillate the patient.
- The device then delivers the controlled shock when the shock button is pressed by the operator.
- The process is repeated if considered necessary.

Before the discharge, the operator selects the desired energy to be delivered into  $50\Omega$  load. The microprocessor determines the corresponding value of stored energy taking into consideration the defibrillator internal resistance and the patient impedance. The corresponding storage capacitor voltage is determined by the microprocessor. The discharge current passes through a current-sensing transformer placed in the circuit. The use of a sensing transformer provides ground isolation for the patient circuit, yielding a simple method for measuring the discharge current. The microprocessor takes the measured peak discharge current and uses this value along with the stored energy to determine patient impedance and delivered energy. It then drives a digital display and annotates peak current, patient impedance, and delivered energy on a strip chart



**Figure 114.6** Block diagram of defibrillator circuit with ECG synchronizer.

recorder. A poor paddle contact warning indicator is also activated when the patient impedance exceeds  $100\Omega$ . The ECG monitor has an automatic gain setting, baseline (offset) restore, 50 Hz filter, and effective heartbeat detector.

Since the patient impedance can vary considerably, it has a strong effect on defibrillation effectiveness. Hence knowledge of peak current, patient impedance, and actual delivered energy will greatly enhance the ability of the operator to assess and improve defibrillation effectiveness. Patient impedance and delivered energy can be directly determined from the peak discharge current if the stored energy and the defibrillator circuit parameters (C, L, R) are known. These measurements are automatically made in the modern equipment.

### **Electrodes**

The electrodes for external defibrillation are usually handheld metal discs about 5–6 cm in diameter ( $70\text{--}100\text{ cm}^2$  in surface area) and are attached to highly insulated handles. Most of the conventional electrode systems are circular, a little concave with sharp rims and an insulated backside. For internal defibrillation when the chest is open, large spoon-shaped electrodes are used. Usually, large currents are required in external defibrillation to produce uniform and simultaneous contraction of the heart muscle fibres. This current not only causes a violent contraction of the thoracic muscles but may also result in occasional burning of the skin under the electrodes.

Chest wall impedance plays an important part in efficient defibrillation. The factors determining this impedance include the size of the electrodes, paddles, the energy of the discharge, the number, and the time interval between previous counter-shocks and the interface material that is used between the paddle electrode and chest wall. Electrode gels are usually employed to reduce contact impedance of the interface and for that the impedance of the gel itself must be very low.

The external electrodes contain safety switches inside the housings, and the capacitor is discharged only when the electrodes are making a good and firm contact with the chest of the patient. This precludes the possibility of an accidental shock to the operator and the risk of burns to the patient. A number of instruments are provided with electrodes, which have a spring contact. When these electrodes are adequately pressed on the thorax, the contacts close and the defibrillator is fired. In this way, burns due to poor electrical contact between electrodes and the skin are prevented.

Flat paddle surfaces do not always conform to the body thus reducing contact areas. Proper paddle sizes for different size patients are not quickly and easily available. In order to meet these requirements, pre-gelled and self-adhesive electrodes have been introduced. Adhesive electrodes are disposable and are applied to the chest before the shock delivery and left in place for reuse if subsequent shocks are needed.

**Monitor/Defibrillators** These are more complex devices that include the ability to monitor different physiological functions such as blood oxygen level, pulse and heart rhythm, blood pressure both by invasive and noninvasive methods, temperature, respiration rate, etc. These devices deliver external cardiac pacing and external defibrillation manually. Some of them also have automatic function like automatic defibrillators. The monitor/defibrillators are used usually by medical professionals and are found mostly in hospitals and emergency medical systems. Figure 114.4 is a typical

monitor/defibrillator that can perform all the functions of a vital signs monitor and that of manual/automatic defibrillator and pacemaker.

## Specifications

*Rated maximum output:* 360 J

*Waveform:* Biphasic

*Charge time:* 200 J in 7 seconds, 360 J in 12 seconds

*ECG display:* Minimum 15 cm × 10 cm, 4 seconds display

*ECG pickup:* Via paddle as well as 3 lead patient cables

*Annotations on record:* Time, date, defibrillator energy, heart rate, event marker

## Applications

In the clinical setting, external defibrillators are used in emergency rooms, in intensive care units (ICUs), and throughout the hospital by trained professionals.

Outside of hospitals, external defibrillators are used by emergency medical personnel in ambulances.

# 115

## Defibrillator: External Automated

### Purpose

Automated external defibrillators (AEDs) are public access defibrillators that are usually placed at public places like airports, train stations, malls, and other such places. They are designed to be operated by a lay person to provide defibrillator therapy to the individual as an emergency measure. AEDs have the capability to analyse the electrical activity of the heart and deliver impulses only if arrhythmia has occurred. These devices are not designed to replace the manual external defibrillators generally used by highly trained professionals. Instead, these devices complement the efforts of medical personnel by delivering immediate shock therapy by the person available at site.

### Principle

The successful implementation of smart AEDs or advisory external defibrillators technology that can accurately analyse the electrocardiogram (ECG) and make reliable shock decisions to determine if a shock is needed by a person has been a significant development in the field of defibrillators. These devices can detect ventricular fibrillation with a

high degree of sensitivity and specificity that is comparable with that of well-trained paramedics and then deliver (automatic) or recommend (advisory) suitable high energy defibrillating shock. The AEDs generally use a single pair of disposable electrodes to monitor the ECG and deliver the defibrilling shock. They also incorporate ECG displays. The simple design and ease of use of automated defibrillators require very little training and operational skill.

AEDs usually employ self-adhesive electrodes instead of handheld paddles because of the two advantages in their use. Firstly, the ECG signal acquired from self-adhesive electrodes usually contains less noise and has higher signal quality, which provides a faster and more accurate analysis of the ECG and, accordingly, facilitates better shock decisions. Secondly, 'hands-off' defibrillation is a safer procedure for the operator, especially if the operator has little or no training. Figure 115.1 shows a typical AED showing the use of adhesive electrodes. Hybrid designs of multifunction electrodes that can be commonly used with defibrillator-monitor-pacer instruments are now available.

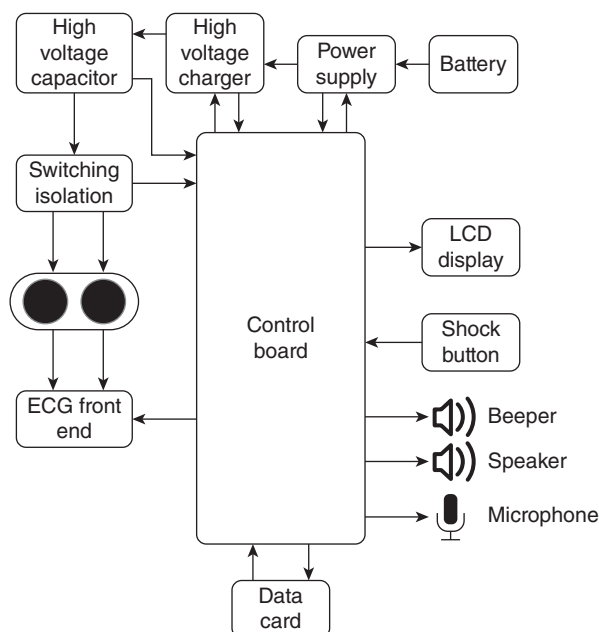
The block diagram of an AED is shown in Figure 115.2. It is a highly sophisticated microprocessor-based device that monitors, assesses, and automatically treats patients with life-threatening heart arrhythmias. The ECG signals are captured by the electrodes, amplified, and subjected to ECG analysis algorithm to identify shockable rhythms, followed by advice to the operator about the need for defibrillation.

The defibrillator part of the circuit contains the usual components such as a high voltage power supply, storage capacitor, patient electrodes, and switching/isolation circuitry to deliver a high amplitude (about 1800 V for the Biphasic waveform) current impulse to the heart. It develops an electrical charge in the capacitor to a desired voltage, creating the potential for current flow. The higher the voltage, the more current can potentially flow. The AED gives out audio instructions and visual prompts to guide the operator through the defibrillation procedure.

The front-end signals of the AED come from the ECG electrodes placed on the patient. These small amplitude signals, in the range from 0.1 to 10 mV, are amplified in an instrumentation amplifier. The instrumentation amplifier has a very high input impedance ( $>10\text{ M}\Omega$ ), very low input leakage current ( $<1\text{ }\mu\text{A}$ ), flat frequency response of 0.1–100 Hz, and high common mode rejection ratio ( $>100\text{ dB}$ ). Some AEDs also have



**Figure 115.1** Automated external defibrillator Philips model HeartStart FR2.



**Figure 115.2** Simplified block diagram of an automated external defibrillator.

the microphone input for recording the audio from the scene of a cardiac emergency. Both ECG and microphone inputs are digitized and processed by the controller circuit. Most AED designs use a 16-bit processor and therefore work well with 16-bit analog-to-digital converters (ADCs) to digitize ECG and voice input. The AED can have synthesized audio instruction with volume control output to either the headphone speaker or the  $8\Omega$  speaker.

The heart of the system is the control board that holds the main processor and all of the circuitry required to control the real-time functions of the AED. The real-time control provides the signals required to sample the ECG data, store ECG and voice data onto the data card, send data to the display, play the voice prompts on the speaker, turn on warning tones, charge the high voltage capacitor, and deliver the shock to the patient. In addition, the processor on the control board runs all of the data processing for the analysis system.

AEDs determine whether defibrillation is needed and automatically charge and discharge to deliver a shock. A critical factor in the safety and performance of an automatic external defibrillator is the ability of the device to accurately assess the patient's heart and make an appropriate therapy decision. The defibrillator performs this evaluation by sensing electrical signals from the patient's heart via electrodes and using a computerized algorithm to interpret the electrical signals. The algorithm used in the modern defibrillators looks at four key indicators to determine whether a rhythm is shockable or non-shockable. These four indicators are heart rate, conduction (flow of electrical waves through the heart indicated by the width of 'R' wave), stability (repeatability of QRS complexes), and amplitude (magnitude of the heart's electrical activity).



AEDs are generally not used, except in the case of an emergency. They are, therefore, required to be optimized for infrequent use. They are normally on standby mode for long periods, but the device automatically self-tests its functioning every day and periodically performs an internal discharge and recalibration processes. The device is powered by a long-life disposable lithium battery with enough capacity for 100 discharges and one year of self-test. The device produces a low energy biphasic waveform with dynamic compensation that can accommodate a wide range of patient impedances.

When the AED is switched on and the pads are applied to the patient, the ECG and the event summary are continually recorded onto device memory. The device also contains a real-time clock that provides time reference for any event that occurs. A temperature sensor incorporated in the device allows the control board to record the ambient temperature of the device.

Most AEDs are designed to enable fast response by the user. The front panel specifies three steps marked as 1-2-3, which guides the user to operate the device. The steps are (i) turn the unit on, (ii) follow the prompts, and (iii) deliver a shock. Some of the units can also be configured to be used as a manual defibrillator. This allows a smooth transition of the patient care from a lay person to a better trained medical person. In order to make them highly visible, public access AEDs are often brightly coloured and are mounted in protective cases at most visible places in the facility.

## Specifications

*Waveform shape:* Biphasic truncated exponential

*Energy delivered:* 150 J nominal into a  $50\Omega$  load

*Charge control:* Controlled by patient analysis system

*Charge time:* <10 seconds typical

*Shock-to-shock cycle time:* <20 seconds typical, including analysis

*ECG frequency response:* 1–20 Hz (–3 dB)

*Pads:* Adults –  $85\text{ cm}^2$  each, infant/child –  $44\text{ cm}^2$  each

*Size:*  $6.6\text{ cm} \times 21.8\text{ cm} \times 21.8\text{ cm}$

*Weight:* 2.1 kg (with battery)

## Applications

AEDs are generally placed at public access places including corporate and government offices, shopping centres, airports, aeroplane, restaurants, hotels, sports stadium, schools and universities, community centres, fitness centres, cruise ships, health clubs, theme parks, workplaces, and any other location where large groups of people are likely to be present. Emergency vehicles such as ambulances, fire vehicles, elevators of high-rise buildings, and other transport facilities are also being advised to carry an AED. There is an increasing trend to have AEDs for use in the home, particularly by those having known heart problems.

## 116

## Defibrillator: Implantable Cardioverter

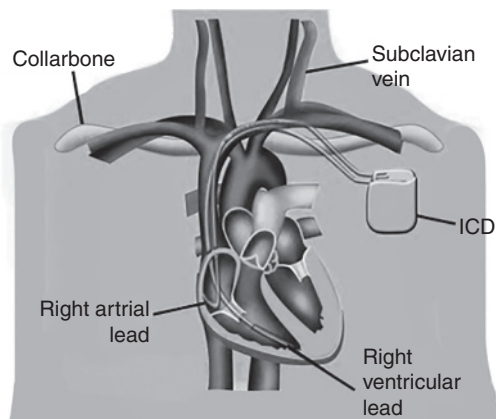
### Purpose

An implantable cardioverter defibrillator (ICD) is a therapeutic device that is recommended in patients who are prone to life-threatening ventricular fibrillation. The device is designed to detect ventricular tachycardia or fibrillation and automatically delivers high voltage shocks (750 V) that may restore normal sinus rhythm. Although an ICD is not a cure for dangerously fast heart rhythms, it does provide treatment for this condition by constantly monitoring the heart rhythm and treating the life-threatening rhythmic situation. Some newer-generation ICDs also include pacemaker function to provide low voltage pacing stimuli if the heart rate is detected to be too slow.

### Principle

An implantable defibrillator is a small life-saving device that helps to correct fast, abnormal heart rhythms. The device may be implanted in the chest or abdomen in the body. The device is mostly referred to as ICD as the device continuously monitors the heart and automatically delivers therapies to correct fast heart rhythms when necessary. Figure 116.1 shows an implantable defibrillator implanted in the chest.

The ICD is basically an implanted computer that stores recordings of the patient's heart signals and collects extensive therapy history and diagnostic data files to assist the physician in deciding individual device behaviour for each patient. Weighing just 50–120 g, having 30–70 cc volume, and with over 30 million transistors, these implantable devices draw



**Figure 116.1** Implantable cardioverter defibrillator implanted in the chest.

less than  $20\mu\text{A}$  current during years of constant monitoring of the patient's cardiac status. The devices delivering one shock per month, with 100% backup pacing, may endure five to seven years before battery depletion. Additionally, the device is hermetically sealed, biocompatible, and able to survive over a large temperature range from  $-30^{\circ}\text{C}$  to  $60^{\circ}\text{C}$ .

After the ICD system is implanted, an external computer, called a programmer, can be used by the doctor to program the heart device noninvasively and retrieve information from the device that will assist the doctor in providing suitable heart failure treatment. Devices available today combine a defibrillator to deliver high energy to very fast and erratic heart rates, with a pacemaker to provide therapies to both increased and decreased heart rates. Other additions to these devices are highly sophisticated algorithms for rhythm classification and storage of patient's heart signals.

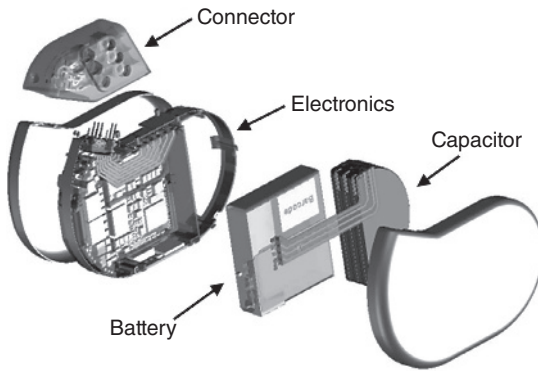
An implantable defibrillator is designed to monitor the heart rhythm 24 hours a day. If the heart is beating too fast or irregularly, small painless electrical signals are first sent to correct the heart rate. If the fast heart rate continues and the device detects fibrillation, the capacitors within the device are charged up to 750 V. The capacitors are then discharged into the heart, which mostly represents a resistive load of  $50\Omega$ . The delivered defibrillator shock will restore the heart to a normal rate. Sometimes, this may require delivery of more than one high energy pulse, but the number of high energy shocks delivered by the device is usually limited to four or five during any single arrhythmic episode. The shock duration for efficient defibrillation is approximately 4–8 ms, which results in the delivery of approximately 30–35 J at 750 V.

Studies have shown that biphasic waveforms are usually used for defibrillation as they are more efficient and probably safer than monophasic waveforms and produce successful defibrillation at lower energies. The discharge current pulse duration (full width at half maximum current) is in the range of 2.5–3.5 ms for most defibrillators and does not increase very much with patient impedance. Based on studies by several research workers, a biphasic truncated exponential waveform has become the standard waveform, among all implantable defibrillator manufacturers.

Implantable defibrillator systems have three main system components: the automatic implantable defibrillator itself (AID), the lead system, and the programmer recorder/monitor (PRM). The AID houses the power source, sensing, pulse generator for defibrillation, pacing, and telemetric communication system. The leads system provides physical and electrical connection between the defibrillator and the heart tissue. The PRM communicates with the implanted AID and allows the physician to view status information and modify the function of the device as needed.

### ***Pulse Generator***

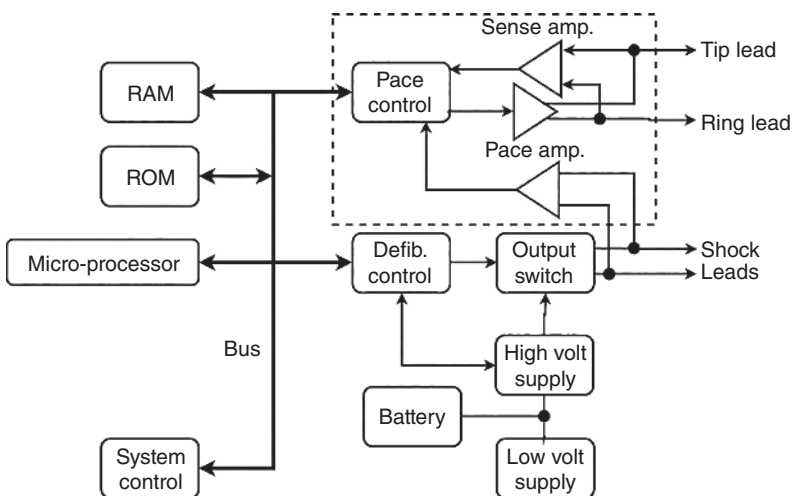
The basic components of pulse generator are shown in Figure 116.2. These include a battery, a high voltage capacitor to store and deliver charges, a microprocessor and integrated circuits for electrocardiogram (ECG) sensing, data capture, processing, storage, and control of delivery of therapeutic shock, arrangement to connect the leads used for sensing, pacing, and defibrillation. All these components are integrated as a package and encased in a titanium can. The combination of these components performs the essential functions of implantable defibrillator that includes sensing, detecting, and classification of tachyarrhythmias, delivering therapy (ventricular defibrillation or anti-tachycardia pacing), monitoring heart rhythm after therapy, and storage of episodes.



**Figure 116.2** Exploded view of implantable cardioverter defibrillator showing its various components. *Source:* van Welsenes, G.H., Borleffs, C.J., van Rees, J.B. et al. (2011). Improvements in 25 years of implantable cardioverter defibrillator therapy. *Netherland Heart Journal* 19 (1):24–30.

Figure 116.3 shows major subsystems of the pulse generator in which the microprocessor controls overall system functions. The electronics usually includes an amplifier to amplify and process sensed mV-range cardiac electrocardiogram signals and to initiate the process of generation and delivery of the therapeutic energy (shock) with high voltage switching capability under software control; DC-to-DC converter to step up the low battery voltages; adequate RAM to store appropriate patient and device data; and RF telemetry systems to allow communication to and from the implanted device and enable noninvasively programmable processing and control functions. Monolithic ICs on hybridized substrates have made it possible to achieve these diverse functions in highly reliable and commercially viable stage.

ROM provides non-volatile memory for system start-up tasks and some program space, whereas RAM is required for storage of operating parameters and storage of



**Figure 116.3** Block diagram of an implantable cardioverter defibrillator.

electrocardiogram data. The power supply to the circuit comes from lithium/silver vanadium oxide (Li/SVO) batteries. Digital circuits operate from 3 V or lower supplies, whereas analog circuits typically require precision nanoampere current source inputs. Separate voltage supplies are generated for pacing (approximately 5 V) and control of the charging circuit (10–15 V).

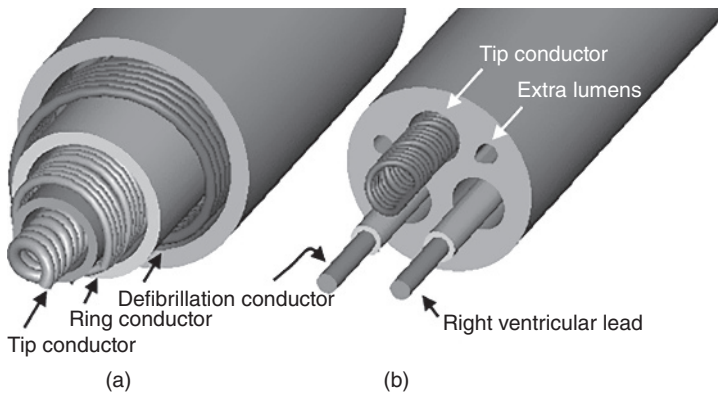
Commercially available implantable defibrillators all utilize Li/SVO cells. The most common configuration involves connecting two of these cells in series to form an approximately 6 V battery. Unlike 2.8 V lithium iodide (Li) batteries that develop high internal impedance as they discharge (up to 20 000  $\Omega$  over their useful life), SVO cells are characterized by low internal impedance (less than 1  $\Omega$ ) over their useful life. The output voltage of SVO is higher than Li ranging from 3.2 V for a fresh cell to approximately 2.5 V when nearly depleted. High power circuits convert the 3–6 V battery voltage to the 750 V necessary for a defibrillation pulse, store the energy in high voltage capacitors for timed delivery, and finally switch the high voltage to cardiac tissue or discharge the high voltage internally if the cardiac arrhythmia self-terminates. The major components of these circuits are the battery, the DC-to-DC converter, the output storage capacitors, and the high power output switches. DC-to-DC converter used to convert the 6 V battery voltage to 750 V is of classical configuration. They are operated at as high a frequency (in the range of 30–60 kHz) as practical to facilitate the use of the smallest possible core.

The storage capacitors are typically aluminium electrolytics because of the high volumetric efficiency and working voltage required. Most designs are based on the use of at least two such capacitors in series to achieve the 750 V working voltage required for defibrillation. Since the load resistance is in the range of 20–50  $\Omega$ , peak currents of the order of 40 A are common in output circuits.

The electrical activity of the heart must be properly sensed and processed to correctly establish tachycardia and ventricular fibrillation. The amplitude of the heart signals lies in the range from 100 to 10 mV, and it is essential that the sense amplifier must accurately respond to the widely varying intracardiac signals, particularly during arrhythmia. The automatic gain control circuit increases the gain if the signal being sensed drops suddenly in amplitude so that the fibrillation signal can be sensed correctly. The power consumption of these circuits has a direct impact on device longevity. Therefore, complementary metal-oxide semiconductor (CMOS) or combination of CMOS and Bipolar technology (BICMOS) IC technologies are generally used to achieve low power designs of ICDs.

Highly advanced arrhythmia detection algorithms are employed to achieve a high degree of sensitivity and reliability. The performance of the device is continuously monitored and documented to accomplish appropriate programming of arrhythmia detection and therapy parameters. Most defibrillator detection algorithms depend primarily on heart rate as a basic parameter to detect the presence of a treatable rhythm. Additional features often include morphology assessments and analysis of rhythm stability and rate variability.

**Leads** Leads are electrode-tipped wires that are placed into the chamber(s) of the heart. They are designed to sense the electrical activity of the cardiac muscles, as well as deliver an electric impulse and shock. All modern ICD systems can also function as pacemakers, being able to conduct an electrical pacing impulse from the *generator* to the tip of the leads and thus to the heart. So, the ICD lead is more complex than the average *pacemaker* lead. The modern implantable defibrillators make use of a single transvenous lead with the multiple electrodes inserted into the right ventricle for ventricular pacing and



**Figure 116.4** (a) Cross section of coaxial lead of a single coil defibrillation lead with true bipolar sensing and pacing (b) cross section of multilumen lead.

defibrillation. Two different kinds of leads used in implantable defibrillators are shown in Figure 116.4. The coaxial lead design was used in the early devices, while the multilumen lead design is used in modern devices. The coaxial lead has a layered design composed of a tip conductor, ring conductor, and defibrillation conductor and an insulation layer between each conductor. The multilumen lead construction is based on parallel running conductors through a single insulating body. Tip and ring conductors are used for pacing and sensing, a defibrillation conductor for the coil located in the right ventricle, and a defibrillation conductor for the coil located in the superior vena cava. The main advantage of multilumen over coaxial leads is that more conductors will fit into overall smaller leads. Currently available transvenous leads are constructed much like pacemaker leads, using polyurethane or silicone insulation and platinum-iridium electrode materials.

### ***Programmer Recorder/Monitor (PRM)***

ICDs are complex technical devices with a multitude of programming options for the physician. Therefore, after the ICD system has been implanted, an external computer, called a programmer, is used to program the heart device and retrieve information from the heart device that will assist the doctor in providing heart failure treatment. A number of combinations of programmable therapy and detection options are available, and it is now usual to alter these prescriptions dozens of times over the life of the implant.

The PRM provides a bidirectional communications link to an implanted ICD. This telemetry link is established from a coil, which is contained within the wand of the PRM, to a coil that is contained within the implanted device. This telemetry channel aids in retrieving real-time and stored intracardiac ECG, therapy history, battery status, and other information pertaining to device function. Programmers are capable of maintaining continuous communication with the pulse generator at a data rate of 2–4 kbps, which is adequate for transmission of one to four channels of ECG signal and other device or patient data.

**Types of ICDs** Depending on the number of leads, their placement into the cardiac chambers, and the therapy offered, there are three types of ICDs: single, dual chamber, and biventricular devices.

*Single chamber:* These have a single lead that is placed in the right ventricle and provide antibradycardia and antitachycardia therapies. A typical single channel ICD is shown in Figure 116.5. Single chamber atrial implantable cardioverters are also available, for example, Model Advisa SR MRI™ A3SR01 from M/s Medtronic, USA. In atrial cardioverters, the device must sense low, variable amplitude atrial signals, while not sensing far-field ventricular waves. During atrial fibrillation, the heartbeats are irregular, which requires a sophisticated algorithm to recognize atrial fibrillation. If the device confirms atrial fibrillation, a shock is delivered.

*Dual chamber:* Dual chamber ICDs are preferred in patients with coexisting atrial and ventricular tachyarrhythmias, as they enable discrimination of the two types of rhythm disturbances. They have two leads that are placed in the right atrium and right ventricle. The processing unit is programmed to detect the type of arrhythmia and decide the corresponding treatment that needs to be delivered. These ICDs can provide antibradycardia pacing through the right atrium and ventricle, as also provide antitachycardia therapies, cardioversion, and defibrillation through the right ventricle only. They have better diagnostic capabilities, making inappropriate shocks during atrial arrhythmias infrequent. The block diagram of a dual chamber of ICD is shown in Figure 116.6.

*Biventricular:* These ICDs have three leads, one of which is placed in the right atrium, and the remaining two are placed in the left and right ventricles each. In addition to the functions provided by a dual chamber ICD, these ICDs are also capable of synchronized pacing to the left and right ventricles, which are useful for individuals at a risk of heart failure.

Implantable defibrillators are now comparable with state-of-the-art pacing systems. Small generator sizes, biosensors, increased longevity, dual chamber pacing, dual chamber sensing and dual chamber inhibiting (DDD) systems, and pectoral implants allow ease of use and increased implantation rate.

## Specifications

*Volume:* 33 cm<sup>3</sup>

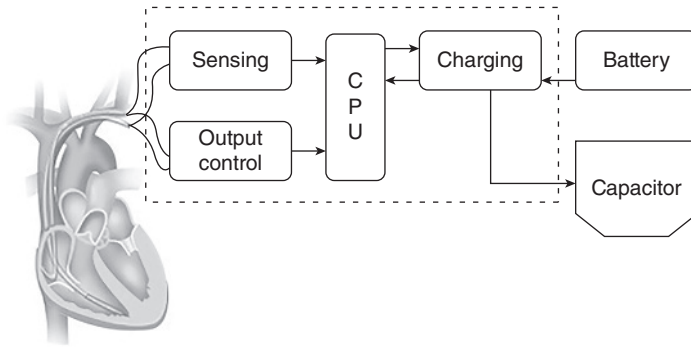
*Mass:* 77 g

*H × W × D:* 64 mm × 51 mm × 13 mm



**Figure 116.5** Single chamber implantable cardioverter model Evera MRI VR SureScan. *Source:* With Courtesy of M/s Medtronic, USA.





**Figure 116.6** Block diagram of a dual chamber implantable cardioverter defibrillator.

*Surface area of device can:* 57 cm<sup>2</sup>

*Materials in contact with human tissue:* Titanium, polyurethane, silicone rubber

*Battery:* Lithium/silver vanadium oxide

*Maximum delivered energy:* 36 J

*Maximum stored energy:* 42 J

*Typical charge time at beginning of service (BOS):* 8.4 seconds

*Typical charge time at recommended replacement:* 12.5 seconds

*Sensitivity:* 0.15, 0.30, 0.45, 0.60, 0.90, 1.20 mV

## Applications

Implantable cardiac defibrillators have proved very useful in preventing sudden death in patients with known, sustained ventricular tachycardia or fibrillation. An ICD is usually recommended for those who have a history of ventricular tachycardia, ventricular fibrillation, or cardiac arrest, an increased risk of sudden cardiac death due to previous cardiac surgery or heart failure or an inherited defect of the heart's electrical system that may increase their risk for dangerously fast heart rhythms.

117

## Defibrillator: Pacemaker Analyser/ECG simulator

### Purpose

Defibrillator analyser/pacemaker analyser/electrocardiogram (ECG) simulator is an integrated biomedical test instrument that combines the complete testing functions of a defibrillator tester, a pacemaker analyser, and a 12 lead ECG/arrhythmia simulator. This instrument is a vital test equipment in the biomedical department of a medical facility and for manufacturers of defibrillators, pacemakers, and ECG machines for quick and reliable testing of these machines.

## Principle

Defibrillator analyser/pacemaker analyser/ECG simulator is a compact device with microcontroller based design and utilizes sophisticated algorithms to control all system activities. The microcontroller with a 16 bit central processing unit contains flash programmable EEPROM, RAM, serial peripheral interfaces, etc. The instrument may be battery or AC mains operated. The instrument allows viewing and selecting the desired waveforms and test data quick and intuitive, with all operational information displayed on the  $240 \times 64$  pixel graphic display.

Figure 117.1 shows a generalized block diagram of the instrument. The device incorporates a 16 bit microcontroller. All functions of the device are controlled by the menu and key interaction. The eight keys are directly interfaced with the microcontroller. The display is a 20 character 4 line LCD that interfaces directly with the microcontroller. The memory consists of 32k internal ROM, 32k external ROM, and 32k RAM. The internal and external PROM contains the software necessary to control the device. The static RAM is used during program execution to hold buffers and stack operation.

A typical instrument for testing defibrillators and pacemakers with an ECG simulator is shown in Figure 117.2. The details of these tests are as follows:

### Defibrillator Test Functions

These tests include measurement of the energy output and information about the defibrillation pulse. These tests are applicable for use on manual, semi-automatic, and automatic defibrillators with monophasic or biphasic outputs. These devices primarily measure the output energy the defibrillating pulse carries. Other information relates to maximum voltage and current as well as the pulse timing with respect to the R wave of the ECG.

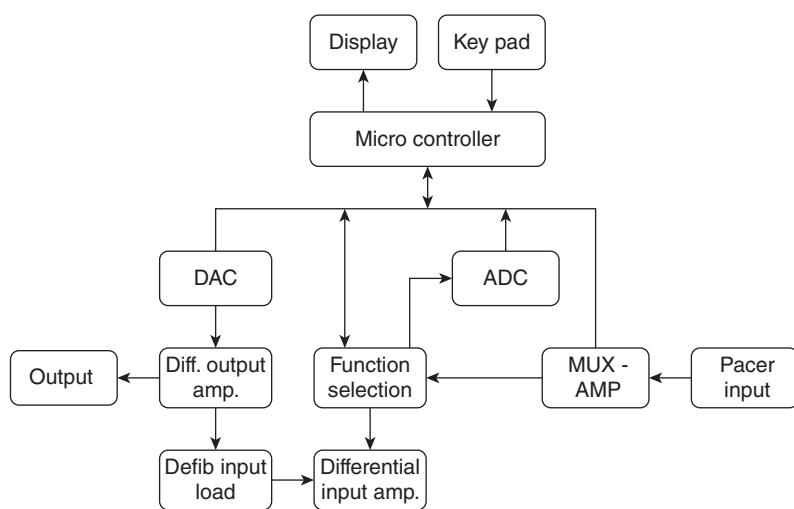


Figure 117.1 Block diagram of a defibrillator/pacemaker analyser/ECG simulator.



**Figure 117.2** Defibrillator/pacemaker analyser/ECG simulator Model Delta 3300. *Source:* Image Courtesy of M/s Netech, USA.

The human body has characteristic impedance that may vary, but  $50\Omega$  is used for comparative defibrillator testing. Accordingly, a large  $50\Omega$  non-inductive, high power resistor is used to simulate human body impedance. The resistance is designed to accept repeated pulses at the maximum energy levels. The energy contained in the discharge pulse is determined mathematically based on the fact that the energy is defined as the integral of the power curve. The following formulas form the basis of computation of the energy:

$$\text{Energy} = E = \int P dt$$

$$\text{Power} = P = \frac{V^2}{R} \Rightarrow \int E = \frac{V^2}{R} dt = \int \frac{V^2 dt}{R}$$

where 'V' is the discharge voltage across the load resistor 'R' and 't' is the duration of the waveform in seconds.

The computation of energy is implemented digitally by measuring the instantaneous voltage by taking timed samples every  $100\mu s$  for 100 ms yielding 1000 readings. The microcontroller computes the energy by summing up the squared voltages multiplied by time and divides the product by 50 (load resistance). The peak voltage measurement is performed by obtaining the largest value of the samples after a pulse measurement is recorded. The delivered energy of a defibrillator is measured in joules (watt-seconds). The energy is usually measured in two ranges: 0–100J (low) or 0–1000J (high). The maximum voltage of the pulse may be limited to +6000 V.

The defibrillator testing circuit consists of a voltage input measurement section and an analog output section. The input circuit measures the defibrillator discharge pulse. The analog output is used to generate ECG or pacemaker test waveforms. The input circuit has two resistors of  $25\Omega$  each, 100 W, non-inductive power resistors that absorb the power from the defibrillator discharge pulse. These power resistors are followed by a series of low power resistors whose function is to divide the voltage of the defibrillator discharge pulse. These resistors are used to provide protection to the output drive circuitry from the defibrillator discharge pulse. The low voltage obtained is amplified in a

differential amplifier followed by an A/D converter to get digital signal. This value is then processed by the microcomputer and displayed on the LCD. The peak voltage and current are usually displayed simultaneously. The cardioversion delay time of a defibrillator in its synchronized mode is measured in milliseconds from the R wave peak of the simulated ECG waveform. The defibrillator pulse waveform can be displayed on an oscilloscope or can be printed on a recorder.

### **Pacemaker Analyser**

Pacing system analyser is useful in the operating room or catheterization laboratory during pacemaker surgical procedures. The analyser can help to determine optimum voltage and pulse width thresholds with the resultant current flow, thus helping to determine the stimulation thresholds. Likewise, the R-wave amplitude of the heart sensed by the implanted electrode is displayed thus helping to determine the sensitivity threshold. The pacer output measurement consists of peak voltage, peak current, pulse width, pulse rate, paced refractory period, sensed refractory period, and pulse energy. They also determine sensitivity levels of on-demand pacemakers. The analysing system has two independent functions as follows:

- (i) *A synchronous pulse generator with variable rate, pulse duration, and output voltage:* These parameters help the physician to determine the stimulation threshold. ECG and arrhythmia waveforms, along with performance waveforms, are generated by an internal digital-to-analog (D/A) converter and are available on the ten patient lead connectors. For sensitivity testing, a square, triangle, or haversine waveform with widths ranging from 10 to 200 ms is used. The input circuitry of the device is protected against damage in the case of an accidental defibrillator discharge into the pacemaker input terminals.
- (ii) *A digital measuring system helps to test the operation of the pulse generator as well as the lead:* The system provides a digital readout of the pulse amplitude, pulse rate, and pulse width available at the output of the pulse generator. The series of test capabilities are useful when verifying the proper operation of a pulse generator to be implanted and when troubleshooting for a suspected malfunction in an implanted system. The pace pulse is analysed by the microcomputer. The load resistance for the pace function can be the same load resistance for the defibrillator pulse or a separate set of internal load resistors from 100 to 1000  $\Omega$  can be used. This allows the user to be able to analyse the pace pulse at many different loads. The system can measure pace pulses with an amplitude of 4–300 mA, with widths from 0.6 to 80 ms and rate limits are from 30 to 800 ppm.

For pre-implantation sensitivity testing of ventricular synchronized and ventricular inhibited pacemakers, it is necessary to simulate the R wave available at the endocardial or myocardial electrode. The sine-squared waveform has been chosen for this test. A function selector is used to select the pacer function. Separate input loads are used for atrial and ventricular pacer inputs. The transthoracic pacer inputs are connected to a fixed 50  $\Omega$  load or a variable load. The appropriate input is selected by the multiplexer switch and fed to a differential amplifier, which is then fed to the A/D converter via the function selector switch.

### ECG/Arrhythmia Simulator

The device generates simulated normal sinus rhythm ECG waveform and several common types of arrhythmias. In addition, it also generates sine, square, triangle, and pulse performance waveforms.

The ECG waveform is generated by a D/A converter. The output of D/A converter is buffered and scaled for the ECG output. ECG and arrhythmia waveforms are available at the ECG leads, the defibrillator paddle contacts, and the pacemaker output attenuator that contains all of the resistive dividers used to generate the individual ECG output voltages. The nominal ECG voltage is 1 mV. This signal is sensed by the automatic defibrillator to trigger the output pulse.

These devices are mostly battery operated using two 9 V alkaline batteries. The battery circuit incorporates low battery detection, and when the battery voltage is lower than 6.5 V, it sends a low battery signal to the microcontroller. An external power jack is provided for use with the AC adapter. When the AC Adapter is plugged, the battery voltage gets disconnected.

## Specifications

### *Defibrillator tester*

*Energy measurement load resistance:*  $50\ \Omega \pm 1\%$  non-inductive

*Range (high):* 1000 J, (low): 2–100 J

*Maximum voltage:* 5200 V (high range), 1750 V (low range)

*Maximum current:* 100 A (high range), 32 A (low range)

*Accuracy:*  $\pm 2\%$

*Cardioversion (sync.) time range:* 0–250 ms

### *External pacer analyser*

*Test load:*  $50\ \Omega$  (fixed) and variable 100–1000  $\Omega$

*Current:* 1–200 mA

*Pulse width:* 0.5–80 ms

*Refractory:* 20–500 ms

### *ECG arrhythmia simulator*

*ECG waveform:* Normal sinus rhythm, rate: from 30 to 300 bpm

*Performance waveforms:* Sine, square, triangle

*Pulse rates:* 0.5, 1, 2, 10, 15, 20, 25, and 40 Hz

*Arrhythmia waveforms:* All commonly encountered Arrhythmia waveforms

*Amplitudes:* 0.5, 1, 1.5, 2, 2.5, and 3 mV

*Waveform output:* 12 lead ECG

## Applications

The defibrillator/pacemaker analyser with ECG simulator is designed to accurately measure the output parameters of defibrillators and external pacemakers, including

both transthoracic and transcutaneous devices. A wide variety of arrhythmia waveforms are useful for testing automatic defibrillators, ECG machines, cardiac monitors, and arrhythmia monitors. They are essential equipment in repair, maintenance, and calibration of laboratories and workshops.

## 118

### Dental Amalgamator

#### Purpose

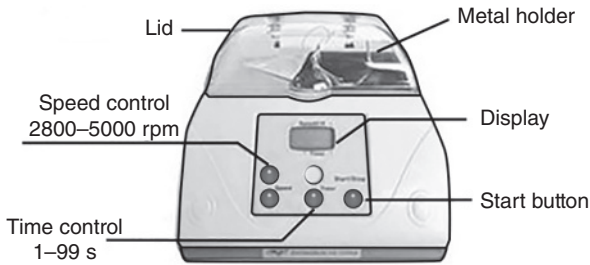
A dental amalgamator is a device that is used in the field of dentistry for the blending of restorative materials such as silver amalgam capsules and glass ionomer. The dental alloys, such as amalgams or cements, are required to be mixed using predetermined constituents in a specific ratio before they can be applied. It is possible to pre-dose the individual components in the required quantity using a dental amalgamator. As a result, the user does not directly come in contact with the constituents of the amalgam. This offers a great advantage in case of amalgams, which may involve handling with the toxic mercury. In addition, automatic capsule mixers allow quick mixing of the components so that adequate time is available for application and the patient has not to wait for too long a period.

#### Principle

A modern amalgamator is a computerized mixing system that works under the control of a microprocessor. This ensures a precise, controlled, and consistent mix. The main components of an amalgamator are a series electric motor and a holder for receiving the capsule with the materials to be mixed for providing the filling compound. Special vibration dampening techniques are used to ensure self-protection, high mixing frequency, and stable performance. The operation of the motor causes the holder to be vibrated and thereby mixing the filling materials in the capsule. The motor must be of low noise type and provide a high mixing frequency and stable performance. The device must be suitable for mixing capsules of different brands and specifications.

In amalgamators, the armature shaft of the electric motor extends to both sides of the motor. A capsule holder is coupled to each of the armature shaft ends so as to enable two movable holders for independently mixing two different dental fillings. The holders are suitably connected with the electric motor to have strokes that are of different lengths and that substantially cancel each other and thereby minimize the vibration of the amalgamator. The typical amalgamator is designed to hold the ends of the capsule in a claw that is oscillating in a figure-of-eight pattern. The design accelerates the mixture towards each end of the capsule during each throw and impacts the mixture with the pestle.

Several types of dental amalgamators are available in the market. A typical dental amalgamator with various controls is shown in Figure 118.1. Some amalgamators operate at a single speed, while others have variable speeds that is categorized as low,



**Figure 118.1** Dental amalgamator with various controls.

medium, or high and path in which the capsule moves during trituration. Manufacturers of amalgamators generally recommend the speed and mixing times that are required for the type of dental alloy to be mixed. In general, the higher the speed, the lesser the trituration time. Usually, 10–15 seconds is adequate to produce a homogeneous and uniform mixture. During operation of the machine, a safety cover ensures that the spillage of any mixing component, if any, does not fall outside the machine. The amalgamator automatically deactivates when the front cover is opened to access the capsule.

## Specifications

- *Motor power:* 40 W
- *Blending speed:* Selectable from 2800 to 5000 rpm
- *Range of timing:* 1–99 seconds
- *Noise level:* Less than 65 dB
- *Amplitude:* 25 mm

## Applications

Amalgamators are used to form amalgam fillings for treating cavities found in teeth. So, they find applications in every dentist's office.

# 119

## Dental Casting Machine

### Purpose

The dental casting machine is used in dental laboratories to make dental restorations such as inlays, onlays, crowns, bridges, and removable partial dentures. The machine is employed for all types of casting requirements in the dental laboratory from non-precious metal alloys to precious metal alloys except titanium.



## Principle

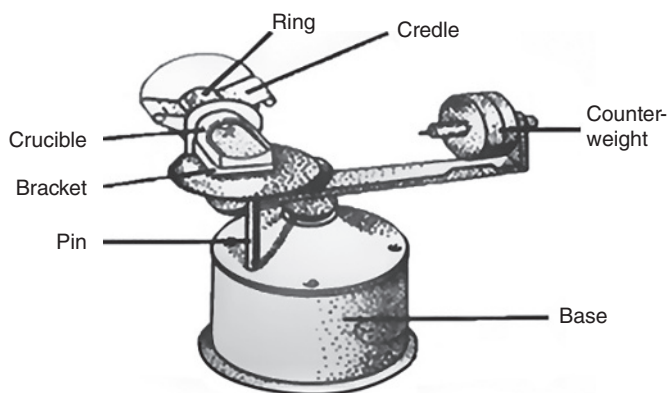
The act of forming an object in a mould is referred to as casting. The object thus formed is also referred to as a casting. The process of casting converts a wax pattern of a restoration to a replicate in dental alloy. Since the restorations and consequently the castings must meet stringent dimensional requirements, the casting process assumes extremely demanding role. A crucible made of heat resistant material serves as a container in which the alloy is melted prior to casting. In dentistry, ceramic or quartz crucibles are generally used.

Casting is a complex process involving a number of steps and equipment. The most important step is forming a wax pattern of the final restoration, taking all precautions to avoid distortions. The dental casting machines can be categorized into two types as follows:

*Centrifugal force type:* Most casting in the dental laboratory is done in a centrifugal casting machine. This type of machine makes use of centrifugal force in which the molten alloy is accelerated outwards by rapid spinning and the liquid metal is thrown into the mould. The machine may be spring driven or motor driven. The purpose is to force the liquid metal under sufficient pressure, so that the pressure can be maintained for at least four seconds after the metal has been cast. Pressure is necessary because the liquid with high surface tension will not enter the mould on its own. The principle of centrifugal force casting machine is shown in Figure 119.1.

Centrifugal casting machine is also known as broken arm casting machine because it has an arm that is supported in the middle by a rotating spindle. One side of the arm carries the weights to balance the machine, while the other side of the arm has crucible to melt the metal and an arrangement to hold the casting ring. This type of machine can be used to cast both large and small castings.

*Air pressure type machine:* In this type of machine, either compressed air or gases such as carbon dioxide or nitrogen are used to force the molten metal into the mould. Some machines employ argon gas to protect the alloy from oxidation, especially when melting titanium. This type of machine is mostly used for small castings. Both centrifugal and gas pressure type casting machines are available with attached



**Figure 119.1** Principle of centrifugal force type casting machine.

vacuum systems. The vacuum assists in creating a negative pressure within the mould, which facilitates drawl of the alloy into the mould.

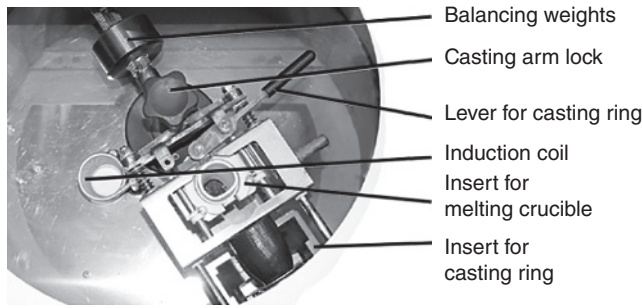
The casting machines are also sometimes categorized based on the heating system used for melting the alloys. Except for pure titanium, all precious metal and non-precious alloys can be cast with casting temperatures of between 700°C and 1550°C. Optimal casting temperatures have been determined for alloys generally used in dentistry and stored in special casting programs for the machine control. The measurement of the temperature is done using a precision optical system (pyrometer) that is fixed to the hinged screen. The pyrometer measures the temperature of the melt without contact. Casting time control is fully programmed and automatic with a multichannel temperature control. Along with proprietary software, the casting process can be largely automated. This assures reproducible quality during casting process, which can be documented and archived on a PC via the USB interface. The commonly employed heating methods are the following:

*Torch melting:* This method employs a torch flame to melt the alloy. The flame is generated by using a combination of natural gas and compressed air or natural air and oxygen or acetylene gas. The latter combination gives higher temperature range from 1100°C to 1300°C. The air and gas mixture is adjusted to get a reducing flame as it is the hottest part of the flame and does not contaminate the alloy. The torch melting is employed for heating low temperature alloys with melting temperature <1200°C.

*Arc melting:* In arc melting, direct current is passed between two electrodes – tungsten and the alloy. The arc produces very high temperatures and is used to melt high fusion metals like titanium. Arc melting can be done under vacuum or in an inert environment like argon.

*Induction melting:* Induction heating is the most common method used for melting most of the dental alloys. The induction heating process operates based on the principle of energy transfer used in transformers and known as induction. It consists in heating an electrically conducting object, usually a metal by electromagnetic induction, when a secondary current is produced through induction that flows on the surface of the metal to be melted, and this current is transformed into heat, which then melts the metal. The electrical turmoil created by the eddy-currents in the molten metal ensures that the metal is thoroughly mixed. The subsequent centrifugal force that casts the molten material into the form also helps with homogenisation.

The induction heater comprises of an electromagnet, through which high frequency alternating current is passed. With this heating, the metal in the crucible that is surrounded by water-cooled metal tubing gets melted. When the metal reaches the casting temperature, it is forced into the mould by air pressure, vacuum, or both. When induction melting is combined with those of vacuum pressure casting, the oxygen level in the casting chamber is greatly reduced within a very short time and the alloy quickly melts. The melt then flows directly under vacuum from the hot area into the mould without temperature loss. Within fractions of a second, the still molten alloy is then pressed into the finest crevices of the object. Induction melting is preferred for melting high-fusing alloys like metal-ceramic and base metal alloys.



**Figure 119.2** Constructional parts of a dental casting machine.

Figure 119.2 illustrates various components of a casting machine based on the induction principle. The heart of the machine is a medium-frequency generator that is enclosed in a sheet steel housing. The frequency generator produces a 110 kHz electromagnetic field that heats and mixes the molten metal to a high homogeneous consistency. The induction coil is water-cooled so as to provide against overheating. The crucible is held by the centrifugal arm in the casting chamber and the mould ring. A counter weight to the centrifugal arm ensures smooth and quiet running. The heating element or the induction coil is usually located in the lower section of the chamber. It rises automatically and encircles the crucible when the program is initiated. After the heating phase, the casting process is started. The induction coil gets lowered and the casting cycle commences. The melting process can be observed through a protective glass integrated in the cover lid.

There does not appear to be much practical difference in the properties or accuracy of castings made with any of the three types of casting machines. The choice is entirely a matter of personal preference and access to a particular equipment. But there are some advantages of induction casting machines that include high melting capacity with low energy consumption, homogeneous melting and casting, minimum material loss, less finishing required, and easy operation.

## Specifications

*Average power consumption:* 1.5 kW

*Melting time:* Within 3 minutes

*Maximum weight of metal to be melted:* 100 g

*Minimum melting quantity:* 15 g

*Maximum melting temperature:* 1750 °C

*Cooling water flow:* Chiller or direct water cooling

*Compressed air or argon:* Air 0.5–1.0 MPa, Argon 0.5–0.8 MPa

*Casting method:* Vacuum and pressure casting with induction heating

## Applications

The casting machines are used in dental laboratories for meeting all types of casting requirements from non-precious metal alloys to precious metal alloys except titanium.

120

## Dental Furnace

### Purpose

A dental furnace is used for producing ceramic dental restorations such as crowns, bridges, inlays, and onlays. They are designed to process the materials that have been milled, layered, or waxed up.

### Principle

The dental ceramics form a part of systems designed to be used as dental prostheses, which in turn replace the missing or damaged dental structures. Ceramics are inorganic, non-metallic materials, usually of a silicate nature, produced by heating of raw minerals at high temperatures. It can be a combination of one or more metals with a non-metallic element, usually oxygen. Ceramics are usually brittle, which implies that they display a high compressive strength, but low tensile strength, and may be fractured under very low strain levels. As restorative materials, dental ceramics do not have the ability to withstand functional forces that are generated in the oral cavity during chewing of the food and other such actions. Thus, they need to be hardened before they can be used. Metal ceramic based systems combine both the aesthetic properties of ceramics and the mechanical strength of metals.

### Types of Furnaces

Dental ceramic furnaces employ high temperatures and pressures to process ceramic materials into a hardened, final state. These furnaces fall into several categories including firing furnaces, pressing furnaces, sintering furnaces, and glazing furnaces.

*Firing furnace:* The firing furnace is the most important equipment of the dental laboratory. The furnace is used to vitrify porcelain. These furnaces require accurate temperature and heat rate control and mostly operate under vacuum. So, maintenance of temperature and vacuum conditions is essential.

*Pressing furnace:* They are primarily employed for pressing materials such as pressable porcelains and ceramics. Pressing furnaces, in addition to having all the same control requirements as the porcelain furnaces, also include pressing hardware and controls.

*Sintering furnace:* These furnaces operate at much higher temperatures than conventional firing or pressing furnaces. Such high temperatures can be achieved by using special ceramic heating elements and power control electronics.

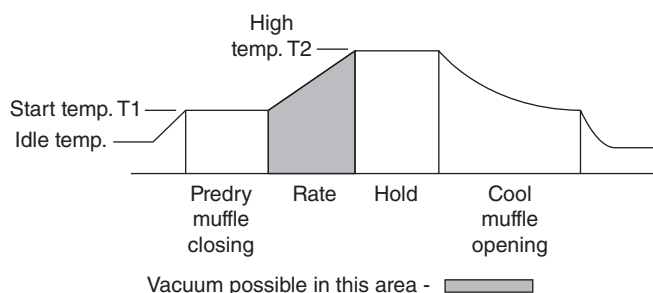
*Glazing furnace:* The glazing furnace is used in dentistry clinics for the purpose of glazing the surface of the dental prosthesis and removing partial defects in the dental model. In a way, glazing furnaces are used for setting certain stains and glazes that add the final shade details to a restoration.

## The Furnace

A typical firing furnace consists of three main components: (i) furnace head with firing chamber, (ii) electronic controller, and (iii) vacuum pump. The firing chamber may be heated up to  $1200^{\circ}\text{C}$  by means of a heating element. The maximum temperature of  $1530^{\circ}\text{C}$  is required by the majority of the zirconium oxides. The firing chamber is designed in such a way that it is possible to create vacuum within the chamber. The electronics control for the firing process is usually based on a microcontroller and associated software. The dental furnace is equipped with a programmer with either one or several configurable programs with up to eight segments. The vacuum level is generally preset by the company and is 71 cm of mercury. The acceptable range is from 22 to 75 cm of mercury. Most modern dental ovens feature touch screen controls, preset programs, and even the connectivity to the Internet.

Figure 120.1 shows a typical temperature cycle in a dental furnace. The functioning of the furnace starts by comparing the ambient temperature with the set T1 temperature. If the ambient temperature is higher than T1, the vacuum pump starts and sends cool air through the chamber. This action continues till the chamber temperature gets lower to within  $5^{\circ}\text{C}$  of T1. Thereafter, the program ramps up the temperature until it reaches the maximum set temperature T2. The ramp up is the number of degrees per minute the temperature will rise after the chamber has been closed. The range of values is  $0^{\circ}\text{C}/\text{min}$  to a maximum of  $100^{\circ}\text{C}/\text{min}$ . During the temperature ramp up, the vacuum will turn on at the programmed vacuum level until the vacuum release or T2 temperature is reached. The range of T2 values is  $25^{\circ}\text{C}$  to a maximum of  $980^{\circ}\text{C}$ . After reaching the T2 level, the temperature is held at the programmed hold time. Hold temperature is the final, highest temperature in a single-stage program and an intermediate stopover temperature in a two-stage program. The range of temperature values is from  $400^{\circ}$  to a maximum of  $1200^{\circ}\text{C}$ . After the expiry of the hold time, the muffle will be opened and cool down at the programmed rate till the initial T1 temperature is reached. This is followed by drawing the cool air through the chamber by turning on the vacuum pump to lower the temperature to the ambient temperature.

The furnace is heated by using one or more silicon molybdenum rods. It includes proportional, integral, derivative (PID) program temperature control and over temperature alarm protection system. Furnace body is made of powder-coated sheet steel or



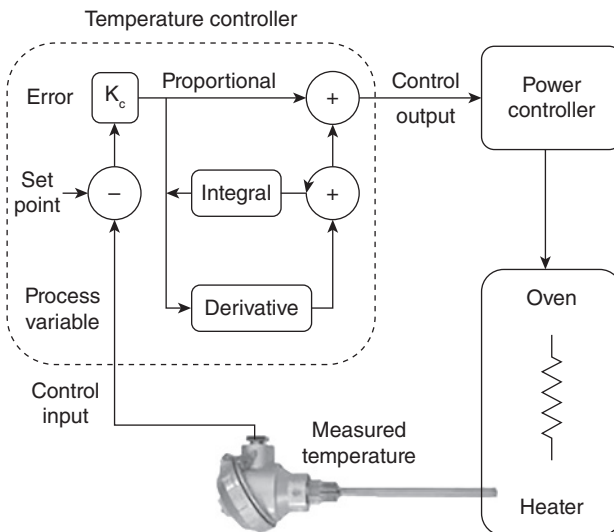
**Figure 120.1** Temperature cycle in a typical dental furnace.

lightweight, high alumina fibre materials. Ceramic furnaces for the fabrication of metal-ceramic and all-ceramic dental restorations are usually operated at a temperature range from 600°C to 1000°C. For zirconium dioxide ceramics, higher temperatures are desirable, which could go up to 1600°C. It is desirable to ensure high-quality temperature control with an accuracy of  $\pm 2^\circ\text{C}$  across the entire temperature range.

Most conventional dental furnaces use a thermocouple for measuring the temperature in the firing chamber. The thermocouple is generally placed in the upper section of the firing chamber and at a close distance from the ceramic object. Thermal imaging technique using an infrared camera can also be used for temperature measurement directly on the object in the firing chamber. This technique has the advantage that even if there are draughts, the infrared technology always measures the correct temperature on the surface of the object in the firing chamber.

Most heating requirements in furnaces can be handled by using a simple proportional control. A proportional controller has the ability to continuously adjust the output so that the power input to the process is in balance with the process demand. However, more sophisticated dental furnaces employ a PID controller that is based on examining the signals that are received from sensors placed in the heating chamber. These signals are called feedback or error signals. When an error signal is received, it is compared with the desired or set-point value on the furnace. The system then calculates the response that is necessary to match the deviation from the set point. A block diagram shown in Figure 120.2 illustrates the working of a PID controller. The PID controller does its job by the following three modes of action:

- *P (proportional)*: It is the factor that determines the basic rate of change at the output in response to changes in the input. Proportional control adjusts the amount of power



**Figure 120.2** Block diagram of proportional, integral, and derivative (PID) temperature controller.

supplied to the heating elements in direct proportion to the difference (the error) between the actual temperature value and the required set value.

- *I (integral)*: This function modifies the proportional element and is based on the time that a difference between set point and actual temperature exists. The integral function prevents the initial overshoot on power-up.
- *D (derivative)*: A function of the rate of change while the actual temperature is moving with respect to the set point. The derivative function eliminates the temperature instability over time once the set point is achieved and the process is under control.

Modern dental furnaces are microprocessor controlled that offer advantage of programmability and memory system that can remember even up to 200 different programs, which can be performed accurately by the user. Multistage programs are used for firing or sintering of ceramics where it is necessary to heat and hold at one temperature and then heat or cool to another programmed temperature. This type of flexibility of the programming allows to create many different types of programs. There is automatic temperature adjustment to  $\pm 1^\circ\text{C}$  every time a program is started. An W display (LCD) digital display shows current program information and the status of the process progress. There is a provision for automatic prevention of condensation in the firing chamber.

The pre-drying of ceramic materials is a critical phase in their processing as it determines the risk of crack formation and the final quality of the restoration. This is usually achieved in conventional furnaces by regulating the set time and temperature, both being based on the empirical data. However, if the ceramic is still too moist after this pre-drying process, there is every likelihood for the cracks to occur in the restoration. The new infrared technology overcomes such different situations and adapts the firing parameters to the respective situation. The system has the ability to identify the exact time when the moisture in the ceramic has evaporated and only then closes the furnace head. Subsequently, the software initiates the actual firing process.

## Specifications

*Housing*: Sheet steel, powder coated

*Firing chamber diameter*: 90 mm

*Firing chamber height*: 55 mm

*Maximum firing temperature*: Maximum 1200–1600°C

*Temperature accuracy*:  $\pm 1^\circ\text{C}$

*Maximum energy usage*: 1.5 kW

## Applications

Dental furnace is used in dental laboratories for baking and drying ceramics relating to restorations into a hardened, final state.



# 121

## Dental Sandblaster

### Purpose

Dental sandblaster units are used in dental laboratories to remove residues, oxides, and ceramics on cast objects, thereby increasing bond strength and effective surface area as well as polishing the surface of castings. In addition, many medical prosthetic implants, such as hips and knee joints and dental implant screws, are blasted to produce a precise keyed surface topography, which improves adhesion of special coatings to assist in their integration into the bone surrounding the implantation site. Sandblasters are also used intraorally in a dental clinic, referred to as air abrasion. Intraoral dental sandblasters have a variety of angled tips allowing the technician to reach any part of the mouth.

### Principle

Sandblasting is a technique in which a stream of abrasive material, usually sand, is forcibly propelled under high pressure typically with compressed air against a surface to smoothen a rough surface, roughen a smooth surface, shape a surface, or remove surface contaminants. Sandblasters used in dental laboratories are generally enclosed cabinets and often operate through a vacuum or via air compressor, with integrated gloves for hand protection and containment of the blast media. The dust is constantly removed by a dust collector from the cabinet, and the blast media is recycled to provide a continuous and reliable cleaning and finishing system. Sandblasting media can be aluminium oxide, glass beads, or silicon carbide grit.

The sandblasters generally use an air-powered pressure gun that fires out the sand at high velocity to impact with the intended surface. The pressurized gun has a ceramic barrel or interior coating to prevent the sand from eroding it over time. As the processing takes place in a closed cabinet, a provision is made to check the work carried out by observing it through a transparent screen mounted on top of the machine. The device has two handpieces as shown in Figure 121.1, with metal carbide sandblasting nozzle and a selecting valve that allows your choice to operate the handpiece. The processing may result in different degrees of finishing, varying from coarse to fine depending upon the particle size of the abrasive material and the type of work pieces. Basically, there are three types of sandblasters:

*Gravity-fed blasters:* This type of unit has three basic parts – an air compressor or pressurized air tank, a handheld pressure gun with air hose, and a hopper on top of the gun. The hose is connected to the pressurized air source, and the hopper is filled with silica sand. When the trigger of the gun is operated, compressed air fires through the gun and an opening at the top of the gun into which the hopper is connected opens. The air flowing through the gun and the force of gravity pulls the sand down through the gun and pushed out of the barrel.



**Figure 121.1** Dental sandblasting unit. *Source:* Image courtesy of M/s Vaniman, USA.

*Pressure blasters:* These are most popular and consist of a large canister containing silica sand under high pressure. The blasting gun is connected to the port at the top of the canister through a specialized hose that can withstand the abrading effects of the sand. When the gun is operated, both the air and sand are forced out as a single entity. The disadvantage is that the fired out sand cannot be collected and reused.

*Siphon sandblaster:* The siphon sandblaster can be used to clean and strip large surfaces. It has a normal pressurized tank or air compressor. It also has a reservoir of loose sand, which may be in the form of a large bucket or container of some kind. The air hose of the blasting gun is connected to the compressor; while the other hose of the gun is connected to the separate sand reservoir. When the gun is fired, the air serves to create a suction, which pulls the sand from the reservoir up the hose and into the gun to be fired out the barrel. As a result of this system, the sand that is fired out the barrel can be collected and placed back in the reservoir to be reused again and again.

*Compressor:* Air compressor size is crucial to the operation of the abrasive blast system as there should be sufficient air supply capacity that is necessary to maintain the system air pressure. The size of the compressor is determined by considering the pressure to be developed and the volume of air that can be moved in one minute (cubic feet per minute [cfm]) by the compressor. The cfm for a particular application is determined by the compressor cfm, the sandblaster cfm, and the size of the nozzle. Clean, dry, compressed air is one of the most important requirements for proper operation of a sandblaster. Contamination by water and or oil

will cause clumping of the abrasive, limiting the abrasive from flowing freely and evenly to the blasting tip.

**Nozzles:** The blast nozzle is an important part of the blast operation since its size determines the air flow and abrasive requirement. The nozzles are available in various materials, sizes, and types for different abrasives used. A ceramic nozzle is ideal for jobs with lower pressure (5 cfm), whereas a nozzle made from tungsten carbide is ideal for jobs up to 25 cfm. Different sizes of nozzles ranging from 0.5 to 2.0 mm can be fitted, suitable for abrasive grain size 25–200  $\mu\text{m}$ .

The sandblasting units often include ‘pencil blaster’ (microetcher), which provides ultra-fine, microblast system for cleaning, preparing, or finishing precision components. This allows the dual function of a larger blast gun for faster cleaning and the pencil blaster for intricate work. The pencil blast unit is a compact air-powered pressure-fed blast system fitted with hard metal stylus-type nozzles available with 0.8, 1.2, or 1.8 mm bore blast nozzle and comes complete with foot pedal control. The pencil blaster measures only 300 mm high by 300 mm wide and 230 mm deep. The microetcher requires compressed air of 40–100 psi (2.6–6.6 bars) at 1 cfm (30 ccm/m). There is a significant reduction in sandblasting action as the pressure is reduced below 60 psi. Bottled highly compressed air or gas such as  $\text{CO}_2$  with a regulator can be used with a microetcher.

The handheld miniblasters such as shown in Figure 121.2 are also available. However, they do not have dust collectors included in them. Micro-abrasive blasting technology derived from sandblasting consists in mixing fine abrasive with dry air that can be streamed through a small nozzle to target small areas accurately. It is usually used to texture the surface finish on the threaded portion of the implant.

Sandblasters can be a major source for very fine toxic dust particles, which are harmful when inhaled. In some machines, a filtering system is used to avoid this situation. The water air filtering system eliminates airborne dust with the combined action of water and air pressure and starts automatically when the sandblaster is switched on.



**Figure 121.2** Typical dental miniblaster.

## Specifications

*Nozzle materials:* Carbide/ceramic

*Nozzle diameter:* 1.2 mm/0.8 mm

*Particles size:* 50–250  $\mu\text{m}$

*Power consumption:* <8 W

*Working pressure:* 14.5–116 psi

*Handpiece:* Twin pencil with different nozzle sizes

*Number of tanks:* Two (0.5–1 l capacity)

*Control:* Pneumatic foot control

*Air output:* 60–70 l/min

## Applications

Dental sandblasters are used in dental laboratories for surface preparation or porcelain clean-up and in dental clinics for various procedures.

# 122

## Differential Counter, Automated

### Purpose

Differential blood counters are designed to measure absolute value of different types of white blood cells (WBCs, leucocyte) in a sample. The results of the differential blood count reveal a wide range of important haematic pathologies. For example, the presence of infections, leukaemia, and some particular kinds of cancers can be diagnosed based on the results of the classification and the count of WBCs. Also, this helps to identify abnormal WBC populations such as blasts, immature granulocytes, or circulating lymphoma cells in the blood. Absolute values of leucocytes are also useful for monitoring during chemotherapy, bone marrow transplantation, or differential diagnosis of some types of patient's underlying disorders.

### Principle

Along with the automated instruments for obtaining the erythrocyte, leucocyte, and platelet counts, there has been a considerable interest in developing automated techniques for identifying and counting the different types of cells within a given class. Examples of this could be the immature red cell count, the differential leucocytes count, and the recognition of normal versus malignant cells in other cell types. Various diseases affect the mechanism of blood cell formation in different ways. In particular,

fractional proportion of the five major leucocytes is a sensitive measure for indicating and assisting in the diagnosis of various diseases, and therefore differential count tests are generally done for them. Reference ranges for differential WBC count in normal adults is as follows:

- *Neutrophils*:  $2.0\text{--}7.0 \times 10^9/\text{l}$  (40–80%)
- *Lymphocytes*:  $1.0\text{--}3.0 \times 10^9/\text{l}$  (20–40%)
- *Monocytes*:  $0.2\text{--}1.0 \times 10^9/\text{l}$  (2–10%)
- *Eosinophils*:  $0.02\text{--}0.5 \times 10^9/\text{l}$  (1–6%)
- *Basophils*:  $0.02\text{--}0.1 \times 10^9/\text{l}$  (<1–2%)

The reference ranges may vary depending on population studies, the individual laboratory, instruments, and methods.

The microscopic inspection of blood smears is an established technique that provides diagnostic information concerning patients' health status. The traditional method for the differential blood count is also performed by experienced operators using a microscope and count the percentage/absolute value of the occurrence of each type of cell counted within an area of interest in smears. The counting is done with a totalizer that shows the sum of all cells and to classify and count WBCs. A typical manual totalizer is shown in Figure 122.1. They are available as 2-key, 5-key and 8-key totalizer window. At 100 increment of total record, there is an audible signal. The reset knobs on both sides can clear all the numbers to zero.

The manual differential counting process is very laborious and time consuming. In addition, the cell classification and counting accuracy is highly dependent on the skill and experience of the operator. There is, thus, a need for automation of acquisition and interpretation of data in routine clinical differential cell count. Two approaches have been employed in the pursuit of automating the differential counting technique. The popular technique is based on the *flow cytometry*, and there are many commercially available systems that adopt this technique for counting cells. The flow cytometry-based systems though offer high throughput, but they cannot produce the images of the blood samples if there is a further requirement for verification of some abnormal conditions.

The other technique of differential counting is based on image processing. Several different approaches have been adopted over the years to implement and refine this



**Figure 122.1** Manual differential cell counters (2-key, 5-key, and 8-key).

technique. The technique is based on the premise that WBCs can be categorized into several classes according to the morphology of their contours and their nuclei. The classification of WBCs into various categories usually involves the following three stages: (i) the segmentation of a WBC from a smear image, (ii) the extraction of effective features, and (iii) the classification. Of all the stages, the feature extraction plays the most important role in the performance of an automatic WBC classification system. Most of the existing methods are based on the following features:

- (i) Geometrical features such as area, radius, perimeter, convex area, major axis length, compactness, and orientation.
- (ii) Textural features such as momentum, contrast, entropy, and skewness.
- (iii) Colour features such as colour distribution and histogram.

Automated count technology uses electrical, laser, or photodetection methods to provide a highly accurate results of differential count based on the size, shape, and number of blood cells in a sample. These methods are very accurate, even across different types of machines that do automatic blood counts. The modern machines utilize digital technology, which allows to share common morphological databases, digital image cells export, creation of digital archives, and their utilization for educational purposes.

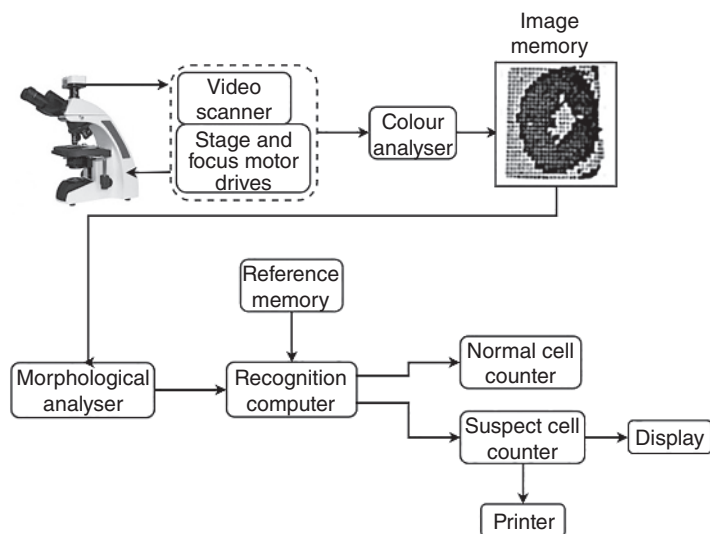
CellaVision DM 9600 from M/s CellaVision, Sweden, shown in Figure 122.2 is a differential cell counter that consists of a slide feeder unit, an optic unit consisting of a microscope and camera (slide scanning unit), and a computer system containing the acquisition and classification software. The magazines are put onto a conveyer belt and the slides are automatically transported to the slide scanning unit and placed under the microscope. The system scans and reads the slide bar code and acquires the patient demographics and order data from the laboratory information system. The slide is automatically placed under the microscope and the monolayer is identified. The system automatically captures digital images of cells from blood smears and body fluid preparations. When processing is complete, pre-classified WBCs and pre-characterized red



**Figure 122.2** CellaVision® DM9600 automated and digital workflow cell morphology system. *Source:* Image Courtesy of M/s Cella Vision, Sweden.

blood cells are extracted by software and presented for review and verification. WBCs are pre-classified into 17 cell types and red blood cells are pre-characterized based on 21 morphological characteristics. The system is designed to classify the following WBC classes: band neutrophils, segmented neutrophils, eosinophils, basophils, lymphocytes, monocytes, promyelocytes, myelocytes, metamyelocytes, blast cells, lymphocytes (variant forms), and plasma cells. The instrument has a loading capacity of 96 slides, with a mechanism for continuous feed. It provides about 30 slides throughput per hour. Body fluids, including cerebrospinal, peritoneal, and pleural fluids, can also be analysed using this instrument.

A block diagram of the cell identification steps of the system are shown in Figure 122.3. The system is built around a motorized upright light microscope with a LED illumination system. It has one 10 $\times$  objective and one 100 $\times$  oil immersion objective and intermediate optics switching between 1.0 $\times$  and 0.5 $\times$  magnification, which combined gives images with 5 $\times$ , 10 $\times$ , 50 $\times$ , or 100 $\times$  magnification. The focusing mechanism is computer controlled. The camera is a high-quality progressive-scan charge coupled device (CCD) colour camera, for maximum image quality and high speed image acquisition. The camera takes images of the identified areas, stores the images of the located cells and the results in a database, displays the images on a monitor, and shows the relative position of the cells in each field. The slide is positioned precisely on the transport to allow reloading, oil is applied from a reservoir, and the objective is focused. The unit automatically applies drops of immersion oil to a slide. An optical drop counter controls the procedure. The oil pack contains 150 ml. The automatic microscope focus mechanism operates from high frequency video information as an error signal to position a special piezoelectric focus drive. The piezoelectric crystal adjusts the lens assembly so as to maximize the high frequency content of the video signal.



**Figure 122.3** Block diagram of an automatic cell identification system.



A robot gripper unit allows fully automated focusing and XY-positioning of the slide feeder during process. It transports a slide from a magazine and back again after the slide has been processed. The magazine can be loaded with up to 12/96 slides. The bar code reader scans the bar code of both the slide and the magazine. For maximum safety, the bar code of the slide is scanned before processing. Usually, the scanning system traverses the slide in 1  $\mu\text{m}$  wide sweeps and the entire sample area is scanned. When a cell nucleus is located, the coordinates of the beam are immediately stored. The light passing through the cell is split and sent through three filters to break it into its red, green, and blue components, with highly sensitive photomultiplier tubes detecting the resulting radiation.

Based on the number of grid positions and three colours, the system has over 3 million data values to use in each cell identification. These are used to first locate and then characterize the nuclei based on size and segmentation. The instrument performs all the functions that a human being sitting at a microscope would be expected to do. However, the system is much faster than a human technologist as it can process up to 100 slides/h.

The control unit controls motors, sensors, oil application, and illumination. It functions as a slave computer to the PC via an unshared 100 Mbit Ethernet connection. A PC system running Microsoft® Windows® XP and CellaVision® DM software carries out the cell classification as follows: As the input device supplies an image, cell segmentation procedure is implemented. Segmentation provides a number of cell counters and their nuclei. This is followed by analysis by feature extraction engine of each segmented cell and its nucleus to form a feature vector from colour, shape, and texture features. The cells are then classified according to their feature vectors.

These instruments provide remote access functionality that facilitates sharing of cell images for collaboration and consultation, from any computer or laboratory sites within a network. This enables sharing of expertise and manpower between labs of all sizes, at one or multiple healthcare units. Also, network integration allows cell images to become part of the patient's medical history providing complete traceability down to the individual cell level.

## Specifications

*Slide capacity:* 12 or 96 slides (slides loaded into 8 magazines with the capacity of 12 slides each)

*Slide image size of 100 WBCs:* ~5 MB

*Digital slides:* Up to 20 slides/h for 10 mm  $\times$  10 mm at 10 $\times$

*Throughput:* Approximately 30 slides/h

*Immersion oil:* Automatic dispensing

## Applications

Differential counters play an important role in a haematology laboratory. They are used to look for quantitative abnormalities in morphologically normal WBC population such as in the diagnosis of infectious or allergic diseases and for therapeutic monitoring of certain drugs.

## 123

## Digital Subtraction Angiography Machine

### Purpose

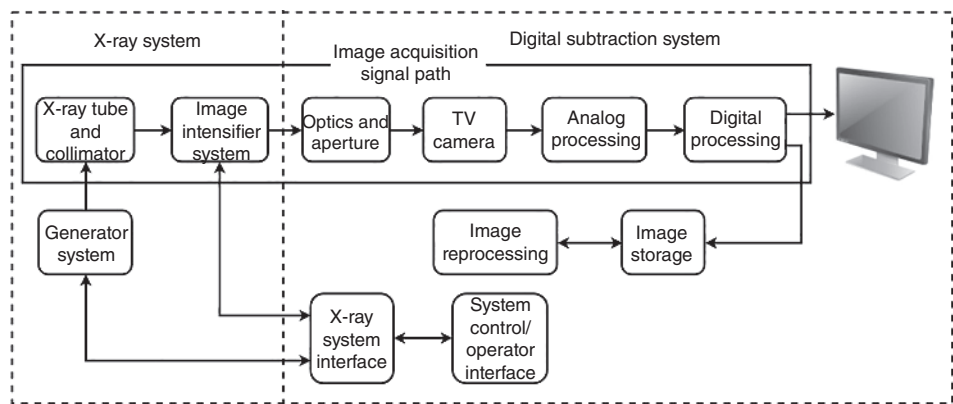
Digital subtraction angiography (DSA) machine is used as a medical diagnostic imaging modality for the visualization of the inside or lumen of blood vessels, especially the arteries, veins, and heart chambers. Traditionally, angiography was used to diagnose vascular disease, particularly the blockage caused by plaque build-up in them. In addition, the technology has been proven useful in the identification of vascular abnormalities including occlusions, stenoses, and aneurysms. In recent times, X-ray angiography procedure has been used to guide minimally invasive surgery of the blood vessels and arteries of the heart.

### Principle

Traditional angiography involves acquiring images by exposing the area of interest with X-rays while injecting contrast medium into the blood vessels. The image obtained is a composite image that includes the blood vessels and all overlying and underlying structures. The images though useful for determining anatomical position of various organs and structures are not very helpful for visualizing blood vessels accurately. The blood vessels can be seen better, if the distracting structures are removed from the image. This is done by using a technique known as DSA to improve vessel contrast. This technique uses a computer to subtract the two images, obtained before and after contrast media is injected into the vessels of interest. The anatomical structures that are same in the two images and are static can be removed or subtracted from the final image. The resulting image leaves a clear picture of the artery of interest, which can then be studied independently and in isolation from the rest of the body.

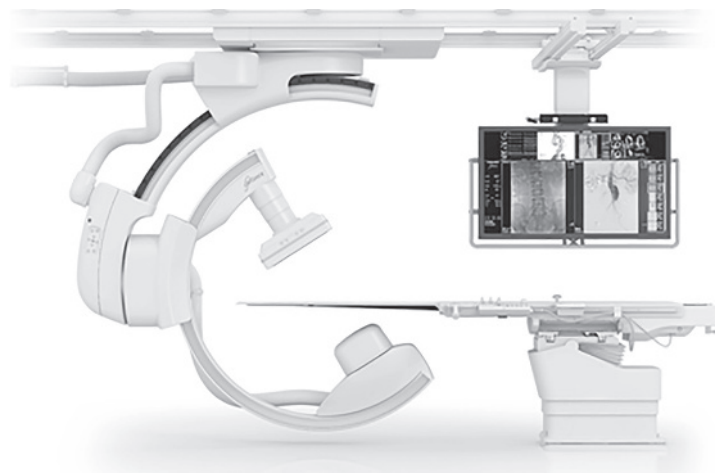
The device used to capture the images is usually an X-ray image intensifier, and the resulting image is picked up by a TV camera. The images of the area are produced at a set rate of 1–30 exposures/s. Each image gets the original 'mask' image subtracted out. Each frame of the analog TV signal is then converted to a digital frame and stored by a computer in memory or on a magnetic disc. The images are produced in real time by the computer or image processor, while the contrast medium is injected into the blood vessels. These X-ray 'movies' can be viewed in real time as the angiography is being performed. Subtraction and enhancement of images performed in real time means that the processing of data is sufficiently rapid and the results are available in time to assist in diagnosis. Advances in digital technology, including DSA, have made it possible to acquire serial images at rates and quantities not possible with conventional film changer and film-cassette technologies.

Figure 123.1 illustrates a block diagram for a DSA system. The basic components of the system include the X-ray tube and *X-ray generator*, the image intensifier, and the video camera. However, they are similar to but are of much higher quality than those



**Figure 123.1** Principle of digital subtraction angiography (DSA) system. In the digital system, the image intensifier, optics, and TV camera are replaced by digital flat panel detector arrays.

used in conventional fluoroscopy. X-rays are produced by an X-ray generator when it receives a timing signal under computer control. The X-rays are transmitted through the patient and received by the *image intensifier* beginning the image acquisition process. Flat panel digital detectors are now rapidly replacing image intensifier tubes. An aperture is usually placed between the image intensifier and the *video camera*, for controlling the amount of light delivered to the camera. A video camera acquires the light image from the image intensifier output window and converts it to an electronic video signal, which is delivered to the image processor in analog form. The images are digitized and stored in the memory by the *image processor* that allows subtraction with another image set acquired under different conditions. The images are displayed for viewing on a video screen for the detection of abnormalities. A typical DSA machine is shown in Figure 123.2.



**Figure 123.2** Digital subtraction angiography system. Source: Reproduced with permission of M/s Canon Medical, Japan.

### ***Image Intensifier***

A technology that is crucial to DSA is the X-ray intensifier tube. The operating principle of this device is to amplify an X-ray signal while simultaneously converting it into visible light for viewing. The image intensifier has a caesium iodide (CsI) input phosphor, which has excellent X-ray absorption properties. The image intensifier consists of a large evacuated glass tube with an input screen diameter ranging from 15 to 32 cm. The input screen converts the X-ray image into a light image. The light image thus produced is transmitted through the glass of the tube to a photocathode, which converts the light image to an equivalent electron image. The image intensification takes place because of the very small output screen size and electron magnification in the tube. A light aperture, similar to those used on single-lens reflex cameras, is mounted behind the output phosphor of the image intensifier. The aperture controls the amount of light reaching the video camera for a given exposure rate.

### ***Flat Panel Digital Detectors***

Flat panel digital detectors are replacing image intensifiers in modern DSA systems. These detectors comprise thin film transistors (TFTs) arranged as two dimensional arrays. The photodiodes in TFT help convert light to electronic signal just as image intensifiers. The photons not absorbed by the patient strike a layer of scintillating material that converts them into visible light photons. These photons then strike an array of photodiodes, which converts them into electrons that can activate the pixels in a layer of amorphous silicon. The activated pixels generate a high-quality image of the target, which is then displayed on a computer monitor. Flat panel arrays require less radiation dose and give image resolution comparable to conventional computed tomography machines.

### ***Video Camera***

Video camera is a critical component in the imaging chain in DSA. The video camera generates an analog electronic signal that is proportional to the amount of light received by the target of the camera. Charge-coupled devices (CCDs) can be used as the image acquisition component of cameras in video and digital photography. Scanning an electron beam across sequential lines of the video target, with the deposited electronic charge passing through the target to form an electrical current, creates the video signal. The analog video signal is a time-varying signal that represents the two-dimensional light image at the target as a temporal record. In conventional broadcast industry, the video image is acquired using interlaced scanning as it helps to reduce bandwidth during transmission while avoiding flicker in the video image. However, this type of interlaced scanning is not preferred in digital radiography as the images are found to be unstable due to lag in the video signal when the X-ray beam is initiated. Progressive mode scanning technique has been developed to resolve this problem and for best dose utilization. However, interlaced scanning is also used in some cases.

### ***Digital Image Processor***

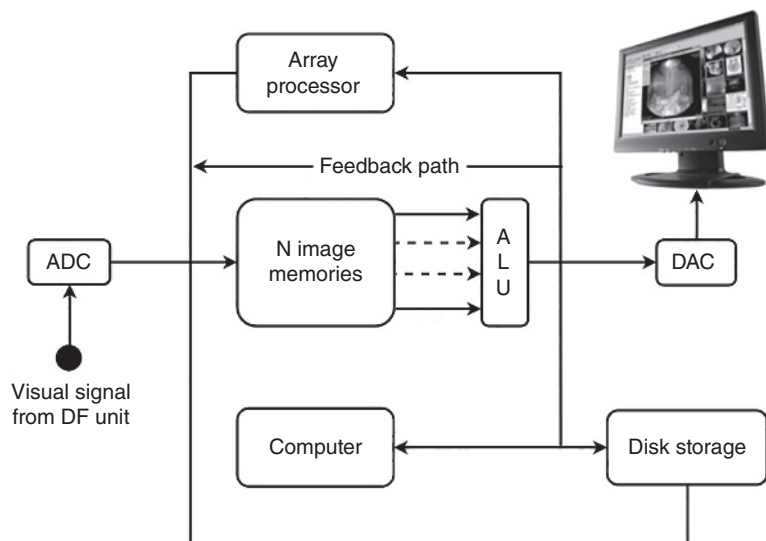
At the heart of the DSA system is a digital image processing system, which acquires images from a video camera, digitizes them and stores them as digital images in the computer

memory. It performs all arithmetic operations such as subtraction, addition, and multiplication on the image data and displays the digital images on video monitors. The image data is also stored on magnetic media or an optical disc. The image processor contains a system controller (microprocessor) that controls the basic operations of the image processor, provides timing signals to both the X-ray generator and the image acquisition system to control the flow of data from the X-ray source into the image processor, and coordinates and controls the operation of the digital imaging system.

The processor has two separate image memories, one for the mask and the other for the images with contrast medium. These two image memories are subtracted from one another arithmetically, and the results are shown on display unit. DSA systems also allow a number of options for post-processing of images. They include windowing that helps in enhancing contrast in the image, filtering, and quantitative measurements. Any motion shift that might occur in the mask image can also be removed.

Figure 123.3 shows a block diagram of a DSA image processor. The signals from the digital detectors are digitized using an analog-to-digital converter (ADC), and the resulting digital data is passed to storage in one of the image memories. There are three image memories that are required for routine DSA: one for each of the mask and live images and the third for the subtracted image. Image subtraction is performed using an arithmetic/logic unit with the subtracted image data being fed along the feedback path so that it can be stored in image memory.

Storage of digital images is required for both online and archival purposes. Online storage is provided by real-time digital discs. Archival needs are mostly met by the storage of hard copy films generated from the digital images. Hard copy devices include multiformat cameras (laser or video) and video thermal printers. Alternatively, digital streamer tape cassettes, and digital optical discs have been used to record angiographic procedures and associated images.



**Figure 123.3** Block diagram of digital subtraction angiography (DSA) system image processor unit.

## Specifications

*X-ray system generator:* High frequency generator, power ratings 100kV

*X-ray tube:* Dual focus

*Digital imaging system:* A flat detector digital system with  $1920 \times 2048$  matrix

*Frame rate:* From 0.5 to 15 frames/s

*Software:* Facility for edge enhancement, positive/negative image display, windowing, contrast/brightness, electronic shuttering, image/pixel shifting, vertical and horizontal image reversal, and zoom functions. Automatic and interactive detection of lesions and stenosis quantification

*Image display system:* Four 19-in. TFT (LCD) flat monitors, two in angio room and two on console for live and reference image display

*Control console:* All system movements of C-arm, table, image display, image review, and image post-processing and quantification controlled both by the operator at the table in the angio room and in the console room

*Digital archiving on compact disk:* System for recording in Digital Imaging and Communications in Medicine (DICOM) 3.0 or higher version

*Mechanical system (C-arm and table):* C-arm motorized with angulations of  $\pm 120^\circ$  floor mounted table with carbon fibre tabletop and swivel capability. The tabletop is equipped with gantry controls, table system controls, collimation controls, and optional intravenous poles

## Applications

Digital subtraction technique is used clinically for diagnostic and therapeutic applications of vessel visualization in the entire body. DSA is routinely used for imaging of the abdominal, cardiac, pulmonary, carotid, intracerebral, and peripheral vessels. The technique is particularly useful for diagnosis of arterial and venous occlusions, including carotid artery stenosis, pulmonary embolisms, and acute limb ischaemia. DSA is the gold standard investigation for renal artery stenosis.

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## DNA Sequencer

### Purpose

A deoxyribonucleic acid (DNA) sequencer is an analytical instrument that is used to automatically determine the precise order of nucleotides within a DNA molecule. The DNA sequencing process includes any method or technology that is used to determine the order of the four bases: guanine (G), cytosine (C), adenine (A), and thymine (T) in a strand of DNA. The developments in the rapid DNA sequencing methods have greatly

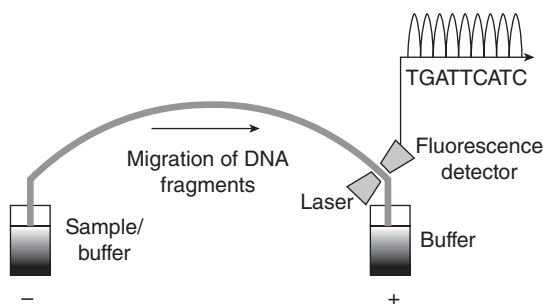
accelerated biological and medical research and discovery. They have become indispensable tools for basic biological research and in numerous associated fields such as medical diagnosis, biotechnology, forensic biology, virology, and biological sciences.

## Principle

DNA sequencing methods have been under development since the mid-1970s. Nucleotide order determines amino acid order and, by extension, protein structure and its function. Any change in a DNA sequence can lead to an altered or nonfunctional protein, indicating a genetic disorder. DNA sequence assumes importance in detecting the type of mutations in genetic diseases and to determine if there is risk of genetic diseases. The technology offers great hope for the eventual development of treatment based on DNA sequencing. The Human Genome Project has spurred the development of cheaper, high throughput, and more accurate platforms for DNA sequencing.

Historically, DNA sequencing products were separated using gel electrophoresis separation technique. During electrophoresis, an electrical field is applied so that the negatively charged DNA fragments move towards the positive electrode. The speed at which a DNA fragment moves through the medium is inversely proportional to its molecular weight. This process of electrophoresis can separate the products by size at a resolution of one base. However, capillary electrophoresis (CE) has now become the dominant technique for this purpose. This technique has largely replaced the use of gel separation techniques due to its significant gains in workflow, throughput, and ease of use. With capillary electrophoresis, DNA sequence analysis can be automated more easily, and more samples can be processed in a given time. The separation of the fluorescently labelled DNA fragments is achieved according to molecular weight as they pass through a long, thin, acrylic fibre capillary.

The principle of DNA sequencing by capillary electrophoresis is shown in Figure 124.1. The sample containing fragments of DNA is injected into the capillary by dipping the capillary and an electrode into a solution of the sample. An electric current is briefly applied that causes the DNA fragments to migrate on to the end of the capillary. Once the sample has been injected, the electric field is reapplied that drives the DNA fragments through the capillary.



**Figure 124.1** Principle of capillary electrophoresis for DNA sequencing.



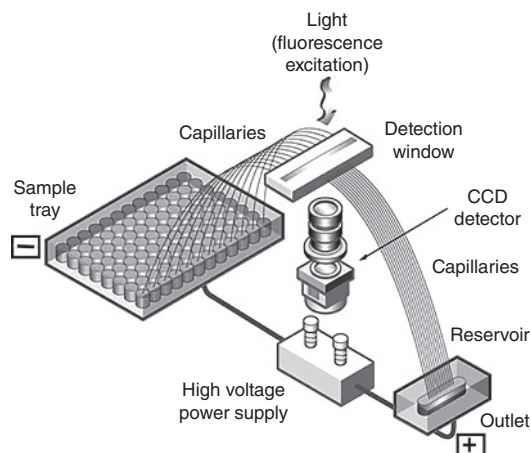
Shortly before reaching the positive electrode, a fluorescence-detecting laser beam is passed through the capillary fibre. The laser beam causes the dyes on the fragments to fluoresce. Each base is labelled with a different colour, for example: A = green, C = blue, G = yellow, and T = red. The colour of the fluorescent bases is detected by a camera. The software converts the fluorescence signal to digital data that is recorded in the sequencing files. The software allows to analyse sequencing files automatically, almost immediately after the electrophoresis run. With autoanalysis, the software applies analysis protocols to sequencing files and the analysed data is saved in the sequencing files. The colours of the bases are then displayed on a computer as a graph of different coloured peaks. Since each dye emits light at a different wavelength when excited by the laser, all four colours, and therefore all four bases, can be detected and distinguished in one capillary injection.

### **Capillary Array**

It is obvious that single capillary operation would not be adequate to meet the general sequencing needs with higher throughput requirements, such as for the Human Genome Project where 3 billion bases are required to be sequenced. The problem was handled with the development of a multiplexing technique for the separation of DNA sequencing fragments by means of the use of arrays of capillaries. The throughput of the system can be increased many times by using capillary array electrophoresis for running multiple capillaries in parallel. Array instruments typically use about 100 capillaries, though instruments using 576 capillaries have also been developed. The capillary array systems require sensitive detection settings applicable to bundles of capillaries. This effort was supported by the introduction of a high sensitivity post-column laser-induced fluorescence detector with a sheath flow cuvette to minimize the background signal originating from the light scatter of the gel-filled capillary. The charge-coupled device (CCD) camera looks at all capillaries at all times, with data rates sufficiently fast for sequencing at >1 base/s/lane. Today, automated multi-capillary DNA-sequencing instruments can handle up to hundreds of DNA samples in continuous operation with good sensitivity for long read lengths.

Figure 124.2 shows a schematic of parallel capillary electrophoresis instrumentation for DNA sequencing. The platform allows to achieve the perfect balance of speed and resolution by adjusting the capillary length. The inlet side of the capillary array is arranged in an 8 × 12 format in a 96 well plate, with electrodes next to each capillary having 0.1 mm inside bore, and 50–80 cm length. This allows direct injection via vacuum or voltage from standard 96-well plates. Capillary sequencers typically use a robot to load a stack of sample plates automatically. One end of the capillary array is positioned in a negatively charged cathode plate so that their ends align with each well of the sample plate. When high voltage is applied, it causes the labelled DNA in each sample well to enter the corresponding capillary and migrate through it toward the positively charged anode reservoir.

The capillaries are aligned in parallel in the detection window, which is positioned between the LED light source and the detector assembly. The labelled dyes are activated by a laser in the detector window, and a photometer reads the fluorescence wavelength of each fragment as it passes a fixed point. The laser and photometer are fixed and can



**Figure 124.2** Multiple capillary electrophoresis arrangement for DNA sequencing. *Source:* Reproduced with permission of M/s Agilent Technologies, Inc., USA.

activate and read multiple side-by-side capillaries simultaneously as separate data streams. The outlets of the capillaries are bundled to a common reservoir, where they are connected to a ground. The capillary arrays are modular and can be exchanged in less than five minutes. Room temperature air is circulated around the capillaries to modulate the temperature during separation.

The optical platform consists of an LED light source (470 nm excitation), camera lens, and CCD detector. Fluorescent light from the LED passes through the array window, exciting the intercalating fluorescent dye in the gel matrices. This is captured by the camera lens and spatially imaged onto the CCD detector. The fluorescence signals from all capillaries are simultaneously recorded at the rate 0.6 frame/s. To eliminate light scattering, detection is performed at a multiple sheath flow region. Optical waveguides are used to collect fluorescence in the detection cell. Imaging is constant, so real-time, online detection of separations is obtained.

The power supply provides appropriate voltage for electrokinetic sample injection and electrophoresis. The recommended operating limits are  $\pm 16$  kV, 3 mA total current (30  $\mu$ A per capillary). A syringe pump provides controlled pressure or vacuum to the outlet reservoir of the capillary array. Built-in software automates capillary conditioning, sample injection, electrophoresis separation, and data processing. Results can be visualized in a preferred format and reports can be shared easily.

High throughput DNA sequencing generates large amounts of data, which puts heavy requirements on software for data handling and data storage. Data analysis software processes the raw data in the sequencing files using special algorithms and carries out several analysis routines. The most important requirement is to separate the four different fluorescent dye signals into distinct spectral components by mathematically filtering fluorescence signal from dyes with emission spectra overlap. Analysed sample data is displayed as an electropherogram, a sequence of peaks in four colours. Each colour represents the base associated with the particular peak. A typical DNA sequencer is shown in Figure 124.3.



**Figure 124.3** DNA sequencer model 3730xl/DNA analyser. *Source:* Image Courtesy of M/s Thermo Fisher Scientific, USA.

### ***Microchip-Based DNA Sequencer***

Substantial effort is being devoted towards microfabrication of a device on a chip for DNA sequencing by capillary electrophoresis. This brings new potentials into DNA sequencing and may become a part of instrumentation of future. The microchip format allows electrophoretic analysis of submicrolitre to nanolitre sample volumes and thus facilitates integration of polymerase chain reaction (PCR) on the microchip, which will further provide automation, improve reliability, and reduce operator intervention. The microchip-based DNA sequencing is based on microfluidics technologies such as compact plates or discs. These are etched and micro-plumbed at high density using photolithography on fused silica or other materials as was done in semiconductor industry.

The lab-on-chip technology includes all sequencing steps such as thermal cycling, sample purification, and capillary electrophoresis integrated on a wafer-scale chip. The thermal cycling unit is a 250 nl reaction chamber with integrated resistive temperature detector, microvalves, and a surface heater. After thermal cycling, the reaction mixture undergoes purification in the purification chamber and is then injected into the CE chamber. The chip allows for significant miniaturization of systems, simplification of fluid handling, and more control options for sample introduction.

## **Specifications**

*Number of channels:* 96 or 384

*Capacity:* 16 sample plates (96 or 384 well)

*Sample volume:* 10–50 µl for 96-well plate, 5–30 µl for 384-well plate

*Capillary length:* 36 or 50 cm

*Temperature range:* Temperature-controlled oven (18–70°C range) and detection cell heater

## Applications

DNA sequencing machine finds a variety of applications that include de novo sequencing of genomes, biological identification, confirmation of clone constructs, and gene expression studies.

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## Dynamometer Exercise System

### Purpose

The dynamometer is a popular and most used piece of equipment for various isokinetic exercises. Isokinetic exercise is a form of exercise that allows maximum muscle contraction throughout the full range of joint movements. The dynamometer is used in physical, therapeutic, and sports medicine and fitness fields. It generally resembles a positioning chair attached to an adjustable strength machine and computer control unit. It is primarily a rehabilitative exercise device intended for medical purposes, such as to measure, evaluate, and increase the strength of muscles and the range of motion of joints.

### Principle

Isokinetic dynamometers are primarily used to measure muscular strength in musculoskeletal rehabilitation with the main aim of restoring their optimal function after injury or surgery. The final stage of rehabilitation process helps the individual to return to normal activities through resistance exercises on the dynamometer machine. Essentially, the device measures performances of different muscle groups based on a wide range of sensitive force measurements for numerous angles and speeds. This information helps to target muscle groups that need additional time, attention, and physical therapy to regain strength and return to normal functioning.

A sequence of test and exercise modes are programmed by the doctor that aims at the movement of all peripheral joints of the body. Measurements may include strength, torque, resistance, and fatigue.

Instruments and gadgets are available that provide precise measurement of resistive force against which the muscle is made to work. A typical example is that of handheld dynamometers that are used for routine screening of grip and hand strength. They also help to evaluate initial and ongoing status of patients with hand trauma or dysfunction. These are easy to use and are commonly used for diagnostic purposes. However, it is likely that readings of such gadgets from different types and brands are likely to vary under similar conditions.

Sophisticated force dynamometers that are used for measuring the back, grip, arm, and/or leg strength of athletes, patients, and workers for evaluating physical status, performance, and task are usually computer controlled. In these machine, isokinetic conditions are created in which the muscle group acts against a computer-controlled resistance that moves the limb at a constant angular velocity. These machines provide for a variety of muscle movement exercises that are designed to guide, measure, and assess the performance of all major muscle groups in the following kinds of muscle activity:

*Passive:* It means movement without exertion.

*Isometric:* It implies exertion without movement.

*Isokinetic:* It relates to variable exertion at a constant rate of movement.

*Isotonic:* It means constant exertion at a variable rate of movement.

These exercises are usually carried out on an exercise station, the dynamometer, that provides the desired form of resistance in the form of hydraulic, electric, or weight dynamometer to the muscular force applied for the patient. It is accompanied by a computerized unit that controls the sequence and duration of the exercise plan and monitors and assesses the patient's performance and progress. A typical dynamometer is shown in Figure 125.1.

There are two major types of dynamometer exercise machines that are available for isokinetic exercises: (i) An active dynamometer allows for exercise in which the speed is kept controlled, while resistance is made variable according to the amount of force throughout the range of movement. (ii) The second type utilizes a change in the moment arm of the selected resistance to coincide with the change in moment arm of the muscle effort and the change in tension due to muscle length change. The system basically comprises three major parts.



**Figure 125.1** Exercise dynamometer. *Source:* Image Courtesy of M/s Biodex Medical Systems, USA.

## Dynamometer

While using isokinetic exercise equipment, patients generally exercise with the help of a wheel, crank, lever, or some type of similar device. A generalized schematic diagram of the machine is shown in Figure 125.2. A mechanism, much like a braking system in a car, assists in allowing for increase or decrease in speed and torque, depending upon the resistance provided by the patient. The dynamometer has provision for more than 20 standard test and exercise patterns, with a stable platform. It allows controlled exercise speeds from 0 to 500° per second and can withstand joint torques of up to 500 ft/lb. It has the facility to rotate the shaft 360+ degrees, which makes it possible to achieve work simulation patterns. The rotation, height, and tilt of the dynamometer can be altered to suit testing or rehabilitation patterns to be used.

The machine must provide impact-free acceleration and deceleration to eliminate joint trauma, allowing patients to exercise and be tested at more functional speeds. The standard patterns can be set with the help of the patient set-up window display that also allows to record the rotation, height, and tilt scale values. The entire system works under the control of software. The automated force limits programmed in the system allow movement within safe ranges and not to exceed desirable force levels. The dynamometers usually have attachments that provide for interfacing with joints such as ankle, knee, shoulder, elbow, wrist, hip, and/or upper body extremity table.

## Reclining Chair

The reclining chair has a provision for multiple adjustment angles that allow the patient to be placed in sitting, prone, or supine position for extremity testing or rehabilitation. The system is mechanically rugged to allow consistent and reproducible patient placement. The seat is designed to move forwards or backwards, thereby providing the

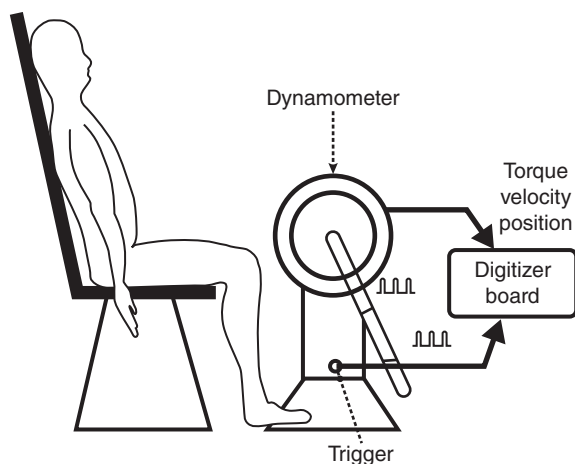


Figure 125.2 Schematic diagram of an exercise dynamometer.

appropriate stabilization of the torso, hips, waist, thighs, and the contralateral limb. The chair ensures system and patient stability during testing or rehabilitation sessions.

### **Data Acquisition System**

An important component of a dynamometer system is its data acquisition system, which typically consists of two units, a controller and workstation that are interconnected. The controller, a desktop computer operated by Windows-based software, issues appropriate commands to the workstation, which is a touch screen-operated unit. The workstation operates the precision load and throttle control systems, collects the data, and sends it to the controller to be processed, stored, and analysed. Pressure transducers are used to measure airflow in the intake manifold, oil pressure, and other fluid pressures.

The dynamometer speed, force, and direction are controlled and monitored electronically. An electrical signal from the dyna motor encoder provides information on dyna shaft position and direction information. The torque or resistance values encountered at the input shaft are also measured. The input signals received from both the position and the force transducers, which are analog, are then digitized in an A/D converter. The force, expressed as torque, is applied in a certain distance from the axis of joint rotation and is measured using load cells. The control and powering of the resistive mechanism of the dynamometer is also done electronically. The controlled work option with proper selection of resistance allows the individual to determine the amount of work, in Newton/metres or joules, to be performed. This enables to regulate the stepper motor attached to the hydraulic valve and cylinder unit to provide rapid and precisely regulated accurate and smooth performance results. The processed signals are provided to the computer and application software to provide visual feedback and data to the user for evaluation and data storage.

### **Specifications**

*Modes:* Isokinetic, isometric, isotonic, reactive eccentric, and passive

*Speed:* Concentric speed up to 500° per second, eccentric speed up to 300° per second, passive speed as low as 0.25° per second

*Torque:* Concentric torque up to 500 ft-lb (680 Nm), eccentric torque up to 400 ft-lb (544 Nm), passive torque as low as 0.5 ft-lb, isotonic torque 0.5 ft-lb

*Attachments:* For ankle, knee, shoulder, elbow, and wrist

### **Applications**

Dynamometer exercise system finds applications in sports and orthopaedic medicine departments. Isokinetic testing is used on old people to identify weakness and to undertake exercise to improve ankle and leg strength. These systems are also employed in paediatric medicine, neurorehabilitation, and industrial medicine.



## 126

# Echocardiograph

### Purpose

An echocardiograph is an instrument that provides a record of the ultrasound images of the heart. The recording is called an echocardiogram that is useful for diagnosis, prognosis, and follow-up of cases with heart problem. It is an important investigation for those suspected of heart failure, heart valve disease, or cardiomyopathy. The instrument allows you to measure ejection fraction, i.e. the amount of blood pumped out of the heart with each heartbeat, that helps to establish the severity of the problem and the likely prognosis.

### Principle

Echocardiography is an important noninvasive technique employed by the cardiologists for diagnostic imaging of the heart to diagnose a wide variety of cardiac diseases and ascertaining the severity of the disease. Echocardiography allows to evaluate cardiac chamber size, wall thickness, wall motion, valvular anatomy, valve motion, and the pericardium.

Echocardiography uses ultrasound waves in the frequency range of 1–20 MHz to generate images of cardiovascular structures and to display information regarding the blood flow through these structures. The imaging is based on the use of ultrasound pulse–echo technique, which was initially employed for non-destructive testing of metallic structures. The technique, basically, consists in transmitting a train of short duration ultrasonic pulses into the body and detecting the energy reflected by interfaces between tissues of different acoustic impedance such as myocardium, valves, and blood. With this technique, the presence of a discontinuity can be conveniently established and its position located if the velocity of travel of ultrasound in the medium is known. Also, it is possible to determine the magnitude of the discontinuity and to assess its physical size.

Since the heart is surrounded by lungs over the majority of its surface and is contained within the bony cage of the thoracic cavity, the ultrasound beam must be aimed through gaps between the ribs, known as acoustic window, in order to produce images of the heart. The transducer is placed between the third and the fourth ribs (acoustic window) on the outer chest wall where there is no lung between the skin and the heart. From this probe, a low intensity ultrasonic beam is directed towards the heart area and echo signals are obtained. The probe position is manipulated to obtain echoes from areas of interest in the heart. Modern echocardiographic equipment also incorporate facilities for Doppler flow imaging, which is based on the scattering of ultrasound waves from moving blood cells, with a resulting change in the frequency of the waves received at the transducer.

The ultrasound is generated by a transducer, which consists of a piezoelectric crystal that also detects received ultrasonic pulses. The piezoelectric material generally used is lead zirconate titanate. The crystal is cut in such a way that it is mechanically resonant

of an increased efficiency of conversion of electrical energy to acoustic energy. It is usually one-half wavelength thick for the particular frequency used. The probes carrying the piezoelectric crystal are designed to achieve the highest sensitivity and penetration, optimum focal characteristics, and the best possible resolution. A train of short duration pulses at a desired repetition frequency are generated by a transmitter circuit and applied to the piezoelectric crystal where these are converted into corresponding pulses of ultrasonic waves. The echoes reflected and received from the target are picked up by the same transducer and amplified suitably for display on a monitor screen. The X-axis is driven by the time base, which starts at the instant when the transmitter radiates a pulse. In this way, the position of the echo along the trace is proportional to the time taken for a pulse to travel from the transmitter to the target and back again. Knowing the velocity of ultrasonic waves and the speed of the horizontal movement of trace on the monitor, the distance of the target from the transmitting end can be estimated.

Ultrasound waves are characterized in terms of its frequency (Hz), wavelength (mm), amplitude or loudness (decibels [dB]), and velocity of propagation (m/s). The velocity of propagation varies according to the type of tissue medium carrying the ultrasound wave and it is approximately 1540 m/s in blood. For ultrasound,  $c = \lambda \times f$  where  $c$  is the propagation velocity in the heart, which is 1540 m/s,  $\lambda$  = wavelength, and  $f$  = frequency. From this relationship, the wavelength for any transducer frequency can be calculated as  $\lambda$  (mm) =  $1.54/f$  (MHz). Wavelength is a clinically important parameter, as the higher the frequency, the shorter the wavelength and the better the image resolution. Also, the depth to which ultrasound waves penetrate the body is directly related to wavelength. That means shorter wavelengths penetrate a shorter distance. Thus, an obvious trade-off exists between image resolution and depth of penetration. For example, a 1 MHz transducer has a penetration depth of 30 cm and resolution of 1.5 mm, whereas a 5 MHz transducer has a penetration depth of only 6 cm, but a higher resolution, about 0.3 mm.

### **Echo Imaging Modalities**

There are various modes found in modern echocardiographic equipment:

*M-mode (motion) echocardiography:* M-mode, or motion mode, echocardiography was the first ultrasound technique used for clinical cardiovascular imaging. However, its use today is primarily limited to assessment of valve motion and reliable reproducible measurements of chamber sizes and function. It can be used to assess cardiac wall thickness, aortic root size, chamber sizes, or ventricular function. The M-mode echocardiography yields a one-dimensional view of the cardiac structures moving with respect to time. It involves scanning a single line in the object and then displaying the resulting amplitudes successively. Thus, the echoes from various tissue interfaces along the axis of the beam that are moving during the cardiac cycle are swept across time, providing the dimension of time. The lines on the recordings correspond to the position of the imaged structures in relation to the transducer and other cardiac structures at any instance in time. Because of the use of high sampling rate or pulse frequency, the technique gives cleaner images of cardiac borders is useful in assessing rates and motion and is used extensively in cardiac and foetal cardiac imaging.

*Two-dimensional (2D) echocardiography (B-mode):* This mode of imaging is performed by sweeping the transmitted sound waves over a plane to produce a 2D image in terms

of both depth and width in real time. Typically, multiple sets of pulses are generated to produce sound waves for each scan line, and each set of pulses is intended for a unique focal point along the scan line. The image that is of a narrow plane in cross section is typically updated at a rate of 15–200 Hz and displayed on a video monitor as real-time display of cardiac motion. This allows the anatomic relationships between various structures to be better appreciated than with M-mode echocardiographic images. An infinite number of imaging planes through the heart are possible; however, standard views are used to evaluate the intra- and extracardiac structures.

*Three-dimensional (3D/4D) echocardiography:* This involves capturing image data from multiple 2D scans sequentially or in real time and displayed in a spatial 3D format. The rotation and slicing of the display are achieved through a software. When the data is displayed continuously, 4D images can be displayed as time becomes the fourth dimension.

*Doppler echocardiography:* Doppler echocardiography allows evaluation of blood flow patterns, direction, and velocity that helps to detect valvular insufficiency or stenosis and cardiac shunts. The blood flow and cardiac output can also be estimated using Doppler imaging. Doppler echocardiography is based on detection of frequency changes (the Doppler shift) that occur as ultrasound waves reflect off individual blood cells moving either away from or towards the transducer. Doppler echocardiography can be performed either by continuous wave (CW) or pulsed wave (PW) modes.

*Continuous wave (CW) Doppler:* Here, a sound wave at a single frequency is continuously transmitted from one piezoelectric element and a second piezoelectric element is used to continuously record the reflected sound wave, which is Doppler shifted in frequency. The frequency difference between the two signals is processed and displayed indicating direction and velocity of blood flow. However, since the sensor is continuously receiving data from various depths, the velocity location cannot be determined.

*Pulsed wave (PW) Doppler:* In this mode, several pulses of ultrasound are transmitted along each scan line and the Doppler frequency is estimated from the relative time between the received signals. Since pulses are used for signalling, the blood flow velocity location can be easily determined. Similarly, by using pulse mode, it is also possible to estimate the velocities of blood or tissue at user-selected depths.

*Colour Doppler:* In colour echocardiography, the PW Doppler is used to create a colour image that is superimposed on top of 2D image. A colour code is used to denote the direction and magnitude of the flow. Red colour typically denotes flow towards the transducer, and blue colour denotes flow away from it. A darker colour usually denotes a larger magnitude, while a lighter colour denotes a smaller magnitude.

### **Duplex Scanning**

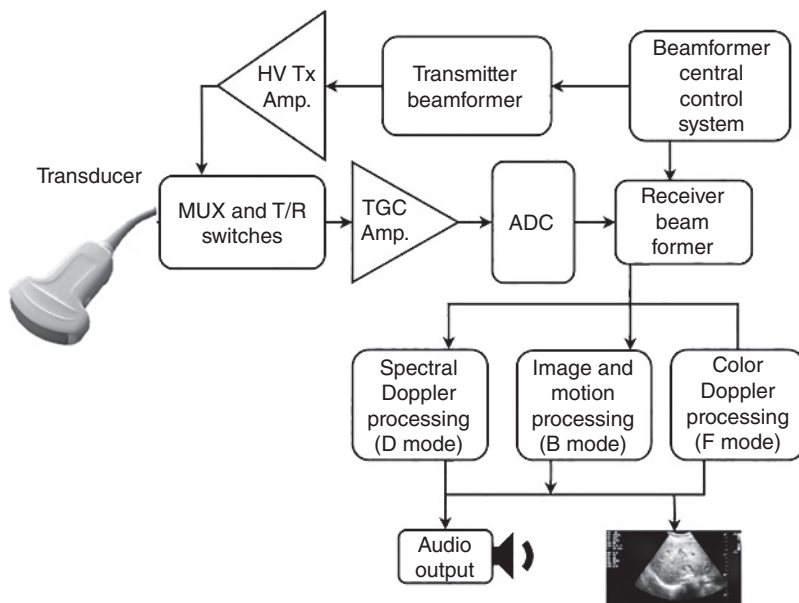
Duplex echo-Doppler scanning has been found to be useful for direct noninvasive measurement of peripheral arterial flow and tissue geometry. Here, the echo image is used to locate the artery and determine the position of the walls of the blood vessels and organs. The echo image is then used as a guide to map out the flow field with the Doppler technique. The incorporation of separate echo and Doppler transducers in a duplex scanner results in high resolution images due to the fact that the echo transducer beam can be aligned perpendicular to the artery wall, while the flow probe is at an angle appropriate for detecting Doppler shift.

## Echocardiography Systems

The development and application of clinical echocardiography has allowed thorough, accurate, and noninvasive evaluation of cardiac structure and function. The basic functional building blocks of a diagnostic ultrasound imaging system, which includes the above listed echocardiographic modalities, are the transducer, processing blocks needed for image formation, and system controller as shown in Figure 126.1. The electronics consists of two main sections: the analog and the digital. The analog section comprises multiplexers, pulsers, time gain compensation amplifiers, and analog-to-digital converters. The digital section contains beamforming, signal processing, and display and audio circuits.

The *analog section* is getting into tremendous amount of miniaturization, resulting in better overall performance of the system. Delineation of signal path operations as front-end, mid-end, and back-end processing varies from one manufacturer to another. It also depends, to some degree, on the type of signal processing device used for carrying out these operations. The commonly used devices include application-specific integrated circuit (ASIC), field-programmable gate array (FPGA), digital signal processor (DSP), or personal computer (PC). These devices provide flexibility of programming the gain and help achieve better gain compensation in the ultrasound image.

The transmit beamformer is responsible for the pulse excitation of the transducer elements, which results in emission of acoustic waves into the region of interest. Immediately following this, the transmit/receive (T/R) switch is positioned to put the front end in receive mode. Transducer elements transform the reflections or echoes into corresponding electrical signals. The analog front end (AFE) suitably amplifies these signals and converts them into digital data streams for further processing. By



**Figure 126.1** Block diagram of an echocardiograph and blood flow monitor.

applying dynamic delays into these data streams, the receive beamformer combines them to form a scan line, which represents the region of interest along a given line of sight. This process is repeated either sequentially or simultaneously to form multiple scan lines to cover the entire region of interest. The front-end controller is responsible for controlling the timing and sequencing of transmit and receive beams. Sampling rates used for analog-to-digital (A/D) conversion in the front end can vary from 16 to 50 MHz depending on system requirements.

Traditionally, the *digital section* is implemented in the proprietary ASICs, FPGAs or DSPs. Today, the multi-core DSPs are capable of performing the high-end, real-time image processing and rendering functions. System-on-chips (SOCs) have been specially designed to process digitized electrical signals generated by transducers that have revolutionized the area of diagnostic ultrasound imaging. A diagnostic ultrasound imaging system generates and transmits acoustic waves and captures reflections that are then transformed into visual images. The signal processing on the received acoustic waves include interpolation, decimation, data filtering, and reconstruction. Programmable DSPs and SOCs, with architectures designed for implementing complex mathematical algorithms in real time, can efficiently address all the processing needs of such a system.

Software image processing has enabled to bring about system-level architecture changes leading to evolution of handheld ultrasound equipment. The image processing has been logically and architecturally divided between a ubiquitous PC and a DSP/processor. The image processing has further advanced from just performing rendering function, to helping doctors diagnose diseases precisely and easily. Disease diagnosis via visualization usually has high dependency on the interpretation expertise of a medical practitioner, which is subjective and can vary from one doctor to another. The modern software packages support a variety of static or real-time cardiac specific imaging applications used to diagnose anatomical defects of the heart and determine blood flow characteristics and functional/anatomical problems associated with myocardial infarction. The software allows to display static or dynamic 2D or 3D images. Modern systems also enable Digital Imaging and Communications in Medicine (DICOM)-compliant image transfer to other facilities that form a part of the network.

Three major modes of ultrasound imaging systems, which are relevant for cardiac studies are: B-mode, colour flow, and Doppler. All these modes are now available in modern systems. *B-mode* operation provides greyscale image that aids in examining tissue structures and organs. *Colour-flow operation* forms a colour-coded display of spatial distribution of mean velocity of blood flow superimposed on greyscale image. The process of *colour-flow* detection requires considerable computing involving high pass filtering of ensembles of scan lines to eliminate contributions from vessel wall or tissue motion. Output of the wall filter is then used to estimate power, mean velocity, and turbulence. *Doppler processing* produces scrolling display of blood flow velocity distribution at a user selected location of blood vessels. It involves a much simpler filter and estimation of velocity distribution using short-time Fourier transform technique. Doppler processing also generates a stereo audio signal that represent the Doppler spectrum. Figure 126.2 shows a typical echocardiogram along with Doppler blood flow velocity profile.

Following the above, B-mode, and colour-flow estimates are subjected to temporal and spatial processing to reduce noise and enhance features of interest. Scan conversion is the operation where B-mode and colour-flow estimates are converted to display raster data. When colour flow is on, B-mode and colour-flow pixels have to be blended to





## Transducers

A 2D image can be produced by having multiple crystals mounted in line, known as linear array. This type of transducer is not suitable for echocardiography as it is difficult to aim the array beam of sound through the acoustic window. However, the technology may allow detection of gross abnormalities such as a pericardial effusion, very poor myocardial contractility, or large vegetations on the heart valves. Alternatively, a sector scan transducer can be used, which emits ultrasound in an arc. The sector can be produced by rotating or oscillating the crystal mechanically; this type of transducer is called a mechanical sector scanner. Alternatively, the sector can be produced by using an array of crystals, which are electronically stimulated in sequence to produce a fan-shaped beam. These are known as phased-array transducers.

Specialized transducers that transmit and receive the ultrasound have been designed for various clinical applications. The common types of echocardiograms are as follows:

- *Transthoracic echocardiogram*: This is a standard, noninvasive echocardiogram in which the transducer is held firmly on the chest aiming an ultrasound beam through the chest to the heart.
- *Transoesophageal echocardiogram*: If there is reason to examine the heart and valves in more detail, the doctor may recommend a transoesophageal echocardiogram. In this procedure, a flexible tube containing a transducer is guided down the throat and into the oesophagus, which connects mouth to the stomach. From there, the transducer can be positioned to obtain more-detailed images of the heart.
- *Doppler echocardiogram*: Doppler techniques are used in most transthoracic and transoesophageal echocardiograms, and they can be used to check blood flow problems in the arteries of the heart that traditional ultrasound might not detect.
- *Intracardiac echocardiogram*: Here, a small transducer is mounted on a catheter, which is inserted into a large vein and moved into the heart. Imaging from within the heart is done to monitor-specialized interventional therapy.
- *Stress echocardiogram*: Some heart problems, particularly those involving the coronary arteries that supply blood to the heart muscle, occur only during physical activity. For a stress echocardiogram, ultrasound images of the heart are taken before and immediately after walking on a treadmill or riding a stationary bike.

The most exciting development in echocardiography has been that echocardiographs can now be used beyond hospitals. There are pocket-sized devices providing access for more patients. Image quality has also got better over the years, with clearer images.

## Specifications

*Imaging modes*: 2D, M-Mode, pulse wave Doppler, continuous wave Doppler, colour-flow imaging, and tissue harmonic imaging

*Frequency range*: 1–15 MHz

*Probes*: Convex probe, 2–5 MHz; phased-array echo probe, 1–5 MHz; linear array probe, 4–15 MHz; and microconvex probe, 5–8 MHz

*Display screen*: At least 14 inch in size with high resolution colour LCD.



*Software:* For measurement and calculation, provision for distance, area, volume, and circumference, complete vascular, cardiac calculation package, and evaluation package. For pulsed Doppler imaging, provision for automatic real-time calculations and display of at least user-selectable parameters like peak systolic velocity, end diastolic velocity, mean diastolic velocity, time average mean velocity, volume flow measurement, pulsatility index, resistive index, etc. 3D or 2D image for cardiac studies in adults, children, and infants. ZOOM facility

*Compatibility:* DICOM

*Hard disk capacity:* At least 10 000 images

## Applications

Echocardiograph is a widely used and valuable instrument for carrying out cardiac examination and assessment of many congenital and acquired cardiac diseases. Echocardiography is often used for the study of the aortic valve, tricuspid valve, and pulmonary valve. Another very important use is in the detection of pericardial effusion, which is the abnormal collection of fluid between the heart and the pericardial sac. The technique helps to study the size and shape of the heart, and the size, thickness and movement of the heart's walls, and the heart's pumping strength. Echocardiograph machines are now widely available in provincial hospitals and specialized hospitals in their radiology departments.

## 127

# Electrical Safety Analyser

## Purpose

An electrical safety analyser is an instrument that is used to perform various electrical safety tests in order to check that the device under test is in compliance with established electrical safety requirements. The typical tests that are generally performed with an electrical safety analyser include ground continuity test, insulation test, high voltage test, and line leakage test along with several other associated tests.

## Principle

Hospitals today are facing the problem of creating a safe electric environment for the care and comfort of the patients in the presence of an increasing number of electronic and electric equipment used for diagnosis and therapeutic purposes. The cases of persons getting shock in hospitals from electric power has been a common experience. Besides, burns and fire hazards are reported to be generally resulting from the careless

use of electricity. When electricity is relied upon to support life with devices like external ventilators and defibrillators, power failure is a continuous threat unless alternative power arrangements are available. Disruption of physiologic function of patients by undesirable leakage current that finds a path internally through the patient remains sometimes hidden and mysterious.

In the past few years, there has been an explosion in the extent and proliferation of medical equipment in the hospitals. In most of such equipment, the patient is included as a part of an electrical system, which has generated a problem of reconsidering the well-established safety conventions. For example, the patient is wired for collecting data important for diagnosis and therapy wherein his/her presence in the system has to be there. In addition, there are catheters and pacing leads that may be connected to the heart directly. In such cases, currents of the order of microamperes, which were earlier ignored, are now considered to be potentially hazardous because the natural protective barrier of the skin is no longer present. Because of these factors, it is essential to good healthcare delivery that the electrical supply be carefully designed, correctly installed, and well maintained.

### ***Gross Shock or Macroshock***

Gross shock is experienced by the subject by an accidental contact with the electric supply at any point on the surface of the body. Most of the electric accidents involve a current pathway through the victim from one upper limb to the feet or to the opposite upper limb, and they generally occur through intact skin surfaces of the person. In all these cases, the body acts as a volume conductor at the mains frequency. The physiological effects of the electric shock depend on the magnitude of current and its pathway through the body, which in turn depends on the location of the contact points with the electric supply.

When a person gets in contact with the electric supply, the value of current passing through him/her would depend upon the contact impedance for a given voltage present on the surface of the body. The value of impedance of the human body to electrical currents through intact skin surfaces can vary from 1 k $\Omega$ , if the skin is damp or scrubbed to over 100 k $\Omega$ , if the skin is dry. Besides this, it depends on many other factors such as age, sex, condition of skin (dry or wet, smooth or rough, etc.), frequency of current, duration of current, and the applied voltage. Depending upon the magnitude of the current, different effects can take place on the human body, such as electrical stimulation of nerves and muscles, resistive heating of the tissue, and sometimes severe burns and tissue damage when very high voltages are present.

***Effects of Electric Current on the Human Body*** Electrical currents can be extremely dangerous to the human body. The energy (power and time factor) released by electrical current passing through human tissue can generate burns and excite or stimulate muscles of the respiratory system (intercostals). The most critical muscles are those in the human heart, which are driven (excited) by very tiny amounts of electrical currents. When the heart is exposed to external electrical currents (electrical shock), the heart can lose its normal sinus rhythm, required to sustain a healthy blood circulation, and move into ventricular fibrillation. This stops the circulation of oxyhaemoglobin (oxygenated blood cells) to the brain and organs and, when left untreated, will result in death within 15 minutes.

The macroshock effect of a 50/60 Hz current on the human body when applied to the skin for one to three seconds (noninvasive) is as follows:

- 0.5–1.1 mA current: Just noticeable when applied to the fingertip
- 6–16 mA: Painful shock, unable to let go, cannot be tolerated over 15 minutes
- 75–400 mA: Ventricular fibrillation, respiratory arrest, leading to death
- >5 A: possible burns, sustained myocardial contraction, respiratory paralysis, and possible death

### **Microcurrent Shock**

When currents are required to be applied internally to the body, a far greater percentage of the current may flow via the arterial system directly through the heart of the patient. Consequently, much less current is required to produce ventricular fibrillation. Such situations are commonly encountered in hospitals; for example, certain medical procedures require that conductive catheters be placed in the body of the patient in the catheterization laboratory or in the operating room. Similarly, a cardiac catheter connected to an electrical circuit for the measurement of internal pressure provides a conductive fluid connection directly to the heart. In such cases, the patient is deprived of the electrical protection of the skin and would offer very little resistance to electric currents. The International Electrotechnical Commission's (IEC) recommendations covering the safety aspects of electrical equipment for medical applications stipulate that the current that flows continuously through the heart shall not exceed  $10\text{ }\mu\text{A}$  for a frequency range of 0–1 kHz.

### **Leakage Currents**

The microshock is mostly caused by the leakage current of extremely small magnitude that can be fatal to a patient when a direct, localized electrical path exists to the heart. Leakage current by definition is an inherent flow of non-functional current from the live electrical parts of an instrument to the accessible metal parts. The leakage current is present in all power line-operated equipment due to capacitive and resistive coupling to the chassis.

Instruments are generally designed so that leakage current flows to the instrument case and then to the ground via the three-wire power cord provided with the instrument. In that case, the leakage current effectively drains off to the earth and then there will no longer be any danger for the patient or the operator. However, when the earth connection gets interrupted due to any reason, the leakage current can become a real danger to the patient or the operator.

**Types of Leakage Current** Leakage currents are divided according to the current path into the following types:

**Enclosure leakage current:** The enclosure leakage current is described as the current that flows, in normal condition, from an exposed conductive part of the enclosure to earth through a conductor other than the protective earth. This current can become hazardous when a person touching the equipment is connected to earth.

*Earth leakage current:* The earth leakage current is the current that flows, in normal condition, to earth from the mains parts of an apparatus via the earth conductor.

*Patient leakage current:* The patient leakage current is the current that flows through the patient from or to the applied part of the patient circuits. This current does not include any functional patient current.

### ***Safety Codes for Electromedical Equipment***

Any electrical equipment for the purpose of treating, monitoring, or diagnosing a patient's condition is classified as a medical electronic device according to IEC 60601, the global standard governing the design and approval of medical devices. The persons responsible for managing medical equipment the world over has been concerned about the problem of ensuring a safe environment for the patients as well as for the operators. Various countries have laid down codes of practice for equipment intended to be used in hospitals. The IEC has brought out a fairly voluminous document, the IEC 60601-1 (General Requirements for the Safety of Medical Electrical Equipment), to provide a universal standard for manufacturers of electromedical equipment as well as a reference manual on good safety practice. This standard has been adopted by all IEC member states. Adopting a common standard implies that construction of equipment shall be universally acceptable, the leakage and earth resistance paths will be assessed in identical manners and the mains leads will be coloured to the same code. All tests relating to the electrical safety of medical equipment and devices are categorized into two categories:

*Means of operator protection:* Means of protection for reducing the risk of electric shock to persons other than the patient.

*Means of patient protection:* Means of protection for reducing the risk of electric shock to the patient.

In IEC 60601, the test requirements for electrical leakage must be carried out under the worst possible conditions to ensure absolute safety. Tests are done under normal condition (no fault conditions) and including any one of the specific and relevant fault conditions. IEC 62353 Medical Electrical Equipment standard defines the requirements for electrical safety testing of medical electrical equipment and systems during routine intervals and test after repairs of equipment.

### ***Electrical Safety Analyser***

The visual inspections form a critical part of the general safety inspections during the functional life of medical equipment. In most cases, 70% of all faults are detected during visual inspection. However, a range of electrical safety analysers are commercially available for testing both medical facility power systems and medical equipment. They vary in complexity from simple volt-ohm-meter to computerized automatic measurement systems that generate hard copies of test results. Modern safety analysers are digital reading meters incorporating facilities for measuring enclosure leakage current, patient leakage current, and ground continuity tests. Besides these, they have provisions to carry out insulation tests at 500V and isolated power system tests. Advanced and

automated electrical safety analysers are commercially available, which meet stringent international standards for electrical safety testing of hospital and laboratory electro-medical equipment. A typical electrical safety analyser from M/s Fluke, United States, is shown in Figure 127.1. The following tests are usually performed for safety testing of medical equipment using the analysers.

**Mechanical Testing of Electrical Outlets** There has been a proliferation of electrical receptacles to accommodate the operation of various medical equipment and devices in various parts of the modern hospital buildings. However, the most vulnerable power delivery point is in the patient area that usually has outlets in the vicinity of the patient. The outlets are generally three-prong wall receptacles, which have spring contacts that become distorted, weakened, and bent over a period of time because of their usage. They can no longer establish a good electrical contact, which can lead to possible heating of the contacts and the attendant fire hazard, arcing, and sometimes complete failure of power supplied to essential equipment. The proper grip force requirements are important as they ensure that plugs on medical devices do not fall out of the receptacle, possibly placing the patient in danger.

Receptacles need to be tested for proper wiring, proper line voltage, low ground resistance, and mechanical tension. The holding tension provided by a set of contacts in the receptacle can be measured with a spring-loaded tester that measures the force required to extract the plug after it is inserted into the receptacle. The tension in the receptacle should not be too high as it will destroy the plug, electrical cable, or the receptacle.

**Electrical Testing of Electrical Outlets** Electrical testing of a wall receptacle should be made to determine whether power is available at the receptacle and if its polarity is correct. The availability of power is checked with a digital multimeter. Proper polarity of the receptacles is checked so as to ensure that the hot, neutral, and ground wires are



**Figure 127.1** Electrical safety analyser model ESA612. *Source:* Courtesy of M/s Fluke Biomedical, USA.

connected to their correct positions. Testing of the outlet can easily be done by a receptacle tester consisting of three LEDs, which can test for 8 of 64 possible states of the outlet. The three lights have only two states ( $2^3$ ), whereas each of the three outlet contacts has four states ( $4^3$ ) – hot, neutral, ground, and open. Testing of the outlet for possible reverse wiring or loss of grounding is important as these are potentially hazardous conditions and should be corrected immediately.

Ground resistance is usually measured by passing up to 1 A current through the ground wire and measuring the voltage between the ground and neutral. The resistance of neutral wiring can be tested similarly by passing the current through the neutral conductor. Ground or neutral resistance should not exceed  $0.15\ \Omega$ . Testing the protective ground circuit design for sufficient current-carrying capabilities is achieved by stressing the design, passing a minimum test current of 25 A RMS through the circuit for a minimum of 10 seconds.

### **Testing of Biomedical Equipment**

The types of tests needed for checking the safety parameters of biomedical equipment are many and varied. However, measurement of leakage current and ground resistance constitutes the majority of the tests and must be carried out periodically on instruments normally applied to the patients. Modern equipment for safety testing are all microprocessor controlled. The below given description of safety tests relate only to the method of measurement of various parameters.

**Enclosure Leakage Current Measurement** Enclosure leakage current is mostly measured with an AC microammeter under normal conditions as well as during single-fault conditions, in which one supply conductor at a time is interrupted, and, also the protective earth conductor is opened. This leads to assessment of the possible hazard arising from an outlet, which is improperly wired. Leakage currents from the chassis should not exceed  $500\ \mu\text{A}$  for equipment not intended to come into contact with patients and should not exceed  $100\ \mu\text{A}$  for equipment that is likely to come into contact with the patients. These are limits on RMS currents from DC to 1 kHz.

To ensure that a valid leakage measurement can be obtained, the following three methods are provided in the IEC 62353:

*Direct leakage:* Measurement of leakage current via a measuring device, placed directly in the path of the leakage current. The direct method is most commonly used. The device under test is powered and the leakage currents are measured from accessible parts and applied parts with interruption of the protective ground. The power supply is then inverted between the two poles and the highest value is recorded.

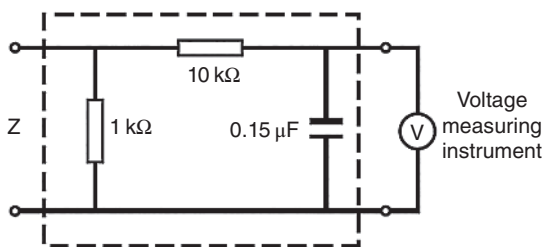
*Differential leakage:* Measurement of the imbalance between current in the hot conductor and the neutral conductor as a result of leakage current.

*Alternative method:* Measurement of leakage when mains voltage is both on the hot and neutral wires.

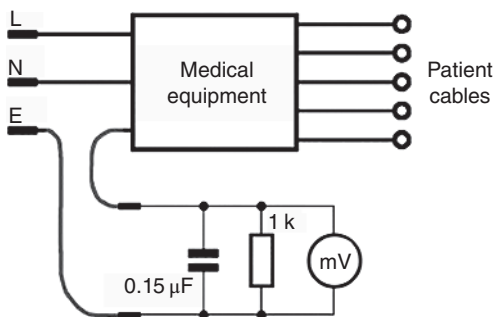
**Measurement of Leakage Current** The instrument for measuring leakage current must have an input impedance  $\geq 1\ \text{M}\Omega$  and a frequency characteristic that is flat from DC to 1 MHz. The leakage current is made to develop a potential across a resistor–

capacitor network as per IEC60601-1 and is as shown in Figure 127.2. The capacitor is employed to imitate the sensitivity of the heart as a function of frequency. The network may be slightly different for different standards representing the impedance of the human body. The load for the current input is specified by the Association for the Advancement of Medical Instrumentation (AAMI, USA) is  $1\text{ k}\Omega$  resistance in parallel with  $0.15\text{ }\mu\text{F}$  capacitor having a series resistance of  $10\text{ }\Omega$ . A number of commercially available instruments are available that are specifically designed to make leakage current measurement. These instruments include typical selectable human body models for several popular standards built right into the instrument. The leakage test is performed with both the power off and on under conditions of normal polarity leakage and reverse polarity leakage. These leakage currents are the maximum values that can occur with any combination of polarity or power. The test for leakage current with power off provides an opportunity for checking a short to the chassis from either side of the line. The range of leakage measurement is  $0\text{--}2000\text{ }\mu\text{A}$ . Figure 127.3 shows a scheme for the measurement of equipment enclosure leakage current.

**Ground Continuity Test** With this test, the resistance of the protective earth conductor is measured between the earth connection of the mains plug and the metal housing of the equipment. This test is considered as the most important test and is the first test to be performed when carrying out all other safety tests. The test is usually performed with an ohmmeter while the equipment is unplugged. This test helps to

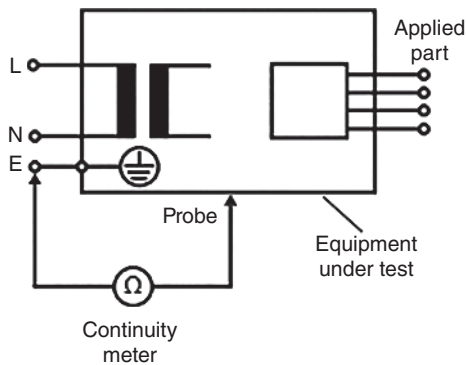


**Figure 127.2** Principle of leakage current meter as per IEC60601-1 standard. All component values are  $\pm 5\%$ .



**Figure 127.3** Measurement of enclosure leakage current using a leakage meter.





**Figure 127.4** Ground continuity tester.

detect complete failures but is not sensitive enough to determine the gradual development of a defect and also does not verify the capability of carrying large fault currents that could be caused by a line to enclosure short circuit. According to many guidelines, ground resistance is measured with a test current of several amperes provided either by a transformer and current limiting resistance or by a regulated DC constant current source.

Figure 127.4 shows arrangement for measuring the resistance of the protective earth conductor between the earth pin on the mains plug and a protectively earthed point on the equipment enclosure as shown. As per IEC60601 standard, the test is conducted using a 50Hz current between 10 and 25 A for a period of at least five seconds. The resistance between the ground pin of the plug and the equipment chassis/exposed metal objects should not exceed  $0.15\ \Omega$  during the life of the equipment.

**Insulation Resistance Test** The risk of unacceptably high electrical fault currents can be minimized by providing higher levels of electrical insulation/isolation in the design of the equipment. Such insulation can be achieved through physical spacing (creepage and clearance) of components and choice of components and dielectric materials, while ensuring the device operates properly. The effectiveness of electrical insulation is tested through electrical leakage measurements, while the level of isolation is often tested using a dielectric or insulation test. The insulation test is performed by applying a high voltage (up to 4000 VAC) across different parts of the electronic design in order to stress the dielectrics. The results are displayed in mA or  $\mu\text{A}$  similar to leakage current measurement. For insulation resistance test, DC voltage, typically applied is between 250 and 500 VDC, across different parts of the electronic design. The results are displayed in mega ohms ( $\text{M}\Omega$ ).

Electrical safety testing of medical electronic devices remains a crucial part of the overall safety validation of medical devices. Although medical equipment is designed and manufactured following all safety regulations, it then becomes the responsibility of the hospital workshop to ensure that the equipment remains functional, calibrated, and safe during usage. Usually, the electrical safety tests should be compulsorily carried out after every repair of a medical equipment and also as a part of the preventive maintenance procedure. National and international organisations like American National Standards Institute (ANSI), British Standards Institution (BSI), European Economic

Community (EEC), International Electrotechnical Commission (IEC), International Organization for Standardization (ISO), National Fire Protection Association (NETA) have defined safety standards and test procedures. For medical equipment IEC 60335 is the most widely applied testing standard.

## Specifications

*Earth resistance*

*Test current:* >200 mA AC

*Range:* 0–2  $\Omega$

*Leakage current*

*Modes:* AC + DC (true-RMS), AC only, DC only

*Patient load selection:* AAMI ES1-1993/IEC 60601-1

*Ranges:* 0–199.9  $\mu$ A, 200–1999  $\mu$ A, 2–10 mA

*Leakage tests:* Ground wire (earth), chassis (enclosure), lead to ground (patient), lead to lead (patient auxiliary), lead isolation (mains on applied part)

*Insulation resistance*

*Ranges:* 0.5–20 M $\Omega$ , 20–100 M $\Omega$

*Source test voltage:* 500 V DC

## Applications

Electrical safety analysers are widely used by biomedical professionals to perform field service on medical equipment throughout their facilities, in clinics, or any place where on-site service is required. These instruments offer the functionality of a simulator, multimeter, and electrical safety analyser in a single test tool.

# 128

## Electrocardiograph

### Purpose

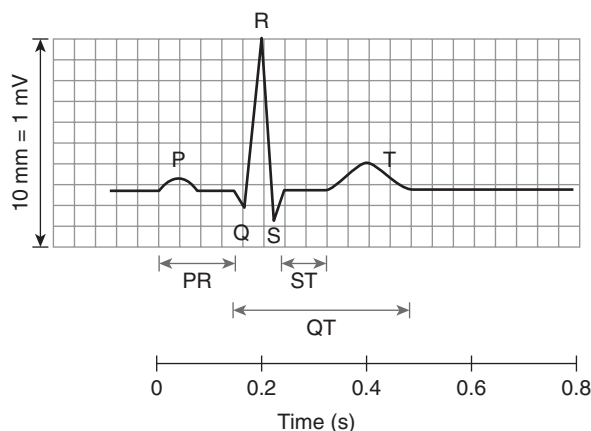
The electrocardiograph (ECG) is an instrument, which records the electrical activity of the heart associated with the heart muscle activity for assessment of cardiac physiology. Electrical signals from the heart characteristically precede the normal mechanical function, and monitoring of these signals has great clinical significance. ECG provides valuable information about a wide range of cardiac disorders such as arrhythmia and the presence

of an inactive part (infarction) or an enlargement (cardiac hypertrophy) of the heart muscle. ECGs are used in catheterization laboratories, in coronary care units, and for routine diagnostic applications in cardiology.

## Principle

ECG is an instrument for surface recording of the electrical activity of the heart by connecting various electrodes through which electrical potentials are acquired from the surface of the skin. Although the electric field generated by the heart can be best characterized by vector quantities, it is generally convenient to directly measure only scalar quantities, i.e. a voltage difference of mV order between the given points of the body. The normal wave pattern of the electrocardiogram is shown in Figure 128.1. The prominent features of this waveform are designated by alphabetic designations. The P wave represents depolarization of the atrial muscles, whereas the QRS complex is the combination of repolarization of the atria and depolarization of the ventricles, which take place almost simultaneously. The T wave represents repolarization of both ventricles.

The PR and PQ intervals, measured from the beginning of the P wave to the onset of the R or Q wave, respectively, marks the time that an impulse leaving the sino-atrial (SA) node takes to reach the ventricles. The PR interval normally lies between 0.12 and 0.2 seconds. The QRS interval, which represents the time taken by the heart impulse to travel first through the interventricular system and then through the free walls of the ventricles, normally varies from 0.05 to 0.10 seconds. The QT interval, therefore, is the period for one complete ventricular contraction (systole). Ventricular diastole, starting from the end of the T wave, extends to the beginning of the next Q wave. Typical amplitude of QRS is 1 mV for a normal human heart, when recorded in lead I position. The shape, polarity, and amplitude of each of these features vary with the placement of the measuring electrodes with respect to the heart. It is for this reason that the ECG recordings are made from several electrode locations.



**Figure 128.1** Normal wave pattern of ECG waveform: P wave (0.08–0.10 second), QRS (0.05–0.10 second), PR interval (0.12–0.20 second).

### The ECG Leads

Two electrodes placed over different parts of the body will pick up electrical signals generated by the heart, which will represent the potential difference between them. For example, if under one electrode a wave of 1 mV and under the second electrode a wave of 0.3 mV occur at the same time, then the two electrodes will record the difference between them, i.e. a wave of 0.7 mV. The resulting tracing of voltage difference at any two sites of the body due to electrical activity of the heart is called a 'lead'. The lead system in an ECG machine is shown in Figure 128.2.

**Bipolar Leads** The bipolar leads represents the difference of electrical potentials existing between two electrodes. They are also called standard leads and have been universally adopted. In standard lead I, the electrodes are placed on the right arm and the left arm (RA and LA). The electrodes in lead II are located on the right arm and the left leg, and in lead III, they are placed on the left arm and the left leg. In all lead connections, the difference of potential measured between two electrodes is always with reference to a third point on the body. This reference point is conventionally taken as the 'right leg' (RL). In defining the bipolar leads, Einthoven proposed that the electric field of the heart could be represented diagrammatically as a triangle, with the heart ideally located at the centre. The triangle, known as the *Einthoven triangle*, is shown in the figure.

**Unipolar Leads (V Leads)** In this arrangement, the electrocardiogram is recorded between a single exploratory electrode and the central terminal, which has a potential corresponding to the centre of the body. In practice, the reference electrode or central terminal is obtained by a combination of several electrodes tied together at one point. Two types of unipolar leads are employed: (i) limb leads and (ii) precordial leads.

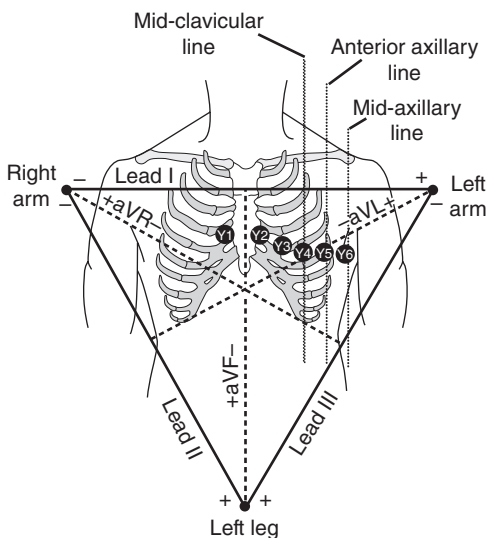


Figure 128.2 The lead system for recording ECG.

(i) *Limb leads*: Unipolar limb leads, also called as augmented leads or 'averaging leads', consist in tying together the two of the limb leads and recording the potential with respect to the third limb. They are designated as augmented vector right (AVR), augmented vector left (AVL), and augmented vector foot (AVF). In the AVR lead, the right arm is recorded with respect to a reference established by joining the left arm and left leg electrodes. In the AVL lead, the left arm is recorded with respect to the common junction of the right arm and left leg. In the AVF lead, the left leg is recorded with respect to the two arm electrodes tied together.

(ii) *Precordial leads*: The second type of unipolar lead is a precordial lead. It employs an exploring electrode to record the potential of the heart action on the chest at six different positions. These leads are designated by the capital letter 'V' followed by a subscript numeral, which represents the position of the electrode on the pericardium. The positions of the chest leads are also shown in the Figure 128.2.

One of the most obvious features of an ECG machine is the number of leads. Some ECGs have only one lead; the maximum number of leads is usually 12. The most common 12-lead ECGs require 10 electrodes. Nine of the electrodes pick up electrical signals and the tenth electrode, on the right leg, serves as a reference. The 12-lead ECGs are capable of operating as 5-, 3-, or 1-lead systems. Single channel ECG machines are usually portable and accordingly rechargeable battery operated.

Figure 128.3. shows the block diagram of a single channel ECG machine. The circuit can be separated into two distinct segments: the analog front end (AFE), which digitizes the signals received from the electrodes, and the digital part, which analyses, displays, stores, and transmits the data, if required. The potentials picked up by the patient electrodes are taken to the lead selector switch. In the lead selector, the electrodes are selected two by two according to the lead program. By means of capacitive coupling, the signal is connected symmetrically to a differential pre-amplifier. The preamplifier is usually followed by amplifiers which provide a gain of about 500.

The design of the AFE is quite complex as there is a need to reject interference from strong radio frequency (RF) sources, pace signals, lead-off signals, common-mode line frequency, signals from other muscles, and electrical noise. In addition, the millivolt-level ECG signal is associated with a DC offset signal that could be hundreds of millivolts. The electrical connections to the patient must not create a shock hazard or interfere with

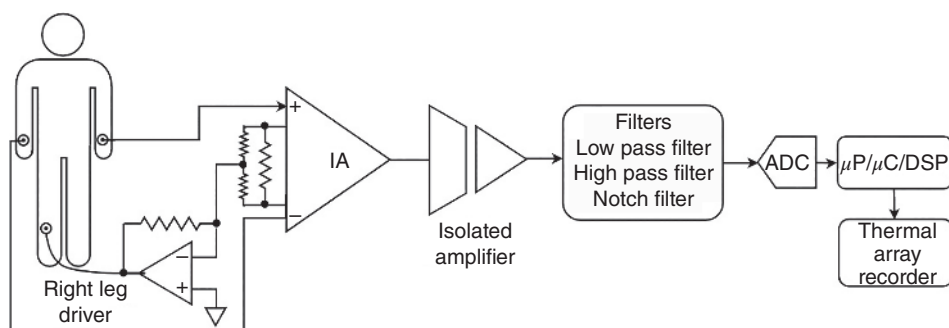


Figure 128.3. Block diagram of a typical single channel electrocardiograph.

other medical equipment that may be connected to the patient. In addition, the ECG machines are required to recover quickly from a defibrillation event, which can saturate the front-end and charge capacitors in the ECG circuit. This creates a long recovery time for capacitively coupled circuits. The frequency range of interest for the ECG varies somewhat with the application but is usually around 0.05–100 Hz. Filtering is required on the input leads to reduce interference caused by electrosurgery and RF. A multistage filter is needed to achieve a suitable reduction in high frequency signal. The filter circuit is followed by high voltage and overvoltage protection circuits so that the amplifier can withstand large voltages during defibrillation.

In view of the complexity of the front-end electronics, manufacturers of semiconductor chips have now come out with integrated circuits suitable for ECG front-end applications, which take care of all problems. Texas Instruments have introduced the ADS1298 single chip solution for the entire AFE, which uses simultaneous sampling low-power delta-sigma converters, which is critical for portable ECG applications.

As the microshock hazard became better understood, particularly when intracardiac catheters are employed, the necessity of isolating the patient from the ground has been greatly stressed. The American Heart Association guidelines state that the leakage current should not be greater than 10  $\mu$ A when measured from the patient's leads to the ground or through the main instrument grounding wire with the ground open or intact. For this, patient leads would have to be isolated from the ground for all line operated units. Initially, optical isolators were used, but now isolation amplifiers are available in the modular form.

Before the amplified ECG signal is passed to the analog-to-digital converter (ADC), it goes through a set of filters. A high pass filter (HPF) with a cut-off frequency of 0.05 Hz, a low pass filter, and notch filter are used to discard signals that are of not much significance in the ECG. Since digital signal processing is relatively of lower cost and provides a great deal of flexibility, it is beneficial to move the signal processing to the digital domain. A sampling rate of 200 samples/s, which will yield 12–20 points in the QRS complex, is considered adequate.

The output of the ADC then goes to a microprocessor or digital signal processor (DSP), which perform necessary processing and computational functions. These devices enable to achieve certain desirable features like removal of artefacts and baseline wander using software techniques. Automatic centring of the tracing is another feature that can be similarly achieved. They can also perform self-testing each time they are switched on. These machines are programmed to check lead continuity and polarity and also indicate lead fall-off or reversal. Use of digital filters considerably improves signal quality during recording and problems like baseline drift and excessive mains hum are thus automatically corrected. Minimizing baseline drift without distorting the signal helps in monitoring the ECG of exercising or ambulatory subjects.

Using microprocessors, the need for the technician to switch from one lead to another during the recording process is eliminated. Microprocessors have also been used for simultaneous acquisition of multiple leads. Stored programs in the ROM direct the operator about entering of patient data. An important feature of modern ECG machines is that it offers the potential for reducing the complexity of analysis algorithms by pre-processing the data. The output from the microprocessor goes to a recorder or can be displayed on a LCD monitor or laptop computer monitor.

Electrocardiograms are almost invariably recorded on graph paper with horizontal and vertical lines at 1 mm intervals with a thicker line at 5 mm intervals. Most ECG machines use what is called a paper strip recorder. After the output records the device, the doctor receives a hard copy of the measurements. Time measurements and heart rate measurements are made horizontally on the electrocardiogram. For routine work, the paper recording speed is 25 mm/s. Amplitude measurements are made vertically in millivolts. The sensitivity of an ECG is typically set at 10 mm/mV. A 'standby' mode of operation is generally provided on the ECG. In this mode, the stylus moves in response to input signals, but the paper is stationary. This mode allows the operator to adjust the gain and baseline position controls without wasting paper.

The writing mechanism used in most strip chart recorders is hot tip or thermal writing. The writing tip is a heated stylus heated by a resistance wire, which is placed inside a hollow metal tube. Thermal writing occurs when specially treated, thermally sensitive paper gets heated to 90–110°C by the heated stylus. The paper, which is initially white or off-white, turns a dark colour (usually blue or black) where heated. The dark colour is caused by a chemical reaction resulting from heating the paper. The functioning of the thermal writing system is entirely digital. For writing, the paper is passed over the writing edge, which is necessary to produce an undistorted recording. The writing paper is driven by a constant speed motor to provide time axis. The paper drive of most machines is provided by a stepper motor, which is controlled by a programmable frequency divider for speed control. Some ECG recorders are also based on dot-matrix technology for printing out numerical data patient name and his/her identity, date, time, heart rate, results of rhythm analysis, and results from other sensors.

ECG machines range from battery-operated low-cost portable handheld units to expensive sophisticated machines of the size of a fax machine. Basic machine may even be embedded in a separate piece of equipment, such as a patient monitor or an automatic external defibrillator (AED).

### ***Interpretative ECG***

Modern ECG machines incorporate computer-based predefined pattern recognition techniques that produces an automated interpretation of the electrocardiogram and identifies normal and abnormal features of the ECG waveform. Each program identifies the complete waveform, locates each waveform component, and determines key measurements. Waveform analysis includes P waveforms, QRS complex, and T waveforms from each lead group or a certain number of successive waveforms. The types of measurements calculated vary among units; the most common types include heart rate, waveform amplitude, waveform widths, intervals between the waveform components, and direction of the electrical activity (axis). Irregularities in the morphology (shape) of any portion of the ECG waveform or in the rhythm (timing) of these waveforms indicate abnormalities. The machine prints the interpretation of a specific cardiac abnormality and a plus or minus code, which reveals the severity of the patient's condition.

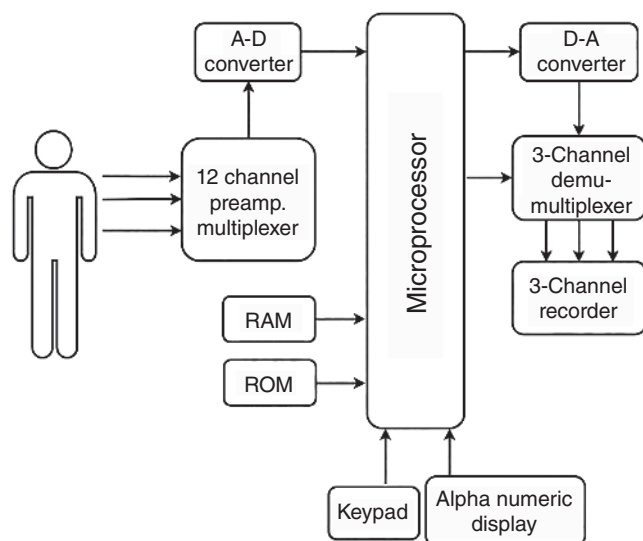


### Multi-channel ECG Machines

Multi-channel ECG machines facilitate recording of several ECG leads simultaneously and thus considerably reduce the time required to complete a set of recordings. Another advantage of multi-channel recording is that the waveforms are recorded simultaneously and they can be shown in their proper time relationship with respect to each other. These machines invariably use microprocessor to capture the heart signals from a standard 12-lead configuration, sequencing the lead selector to capture four groups of three lead signals and switching groups every few seconds.

Figure 128.4 shows the block diagram of a three channel microprocessor-based ECG machine. The operating program controlling the lead selection and other operations is stored in a ROM. The ECG signals selected by the microprocessor are amplified, filtered and sent to a three-channel multiplexer. The multiplexed analog signals are then given to an ADC. For a  $10\mu\text{V}$  resolution referred to as the input, it is necessary to use at least a 10-bit ADC. The sampling rate is usually 200–1000 samples/s. The microprocessor stores the digitized signals in a RAM. The contents of the RAM are sent to a digital-to-analog converter for reconstructing the analog signals. The analog signals are demultiplexed and passed to the video display or chart recorder.

The modern digital multi-channel ECG machines make use of an individual single-ended amplifier for each electrode on the body. Each potential signal is digitally converted, and all the ECG leads can be calculated mathematically in software. The standard 12 ECG leads are derived from various signals obtained through 9 electrodes placed on the skin surface – 1 on each of 3 limbs and 6 on the chest. An additional electrode, which is typically placed on the right leg, is used as a reference to reduce external electrical interference. This would necessitate a nine amplifier system. The machines make



**Figure 128.4** Block diagram of a multi-channel ECG machine.



**Figure 128.5** Typical single channel, three channel, and twelve channel ECG machines.

use of a 16 bit ADC, all within a small amplifier lead stage. The digital signals are optically isolated and sent via a high speed serial link to the main ECG instrument. Here the 32 bit CPU or DSP chip perform all the calculation and hard copy report is generated on a standard A4 size paper. The recording system also operates digitally.

Some ECG machines provide capabilities to control a treadmill, store exercise protocols, and print stress test reports, while others simply print the 12-lead ECG at fixed time intervals. The machines also vary in their capability to electronically store ECG waveforms. Some machines store the waveform, which can be later retrieved, printed, and analysed. In addition, most of the modern machines can be interfaced with RS232, USB, or modem to computer-based data management systems that provide long-term storage of ECG waveforms, for use either within the hospital or at a remote location. Figure 128.5 shows single channel, 3 channel and 12 channel ECG machines.

## Specifications

*Number of channels:* Single channel, 3 channel, 12 simultaneous ECG recording

*Sensitivity:* Selectable from 2.5 to 20 mm/mV

*Frequency range:* At least 0.05–150 Hz

*Input impedance:* 2.5 M $\Omega$  at 10 Hz

*Chart speed:* Selectable between 25 and 50 mm/s

*Patient leakage current:* Not higher than 10  $\mu$ A

*Common mode rejection (CMR):* Not less than +100 dB

*Software:* (i) arrhythmias detection and analysis; (ii) ventricular fibrillation detection and analysis; (iii) ventricular tachycardia detection and analysis; (iv) ST segment analysis

*Memory:* Minimum 40 ECG storage inbuilt memory

*Printer:* Digital thermal array printer

## Applications

ECG machine is one of the most useful noninvasive medical diagnostic device, which is in very wide use. It finds numerous applications in modern patient care as ECG machines, cardiometers, Holter monitors, and exercise and stress testing. Compared to single-channel recorders, multi-channel ECGs improve diagnostic ability by providing a more complete view of the heart during the same beats and are finding increasing applications.

## 129

## Electroconvulsive Therapy Machine

### Purpose

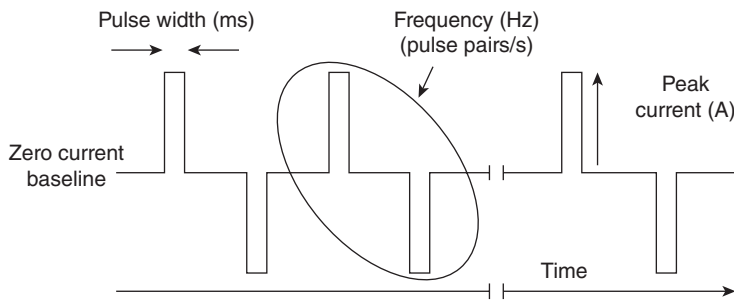
Electroconvulsive therapy (ECT) machine is a device that is used to treat severe, treatment-resistant depression. It is also employed in other mental disorders, such as bipolar disorder or schizophrenia. Its use is mostly recommended in life-threatening circumstances, such as when a patient is unable to move or respond to the outside world and could be having a suicidal tendency as a result of severe depression.

### Principle

ECT, sometimes also referred to as electroshock therapy, or shock treatment, is a technique for the treatment of severe psychiatric disorders in which electric currents are passed through the brain, causing changes in brain chemistry that relieve symptoms of certain mental illnesses by deliberately triggering a brief seizure. ECT is mostly used with informed consent as a last line of intervention for major depressive disorder, mania, and catatonia and as a long-term maintenance treatment (maintenance electroconvulsive therapy [M-ECT]) for the same indications as for acute treatment. ECT machines are classified as Class III equipment category (high risk) by the United States Food and Drug Administration (US FDA), since 1976.

In practice, the patient is connected to a stimulus generating device with two cables. The output cable that delivers the electric stimulus is attached to two electrodes attached to the patient. In the early ECT devices, the stimulus delivered was in the form of sine wave, as it could be easily obtained from electric mains supply. However, most modern ECT machines deliver a stimulus that consists of brief bidirectional rectangular pulses of current, having alternate positive and negative phases, with adjacent pulses separated by brief periods of no electrical activity. Typical pulse shape for ECT is shown in Figure 129.1. The actual number of pulses delivered per second is twice the frequency. The stimulus delivered by these devices is characterized by a number of parameters. These parameters include frequency, pulse width, duration, and peak current. Typical parameters provided in the devices are a pulse width of 0.5 ms at a frequency of 70 Hz, for a total duration of 8 seconds and a maximum current of about 800 mA. The user has the option of individually adjusting each parameter depending on the requirement. The ECT devices are equipped with a method of measuring circuit impedance and a safety mechanism for the treatment to prevent accidental discharge.

Most ECT devices deliver 'constant current' stimulus as opposed to 'constant voltage'. Constant current stimulation is more physiological and preferred method of the two for inducing neuronal depolarization. A constant current device ensures stable delivery of the stimulus over a wide range of impedances, in contrast to constant voltage or energy. Constant current is also more likely to induce a seizure in the presence of a high



**Figure 129.1** Typical pulse shape for electroconvulsive therapy.

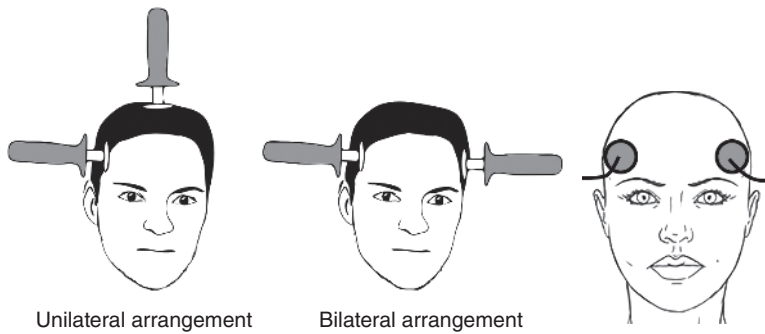
impedance because of insufficient current delivery with constant voltage or constant energy devices. The advantage of using constant current is that the physician is able to deliver predetermined quantity of charge by varying the time interval of exposure to the current.

For delivering constant current to the patient, the voltage has to be varied directly with the dynamic impedance of the patient. In case of extremely high impedances, correspondingly high voltages will be required to maintain the same current across the electrode. However, brief-pulse devices are designed to limit the maximum voltage that can be applied to about 500 V. Most constant current stimulators have maximal charge outputs of 500–600 mC. Assuming an inter-electrode impedance of  $200\ \Omega$ , this output translates into a stimulus energy of less than 100 J (W s). As the stimulus energy is related to inter-electrode impedance, the ECT stimuli are usually quantified in units of charge rather than units of energy.

### Electrodes

ECT provides brief but powerful shocks via one or two *electrodes*, called ‘paddles’, placed on the patient’s forehead. The electrodes are usually either handheld devices or metal plates contained in a band that is affixed to the patient’s head. Handheld electrodes are easier to position, but the position may change as pressure is applied to form a good electrical contact. The stimulus is transmitted to the head of the patient (and, indirectly, to the brain) through externally applied scalp electrodes. The electrodes may either be stainless steel discs held in place with an elastic band or self-adhesive flexible conductive pads. Prior to positioning the electrodes, the skin must be carefully prepared to improve electrical contact and minimize inter-electrode impedance. This is done by cleaning the electrode area with a saline-soaked pad and coating the electrodes with a conducting gel. The inter-electrode area should be dry. The electrodes should be applied very firmly. This firm pressure should be continued throughout the passage of current. There are three types of electrode placement, which can be used depending on the person’s condition.

**Unilateral Placement** The position of the electrodes for unilateral ECT is shown in Figure 129.2a. The flat temporal electrode is placed over the right temporal fossa, with the centre of the electrode 2.5 cm above the midpoint of a line drawn between the tragus



**Figure 129.2** Scheme for electrode placement for electroconvulsive therapy: (a) Unilateral arrangement. (b) Bilateral arrangement. (c) Bifrontal arrangement.

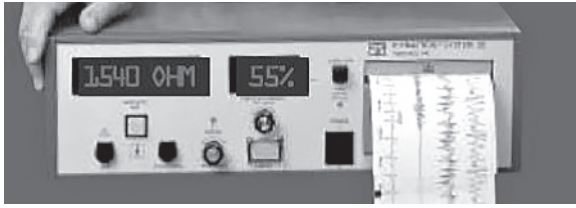
and the outer canthus of the eye. The centre of the second electrode (concave) is placed slightly to the right of the vertex, which is at the intersection of the line drawn between the nasion and the inion (occipital process), and the line drawn between the tragus of each ear. The unilateral arrangement directs the current across the motor cortex, the area of the cortex with the lowest seizure threshold.

**Bilateral (Bi-temporal) Placement** Each electrode (flat) is placed in the temporal fossa bilaterally, as shown in Figure 129.2b. Bilateral placement is generally regarded as the most effective form of ECT, but it is also associated with the greatest degree of cognitive impairment, particularly retrograde memory loss, which may not be fully reversible. It is usually recommended that its use be restricted to situations where other electrode placements have been ineffective and when there is some urgency to achieve a rapid response.

**Bi-frontal Placement** In this arrangement, the midpoint of each treating electrode is placed five centimetres above the outer canthus of each eye, in a parasagittal plane (Figure 129.2c). Concave metal electrodes or disposable adhesive electrodes are generally used.

### Monitoring System

Most modern ECT devices typically include arrangement for monitoring several parameters during the ECT, the most common being ECG, EEG, and EMG. *Four-channel EEG* is usually monitored, recorded, and analysed between treatments to measure ECT-induced EEG manifestations reported to reflect treatment impact and efficacy. A powerful 32-bit built-in computer employs power spectral analysis (Fast Fourier Transform [FFT]) to process and store up to 10 minutes of digitized EEG for the special features. Two analog methods are typically incorporated in ECT instruments for amplifying and presenting unprocessed EEG activity during ECT. One uses a chart drive and pen writer to record the EEG signal on paper; the resulting record is then read by the clinician as it is generated to determine the occurrence, duration, and end point of the induced seizure. A second



**Figure 129.3** ECT machine with EEG and ECG recording and anaesthesia depth monitoring facility. Model Thymatron® System IV. Source: Image courtesy of M/s Somatics, LLC USA.

method provides an auditory representation of the EEG signal in the form of a tone that fluctuates with the frequency of the seizure activity and becomes a constant when the seizure ends.

Two *EMG* electrodes are placed on a foot, usually the right foot to observe and record motor seizure activity in the foot. A continuous *digital heart rate meter* monitors and prints digital heart rate each second on the chart and also prints the baseline and peak heart rates that are important parameters that reflect seizure quality, in the end-of-treatment report.

*Anaesthesia depth monitor* is the latest addition to the modern ECT machines. This monitor provides a continuous front-panel display of three parameters known to correlate highly with anaesthesia depth and with the Bispectral Index® (BIS®): 95% spectral edge frequency (SEF-95), relative delta power (% delta), and median frequency (MF). Although these parameters are presently available in the operating room monitors and are quite expensive, they are now included in the ECT machines. The hard copy printout provides two channels of EEG, ECG, and EMG, plus 2 derived channels: digital heart rate and anaesthesia depth index for documentation for the patient's chart. Figure 129.3 is a state-of-the-art ECT machine Model Thymatron® System IV from M/s Somatics, United States.

## Specifications

*Current:* 0.9 A constant, isolated from line current

*Frequency:* 10–70 Hz in 10 Hz increments

*Pulse width:* 0.25–1.5 ms in 0.25 ms increments

*Duration:* 0.14–8.0 seconds in increments of equal charge

*Maximum charge:* 504 mC (99.4 J at 220 Ω); 1008 mC (188.8 J at 220 Ω)

*Recording:* ECG, EEG, and EMG

## Applications

ECT finds applications in the modern treatment of psychiatric disorders, particularly in the case of major depressive disorders.

# 130

## Electroencephalograph

### Purpose

Electroencephalograph (EEG) is an instrument for recording the electrical activity of the brain, by suitably placing surface electrodes on the scalp. EEG machines are used for diagnosing a variety of neurologic diseases, such as epilepsy, convulsive disorders, brain death, cerebrovascular lesions, ischaemia, and problems associated with trauma. They can also be used to evaluate psychiatric disorders and differentiate among various psychiatric and neurologic conditions. It is also effectively used in the operating room to facilitate anaesthetics to establish the integrity of the anaesthetized patient's nervous system. In addition, routine EEG monitoring in the operating room and intensive care units is also becoming popular. This has become possible with the advent of small, computer-based EEG analysers.

### Principle

The brain generates rhythmical potentials, which originate in the individual neurons of the brain. These potentials are summated as millions of cells discharge synchronously and appear as a surface waveform, the recording of which is known as the electroencephalogram. The EEG signals are of great diagnostic value both in terms of their amplitude and frequency. Frequency information is particularly significant since the basic frequency of the EEG range is classified into the following four bands, and labelled with Greek letters, for the purposes of EEG analysis:

Delta ( $\delta$ ): 0.5–4 Hz

Theta ( $\theta$ ): 4–8 Hz

Alpha ( $\alpha$ ): 8–13 Hz

Beta ( $\beta$ ): 13–22 Hz

Four mind states – alertness, rest, sleep, and dreaming – have associated brain waves named alpha, beta, theta, and delta. Each of these brain wave patterns have different frequencies (Figure 130.1) and amplitudes of waves. The alpha rhythm is one of the principal components of the EEG and is an indicator of the state of 'alertness' of the brain. It serves as an indicator of the depth of anaesthesia in the operating room. The EEG wave patterns usually get altered by pathological processes such as the presence of a tumour in the brain.

EEG signals picked up by the surface electrodes are usually small as compared with the ECG signals. Their amplitude varies from 10  $\mu$ V to over several hundreds of microvolts, but 50  $\mu$ V peak to peak is the most typical. The brain waves, unlike the electrical activity



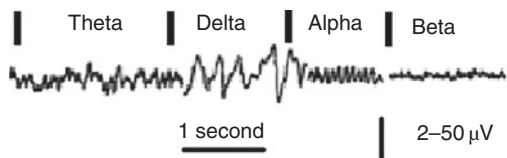


Figure 130.1 Typical EEG waveform with classification in different frequency components.

of the heart, do not represent the same pattern over and over again. Therefore, brain recordings are made over a much longer interval of time in order to be able to detect any kind of abnormalities. The EEG signal bandwidth is from below 1 Hz to over 100 Hz.

**Block Diagram**

EEG machines employ electrodes placed on a patient’s scalp to measure, amplify, display in graphic form, and record the weak electrical signals generated by the brain. The processed EEG signals are usually recorded in graphic form over a period of time so that waveform and pattern changes can be readily studied for possible diagnosis. Modern EEG monitors use computers to analyse and generate large amounts of electroencephalographic data, which are processed and displayed in various formats. Most systems can produce and display certain types of event-related EEG signals that occur in response to a periodically applied external stimulus.

The basic block diagram of an EEG machine with both analog and digital subsystems is shown in Figure 130.2.

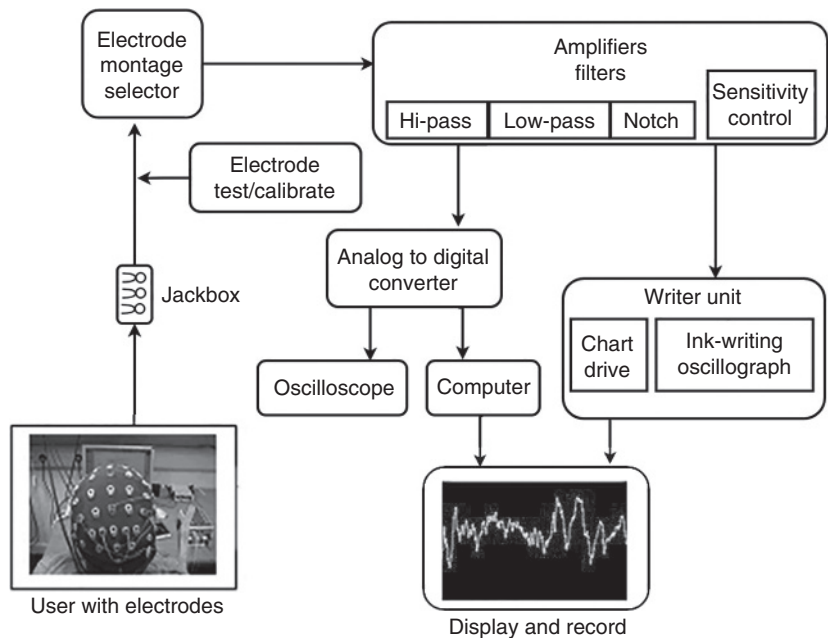


Figure 130.2 Block diagram of a typical EEG machine.

**Electrodes** The electroencephalogram is typically recorded by picking up the voltage difference between an active electrode on the scalp and a reference electrode on the ear lobe or any other part of the body. This type of recording is called ‘monopolar’ recording. However, ‘bipolar’ recording is more popular wherein the voltage difference between two scalp electrodes is recorded. Such recordings are done with multi-channel EEGs.

Several types of electrodes may be used to record EEG. They are usually smaller in size than ECG electrodes and include peel and stick electrodes, silver-plated cup electrodes, and needle electrodes. In general, needle electrodes provide greater signal clarity because they are injected directly into the body. For surface electrodes, there are disposable models such as the tab, ring, and bar electrodes. There are also reusable discs that may be combined into an electrode cap that is placed directly on the head. EEG surface electrodes are smaller in size than ECG electrodes. They may be applied separately to the scalp or may be mounted in special bands, which can be placed on the patient’s head. In either case, electrode jelly or paste is used to improve the electrical contact by minimizing skin–electrode impedance.

EEG electrodes give high skin contact impedance as compared with ECG electrodes. Good electrode impedance should be generally below 5 k $\Omega$ . Impedance between a pair of electrodes must also be balanced or the difference between them should be less than 1 k $\Omega$ . Before measurement, contact impedance should be measured, and EEG trace should be observed while recording. EEG preamplifiers are generally designed to have a very high value of input impedance to take care of high electrode impedance. Using today’s technology, high input impedance (1 G) amplifier chips and active electrode approaches decrease dependency of the contact impedance.

**Montages** EEG machines are multi-channel machines and they require many electrodes to pick the EEG signal. Many systems typically use electrodes, each of which is attached to an individual wire. However, some systems use caps or nets into which electrodes are embedded. This system is particularly common when high-density arrays of electrodes are used. In this case, there are several ways of choosing the electrode pairs according to specific montages. A pattern of electrodes on the head and the channels they are connected to is called a *montage*. The reference electrode is generally placed on a non-active site such as the forehead or earlobe. EEG electrodes are arranged on the scalp for most clinical and research applications according to a standard known as the 10/20 system, adopted by the American EEG Society. This system ensures that the naming of electrodes is consistent among laboratories.

Conventionally, there are 21 electrode (19 recording electrodes plus ground and system reference) locations in the 10/20 system. This system involves placement of electrodes at distances of 10 and 20% of measured coronal, sagittal, and circumferential arcs between landmarks on the cranium. Electrodes are identified according to their position on the head: Fp for frontal polar, F for frontal, C for central, P for parietal, T for temporal, and O for occipital. One electrode is labelled isoground and placed at a relatively neutral site on the head, usually the midline forehead or a metal clip on the earlobe. A new montage convention has been introduced in which electrodes are spaced at 5% distances along the cranium. These electrodes are closely spaced and have their own naming convention.

**Amplifiers** Every EEG channel is provided with individual, multistage amplifier with differential input and adjustable gain in a wide dynamic range. A typical adult human EEG signal is about 10–100  $\mu\text{V}$  in amplitude when measured from the scalp and is about 10–20 mV when measured from subdural electrodes. The preamplifier used in EEGs must have high gain and low noise characteristics as the EEG potentials are small in amplitude. In addition, the amplifier must have a very high common mode rejection to minimize stray interference signals from power lines and other electrical equipment. The input impedance should be greater than 20 M $\Omega$ . The common mode rejection ratio (CMRR) should be at least 100 dB for each input. The amplifier must be free from drift so as to prevent the slow movement of the recording pen from its centre position as a result of changes in temperature. EEG amplifiers must have high gain in the presence of unbalanced source resistances and DC skin potentials at least up to 100 mV. Noise performance is crucial in EEG work because skin electrodes couple brain waves of only a few microvolts to the amplifier.

Each individual EEG signal is preferably amplified at the bedside. Therefore, a specially designed connector box, which can be mounted near the patient, is generally employed with EEG machines. This results in the avoidance of cable or switching artefacts and also eliminates undesirable crosstalk effects of the individual electrode potentials. The section of the amplifiers, which receive direct signals from the patient, uses optical isolators to separate the main power circuitry from the patient to separate the possibility of accidental electric shock.

The connector box also carries a circuit arrangement for measuring the skin contact impedance of electrodes. Thus, poor electrode-to-skin contacts above a predetermined level can be easily observed. The preamplifier is followed by a high gain amplifier in which the analog signal is converted to a digital signal, which is more suitable for output. These amplifiers together amplify the voltage between the active electrode and the reference, typically 1000–100 000 times, or 60–100 dB of voltage gain. A typical value of the calibration signal is 50  $\mu\text{V}/\text{cm}$ .

**Filters** Just like in an ECG, an EEG record may also contain muscle artefacts when recorded by surface electrodes. The artefacts could be large and sharp, in contrast to the ECG, causing great difficulty in both clinical and automated EEG interpretations. The most effective way to eliminate muscle artefact is to use low pass filters. In addition, high pass filters are employed, which typically filters out slow artefact, such as DC signals and movement artefact, whereas the low pass filter filters out high frequency artefacts, such as EMG signals. EEG machines also have a notch filter sharply tuned at 50/60 Hz so as to eliminate mains frequency interference. Typical settings for the high pass filter and a low pass filter are 0.5–1 Hz and 35–70 Hz, respectively. Selecting the proper filter band (at least bandwidth must be 0.5–70 Hz) is important to acquire proper signal. This is important for digitizing and data storage.

**Recorder** In analog EEG machines, after the signal is filtered, it is given to the paper recorder. However, most EEG systems today are digital, and the amplified signal is digitized via an analog-to-digital converter. Analog-to-digital sampling typically occurs at 256–512 Hz in clinical scalp EEG and sampling rates of up to 20 kHz are used in some research applications. The writing part of an EEG machine in older versions was direct writing thermal recorder. The best types of pen motors used in EEG machines have a frequency response of about 90 Hz. The modern PC-based machine can give a printout from a laser printer.

In direct writing recorders, the paper drive is provided by a synchronous motor. An accurate and stable paper drive mechanism is necessary, and it is normal practice to have several paper speeds available for selection. Speeds of 15, 30, and 60 mm/s are commonly used. A timescale is usually registered on the record by one or two time marker pens, which make a mark once per second. Timing pulses are preferably generated independently of the paper drive mechanism in order to avoid difference in timing marks due to changes in paper speed.

**Channels** An electroencephalogram is recorded simultaneously from an array of many electrodes. Commercial EEG machines have up to 32 channels, although 8 or 16 channels are more common. Microprocessors are now employed in most of the commercially available EEG machines to permit customer programmable montage selection. These machines use a video monitor screen to display the selected pattern (montage) as well as the position of scalp sites with electrode-to-skin contact. Individual channel control settings for gain and filter positions can be displayed on the video monitor for immediate review.

Modern EEG machines are mostly PC based. The EEG is displayed on a large screen colour monitor with a resolution of  $1280 \times 1024$  pixels. The user interface is through an ASCII keyboard and the output is available in the hard copy form through a laser printer. Specialized medical software is used to analyse, display, and provide special functions and options, which can be helpful in diagnosis of brain-related diseases.

### ***Recording of Evoked Potentials***

A special technique in electroencephalography is the recording of electrical potentials from the surface of the skull, when an external stimulus is applied to a sensory area of the brain. The electrical potentials generated as a result of the stimulus response are known as the 'evoked potentials'. Evoked potential activity is distinct from spontaneous potentials as detected by EEG, EMG, or other electrophysiologic recording method. Evoked potential amplitudes are generally low as compared to the EEG signal. They are in the range of less than a microvolt to a few microvolts. The most frequently used evoked potentials for clinical testing include visual evoked responses, brainstem auditory evoked responses, and somatosensory evoked potentials.

*Visual evoked potential (VEP):* The VEP tests the function of the visual pathway from the retina to the occipital cortex and thus helps in diagnosis of problems with the optic nerves that affect sight. VEPs are usually evoked by light flashes or visual patterns such as a checkerboard or a patch. A healthcare professional places electrodes along the scalp to record the electrical signals as the patient watches a checkerboard pattern flash for several minutes on a screen.

*Brainstem auditory evoked potentials (BAEPs):* The BAEP measures the functioning of the auditory nerve and auditory pathways in the brainstem. Auditory evoked potentials are usually elicited by tones or clicks. BAEPs are helpful in estimating the assessment of hearing ability and can point to possible brainstem tumours or multiple sclerosis. A healthcare professional places electrodes on the scalp and earlobes and delivers auditory stimuli, such as clicking noises and tones, to one ear. The frequency of stimulation is 50–70 Hz, and at least three different intensities are generally used.

The evoked potentials are generally superimposed with EEG signals. To isolate these low-amplitude signals from EEG signals and ambient noise, signal averaging technique is usually adopted. Here, the signal is time locked to the stimulus and most of the noise that occurs randomly is averaged out with averaging of repeated responses. Since the background EEG and other unwanted signals often appear irregular, or do not synchronize to stimuli, they are markedly reduced by averaging across multiple trials. Since many evoked potential components are of short duration, about 2 ms–1 second, rapid sampling rates are needed to digitally record such low level potentials.

## Specifications

*Number of channels:* 32 channels

*Frequency response:* 0.1–70 Hz

*Input impedance:* >20 M $\Omega$

*CMRR:* 100 dB

*Noise:* <1.5  $\mu$ V peak to peak

*Input range:* 5000  $\mu$ V peak to peak

*High pass filter for each channel:* 15, 35, and 70 Hz

*Low pass filter for each channel:* 0.1, 0.3, 1.5, 3, and 5 Hz

*Display:* Split screen to compare the data of same time/different times with individual selection of filters, sensitivity, and montages

*Software:* Standard software with patient annotation, create a map of the brain

*Stimulator:* Photic using LED or xenon flashlights

## Applications

The main diagnostic application of EEG machine is for the diagnosis of epilepsy, which manifests itself as clear abnormalities on a standard EEG study. The other applications are in the diagnosis of coma, encephalopathies, and brain death. EEGs can also help to identify causes of other problems such as sleep disorders and a first-line method for the diagnosis of tumours, stroke, and other brain disorders.

131

## Electrogastrograph

### Purpose

The electrogastrograph machine is used for recording of gastric myoelectrical activity that controls gastric motility. The technique is noninvasive, and recording of electrical activity is done by means of electrodes placed on the abdominal surface. Electrogastrograph is used when it is suspected that the muscles of the stomach or the

nerves controlling the muscles are not working normally. The electrogastrograph helps to evaluate normal and abnormal gastric electrical activity, leading to diagnosis of the gastric motility dysfunction.

## Principle

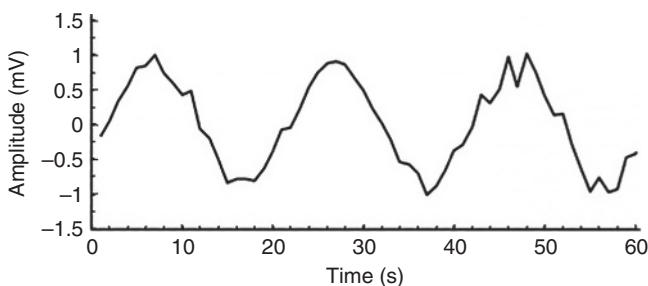
The graph generated by an electrogastrograph is called electrogastrogram (EGG), which represent the electrical signals that travel through the stomach muscles and control the muscles' contractions. An electrogastroenterogram or gastroenterogram is a similar procedure, but records electrical signals not only from the stomach but also from intestine. In practice, both electrogastrography and electrogastrogram are both abbreviated as EGG. The EGG technique has become popular, both in research and clinical situations, due to its noninvasive nature and availability of computerized signal analysis tools.

### *The EGG Signal*

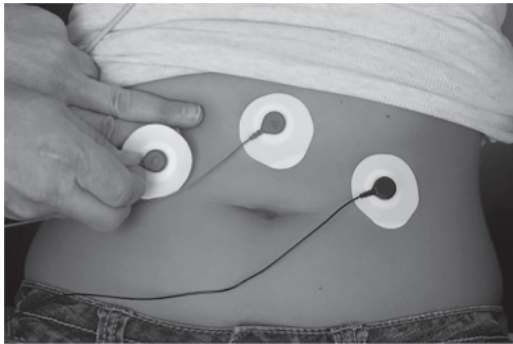
Gastric electrical activity consists of spontaneous rhythmic electrical activity that determines the timing and frequency of the contractile activity. The electrical activity of the stomach is of two types: electrical control activity (ECA) and electrical response activity (ERA). ECA is characterized by regularly recurring electrical potentials, which originate in the gastric pacemaker located in the corpus of the stomach and sweeps in an annular band with increasing velocity towards the pylorus. When motor activity is present, ECA is associated with or without superimposed fast oscillating potential changes, referred to as ERA. EGG signal for the normal activity is a regular electrical rhythm signal at a frequency of 3 cycles/min as shown in Figure 131.1. The voltage (power) of the electrical current increases normally after the meal. In patients with abnormalities of the muscles or nerves of the stomach, the rhythm often is irregular or there is no post-meal increase in the voltage.

### *EGG Electrodes*

Electrodes are used as sensors for capturing the electrical signals from the outer layer of the stomach. Surface electrodes generally used for monitoring electrocardiogram



**Figure 131.1** Typical electrogastrograph (EGG) waveform.



**Figure 131.2** Position of abdominal electrodes for the measurement of one-channel EGG.

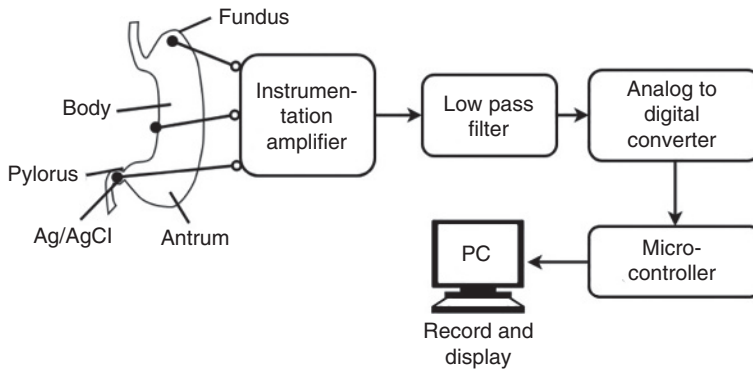
(ECG) like silver/silver chloride (Ag/AgCl) are used for recording EGG also. The electrodes are available in two sizes, standard 20 mm and miniature 11 mm. These cover a small area and provide accurate, stable, and optimal recordings. EGG signals are very weak, so it is very important to minimize the impedance between the skin and electrodes. The abdominal skin, where the electrodes are to be positioned therefore, should be thoroughly cleaned to ensure that the impedance between the pair of electrodes is below  $5\text{ k}\Omega$  followed by application of a thin layer of electrode jelly. For recording single channel EGG, one electrode is placed at the midpoint on a line connecting the xiphoid and umbilicus, and the other electrode 5 cm away (up and  $45^\circ$ ) to the patient's left as shown in Figure 131.2. The ground electrode is placed on the left costal margin horizontal to the first active electrode. For recording multiple channels, the electrodes are placed on the abdomen along the gastric axis with a common reference electrode placed near the xiphoid process. The usual practice is to record several cutaneous electrogastragram (EGG) signals from various standardized positions on the abdominal wall and to select the one with the highest amplitude for further analysis.

### System Block Diagram

A block diagram of the electrogastragraph machine is shown in Figure 131.3. The EGG signal from the stomach due to motility is picked up by Ag/AgCl surface electrodes cutaneously. Since the EGG signal is of low amplitude ( $50\text{--}500\text{ }\mu\text{V}$ ), it is amplified using a signal conditioning unit, which is responsible for data acquisition, in which sensor signals are normalized and filtered to levels suitable for analog-to-digital conversion for recording and analysing using a computer processor. Instrumentation amplifier is the first stage of the signal conditioning unit. The instrumentation amplifier is a closed-loop fixed-gain amplifier, usually differential, and has high input impedance, low drift, and high common mode rejection ratio (CMRR) over a wide range of frequencies. As in the case of ECG recording, all components of the EGG recording system must be electrically isolated from the patient to ensure patient safety.

The EGG signal is accompanied by the surrounding background 'noise' related to unwanted signals, such as cardiac, respiratory, duodenal, and colonic electrical activity and, therefore, it is necessary to filter out the background noise by using bandpass and notch filters. Filter setting determines the frequency range of the EGG signal to be





**Figure 131.3** Block diagram of an electrogastrograph.

maximally amplified. The interesting frequency range of the EGG signal is in the range of 0.0083–0.15 Hz. In addition to the basic fundamental frequencies, it is also important to record certain harmonics of the fundamental frequency, so an appropriate frequency setting should be in the range of 0.0083–1 Hz.

The signal conditioning unit is followed by an analog-to-digital converter, microcontroller, and PC connected with a serial interface circuit.

The PC acts as a monitoring, analysing, and display device. Direct visual analysis of the EGG signals is problematic and, therefore, various automated methods of analysis have been developed, among them, the spectral analysis (SA) method is most common. The signals are analysed to classify normal EGG or abnormal EGG usually based on the amplitude and frequency and displayed on the monitor. It also displays the name, age, amplitude, and frequency, which are saved and kept in an EGG database for future reference.

EGG systems are available from a number of manufacturers. The device is a workstation that consists of an amplifier with custom filters, strip chart recorder, and computer with proprietary software. The systems are usually provided with an automatic impedance check function, which allows to verify all EGG electrodes to be in good electrical contact with the skin. Some machines also include a motion sensor that can record respiration and patient movements during data capture, which can assist in easily identifying motion artefacts, which can be excluded from subsequent analysis.

### Data Analysis

Unlike ECG record that can be visually examined for diagnosis, the EGG requires to be subjected to computerized analysis. This is because the EGG signal represents integrated all gastric slow waves present in the stomach; its waveform has many uncontrollable factors and no diagnostic criteria have been established for the EGG waveform. In addition, artefacts are also present in the recorded waveform sometimes due to the ECG, respiratory activity, and slow wave of the small intestine.

EGG can be analysed using three methodologies namely fast Fourier transform (FFT), wavelet transform, and neural network. Since the frequencies of these artefacts do not overlap with that of the EGG, *spectral analysis* by FFT can be gainfully performed to separate the gastric slow waves from interferences. The data file that is generated during the A/D conversion of the EGG signal is subjected to Fourier transform, an analysis

of the frequencies contained in the EGG signal, and a running spectral analysis (SA). The spectral analysis gives clinically established EGG parameters that include dominant frequency and power, power ratio, percentage of normal gastric slow waves, percentage of gastric dysrhythmias, and percentage of power distribution.

### ***Ambulatory EGG***

An ambulatory multichannel EGG recording system is now available for recording of normal and impaired gastric electrical activity over a long period (24 hours) along with a specific software for EGG frequency analysis. These devices are required for both research and clinical purposes and the development of a small, pocket size EGG recorder has met this need. The stored data can be subsequently analysed on a personal computer by means of dedicated software.

## **Specifications**

*Frequency response:* DC – 1 Hz (maximum bandwidth)

*Low pass filter:* 0.1 Hz, 1 Hz

*High pass filter:* DC – 0.005 Hz, 0.05 Hz

*Notch filter:* 50 dB rejection at 50 or 60 Hz

*Noise voltage:* 0.1  $\mu$ V RMS

*Signal source:* Surface electrodes

*Z (input) differential:* 2 M $\Omega$

*Common mode impedance:* 1000 M $\Omega$

*CMRR:* 110 dB minimum (50/60 Hz)

## **Applications**

The applications of electrogastrography include detection of slow wave abnormalities in patients with gastric motility disorders or suspected gastric motility disorders, assessment of the efficacy of therapy or intervention, and electrophysiological studies.

# **132**

## **Electrolyte Analyser**

### **Purpose**

The electrolyte analyser is a device for measuring the electrolytes in the human body. An electrolyte is a substance that contains free ions that behave as an electrically conducting medium. They are primarily used in the quantitative measurement of sodium,

potassium, and chloride in whole blood, serum, or plasma. The measurements performed by this device are used for the diagnosis, monitoring, and treatment of diseases involving electrolyte imbalance.

## Principle

Electrolytes play an important role in the maintenance of multiple body functions. In physiology, the primary ions of electrolytes are sodium ( $\text{Na}^+$ ), potassium ( $\text{K}^+$ ), calcium ( $\text{Ca}^{2+}$ ), magnesium ( $\text{Mg}^{2+}$ ), chloride ( $\text{Cl}^-$ ), hydrogen phosphate ( $\text{HPO}_4^{2-}$ ), and hydrogen carbonate ( $\text{HCO}_3^-$ ). The electric charge symbols of plus (+) and minus (−) indicate that the substance is ionic in nature and has an imbalanced distribution of electrons as a result of chemical dissociation.

Among all the electrolytes, sodium, potassium, calcium, and chloride are most commonly measured. *Sodium* is the major electrolyte found in extracellular fluid. Its primary functions in the body are to chemically maintain osmotic pressure and acid–base balance and to transmit nerve impulses. Sodium ions are involved in fluid balance, regulating function of the heart, especially blood pressure control. *Potassium* is the major cation in the intracellular fluid and functions as the primary buffer within the cell itself. Most of the potassium is concentrated within the cell and plays an important role in nerve conduction, muscle function, and maintenance of acid–base balance and osmotic pressure. In case of damaged cells, potassium is released into the blood.

*Calcium* is mostly present in the blood as free calcium ions (50%), whereas about 40% is bound to protein, mostly albumin, and only 10% bound to anions such as bicarbonate, citrate, phosphate, and lactate. However, only ionized calcium is used by the body in such important processes as muscular contraction, cardiac function, transmission of nerve impulses, and blood clotting. *Chloride* is another anion that is present predominantly in extracellular spaces. Its function is to maintain cellular integrity through its action on osmotic pressure. Chloride is also important in monitoring acid–base balance and water balance. In view of the importance of these parameters, electrolytic analysis is a key factor in patient diagnosis and treatment.

## Measurement Methods

The most common methods of electrolyte analysis are the flame emission photometry (FEP) and ion-selective electrode (ISE). Flame photometry is an indirect measurement technique and mostly used to measure  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Li}^+$ . The ISE method gives direct measurements of the concentration of electrolytes and are therefore more popular.

### ISE Method

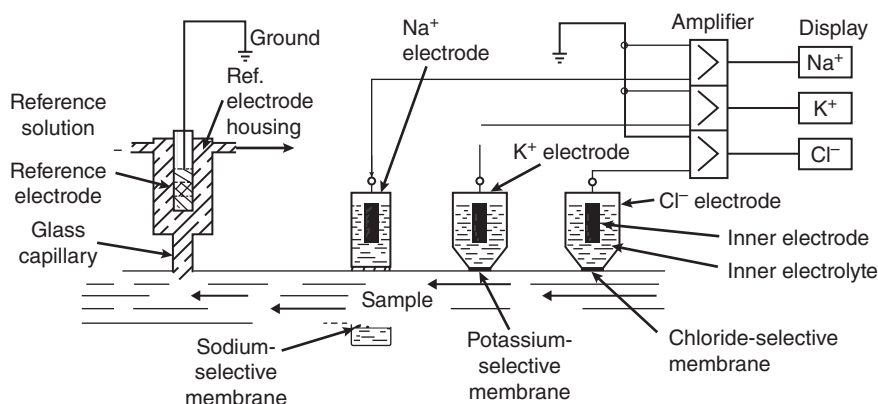
The ISE method of electrolyte measurement is based on the principle of potentiometry in which the voltage that develops between the inner and outer surfaces of an ISE (membrane) is measured. The membrane is made of a material that is selectively permeable to the ion being measured. For example, sodium electrodes are made from a special glass formula that selectively binds sodium ions. The inside of the electrode is

filled with a fluid containing sodium ions, and the outside of the glass membrane is immersed in the sample. The membrane acts as an ion exchanger, thereby causing a change in the membrane potential.

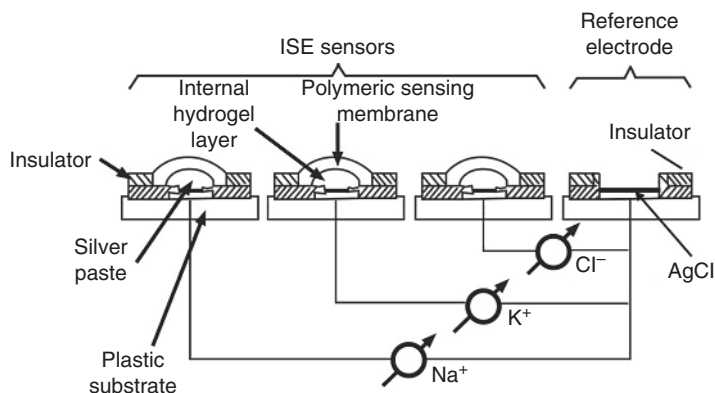
The potential difference developed across the glass membrane is dependent upon the difference in sodium concentration or activity on the inside and outside of the glass membrane. This potential is measured by comparing it to the potential of a reference electrode. The potential of the reference electrode is kept constant, the difference in voltage between the other two electrodes is thus due to the concentration of sodium in the sample. Referring to the Figure 132.1, the potential is conducted by the inner electrode to the input of a very high input amplifier. The reference electrode is connected to the ground as well as the second input of the amplifier. The signal is further amplified, digitized, and processed to calculate ion concentration in the sample and displayed as numerical values. The calibrations curve is done by two measured points of standard solutions with precisely known ion concentrations. Ion-selective membranes are specific for different electrolytes.

### Solid State ISEs

Some electrolyte analysers employ miniaturized ISE, which are fabricated in planar type as shown in Figure 132.2. Each sensor (electrode) is composed of polymeric sensing membrane dispensed over internal hydrogel layers on a thin plastic substrate. For a reference electrode, the Ag/AgCl reference electrode is used. A liquid junction between the sensors and the reference electrode is formed where the reference solution flowing over the reference electrode meets the sample or calibration solution flowing over the sensors. The development of solid state ISE has led to their encapsulation in the form of multi-usable cartridges for the electrolyte analyser. The cartridge incorporates all consumable parts such as reagent, electrode, valve, tubing, sampler, and especially waste bag. The cartridges are cleaned automatically and can be removed after use or expiration date. The use of cartridge allows easy maintenance except for regular cartridge change, replacing reagents, or other consumable part. The i-Smart 30 Pro analyser calibrates the sensors according to the predetermined two-point calibration schedule during the lifetime of the cartridge.



**Figure 132.1** Measurement system in an electrolyte analyser using ion-selective electrodes.



**Figure 132.2** A cross-sectional view of the sensors based on microfabrication technique.

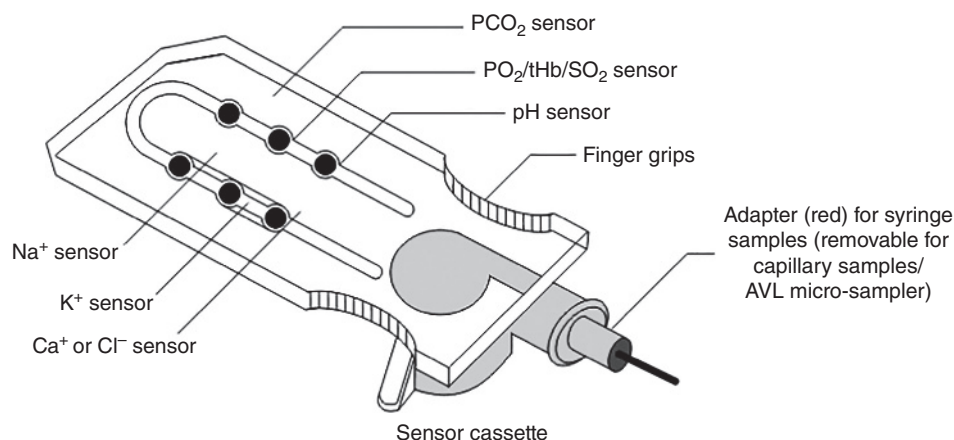
In addition, the analyser performs one-point calibrations between two-point calibration intervals to periodically correct the baseline drift of the sensors.

The electrolyte analyser based on microfabrication technique is usually a small device that can operate on rechargeable built-in batteries. It can be conveniently moved to the point-of-care testing places such as emergency diagnosis room or intensive care unit in the hospitals. Built-in memory allows to store more than 300 000 results. Data can be downloaded via USB data storage devices and software upgrade is convenient. The results are displayed on 7 in. colour touch screen display and printed with a thermal printer.

### ***Ion-Selective Optodes***

An optode is an optical sensor or optical electrode that optically measures a specific substance usually with the help of a chemical transducer. The sensor is referred to as an optode, because it uses the properties of light, rather than depending upon a chemical reaction or electricity to make measurements. The function of an optode, also known as optrode, is similar to that of ISEs. For example, the Na<sup>+</sup> ion optodes use ion-selective recognition elements, called ionophores, similar to those used in ISEs. However, in optodes, the ionophores are linked to fluorescent dyes instead of electrodes. The optode emits a specific wavelength of light that excites the molecules of the substance being measured. These molecules then emit a slightly different wavelength of light in response to excitation, which the sensor detects. As the ion concentration increases, these ionophores bind larger amounts of ions and cause the fluorescence intensity to increase or decrease, depending on the particular ion. Using various calculations, the sensor then determines how much of the substance (Na<sup>+</sup>) is present in the sample. The functioning of the K<sup>+</sup>, Ca<sup>2+</sup>, and Cl<sup>-</sup> are similar to the Na<sup>+</sup> optode except that ion-selective recognition elements (ionophores) are different in each case.

The instruments based on the use of optodes are not exclusive electrolyte analysers, but are mostly composite instruments that allows to perform measurement of several other parameters such as hydrogen ion concentration (pH), carbon dioxide partial pressure (PCO<sub>2</sub>), oxygen partial pressure (PO<sub>2</sub>), sodium (Na<sup>+</sup>), potassium (K<sup>2+</sup>), ionized calcium (Ca<sup>2+</sup>), chloride (Cl<sup>-</sup>), total haemoglobin concentration (tHb), and haemoglobin oxygen saturation (SO<sub>2</sub>).



**Figure 132.3** Optical fibre-based sensors mounted on a single disposable cassette.

After the development of fibre optic-based sensors, there has been a tendency to mount several sensors on a single cassette. A syringe adapter allows automatic aspiration of the sample from the syringe. When adapter is removed from the capillary, direct sample aspiration occurs. Calibration of sensor is verified after insertion of cassette. After entire sample analysis, the cassette is removed. Figure 132.3 shows the constructional details of a disposable, single-use cassette, which carries a number of sensors, including essential electrolyte sensors. The cassette contains all of the elements needed for calibration, sample measurement and waste containment. The pH and electrolyte channels are calibrated with precision buffer solution contained in the cassette. After verification of the calibration, the sample is aspirated into the cassette and across the optode sensors. After a single measurement, the cassette, containing the blood sample, is removed from the analyser and discarded. The analyser contains no reagents, blood, or waste. During each measurement, light emitted by the lamps in the analyser is passed through optical filters so that photons of a specific colour are transmitted to the sensors, causing them to emit fluorescence. The output signal of the fluorescence detectors is converted by the microprocessor to a numeric readout and displayed. A cartridge peristaltic pump is used to transport liquids and gases. All liquids are contained within the cassette and do not enter the instrument. The optode technology does not use electrodes or contact points, which eliminates the need for costly electrode maintenance. The instruments generally accept samples of whole blood, plasma, and serum.

## Specifications

*Sample type:* Whole blood, plasma, and serum

*Sample volume:* 60  $\mu$ l

*Sample introduction:* Syringe and capillary

*Temperature:*  $37 \pm 0.2$   $^{\circ}$ C

*Measuring principle:* Electrochemistry (direct ISE)

*Cartridge capacity:* 50/100/150/200 samples/2 weeks

*Cartridge dimensions (mm) per weight:* 138 (H) × 139 (W) × 80 (D) / 0.8 kg

*Cartridge shelf life:* 12 months

## Applications

Electrolyte analysers find applications for measurement of electrolyte levels in the human body to detect metabolic imbalances and measure renal and cardiac functions. These instruments are mostly used in hospital and reference laboratories and also for point-of-care setting.

## 133

## Electromyograph

### Purpose

An electromyograph (EMG) is an instrument used to study neuromuscular condition and function, extent of nerve lesion, reflex responses, etc. It is specifically used for recording the electrical activity of the muscles to determine whether the muscle is contracting or not; or for displaying the action potentials spontaneously or those induced by voluntary contractions for detecting the nature and location of motor unit lesions; or for recording the electrical activity evoked in a muscle by the stimulation of its nerve. EMG measurements are important for the myoelectric control of prosthetic devices (artificial limbs). Electromyography is the technique that deals with the detection, analysis, and use of the electrical signal that emanates from the muscles. The resultant record obtained via the electromyograph is known as electromyogram.

### Prinzciple

#### *EMG Signal*

The EMG signal is the electrical manifestation of the neuromuscular activation associated with a contracting muscle. The activity is similar to that observed in the cardiac muscle, but in the skeletal muscle, repolarization takes place much more rapidly, the action potential lasting only a few milliseconds. Since most EMG measurements are made to obtain an indication of the amount of activity of a given muscle, or a group of muscles, rather than of an individual muscle fibre, the EMG pattern is usually a summation of the individual action potentials from the fibres constituting the muscle or muscles being studied. The signal is effected by the anatomical and physiological properties of muscles and the control scheme of the nervous system.



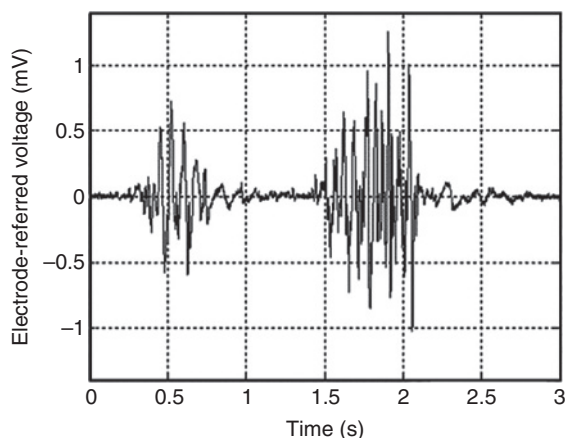
In voluntary contraction of the skeletal muscle, the muscle potentials range from  $50\mu\text{V}$  to  $5\text{ mV}$  and the duration from 2 to 15 ms. The signal lies in the frequency range 0–500 Hz and most dominant in between 50 and 150 Hz. The values vary with the anatomic position of the muscle and the size and location of the electrode. In a relaxed muscle, there are normally no action potentials. Figure 133.1 shows a typical EMG signal characterized by positive and negative peaks. The amplitudes and frequency content of this signal provides information about the contraction or resting state of the muscle under study.

### Electrodes

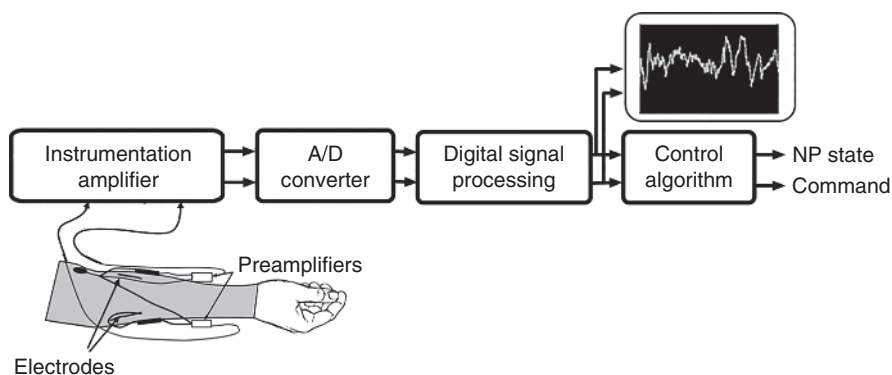
The electrical activity of the underlying muscle mass can be observed by means of surface electrodes on the skin. The surface electrodes may be disposable, adhesive types or the ones that can be used repeatedly. A ground electrode is necessary for providing a common reference for measurement. However, it is usually preferred to record the action potentials from individual motor units for better diagnostic information using needle electrodes, which are inserted directly into the muscle. The needle electrodes may be monopolar having a Teflon-coated stainless steel wire, which is bare at the tip or bipolar containing two insulated wires within a metal cannula.

### System Description

The block diagram in Figure 133.2 shows the various subsystems in an EMG machine. The myoelectric signals are amplified by using a preamplifiers followed by a differential amplifier together having an effective passband of 10–1000 Hz. The signals are sampled at 10 kHz with 16 bit analog-to-digital converter (ADC), rectified, and smoothed with a running time window averager with a window length of 240 ms that is updated every 80 ms. The processed signals are normalized by the amplitudes of the maximum voluntary contractions and are displayed on a computer monitor. The waveforms can be



**Figure 133.1** Waveform of a typical EMG signal recorded over bicep during two brief muscle contractions.



**Figure 133.2** Block diagram of an EMG machine.

stored to facilitate playback and study of the EMG waveforms at a later convenient time. The waveform can also be printed as a hard copy for records. The output is also applied to an audio-amplifier connected to a speaker. A trained EMG interpreter can diagnose various muscular disorders by listening to the sounds produced when the muscle potentials are fed to the speaker.

The amplitude of the EMG signals depends upon the type and placement of electrodes used and the degree of muscular exertions. The needle electrode in contact with a single muscle fibre will pick up spike-type voltages, whereas a surface electrode picks up many overlapping spikes and therefore produces an average voltage effect. A typical EMG signal ranges from 0.1 to 0.5 mV. They may contain frequency components extending up to 10 kHz. Such high frequency signals cannot be recorded on the conventional pen recorders and therefore are usually displayed on the PC monitor screen.

**Preamplifier** The preamplifiers used for EMG are generally of differential type with a good bandwidth. The input impedance of the amplifier must be greater than  $2 \times 50 \text{ M}\Omega$ . Present-day differential amplifiers easily provide input impedances of the order of  $10^{12} \Omega$  in parallel with 5 pF. The signal from the EMG detecting surfaces is captured by appropriate electrodes with respect to a reference electrode that acts as a ground for the signal. It should be placed far from the EMG detecting surfaces, on an electrically neutral tissue.

The leads to the input of the preamplifier should be as short as possible and should not be susceptible to movement. This can be achieved by building the first stage of the preamplifiers very near the subject using very small electrode leads. This minimizes the undesirable effects of stray capacitance between connecting cables and the earth. Also, any movement of the cable from the output of the electrode will not generate significant noise signals in the cable, which feeds into the subsequent amplifier. The property of a differential amplification to reject signals common to both inputs is determined by common mode rejection ratio (CMRR). A CMRR of 90 dB is adequate for elimination of common signals for instrumentation amplifiers, but today's technology provides us with a CMRR of 120 dB. A calibrating square wave signal of  $100 \mu\text{V}$  (peak to peak) at a frequency of 100 Hz is usually available. The main amplifier has controls for gain adjustment from  $5 \mu\text{V}/\text{div}$  to  $10 \text{ mV}/\text{div}$  for selecting the sensitivity most appropriate to the

incoming signal from the patient. To ensure patient safety, the subject should be electrically isolated from any electrical connection to the power line or ground. This isolation is achieved either through the use of optical isolators or through the use of isolation transformers.

**Filters** The noise frequencies containing both high and low frequency components are present as contaminating signals in the raw EMG signal. Low frequency noise is caused from amplifier DC offsets, electrode drift on skin, and temperature fluctuations and can be removed using a high pass filter. High frequency noise can result from nerve conduction and high frequency interference from radio broadcasts, computers, cellular phones, etc., and can be removed using a low pass filter. The low frequency 3 dB point may be selected over the range of 0.016–32 Hz, while the high frequency 6 dB point can be selected over the range 16–32 kHz.

**Digitization** After proper amplification of the signal, a suitable band of EMG signal frequency is obtained. The signal is further amplified in a non-inverting amplifier to a suitable level. The amplified analog signal is then digitized with an ADC. Once the signal is digitized, it is given to a microcontroller followed by its display and printer. The quality of an EMG signal is largely dependent on the *resolution*, *accuracy*, and *sampling rate* of the ADC used. Present-day ADCs used in EMG equipment range in 10–24 bit systems. The sampling rate used in any EMG system must at least follow Nyquist's theorem, whereby the minimum sampling rate must be twice that of the signal frequency in question. In all present-day EMG applications, the upper limit on the frequency of interest is around 500 Hz, and so the sampling frequency may be kept at 1000 samples/s.

Most EMG machines are PC based and are available in both console and laptop models. They provide full colour waveform display, automatic cursors for marking and making measurements, and a keyboard for access to convenient and important test controls. The system usually incorporates facilities for recording of the EMG and evoked potentials. The stimulators are software controlled. For report generation in the hard copy form, popular laser printers can be used. A typical EMG machine is shown in Figure 133.3.

Recent developments in electronic technologies have enabled EMG equipment to include a range of new features and networking capabilities. The RS-232 serial data transfer protocol previously used in the PC-based systems is now replaced by the Universal Serial Bus 2.0, which provides faster data exchange rates and even a means of supplying power to the EMG handheld device to recharge the device. Increased storage capacity of data recordings on digital storage media has become a common feature. Wireless technologies such as Wi-Fi and Bluetooth have also been incorporated into today's EMG equipment to provide the user with extended mobility from the PC on PC-based systems. Acquired EMG signals can now be picked up on the body and sent wirelessly to a PC where it is recorded, processed, and analysed.

**Signal Analysis** Usually, the electromyographic changes in an advanced diseased state are readily recognized on a monitor screen display and by the audio signal. However,

**Figure 133.3** Typical EMG machine. *Source:* Image courtesy of M/s Natus Neurology Incorporated, USA.



since the loss of muscle fibres and, therefore, the action potential changes are relatively small in early or mild disease states, changes in the EMG signals may be obscured by the usual variability of action potentials. Computer-based quantitative analysis methods are thus adopted to determine when the waveforms have changed beyond the normal range. Quantities measured for such analysis include zero-crossing rate, peak rate, negative wave duration, and wave rise time. These *time-domain* techniques are somewhat different from the classical frequency spectrum and correlation function methods but are much simpler to implement with software techniques. Analysis of the EMG signal in the frequency domain involves processing of the parameters that describe specific aspects of the frequency spectrum of the signal. Fast Fourier transform techniques are available for obtaining power density spectrum of the signal. A *frequency domain* representation reveals information about motor unit potential amplitudes and durations as well motor unit firing patterns. Calculation of root-mean-square value of an EMG signal can give useful information regarding time- and force-dependent parameters.

### **Common Artefacts in EMG**

While recording EMG, many types of artefacts may be present, if proper care is not taken. *Power line interference* (50–60 Hz) is caused by the electrical devices present around the EMG equipment. Typically, this interference is removed by using a software implemented notch filter. The instability of electrode skin interface and movement of the electrode cable result in *movement artefacts*, which are caused whenever a patient

moves and the electrodes are disturbed or the cables are pulled. To minimize these artefacts, the electrodes must be placed in firm contact with the skin and electrode cables must be fastened firmly. The electrical signals generated by muscles other than the one under investigation results in *muscle crosstalk*. This type of interference can be minimized through the appropriate placement of the electrodes. The recommended inter-electrode distance is about 2 cm.

**Stimulators** The modern EMG machines include another important feature in the form of a built-in stimulator. The stimulator aids in nerve conduction or nerve velocity measurements. Stimulus amplitude, duration, repetition, and delay are all adjustable, and facilities are provided for external triggering. The output is either of the constant voltage type or of the constant current type. The constant voltage type stimulator provides square wave pulses with amplitudes in the range of 0–500 V, a pulse duration of 0.1–3 ms, and frequency between 0 and 100 Hz. Output of the constant current generator can be adjusted from 0 to 100 mA.

**Electroneurography** The recording and study of action potential propagation along peripheral nerves is known as electroneurography. The technique is primarily used in nerve conduction study and is considered as a reliable diagnostic test of peripheral nerve function. It is used routinely for localization of the site of a nerve lesion and the diagnosis of conditions such as diabetic neuropathy, which affects primarily nerve fibres. Electroneurography recordings can be done using EMG machines.

## Specifications

*Amplifier channels:* 2 or 4

*Sensitivity:* Adjustable from 1  $\mu$ V/div to 10 mV/div in steps

*High cut filters:* Selectable from 30 to 10 kHz

*Low cut filters:* Selectable at 0.04 Hz, 2 kHz

*Notch filter:* 50 or 60 Hz

*Common mode rejection:* >100 dB

*Input impedance:* >1000 M $\Omega$  (common mode)

*Noise:* <6  $\mu$ V peak to peak

*Number of averages per channel:* 1–10 000

*Stimulators:* Repetition rates at 0.1–90 pulses/s

## Applications

Clinically, electromyography is being used as diagnostic tool for neurological disorders, such as neuromuscular diseases and low back pain, and disorders of motor control. EMG is routinely employed as an evaluation tool in applied research, physiotherapy, rehabilitation, sports medicine and training, and biofeedback and ergonomics research.

# 134

## Electronystagmograph

### Purpose

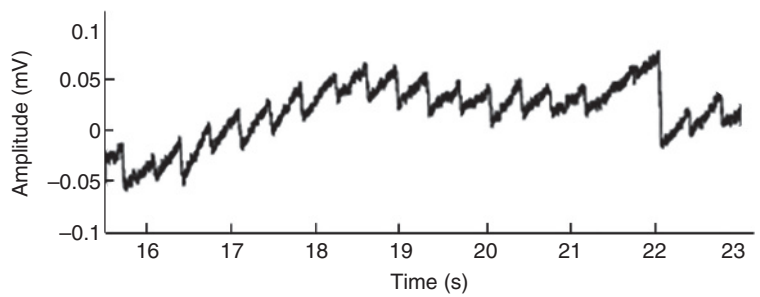
Electronystagmograph (ENG) is an instrument that measures movements of the eye and analyses them to evaluate the functioning of the muscles that control these movements. ENG is the most commonly used test for the assessment of vertigo that refers to a false sense of spinning or motion that can cause dizziness, unsteadiness, and imbalance, which may be due to certain disorders that affect hearing and vision. Such problems may be due to damage or problem in the inner ear, brain, or nerves connecting them. The test is also used to distinguish between lesions in various parts of the brain and nervous system.

### Principle

Electronystagmography is a test that is designed to evaluate eye movements to determine how well the two nerves (acoustic nerve and oculomotor nerve) in the brain are working. The acoustic nerve runs from the brain to the ears, and the oculomotor nerve runs from the brain to the eyes. The vestibular system is important to the maintenance of the static and dynamic equilibrium systems of the human body. Malfunctioning within this system may lead to abnormal reflex eye movements named *nystagmus*. The test helps to understand whether a balance or nerve disorder is the cause of dizziness or vertigo and if there is a suspected damage to the inner ear for various reasons. There are various senses and control systems that are involved in the process of maintaining the body balance. Eye movements are a manifestation of a patient's ability to respond to various tests that indicate which balance component is not functioning properly.

### *The ENG Signal*

The electronystagmography is based on the fact that there exists an electric field around the eye because of the corneal–retinal potential difference. Since a positive charge exists at the cornea with respect to the retina, the change in the electrical dipole by the eye movements are recorded by placing electrodes around eye. The amplitude of the ENG signal varies in the range from about 50–3500  $\mu\text{V}$  and frequency from about DC to 100 Hz. A typical ENG signal is shown in Figure 134.1. The characteristic shape of the ENG signal is a sawtooth waveform. The slope on one side of each peak is smaller (slow component) than on the other side, which is rapid (fast component). These fast components are called saccades. The slow component of the signal is related to the stimulus, while the saccade refers to a rapid reset of eye position by the oculomotor system. The instrument is designed to provide independent recordings of each eye movement activity separately.



**Figure 134.1** Typical ENG signal.

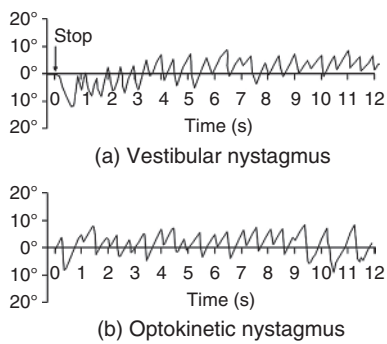
Based on the origin of the unstable eye movement (nystagmoid movement), it is possible to separate it into *vestibular* and *optokinetic* nystagmus as shown in Figure 134.2.

**Vestibular Nystagmus** The vestibular system senses head motion from the signals generated by receptors located in the labyrinths of the inner ear. Under normal conditions, the oculomotor system uses vestibular input to move the eyes to compensate for head and body motion. If there is a damage to the vestibular system, then the signals sent to the oculomotor system will be erroneous and the patient will be in a state of confusion, resulting in dizziness. Therefore, if the patient experiences dizziness, the eye movements can help to identify whether the dizziness is due to vestibular damage.

**Optokinetic Nystagmus** When the subject is stationary, but the target is in rapid motion, the oculomotor system endeavours to keep the image of the target focused at the retinal fovea. However, when the target can no longer be tracked, a saccadic reflex (a saccade is one of the characteristic types of eye movements) returns the eye to a new target. The movements of the eye describe a sawtooth pattern. This is called as *optokinetic nystagmus*. This test is generally done in the laboratory by rotating a cylinder with dark stripes on a light background in front of a person's eyes.

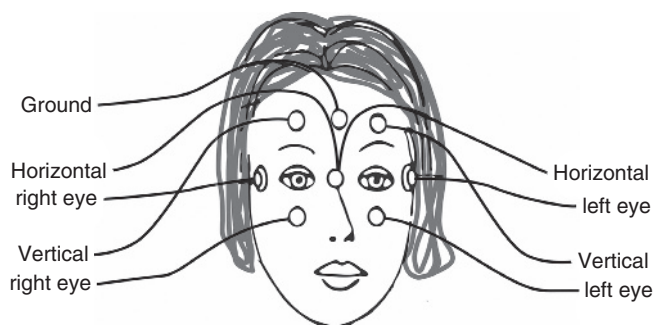
### ENG Electrodes

The eye movements are recorded by using disc or patches called electrodes that are placed above, below, and on each side of the eyes as shown in Figure 134.3. They may be



**Figure 134.2** (a) An illustrative record of saccades arising from vestibular nystagmus. *Saccades* are rapid, ballistic movements of the eyes that abruptly change the point of fixation. (b) An illustrative record of saccades arising from optokinetic nystagmus.





**Figure 134.3** Arrangement of electrodes for recording ENG.

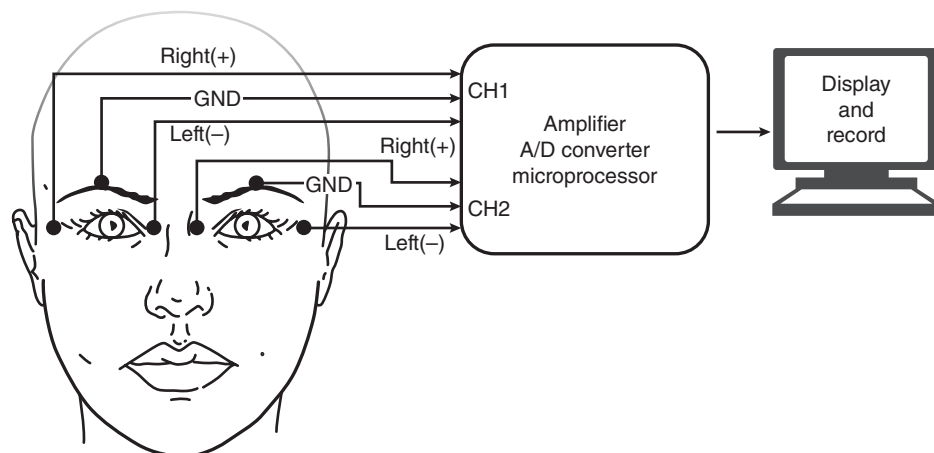
self-adhesive-type patches or attached to a headband. Another patch is attached to the forehead that acts as ground. Because the cornea is electropositive and the retina is electronegative, these electrodes accurately record lateral eye movements. By measuring the changes in the electrical field within the eye, ENG can detect nystagmus (involuntary rapid eye movement) in response to various stimuli. If nystagmus does not occur on stimulation, a problem may exist within the ear, nerves that supply the ear, or certain parts of the brain.

### **System Description**

Modern ENG machines are computer based that perform various functions such as stimulus generation, response acquisition, and interpretation of acquired data. The ENG equipment consists of a PC or computer console with the appropriate software. The electrodes are attached to the face around the eyes and the neutral lead is fixed on the forehead. An electroconductive gel is used as interface between skin and the sensor leads for minimizing contact impedance. The electrodes deliver data into the electrode box, where the signals from different leads are integrated and passed on to the amplifier. The amplifier feeds the amplified signal to an analog-to-digital converter which in turn is connected to the analysing computer as shown in Figure 134.4.

Stimulus generation was earlier done using manually controlled objects. For example, for gaze and saccadic tests, dots could be placed on the wall and/or ceiling at specified places and angles. For optokinetic testing, a rotating drum with stripes of contrasting colours was used to conduct the tests. Though these tests can provide gross assessment of the various oculomotor subsystems, but it is not possible to have fine analysis of latency and accuracy of eye movements in response to the stimulus. Computerized stimulus generation is done by using light emitting diodes arranged in specific pattern on a light bar that is anchored to the wall or in a self-contained stimulator. The light bar is usually placed at a distance of 1 m from the foot end of the patient's bed. The elevation of the light bar can be adjusted and fixed at the desired angle. The light bar is connected to and controlled by the amplifier box. Alternatively, computer-generated stimuli can be projected on a screen or video monitor.

In such systems, the stimuli are locked to the acquisition of the responses that allow for more sophisticated analysis in terms of latency and amplitude.



**Figure 134.4** Signal acquisition system for ENG.

### Data Processing

Manual analysis of the ENG record is time consuming; therefore computerized systems have been developed for data processing. An algorithm for the automatic evaluation of the ENG parameters enhances the diagnostic capability of ENG. It has become a simple, noninvasive, and reasonably accurate test procedure for routine vestibular assessment. However, there are some disadvantages, such as interference from muscle electrical activity and ambient electric noise accompanying the ocular signal. The resolution of the system is poor, about  $1^\circ$  and does not separate eye movements below  $2^\circ$ – $3^\circ$ . Further, ENG does not measure or record torsional eye movements. An ENG data acquisition module is shown in Figure 134.5.

A complex data processing software greatly simplifies the task of the clinician as several parameters are automatically analysed. They include measurement of amplitude, frequency, latency, phase, and distortion of the recorded waveform. The other measurements



**Figure 134.5** ENG signal acquisition instrument. The output can be given to a PC for data processing and display. *Source:* With permission of M/s DIFFRA S.A.

made are the ocular movements, comparing the response from opened eyes and closed eyes, low phase velocity of the nystagmus, and symmetry or asymmetry of the response.

The response acquisition process involves choosing a minimum of two channels, which provides for evaluation of both horizontal and vertical eye movements. A three-channel recording system can further help in increasing the power of analysis by facilitating horizontal recording of each eye and vertical recording of one of them. More sophisticated systems allow acquisition of both horizontal and vertical movements of each eye.

### ***Type of Measurements***

Several types of measurements are made in ENG, the most common of which may include the following:

*Gaze nystagmus test:* This test involves staring at a fixed light placed either to the centre or side as you are seated or lying down. This test measures how well you can fix your gaze at an object without your eyes moving involuntarily.

*Optokinetics test:* This test measures your ability to track a light as it moves quickly across and out of your field of vision and back again while you keep your head still.

*Water caloric test:* This test evaluates vestibular function and can help to differentiate peripheral from central causes of vertigo. The test involves introducing warm or cool water into the ear canal with a syringe so that it touches the tympanic membrane. If no problem exists, your eyes will move involuntarily to this stimulus. Air instead of water may be used as the stimulus for this test, especially in those who have a damaged tympanic membrane.

*Pendulum-tracking test:* This test measures how well you can follow a light with your eyes as it moves like the pendulum of clock.

### ***Videonystagmography***

Videonystagmography (VNG) is a computerized system that consists in recording the eye movements by using infrared sensors mounted in special spectacles or masks. The system does not require the use of electrodes but employs a source of invisible infrared light that can record eye movements under any conditions of ambient light, and even in darkness. Video cameras are installed in lightproof binocular lenses that make it possible to directly observe and record horizontal, vertical, and torsional eye movements with eyes open and in darkness. The computer software measures and analyses eye movements, which are presented on a video monitor and recorded. The system employs digital image processing techniques to measure movements from the centre of the pupils. It is also possible to measure the slow component velocity of horizontal and vertical nystagmus.

VNG system evaluates eye position over about 30° horizontally and about 20° vertically with a resolution of about 0.1°. It may detect eye movements of 0.5° in laboratory conditions. One of the main advantages of VNG is to visualize and record the exact direction of eye movements. It is a functional, differential diagnostic, and monitoring test for several conditions. VNG has gradually replaced ENG in recent years.

## Specifications

*Number of channels:* 2 or 4

*Amplification:* Adjustable from 100 to 25 000

*Low pass filter:* 10–100 Hz

*Sampling frequency:* 200 Hz

*Accuracy:* 0.05% (12 bit)

*Weight (portable part):* 500 g

## Applications

ENG is used to detect disorders of the peripheral vestibular system or the nerves that connect the vestibular system to the brain and the muscles of the eye. It is most widely used clinical laboratory test to assess ENG abnormalities which can be useful in the diagnosis and localization of the site of lesion.

# 135

## Electrooculograph

### Purpose

Electrooculograph (EOG) is an instrument for recording the corneo-retinal resting potential of the retina, i.e. the potential that exists between the front and the back of the human eye. The main applications of EOG are for recording eye movements, and consequently the test is useful for ophthalmological diagnosis. An eye movement-controlled system for assisted mobility (wheelchair) based on EOG measurements can be helpful to improve the quality of life for disabled people. The feasibility of recognizing human activity using eye movement analysis, which allows a system to best assist the user with his or her task is being assessed.

### Principle

Both the terms electronystagmography (ENG) and electrooculography refers to the recording of eye movements by using surface electrodes around the eyes. ENG records nystagmus (involuntary and rhythmically repeated oscillations of one or both eyes) during fixation and in response to vestibular, visual, caloric, rotational, or positional stimulation while in EOG, the patient is asked to switch eye position repeatedly between two points, alternating looking from centre to the left and from centre to the right. Since these positions are constant, a change in the recorded potential results from a change in the resting potential. In instrumentation, there is no major difference in ENG and EOG,

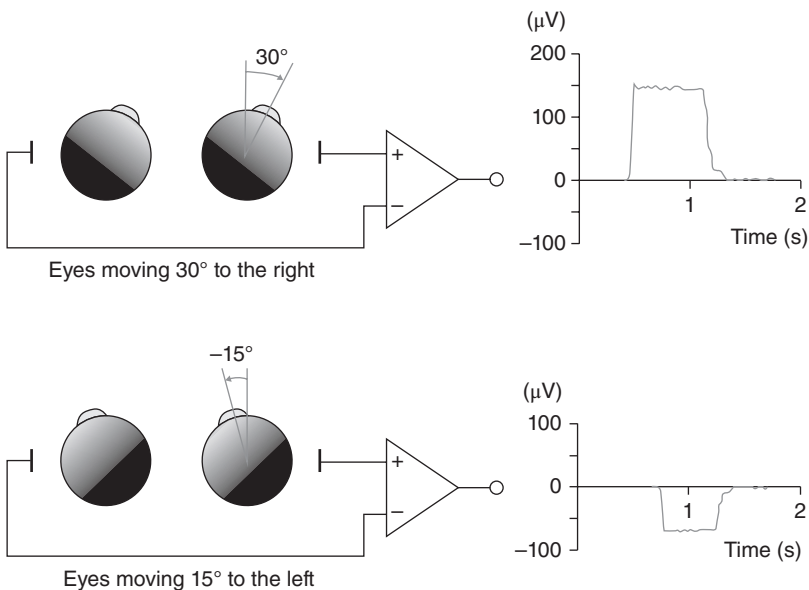
except that the classical EOG uses DC amplification especially during visual fixation, whereas ENG in clinical routine often uses condenser coupled AC, in which the amplifier has a high pass filter (HPF) signal, to damp the slow baseline drifts.

### EOG Waveform

The eye can be considered as a dipole with its positive pole at the cornea and its negative pole at the retina. Since this potential is not affected by the presence or absence of light, it is thought of as a resting potential. The resting potential ranges from 0.4 to 1 mV. This potential difference is due to the large presence of electrically active nerves in the retina compared to the front of the eye. This electric field may be detected with the eye in total darkness and/or with the eyes closed. The EOG amplitude ranges from 0.05 to 3.5 mV in humans and is linearly proportional to eye displacement. The movements of the eye will respectively generate voltage up to 16 and 14  $\mu\text{V}$  per  $1^\circ$  in horizontal and vertical directions. The electrical signal that can be measured due to movement of the eyes is called the electrooculogram.

Figure 135.1 illustrates the measurement of horizontal eye movements by the placement of a pair of electrodes at the outside of the left and right eye. When the eye is at rest, the electrodes are effectively at the same potential and no voltage is recorded. When the eye moves in the right direction, it results in a difference of potential, with the electrode in the right direction becoming positive relative to the second electrode. Ideally the difference in potential is proportional to the sine of the angle. The effect is opposite, with the eye moving to the left.

When the EOG is recorded in the dark, the resting potential evoked by moving the eyes in the dark is called *dark phase* or *dark current*. This potential originates from the



**Figure 135.1** An illustration of the electrooculogram (EOG) signal generated by horizontal movement of the eyes. The polarity of the signal is positive at the electrode to which the eye is moving.

retinal pigment epithelium. The potential evoked by moving the eyes in a lighted environment originates from the photoreceptors and is known as *light potential* or *light rise*. The measurement of the minimum amplitude of the standing potential in the dark and then again at its peak after the light rise is usually expressed as ratio of 'light peak to dark trough' and is clinically known as the Arden ratio.

### EOG Electrodes

The eye movement is recorded by using pairs of electrodes, typically placed to the left and right (for lateral eye movement) and above and below (for vertical eye movement) of the eye. The inner electrode is closest to the nose and the outer electrode is closest to the nearest ear corners of the eye. A ground electrode is placed on the centre of the forehead or on the auricle. If the eye moves from centre position towards one of the two electrodes, this electrode 'sees' the positive side of the retina and the opposite electrode 'sees' the negative side of the retina. Consequently, a potential difference occurs between the electrodes. This technique is an indirect way to evaluate the tracking and scanning of visual targets.

The surface electrode used is usually pre-gelled self-adhesive silver/silver electrode, which is simple in construction and has stable potential. The electrode consists of a silver disc that is coated with a thin layer of silver chloride. Small metal disk electrodes, which are generally made of high purity tin, silver, or even surgical steel, can also be sometimes used. The diameter of these electrodes is usually in the range of 4–10 mm. The recording should be done after a few minutes of the attachment of the electrodes to allow for the electrode gel to soak into the skin and the baseline becomes fairly steady.

### System Description

Figure 135.2 shows front end of the EOG recording circuit. Since the EOG signals are too small to be displayed directly on a monitor, they are amplified using an instrumentation amplifier at the input stage. Usually, the amplifier is switchable for DC recording or AC recording with time constants of 5 or 10 seconds. For recording horizontal EOG, direct-coupled amplifiers are preferred, which provide a better record of actual eye position. In the DC mode, the drift of the baseline is inevitably present, which is

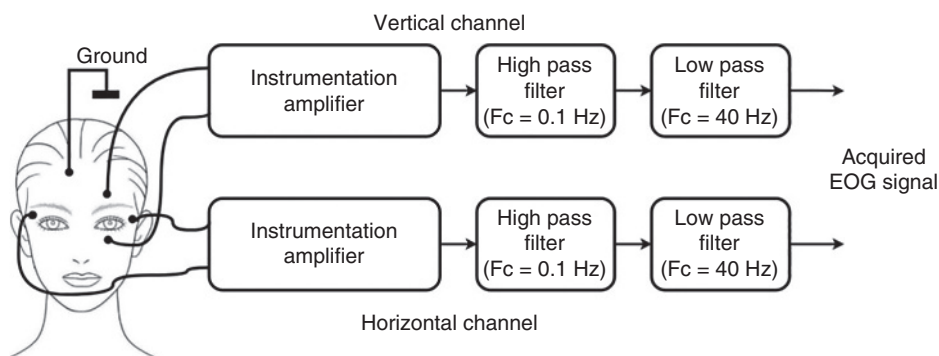


Figure 135.2 EOG signal acquisition and filtering system.

overcome by automatic reset circuit. For recording vertical EOG, AC mode may be adopted as the signal has multiple artefacts. Still, it would be preferable to use the DC mode. The front end has an isolation circuit whose function is to isolate the signal and line power source and is implemented by using either an optical or voltage-transformed method. A typical EOG amplifier is shown in Figure 135.3.

The system receives signals from three sources: the EOG differential voltage from the electrodes, noise, and offset. In order to minimize interference from the sources of noise, the bandwidth of the bandpass filter (BPF) is limited from 0.05 to 30 Hz (two active second-order HPFs and two active second-order low pass filters [LPFs]). The amplifier with an amplification factor of 50 is adequate to magnify the weak signal that has passed through the filter. Most of the circuits also include a band reject filter (BRF) to reject the mains power line with 50 Hz frequency signal. Then, the amplified EOG signals is directly sent to the control circuit for stimulus control, response signal acquisition, and data processing and recording. The analog signal then goes to an analog-to-digital converter for digitization and is then fed to a computer for analysis. The signal can also be directly recorded by a pen recorder on a graph paper. Typical achievable accuracy is  $\pm 2^\circ$ , and maximum rotation is  $\pm 70^\circ$ . Typical signal magnitudes range from 5 to 20  $\mu\text{V}/\text{degree}$ . The new systems, such as video-oculography systems or infrared oculography, have also been introduced, which are based on detection of the eye position using a camera.

The instrument has minimum two channels, one for recording horizontal eye movements across both eyes with electrodes placement at the outer canthi of both eyes and one for the vertical EOG of one eye with electrodes placed above and below. The vertical EOG is used mainly for identifying lid artefacts during blinks or eye closure. Additional channels may be added for recording horizontal EOG from each eye separately or the vertical EOG from the second eye. It is better to record the visual or vestibular stimulus on a separate channel. The preamplifiers are usually placed/mounted near the site of signal acquisition for achieving a higher signal-to-noise ratio.

**Figure 135.3** Typical EOG or biomedical amplifier, which can be connected to any recording or display device. *Source:* Reproduced with permission from LKC Technologies.





The most important disadvantage of EOG is that the corneo-retinal potential difference is not fixed but has been found to vary and affected by light, fatigue, and other qualities. This necessitates frequent calibration and recalibration of the system. Additional difficulties arise owing to muscle artefacts and the basic nonlinearity of the method.

## Specifications

*EOG amplifier*

*Input channels:* 4

*Input impedance:*  $\geq 10\text{ M}\Omega$

*Background noise:*  $< 0.7\text{ }\mu\text{V p-p}$  at 100 Hz

*CMRR:*  $> 110\text{ dB}$  at 50–60 Hz

*Frequency range:* 0.1 Hz to 15 kHz

*Input gain:* 1, 2, 4, 8, 16, 32, and 64 (user selectable)

*DC input range:*  $\pm 2\text{ V}$

*Stability:*  $< 250\text{ nV}/^\circ\text{C}$  drift

*Data resolution:*  $0.25\text{ }\mu\text{V/bit}$  (gain = 1)

*Sampling rate:* 5–3750 Hz

*Safety:*  $< 1\text{ nA}$  leakage current

*System interface:* USB

## Applications

The most common use of the EOG is to diagnose macular dystrophy and variants of this disease, which is usually identified by the appearance of a retinal lesion early in the disease. Assistive devices such as a wheelchair are designed to operate under EOG guidance using eye movements. A portable wireless eye movement-controlled human–computer interface for the disabled is another application. In addition, there are many assistive systems to control and guide autonomous mobile robots. All these systems are intended to enable their users to travel more efficiently and with greater ease.

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## Electrophoresis Apparatus

### Purpose

Electrophoresis is a powerful molecular separation technique that finds applications in the fields of forensics, biochemistry, genetics, and microbiology requiring analysis of nucleic acid and protein molecule size and characteristics. The technique is also useful

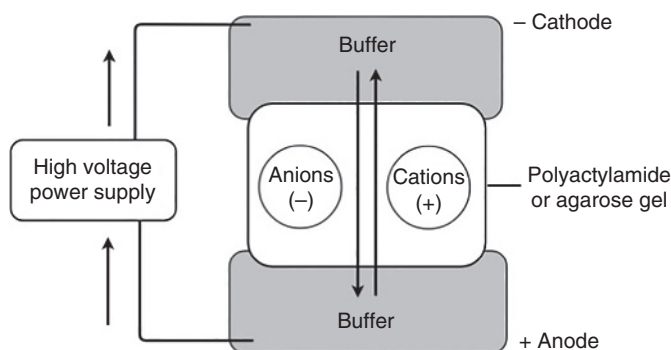
for separation and analysis of macromolecules such as DNA, RNA, and proteins and their fragments. It is often employed as a preparatory technique prior to cloning and DNA sequencing. The technique is widely used in all research and clinical laboratories utilizing DNA and protein applications and provides considerable information about size, shape, composition, and interactions of specific macromolecules and distribution of large numbers of macromolecules at one time. Protein electrophoresis is a common method for analysing blood plasma in medical applications.

## Principle

Electrophoresis is an empirical separation technique used in molecular biology to separate and identify molecules such as DNA, RNA, protein, and complexes by size. The separation of these molecules is achieved by placing them in a gel made up of small pores and applying an electric field across the gel. The principle of gel electrophoresis is illustrated in Figure 136.1. This separation technique is based on the differential rate of migration of charged species in an applied DC electric field. The particles of similar geometry but different charge and particles of like charge but different geometry migrate at different rates towards an oppositely charged electrode. Therefore, when the current is passed for a certain time through such a solution, various components present in the solution would move through different distances in their effort to migrate towards the electrodes. Therefore, a substance, which may be a mixture, is thus separated into its components along the migration path. Measurement of the concentration along this migration path, therefore, would provide a quantitative result of analysis.

It is established that the electrophoretic mobility is proportional to the charge on the molecule and inversely proportional to the radius of the molecule: i.e. the larger the radius, lower the electrophoretic mobility. Several factors affect the outcome of electrophoresis, including net charge, mass of molecule, and buffer and electrophoretic media like paper or gel. Furthermore, molecules with smaller mass move faster or separate faster than molecules with larger mass.

Currently, electrophoretic separations are performed by two popular quite different formats:



**Figure 136.1** Principle of gel electrophoresis.

- Slab electrophoresis
- Capillary electrophoresis

Electrophoresis equipment includes horizontal gel electrophoresis units for DNA separation and vertical gel equipment for protein separation. Capillary electrophoresis systems are used for applications such as DNA sequencing.

### ***Slab Electrophoresis Apparatus***

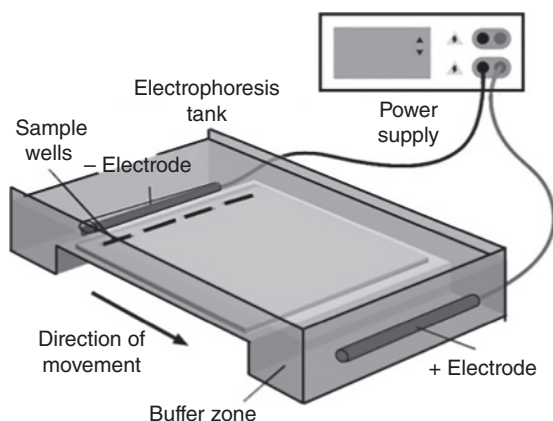
The slab electrophoresis is a classical method that is used to separate complex, high molecular mass species of biological and biochemical interest. The separations are achieved on a thin flat layer or slab of a porous semi-solid gel containing aqueous buffer solutions within its pores. The dimensions of the slab are of a few centimetres on a side. Samples are introduced as spots or bands on the slab. A DC electric field is applied across the slab for a fixed period. When the separations are complete, the electric field is disconnected. For safety reasons, one electrode is usually at ground and the other is biased positively or negatively. The separated species are then visualized by staining as is done in thin layer chromatography. The apparatus is capable of separating several samples simultaneously.

The main components of slab paper electrophoresis apparatus are an electrophoresis cabinet, a high voltage power supply, electrodes, buffer, and a support for the buffer such as filter paper, cellulose acetate strips, and polyacrylamide gel. A typical set-up used to separate DNA fragments by size is shown in Figure 136.2. A gel sits within a tank of buffer. The DNA samples are placed in wells at one end of the gel and an electrical current passed across the gel. The negatively charged DNA moves towards the positive electrode. A scanner or densitometer is used for making direct photometric measurements on stained electrophoretic strips.

The types of gel most commonly used are agarose and polyacrylamide gels. Their choice depends upon the types and sizes of analyte. Polyacrylamide gels are usually used for proteins, and they have very high resolving power for small fragments of DNA (5–500 bp). Agarose gels on the other hand are used for DNA fragments of usually 50–20 000 bp in size. Polyacrylamide gels are run in a vertical configuration, while agarose gels are typically run horizontally. The reagents act as supporting media and provide the ions for conduction through the apparatus. Generally, buffers and salts with low ionic charges are preferred.

***Electrophoresis Cabinet*** Electrophoresis cabinet is made of a methacrylate plastic cabinet and gable cover, and a carrier rack of phenolic plastic. The purpose of gable cover is to prevent condensation droplets from falling on paper strips. The carrier is provided to support paper or cellulose strips. End surfaces of the carrier are usually roughened to grip wet paper. The cabinet is of a moulded construction that eliminates the possibility of buffer leakage from box joints. The thumb supports at either end of the box assist in removal of the lid.

Electrophoresis baths are generally designed to take up multiple strips. In one design, up to six strips, each 34 cm long and 5 cm wide can be accommodated. The strips are supported on removable plastic bridges, which are provided with a number of supports to carry the paper and to prevent undue sagging. The buffer solution is contained in two



**Figure 136.2** Typical set up for separation of DNA fragments. *Source:* Image credit: Genome Research Limited (help@yourgenome.org).

compartments provided at each end of the bath. The ends of the paper strips dip into the solution in the outer of these two compartments, while three platinum electrodes are mounted in the inner compartments. The electrodes are wired to a lead and connected to the power unit. The bath should be properly sealed, and it should not leak electrically as well as mechanically.

The cabinet lid is moulded from UV transparent acrylic material. High tension (HT) cables are attached to the lid by suitable connectors. Holes in the lid close to the connectors are provided for positioning of the thumb supports. Small holes are also provided to allow access for probes for the measurement of temperature and electrical field strength. The cabinet contains platinized titanium electrodes at each end. Both electrodes are rods of 1.5 mm diameter, which are rigid enough and do not get distorted during normal usage of the apparatus.

**Regulated Power Supply** Electrical current is applied to the electrophoresis apparatus by DC power source. Regulated DC power supply may be either constant voltage (0–250, 0–500, or 0–1000 V or higher) or constant current (0–20, 0–100, or 500 mA range). The power supplies typically have a variable output voltage enabling the user to set the output voltage for gel tanks of different sizes and modify voltage for optimum results and convenience. The supplies are provided with two digital numeric indicators, one for indicating current and other for voltage. The polarity reversal facility and overload protection are provided in the power supplies. The ripple content in the power supply should be less than 0.1%.

Power supplies designed specifically for gel electrophoresis have programming capabilities, including preset and customer preferred settings. They provide constant voltage, constant current, or power setting facilities. Most of them are fully protected offering open circuit detection, short-circuit detection, thermal shutdown, overvoltage, and current wattage detection.

High voltage electrophoresis is a rapid and highly effective technique for the separation of a wide range of compounds, especially those with low molecular weights. The high voltages normally employed are 10 000 V at 100 mA or 5000 V at 200 mA. Although higher

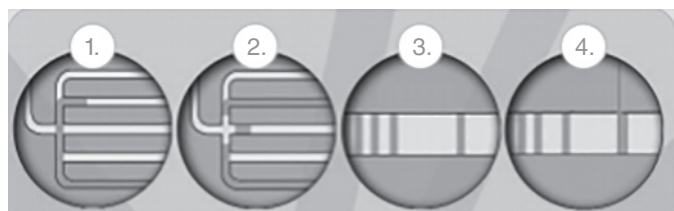
the voltage applied, the faster the samples migrate, but too high a voltage can cause heating and may melt the agarose gel during electrophoresis and cause distortion of results.

**Densitometers** After a separation is completed, the support is stained to visualize the separated components. Transilluminators are used for this purpose and documentation systems create permanent experimental records, which can be analysed and compared with compatible data. A recorder plots curves on the graph paper according to the concentrations of the analyte in the samples. A double-beam recording spectodensitometer can be used for measuring the optical density of dry agar electrophoretograms, which enable to automatically obtain a graphical representation of the density profile, with trough detection marks, peak positions, peak heights, peak integrals, relative percentages, and total integral. Alternatively, the image is recorded with a computer-operated camera, and the intensity of the band or spot of interest is measured and compared against the standard or markers loaded on the same gel. The measurement and analysis are mostly done with specialized software.

### **Automated Electrophoresis System**

Automated electrophoresis systems integrate the process of separation, detection, and data analysis of proteins or nucleic acids in a single platform. They require much smaller sample and reagent quantities and reduce separation time than manual methods. Also, the errors in automated systems are much less during the various steps of the electrophoresis process. These systems yield digital data at a much higher resolution scale compared with manual methods.

Automated electrophoresis systems depend upon the use of microfluidic chip-based technology, which integrate the functions of electrophoretic separation, fluorescence detection, and data analysis of various biomolecules. Essentially, the electrophoretic assays based on the principle of traditional gel electrophoresis are transferred to a chip format. The working of a typical chip is shown in Figure 136.3, which utilizes lab-on-chip technology. Microfluidics chips require only 1  $\mu\text{l}$  of sample at concentrations as low as the ng/ $\mu\text{l}$  or pg/ $\mu\text{l}$  range (as per Agilent Technologies Bioanalyzer 2100 Manual). The chip is a miniature device and functions much like a tiny laboratory and becomes an integrated electrical circuit. The chip incorporates sample wells, gel wells, and a well for an external standard, which are interconnected network by a series of microchannels



**Figure 136.3** Principle of lab-on-chip technology. Microchannels are filled with a sieving polymer and fluorescence dye. (1) The sample moves through the microchannels from the sample well. (2) The sample is injected into the separation channel. (3) The sample components are electrophoretically separated. (4) The detection of the components is by their fluorescence emission and translated into gel-like images (bands) as peaks.

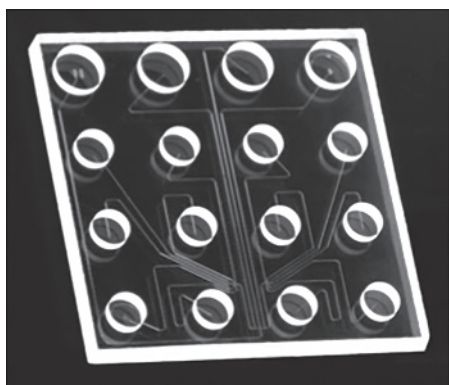
fabricated in glass surface as shown in Figure 136.4. A set of electrodes in the electrophoresis station applies a voltage across the microchannels, which causes charged molecules in the samples to migrate into and through the separation channel.

The detection of the components is by their fluorescence emission and translated into gel-like images (bands) and electropherograms as peaks. As sample molecules approach a waste well that serves as the positive pole, dyes mixed within the gel matrix bind the molecules of interest, are excited by a laser, and fluoresce, thus providing the means of sample detection as they pass a laser and photodiode detector. Data are automatically collected, saved, and presented in several formats with the help of software.

The Agilent 2100 Bioanalyzer is a typical example of an automated electrophoresis system. It uses different cartridges for electrophoretic and flow cytometric assays. For electrophoretic measurements, the electrode cartridge is required. The electrode cartridge contains 16 electrodes that fit into the wells of DNA, RNA, and protein chips. Each electrode in the cartridge has an individual power supply.

A typical system based on lab-on-chip technology represents a complete package that includes the main automated electrophoresis station, chip priming station, vortex station, system operation, and software for instrument control and data analyses. Each assay allows for analysis of up to 12 samples within 1 hour with only about 30 minutes 'hands-on' time.

The electrophoresis station houses all the electrical, optical, and hardware components necessary to perform the separation, staining, destaining, detection, and imaging of samples in a single step. It connects to a computer (PC) running the software. The priming station is used to prepare the microfluidic chips for sample analysis. The priming station applies pressure to the priming well of the chip and fills the network of microchannels with the gel stain solution. The vortex station ensures complete mixing of RNA or DNA samples and loading buffers in the chip wells. At the heart of the system is the microfluidic chip in which sample separation occurs. Each chip contains a series of plastic wells bonded over a small glass plate. The glass plate is etched with a network of microchannels that connects with the base of the plastic wells. The electrophoresis station directs the samples through the microchannels by controlling the voltages and currents that are applied. The software includes the controls required to operate the



**Figure 136.4** Lab-on-chip sample wells, gel wells, and a well for an external standard, which are interconnected network by a series of microchannels fabricated in glass surface.

electrophoresis station and the data analysis tools needed to assess the results. During a run, the software provides the ability to monitor run progress or review previous sample results.

## Specifications

*Gel tray dimensions:* 76 mm × 100 mm

*Gel thickness range:* 2–6 mm (on gel tray)

*Buffer volume:* 300 ml

*Electrical range:* Voltage, 0–500 V; current, 0–500 mA; maximum power, 200 W

*Timer:* 1–999 minutes with alarm buzzer

*Safety protection:* Automatic output shutdown, against short or open circuit

## Applications

Gel electrophoresis is useful in forensics, biochemistry, genetics, microbiology, and other applications requiring analysis of nucleic acid and protein molecule size and characteristics.

# 137

## Electrophoresis, Capillary

### Purpose

The capillary electrophoresis (CE) is a high resolution analytical separation technique that is widely used because it is a non-chromatography separation technique, which has low operating cost and requires smaller amounts of sample. The method can be used for small ions to macromolecules like proteins, peptides, chiral compounds, nucleic acid, etc. Capillary electrophoresis is an attractive technique for DNA analysis because the narrow-bore, gel-filled capillaries provide high speed, high resolution separations with increased separation efficiency.

### Principle

Electrophoresis involves separation of ions based on the electrophoretic mobility of ions under an applied voltage. The conventional method of electrophoresis is flatbed gel electrophoresis whose major drawback is the speed of analysis. Speed can only be improved by increasing the applied electric current. However, with increase in current, a large amount of heat would be generated requiring an efficient cooling system. The

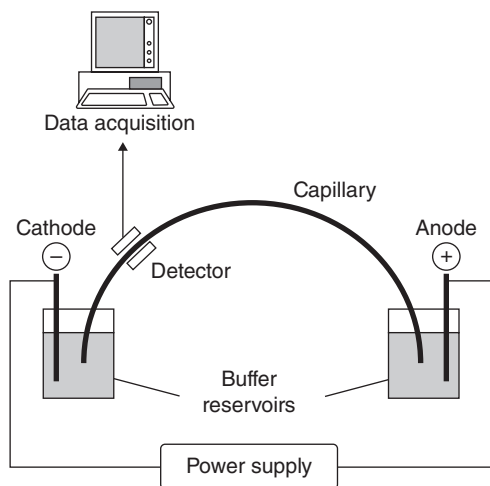


development of CE has resolved the heating problem in which the silica-fused capillaries efficiently dissipate the heat that is produced. Increasing the electric field produces very efficient separations and reduces separation times.

In a CE separation, a very small amount of sample (0.1–10 nl) is required. The sample solution is injected at one end of the capillary and an electric field of 100–700 V/cm is applied across it. Proteins in the solution migrate through the capillary due to the applied electric field. Differing electrophoretic mobility drive each of the components into discrete bands. Fluorescence and absorbance detectors can be used to identify and quantify the proteins in the solution.

Figure 137.1 shows the basic set of a capillary electrophoresis apparatus, which is remarkably simple in design. It comprises a fused silica capillary, a high voltage power supply, two buffer reservoirs, two platinum electrodes, and an on-column detector. The ends of a capillary are placed in separate buffer reservoirs, each containing an electrode connected to a high voltage power supply capable of delivering up to 30 kV. The sample is injected onto the capillary by temporarily replacing one of the buffer reservoirs (normally at the anode) with a sample reservoir and applying either an electric potential or external pressure for a few seconds. The sample is usually introduced by pressure injection and the amount of sample is controlled by controlling the injection pressure. A high voltage is applied over the capillary, and due to this electric field, the sample components migrate through the capillary at different speeds. Positive components migrate to the negative electrode, while negative components migrate to the positive electrode.

In capillary electrophoresis, the mobile phase moves through the capillary under the effect of an electromotive force. The mobility or the migration of ions depends on several factors including charge of the ion, the viscosity, and the size of atom or its radius. The smaller ions have high migration rate due to their smaller size and so they move with less friction. Capillary electrophoresis detection is similar to detectors in high pressure liquid chromatography (HPLC) and include absorbance, fluorescence, electrochemical, conductivity measurements, and mass spectrometry. However, UV–visible detectors are among the most popular detectors.



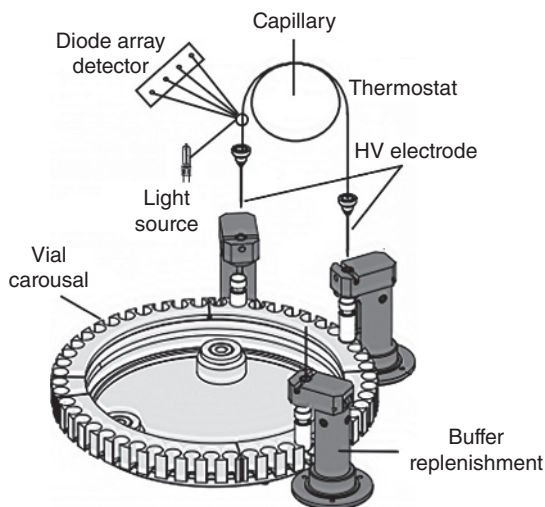
**Figure 137.1** Basic set-up of capillary electrophoresis apparatus.

### Instrumentation

A schematic diagram of a generic capillary electrophoresis system from M/s Agilent, United States, is shown in Figure 137.2. The ends of a narrow-bore, fused silica capillary are placed in buffer reservoirs. The content of the reservoirs is identical to that within the capillary. The reservoirs also contain the electrodes used to make electrical contact between the high voltage power supply and the capillary. Sample is loaded onto the capillary by replacing one of the reservoirs (usually at the anode) with a sample reservoir and applying either an electric field or an external pressure. After replacing the buffer reservoir, the electric field is applied and the separation performed. Optical detection can be made at the opposite end, directly through the capillary wall.

**Capillary** Fused silica capillaries with internal diameters ranging from 10–100  $\mu\text{m}$  to 150–400  $\mu\text{m}$  optical density (OD) are typically used in CE. Effective lengths range from as short as 10 cm for gel-filled capillaries and as long as 80–100 cm for complex sample separations. From an analysis time perspective, capillaries as short as possible should be used. Most commonly, 50–75 cm effective lengths are employed. Similar to gas chromatography (GC) columns, the capillaries are coated with a protective layer of polyimide to make them strong and easy to handle. For detection, an optical window can be placed in the capillary by removal of a small section of the protective polyimide coating. The capillaries are housed in user-assembled cartridges, which integrate with the optical assembly, providing automatic alignment. Optical slits may be physically changed to optimize sensitivity and resolution.

**Capillary Thermostating** Temperature and therefore viscosity plays a major role in ensuring reproducible operation and so it is important to control capillary temperature. Temperature regulation to  $\pm 0.1^\circ\text{C}$  is beneficial due to the strong viscosity dependence of sample injection and migration time. Further, the capillary is isolated from changes



**Figure 137.2** Schematic of capillary electrophoresis instrumentation.

in ambient temperature. The two approaches generally used are to bath the capillary in a high velocity air stream or in a liquid. While liquid thermostating is theoretically more efficient, forced air thermostating at 10 m/s air velocity is usually sufficient for the quantity of heat generated in CE.

**High Voltage Power Supply** In CE, a DC power supply is used to apply voltages up to about 30 kV and current levels of 200–300 mA. The voltage must be highly stable ( $\pm 0.1\%$ ) to ensure high migration time reproducibility. Another desirable power supply feature is to provide programming facility with the ability to control voltage, current, or power gradients during an analysis. Field programming can be used to ramp the voltage at the beginning of an analysis to avoid rapid heating, thermal expansion of buffer, and an expulsion of sample from the capillary. Field programming allows reduced analysis time of complex samples and is often necessary for fraction collection.

**Detectors** UV–visible absorption-based detection is the most widely used method. The fused-silica capillaries allow detection below 200 nm up through the visible spectrum. Diode array detection (DAD) is an efficient alternative to single or multiple wavelength detection. Instrumentally, a DAD consists of an achromatic lens system to focus light into the capillary. The beam is then dispersed by a diffraction grating and falls on the photodiode array. An array consists of numerous diodes (say 211), each of which is dedicated to measuring a narrow band spectrum. With a diode array, a whole wavelength range can be selected, for example, from 190 to 600 nm giving a bandwidth of over 400 nm. In a single analysis, all solutes absorbing within this range will be detected. In addition, there is a provision for incorporating laser-induced fluorescence detection module. A commercial system has been introduced that makes it possible to couple CE to a mass spectrometer (MS) in real time. Besides adding sensitivity and selectivity, MS also provides structural information about the separated molecules.

Figure 137.3 shows a typical commercial capillary electrophoresis system from M/s Agilent. The instrument comprises a high voltage power supply, 48-position carousel for autosampling and fraction collection, injection system, high sensitivity

**Figure 137.3** Capillary Electrophoresis 7100 System.  
Source: Reproduced with permission of M/s Agilent Technologies, Inc., USA.



diode array detector mounted on capillary, separate buffer replenishment station, and capillary cartridge. The carousel is thermostated by connecting an external water bath to the instrument. The capillary thermostating is provided through the use of high velocity recycling air flow (10 m/s), which is thermostatically regulated by a Peltier element. The capillary temperature can be regulated between 10° below ambient (minimum 4 °C) up to 60 °C.

The power supply for the system is capable of supplying voltages over the range from -30 to +30 kV. The high voltage power supply must supply a stable voltage during the course of an analytical procedure. The polarity of the applied voltage is fully controlled by software. The software control also allows the construction of voltage, current or power gradients, and control of voltage ramps, which is of great importance when analysing heat sensitive analytes in low conductivity solutions.

The system uses a high sensitivity diode array detector and the capillary itself acts as the detector flow cell. Wavelength calibration is performed automatically on replacing the capillary cassette and can be performed manually at any time. The response time of the detector is sufficient to detect and acquire spectra of high efficiency peaks with peak widths less than 0.02 minutes.

The Agilent CE ChemStation software provided in PC performs a range of tasks. Simple spectra, iso-absorbance plots, 3D plots, and other evaluation can take place online while analysis is in progress. The software controls the system and enables full spectral information to be retrieved as well as single wavelength and multiple wavelength detection capability.

## Specifications

*Autosampler:* 48-position carousel

*Vials:* 100 µl (polypropylene or glass), 1 ml (polypropylene), and 2 ml (glass)

*Capillary cassette:* High speed forced-air cooler with Peltier element

*Temperature range:* 10 °C below ambient, up to 60 °C

*Minimum total capillary length:* 31 cm

*Capillary compatibility:* 365 µm o.d.

*Detector:* Real time UV–visible diode array detector (190–600 nm)

*Wavelength resolution:* 1 nm

*Response time:* 0.025–10 seconds

*Light source:* Pre-aligned deuterium or high brightness lamp

## Applications

Capillary electrophoresis has numerous applications in biological sciences, pharmaceutical, biotechnology, forensics science, and environmental and food safety. It is considered as a revolutionary technique and serves as a workhorse in analytical laboratories. It has excelled in the rapid analysis of ions and has become predominant for impurity analysis of basic and chiral pharmaceuticals.

## 138

## Electroretinograph

### Purpose

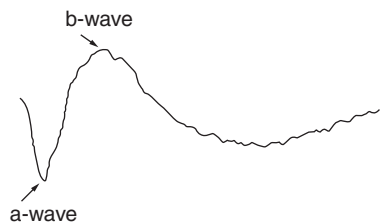
Electroretinography (ERG) is a diagnostic instrument intended for measuring the electrical activity generated by the cells in the retina. The retina is a part of the eye that is responsible for detecting light and images, similar to the film in a camera. After detecting an image, the retina transmits resulting electrical signals to the brain, where the picture is finally registered. ERG measures the electrical activity of the retina, thereby giving an accurate assessment of function of the retina. The ERG can provide important diagnostic information on a variety of retinal disorders and is useful in evaluating both inherited (hereditary) and acquired disorders of the retina. The ERG also helps to distinguish retinal degeneration and dystrophies.

### Principle

The retina is composed of rod and cone cells in the photoreceptive layer of tissue at the back of the inner eye. There are around 120 million rods in the human eye and 6–7 million cones. The cones are responsible for the eye's colour sensitivity. The rods are more sensitive to light than the cones, but they are not less sensitive to colour. When the retina is stimulated with light, electrical currents are generated in the cells of retina and flow through, around, and outside of the eye resulting in an electric field. ERG signal is actually a measurement of the difference in potential between any two locations in this three-dimensional electric field. ERG signal depends upon the function of the retina, stimulus parameters, and properties of other structures of the eye.

### ERG Waveform

During ERG recording, the patient's eyes are exposed to standardized stimuli and the resulting electrical signal is recorded showing the time–signal amplitude (voltage) graph. The electrical response is a result of a retinal potential generated by light-induced changes in the flux of transretinal ions, primarily sodium and potassium. The amplitude of the ERG signal is very small and typically in the microvolts or nanovolts range. The ERG is essentially an integrated display of electrical potentials contributed by different cell types within the retina and the stimulus conditions. In practice, ERG is recorded by stimulating the eye with a bright light source such as a flash produced by light emitting diodes (LEDs) or a strobe lamp. The flash of light results in generating a biphasic waveform as shown in Figure 138.1, which can be recorded at the cornea. The two prominent components of the waveform are the a- and b-waves. The a-wave is the first large negative component, followed by the b-wave, which is corneal positive and usually larger in amplitude.



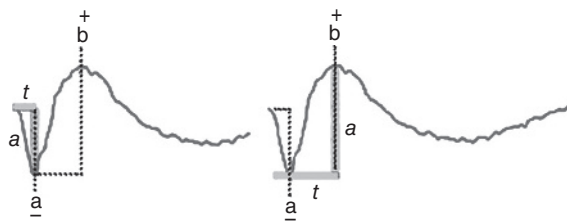
**Figure 138.1** The biphasic ERG waveform of a normal patient.

The two important characteristics of the ERG waveform as illustrated in Figure 138.2 are (a) the amplitude where (i) a-wave amplitude is measured from the baseline to the negative trough of the a-wave and (ii) b-wave amplitude is measured from the trough of the a-wave to the following peak of the b-wave and (b) the time measured from flash onset to the trough of the a-wave and the time from flash onset to the peak of the b-wave. The length of ERG signal is typically 200 ms, with the first 80 ms as the most essential time segment as it contains most of the ERG components. This suggests that the ERG signal is relatively a short signal and provides a significant challenge to the analysis of the signal. The a-wave is an indicator of the general condition of the photoreceptors in the outer retina, while the b-wave reflects the condition of the inner layers of the retina.

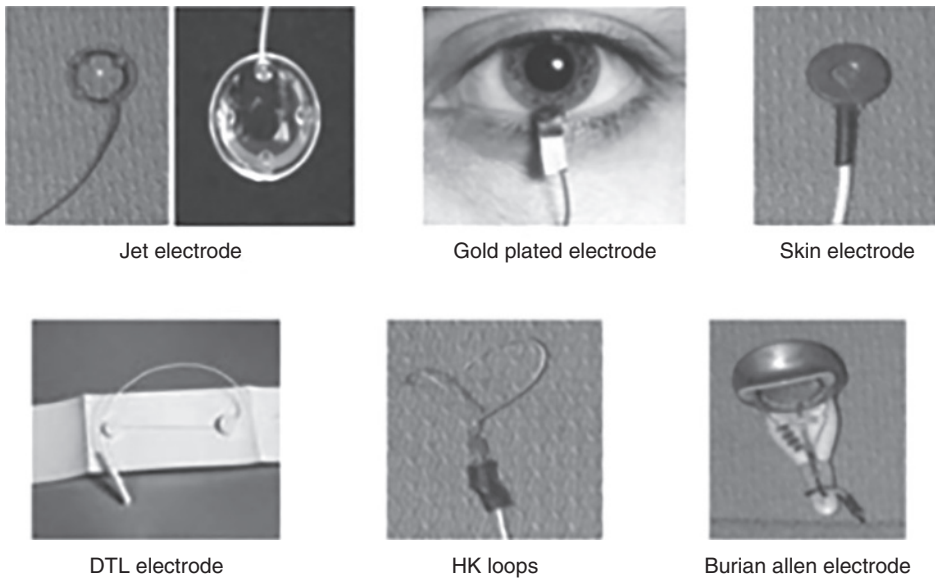
### ERG Electrodes

The choice of electrode is one of the important factors that must be considered when recording the electroretinogram. Several types of electrodes have been developed and tried over the years to measure the tiny voltage signals associated with ERG. Figure 138.3 shows the most commonly used ERG electrodes. Broadly, there are two types of electrodes: (i) with contact lens electrodes or (ii) non-contact lens electrodes that are in contact with either the cornea or the bulbar conjunctiva.

Most often, the small ERG signals are obtained using electrodes embedded in a corneal contact lens and placed on the surface of the cornea. This allows to measure a summation of retinal electrical activity at the corneal surface. These electrodes are centrally transparent with a large optical opening and may include a speculum to hold the lids apart. Contact lens electrodes give larger signal amplitudes. However, they are expensive and often uncomfortable to wear. Contact lens electrodes can be unipolar like the Jet electrode and some of the Burian-Allen electrodes or bipolar like other Burian-Allen electrodes. The non-contact lens-type varieties include gold foil, H-K loop, the



**Figure 138.2** Amplitude and implicit time measurements of the ERG waveform.



**Figure 138.3** Various types of electrodes used in ERG recording. *Source:* From Electrophysiological studies in ophthalmology: Dr. Vaibhav.K P.G.Ophthalmology Navodaya Medical College. Published in: Health & Medicine, Aug 31, 2015.

DTL-fibre, and the LVP-Zari electrodes. In all cases of unipolar electrodes, a reference electrode is usually placed on the forehead, temple, or earlobe. A summary of the commonly used electrodes is given as follows:

*Burian-Allen electrode:* It consists of an annular ring of stainless steel surrounding the central polymethylmethacrylate (PMMA) contact lens core with a lid speculum. The electrode is available in variable lens sizes. These electrodes are bipolar and reusable contact lens type.

*Dawson-Trick-Litzkow electrode:* These electrodes are disposable, mono-polar with adhesive fasteners. They consist of low-mass conductive Mylar thread consisting of individual fibres impregnated with metallic silver.

*ERG-Jet electrode:* A disposable plastic lens with a gold-plated peripheral circumference.

*Mylar electrode:* Aluminized or gold-coated mylar.

*Skin electrode:* These electrodes are used as a replacement for corneal electrodes by placing an electrode on the skin over the infra-orbital ridge near the lower eyelid. They are mostly used for screening purposes only. Since skin electrodes are not in direct contact with the eye, there is significant attenuation in amplitude of the ERG signal. For all skin electrodes, good contact is essential with low impedance.

*Cotton wick electrode:* Burian-Allen electrode shell fitted with a cotton wick, which is useful for minimizing light-induced artefact.

*Hawlina-Konec electrode:* The electrodes are constructed in the form of small 'hooks' and 'loops'. Being lightweight and of such shape, they do not cause the unpleasant feelings in a patient. They are made of Teflon-insulated thin metal wire of silver, gold, or platinum with three central windows, 3 mm in length.



### System Description

The ERG recording system is similar to other types of bioelectric events recorders such as electrocardiogram (ECG) or electroencephalogram (EEG). Figure 138.4 shows a block diagram of the signal acquisition and processing system. The electrical signal generated by the retinal cells is picked up by the electrodes and given to a preamplifier followed by another for amplification and filtration of noise. The patient is electrically isolated to ensure safety from leakage currents, if any. A bandpass filter is used to remove undesired frequencies and bandwidth of the amplifiers is usually kept in the range of 0.3–300 Hz. This frequency range is adequate to record oscillatory potentials and to meet other specialized requirements. The amplified analog ERG signal then goes to an analog-to-digital converter for digitization followed by its processing in the microprocessor. The sampling rate for digitization should be at least 1000 Hz or more. The analog output from the microprocessor goes to the display/recorder unit for displaying the ERG response in time domain. It can also store data for further analysis, capture multiple ERG signals, and average them in order to remove noise. The software provided in the system is usually capable of averaging multiple responses to increase signal-to-noise ratio.

An important part of the hardware is the *stimulating equipment*. Many light-stimulating systems or photostimulators have been developed in order to obtain stimulation of the retina. For ERG recording, two types of illumination arrangements are required. These are the background and the stimulus. A stable background is ensured by a Ganzfeld bowl that provides a uniform whole field illumination to the retina. The inside surface of the bowl is provided with three to five LEDs to enable accurate and constant fixation eye and also allow appropriate excursion of the eyes during electrooculogram (EOG) recordings. The Ganzfeld provides white luminance of 17–34 cd/m<sup>2</sup> across the full field.

The stimulating equipment include xenon strobes, tungsten bulbs, or the LEDs. The duration of each flash stimulus should be less than 5 ms, which should be less than the integration time of any photoreceptors. The flash should be capable of delivering about 12 cds/m<sup>2</sup> of luminous energy at the surface of the Ganzfeld bowl. The flash strength is usually selectable. The stimulus circuit operates under the control of the microprocessor of the recording unit. The stimulus can be delivered with different pattern displays, and the response of the central retina to such a pattern is called pattern ERG (PERG). The pattern is usually a reversing black and white checkboard. The response signal is generally much smaller than conventional ERG signal and requires application of computerized signal averaging techniques to extract PERG. The responses of rods and cones

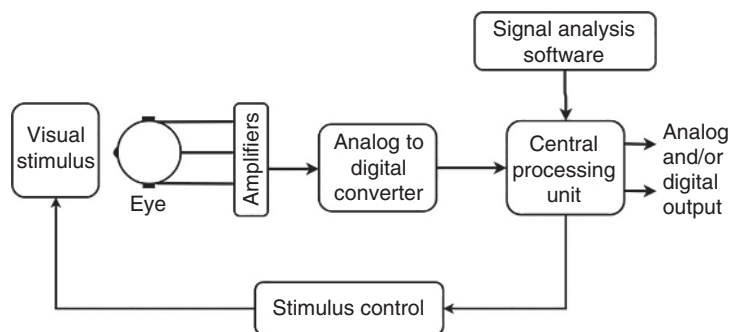


Figure 138.4 Block diagram of signal acquisition system in ERG.

can be isolated using different test settings such as manipulating colours, amplitudes, and intensity of the light simulator.

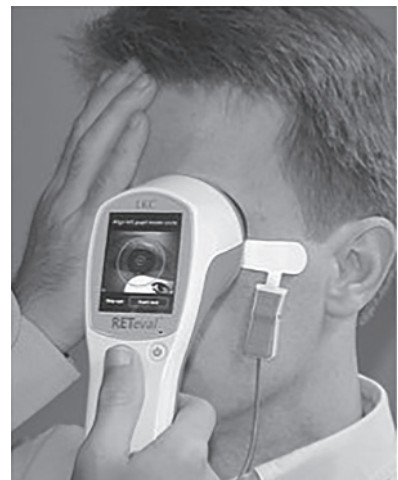
The ERG response signal is a short non-stationary signal that contains overlapping components. The analysis of the signal has been mostly done in the time domain in which a-wave and b-wave have only been studied and their features are defined in terms of amplitudes and implicit times. However, different digital signal processing (DSP) techniques have been used to investigate the time frequency responses of the ERG signal such as short time Fourier transform (STFT), continuous wavelet transform (CWT), and discrete wavelet transform (DWT). The use of different methods and techniques of signal processing offers additional details of the ERG that can help to study the different ERG signal components.

Systems using a contact lens electrode with a built-in LED together with a recording system have been introduced for use in human studies. A typical example is that of the RETeval<sup>®</sup> device, which is the first completely portable, handheld, comprehensive full field flash ERG testing device. This is shown in Figure 138.5. The device is specifically designed as an aid in diagnosis and disease management of visual pathway dysfunctions or ophthalmic disorders such as diabetic retinopathy (DR). The stimulation is provided by focal stimulation or by patterned stimulation. The device incorporates an infrared (IR) camera to view the eye during testing. The test time is only three minutes per patient and the results are available immediately on the device. The DR assessment protocol combines implicit time, amplitude, age, and pupil response. The protocol creates a unified result score, which is shown immediately after test completion. The DR assessment protocol classifies the test result as either high, normal, or low depending upon the reference interval selected. The device monitors the electrical impedance of the connection between pads on the sensor strip. If the impedance is too high, the next operation cannot be performed.

### **Multifocal ERG**

The multifocal ERG is used to record separate responses from different retinal locations and usually produces images with higher resolution than conventional ERG. It consists in stimulating areas of multiple spots simultaneously, and mapping the response, which gives more diagnostic information. Multiple ERG recordings reflecting the retinal

**Figure 138.5** A portable ERG system RETeval. Source: Image Courtesy of M/s LKC Technologies, USA.



response of each of the corresponding stimulated area are produced. The responses can be displayed by the multifocal ERG traces or in a three-dimensional plot, reflecting the response density distribution across the stimulated area.

## Specifications

*Light source:* Red, green, blue, and white LEDs

*Frequency range:* DC coupled

*CMMR:* >100 dB

*Noise:* <0.1  $\mu$ V

*Sampling rate:* 2 kHz

*Flicker frequency:* 28.3 Hz

*Power source:* Li-ion battery

## Applications

The main application of ERG is for the diagnosis of various retinal diseases. It is used by ophthalmologists and optometrists specifically to determine progressive retinal atrophy, a genetic condition that causes slow, gradual but non-painful vision loss. The ERG is also used extensively in eye research, as it provides information about the function of the retina that is not otherwise available.

# 139

## Electrosurgical Machine

### Purpose

Electrosurgical units (ESUs) are used in hospital operating rooms for surgical cutting and coagulating the blood for controlling bleeding at the surgical site. These units are a crucial piece of equipment in the majority of operative settings and are the most useful and common instruments used by surgeons today. The applications of electrosurgery in the medical field are in diverse areas such as general surgery, dermatology, gynaecology, cardiology, plastic surgery, ophthalmology, otolaryngology, orthopaedics, urology, spinal and neurosurgical procedures.

### Principle

Electrosurgery unit, also known as surgical diathermy, is a treatment method that involves the generation of electrically induced heat through the passage of high frequency AC

currents through the biological tissue. The technique utilizes high frequency current to incise, destroy, and remove tissue and to seal blood vessels in order to maintain haemostasis, thereby minimizing blood loss and operating time.

The frequency of currents used in ESU is in the range of 500 kHz–4 MHz in contrast with much higher frequencies employed in a short-wave therapeutic diathermy machines. This frequency is, of course, quite high in comparison with that of the 50 Hz mains supply. This is necessary to avoid the intense muscle activity and the electrocution hazards, which would occur if lower frequencies are employed. The power levels required for electrosurgery are below the threshold of neural stimulation provided that the frequency is in the radio frequency (RF) range. When the frequency is at least 300 kHz, both the faradic and the electrolytic effects are largely eliminated during the flow of current through the human tissue. This then allows the exclusive utilization of the thermal effect in high frequency surgery providing both cutting and coagulation actions.

For their action, surgical diathermy machines depend on the heating effect of electric current. The active electrode in the form of a needle, which the surgeon holds, has a very small surface area as compared to the large pad (ground) electrode. When high frequency current flows through the tip of the needle electrode into the tissue, as seen in Figure 139.1, there is a high density of current at this point. The high current density heats the tissue to such an extent that the cells, which are immediately under the electrode, are torn apart by the boiling of the cell fluid. The current density falls off significantly further away from the active electrode. The larger passive electrode establishes a large area contact with the patient and the RF current is therefore dissipated resulting in negligible heat production at the site distal to the surgical site. This type of action forms the basis of electrosurgical *cutting*. Electric cutting does not require any application of force. Instead, it facilitates elegant and effortless surgery.

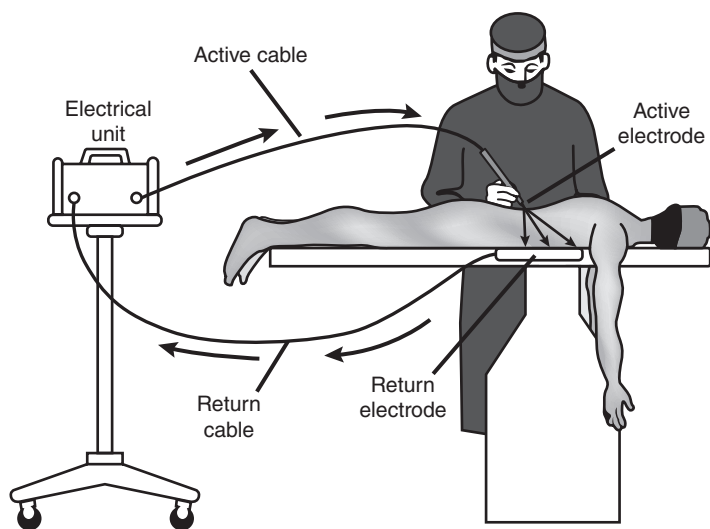


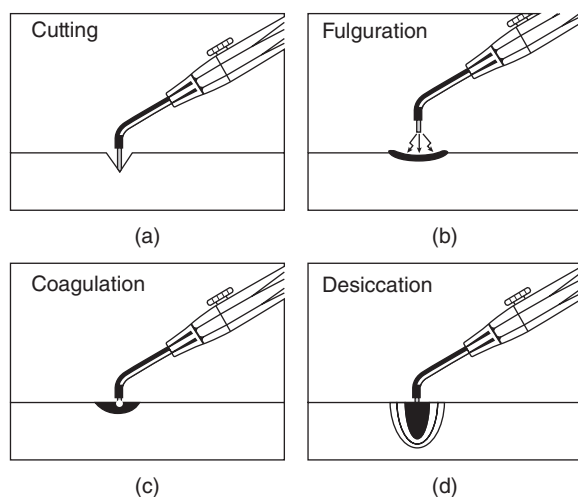
Figure 139.1 Principle of operation of electrosurgery machine.

A voltage of approximately  $200 V_p$  is usually required in order to produce the electric arc for cutting action between a metal electrode and biological tissue. If the voltage is less than  $200 V_p$ , the electric arcs do not get produced and the tissue cannot be cut. The voltage suitable for cutting biological tissue ranges between 200 and  $500 V_p$ . If the voltage applied is above  $500 V_p$ , the tissue will be increasingly carbonized due to the intense electric arcs, which may damage the cutting electrode. A visible arc is generated when the electric field strength is more than  $1 \text{ kV/mm}$  in the gap between the electrode and the tissue. The arc disappears when the field strength drops below this threshold level.

Electrosurgical *coagulation* of tissue is caused by the high frequency current flowing through the tissue and heating it locally so that it coagulates from inside. The coagulation process is accompanied by a greyish-white discolouration of the tissue at the edge of the electrode. Biological tissues are coagulated by thermal means if the requisite temperature is maintained at around  $70^\circ\text{C}$ . While performing coagulation, the surgeon holds the electrode in physical contact with or against the tissue. Using this method of coagulation saves valuable time since bleeding can be arrested immediately by touching the spot briefly with the coagulating electrode.

*Fulguration* is a process of superficial tissue destruction without affecting deep-seated tissues. This is achieved by producing electric arc by holding a needle or a ball electrode of small diameter near to the tissue without touching it. The heat from the electric arc dries out the tissue. Fulguration finds applications in cauterizing fistulas and residual cysts and stopping minor haemorrhages.

*Desiccation* is a direct contact form of coagulation where 100% of the electrical energy is converted into heat within the tissue, not observed with other current waveforms. Needlepoint electrodes are stuck into the tissue and then kept steady. Depending upon the intensity and duration of the current, a high local increase in heat will be obtained. The tissue changes due to drying and limited coagulation. Figure 139.2 shows various types of electrosurgery techniques that are commonly employed in practice.



**Figure 139.2** Various types of electrosurgery techniques commonly employed in practice: (a) cutting, (b) coagulation, (c) fulguration, and (d) desiccation.

The risks associated with electrosurgery fall into four main categories: burns, electrical interference with the heart muscles (ventricular fibrillation), the danger of explosions caused by sparks, and electrical interference with pacemakers and other medical electronic equipment.

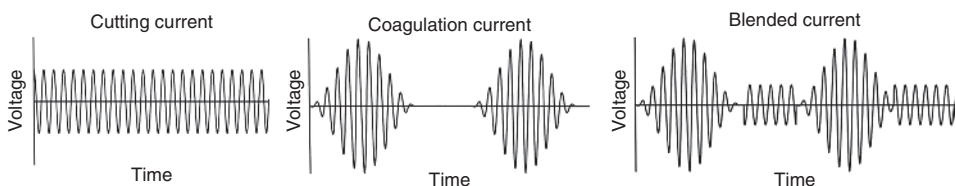
*Electrocautery* is another process in which a direct current is passed through a metal wire electrode, generating heat. The heated electrode is then applied to living tissue to achieve haemostasis. The procedure does not involve passing the current through the patient; thus, the procedure can be safely used in patients with implanted electrical devices. Electrocautery can be used in various minor surgical procedures in dermatology, ophthalmology, otolaryngology, plastic surgery, and urology.

### Types of Waveforms

Different types of waveforms are applied to produce different effects for surgical procedures. Modern ESUs can be programmed to function in several modes with distinct tissue characteristics. There are three types of current waveforms: cutting, coagulation, and blended currents, which are found in commercial equipment. The shape of these waveforms is shown in Figure 139.3.

**Cutting Currents** An uninterrupted sinusoidal waveform has been found to be most suitable for cutting action. The electrode is held slightly away from the tissue to generate a discharge arc at the specific locations that allows for precise cutting and focused heat, minimizing widespread thermal damage. The advantage of using continuous sine wave current is that it does not allow for tissue cooling.

**Coagulation Currents** Coagulation currents are characterized by high voltage intermittent bursts of dampened sine waves. The current through the tissue is relatively low due to the low duty cycle of 6%. Coagulation is the process of electrical sparking over a wider area. Therefore, it produces less heat resulting in evaporation and relatively slow dehydration, which seals blood vessels while keeping cells intact. For coagulation, the power setting is kept between 30 and 50 W with voltage spikes as high as 9000 V at 50 W. In between bursts of current, the heat dissipates into the tissues reducing the cutting effect while enhancing the coagulation during the 94% off cycle.



**Figure 139.3** Types of waveforms generated by electrosurgery units. (a) Cutting current: a pure sine wave. (b) Coagulation current: intermittent bursts of high voltage current. (c) Blended current: a combination of cutting and coagulation current.

**Blended Currents** A combined waveform is usually referred to as 'blended', which is used during specialized requirements. The cutting current usually results in bleeding at the site of incision, whereas the surgeon would require bloodless cutting. The machines achieve this by combining the two waveforms of cutting and coagulation. The frequency of this blended waveform is generally the same as that used for cutting current. Surgeons have the option to combine the cut and coagulate currents to produce different tissue effects. A blended current is not a mixture of both cutting and coagulation current but rather a modification of the duty cycle.

The concurrent use of continuous RF current for cutting and a burst wave RF for coagulation is called *haemostasis* mode.

### **Surgical Diathermy Machine**

The electrosurgery machine typically includes a high frequency power-producing generator with monitoring functions, a handpiece with electrodes to apply the energy to the surgical site, connecting cables, and a foot switch to control output. The earlier types of machines consisted of spark gap oscillators, followed by later designs that utilized vacuum tube oscillator circuits. Modern machines, however, use solid state generators, which could provide much more sophisticated waveforms, better security features, and of course in smaller packages. The designs of these machines include microprocessors that handle all important tasks such as mode selection, output power control, and self-diagnostic features.

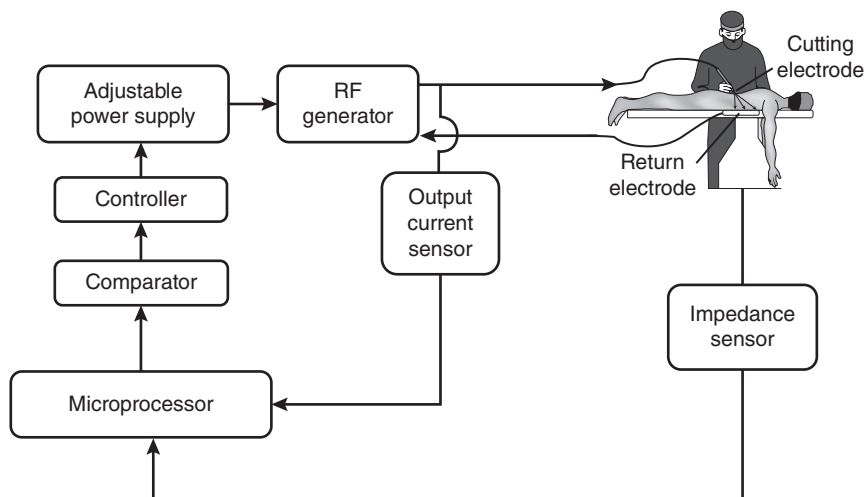
Despite the fact that electrosurgical machines have been in routine use for over a century, the most significant technological developments have been introduced within the past three decades only after the introduction of solid state microprocessor-based generators. Disposable, self-adhering dispersive electrodes are now routinely used in place of the large area buttplates. A number of design features have enhanced safety. These features include a variety of circuit integrity monitors like isolated output, dispersive electrode cable continuity, and patient circuit continuity, among others.

The frequency of operation of most commonly used solid state diathermy machines is in the range of 250 kHz–1 MHz. They deliver 400 W in 500  $\Omega$  load at 2000 V in the cutting mode and around 150 W in the coagulation mode. In coagulation, the burst duration is 10–15 seconds and repetition frequency of the burst is 15 kHz.

Figure 139.4 shows a block diagram of the solid state electrosurgery machine. Unlike the vacuum tube designs in which the oscillator circuit and power amplifier circuits were combined into one stage, modern circuit designs use wave synthesis networks that further drive the output power amplifier stage. This allows to generate even desired waveform shapes for cutting and coagulation. The heart of the system is the RF generator (master oscillator), which generates 500 kHz oscillations, using a stable multivibrator. The oscillator is controlled by a modulator to produce the necessary waveforms. The modulation is done with a 15 kHz gating signal that produces the repetition rate for the three cycles of the 500 kHz signal, which make up the coagulating output. The pulse width of this output is set at about 12  $\mu$ s. The duty cycle of the coagulating waveform is typically 10–20%.

The 500 kHz signal used for cutting is given to power output stage where it controls the push–pull parallel power transistor output stage. The output of this high power push–pull amplifier is applied to a transformer, which provides voltage step-up and





**Figure 139.4** Block diagram of an electrosurgery machine.

isolation for the output signal of the machine. In order to meet the high power requirements, as much as 20 transistors are used in a parallel Darlington circuit. However, the power output amplifier circuitry varies considerably among the different commercial equipment. The modern machines employ both bipolar junction transistors and power metal oxide semiconductor field-effect transistors (MOSFETs) in a cascade configuration or the use of a bridge connection of MOSFETs.

The output circuit in the diathermy machine is generally isolated and carefully insulated from low frequency primary and secondary voltages. Blocking capacitors serve to effectively prevent any low frequency from appearing in the output circuit, and the isolated output reduces the possibility of burns due to an alternate path to ground. The circuitry normally contains a  $0.01\ \mu\text{F}$  capacitor from the ground electrode to earth. This capacitor in the diathermy circuit provides a low impedance ( $20\ \Omega$ ) route to earth for the high frequency diathermy current, but a high impedance ( $300\ \text{k}\Omega$ ) to any incidental low frequency mains current.

The continuity or impedance detector separately evaluates the continuity of all the separate RF output circuits: bipolar, hand controls and dispersive electrode. A low voltage DC supply is connected to each one of them so that when activated, the corresponding LED lights up. This test ensures that the dispersive electrode is actually connected to the proper output connector on the machine.

Microcontroller-based automated systems have been developed so that the output voltage or the spark intensity remain constant. Most electrosurgery machines are programmable and user-friendly. For instance, frequently used standard settings can be earlier programmed by the manufacturer before delivery and individual customized settings can easily and swiftly be programmed later. Continuous monitoring of current and voltage levels and making automatic adjustment under the control of a microprocessor provides for a smooth cutting action throughout the procedure.



**Figure 139.5** Typical electro-surgical machine.

A typical diathermy machine is shown in Figure 139.5. In order to facilitate identification of each mode of operation, the machines incorporate an audio tone generator. The tone signals are derived from the counter at 1 kHz (coagulation), 500 Hz (cutting), and 250 Hz (haemostasis). A thermostat is mounted on the power amplifier heat sink. In case of over temperature, it becomes open-circuited, signalling an alarm and interrupting the output. The gases used in anaesthesia tend to settle near the floor. Therefore, the construction of the foot switch should be such that no explosion should occur in the atmosphere surrounding this switch caused by the operation of the electrical contacts within the switch.

Solid state machines mostly incorporate an independent bipolar RF generator for microsurgery procedures offering a fine output power control. The output waveform is a damped sinusoid at a repetition frequency of 30 kHz. The power output across  $300\ \Omega$  is about 20 W, with peak-to-peak voltage of 1500 V open circuit.

Modern electro-surgical generators use closed-loop control to adjust the voltage and current to keep the output power constant as the active monopolar electrode moves through tissues of varying impedance. These 'adaptive' generators are a significant improvement over those used in traditional electro-surgery. In addition, these machines are provided with numerous safety features such as an error detection system. If a certain error arises, it is immediately displayed and the cause of the error can be readily determined. A variety of safety features that help in reducing the risks in high frequency surgery for both the patient and the users are provided in the machines.

### ***Electrosurgery Techniques***

In terms of current flow, there are basically two types of electro-surgical techniques: the monopolar and the bipolar techniques.

**Monopolar technique:** In the monopolar mode, the current flows from the active electrode through the patient to the neutral electrode (dispersive electrode) from which it returns to the generator. The cutting or coagulating effect depends on the contact area between the monopolar active electrode and the tissue, which is very small compared with the contact area between the patient plate and patient's skin.

**Bipolar technique:** In this technique, both the electrodes (active and dispersive) are at the site of surgery, within the instrument tip. The current in this case flows only through the tissue between the tips of the two electrodes and returns to the generator without passage through the patient. The bipolar surgery is not only safer than monopolar but also more precise since the current only flows locally at the specific site where it is actually required for heat generation. In addition, the risk of inadvertent burning of the patient at the patient plate is very low.

### **Electrodes Used with Surgical Diathermy**

#### **Cutting and Coagulating Electrodes**

The high potential terminal of the diathermy is connected to the cutting electrode, which is mounted in an insulated handle. The cutting electrodes are available in a variety of shapes as shown in Figure 139.6, the choice depending upon the nature of application. Lancet electrodes are normally used for cutting applications, whereas specific types of needle electrodes are preferred for epilation and desiccation. Loop electrodes are employed for exsecting or opening up channels and extirpating growths. The active electrodes for coagulation purposes are of ball type shown in Figure 139.7 or plate type.

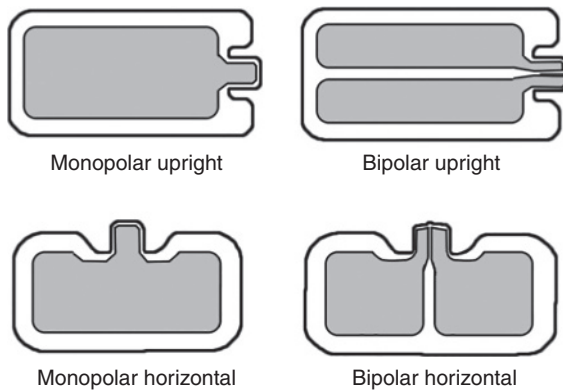
In electrosurgery, the surgeon must be able to switch the high frequency current on and off himself. This can be done with a fingertip switch in the electrode handle or a foot switch. Consequently, the electrodes are used either with electrode handles with fingertip switch, or with handles without fingertip switch with the latter being used in conjunction with foot switches.



**Figure 139.6** Shapes of various cutting electrodes.



**Figure 139.7** Monopolar coagulation, bipolar coagulation, and monopolar cutting electrodes.



**Figure 139.8** Different configurations of dispersive electrodes.

**Dispersive Electrode** A dispersive electrode is an electrode with a relatively large surface area, which is positioned on the patient in order to allow the high frequency current to flow back with a low current intensity in order to prevent any physical effects, such as undesired burns. Typical dispersive electrodes are shown in Figure 139.8. This electrode consists of a lead plate (15 cm × 20 cm) wrapped in a cloth bag, soaked in saline solution and strapped onto the patient's thigh. An alternative arrangement is to use a flexible non-crumpling stainless steel sheet plate without any covering. The large surface area of the dispersive electrode generates little heat, due to the low current density. Good contact is established with the film of perspiration rising between the plate and the patient's body. Quite often, a liberal amount of conductive paste like ECG paste is applied to the plate. This gives excellent electrical contact and removes the need to keep a wet gauze pad. Indifferent electrodes currently available range from 50 to 200 cm<sup>2</sup>.

**Anti-explosion Device** Some diathermy machines are fitted with automatic anti-explosion devices, which make the sparks occurring at the active electrodes innocuous. When the foot switch is actuated or the fingertip switch in the electrode handle is operated, this device causes a stream of nitrogen to emanate from the electrode handle to form a protective cloud around the cutting and coagulating electrode before the high frequency generator is switched on. Hence the explosive gas mixtures in the immediate vicinity of the electrode cannot ignite. An automatic control is incorporated in the unit, which ensures that the high frequency current is not switched on until the active electrode is surrounded by protective gas. This is achieved by using an electrically heated thermistor in the handle, which gets sufficiently cooled by the flow of protective gas. This ensures that an adequate stream of gas is emanating from the handle.

## Specifications

*Modes of operation:* Pure cut, pure coagulation, and blended

*Cutting frequency:* 470 kHz sinusoid

*Coagulation frequency:* 250 kHz

*Monopolar maximum power:* 300 W (cut) and 200 W (coagulate) at 500 Ω

*Bipolar maximum power:* 100 W at 500  $\Omega$

*Desiccate:* 240 kHz sinusoid

*Fulgurate:* 390 kHz damped sinusoidal

*Memory:* For at least 10 programs with their waveforms and power levels

*Monitoring system:* Electrode patient impedance

*Protection:* Against defibrillator discharges

## Applications

A high frequency apparatus is regarded as standard equipment in the operating theatre. It finds applications in at all levels of healthcare facilities such as health centres, district hospitals, provincial hospitals, and specialized hospital.

# 140

## Electrosurgical Tester/Analyser

### Purpose

The electrosurgical analyser is an instrument intended for use in conducting performance tests on high frequency electrosurgical units (ESUs). The tests are performed in accordance with national and international standards. The instrument is used in clinics, hospitals, clinical engineering departments, and independent service organizations and by manufacturers of electrosurgery units.

### Principle

Electrosurgical unit are frequently used piece of equipment in the hospital operating rooms. Electrosurgery is based on the transformation of a high frequency electrical current into heat, with the resulting effect of cutting, coagulating, desiccating, and fulguration of biological tissues at the point of current application. In electrosurgery, the patient forms a part of the electrical circuit as the current flows through the patient's body, which acts as a conductor. Therefore, it is essential to ensure correct operation of the ESU and the highest level of patient safety. It is therefore desirable that performance of ESU is verified on a regular basis so as to manage the risks associated with its use. Manufacturers of electrosurgical generators generally follow the design criteria of IEC 60601-2-2, which specifies the specific requirements in order to provide a controlled approach to patient safety when using electrosurgical devices.

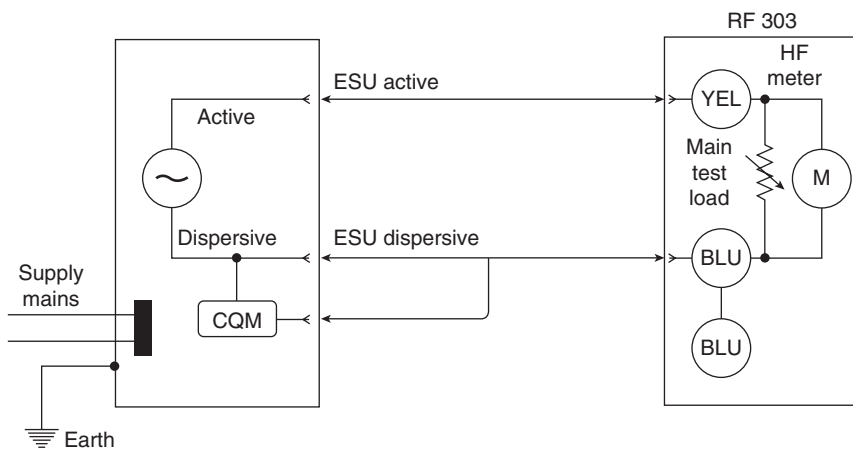
The commonly performed tests on ESU include output current, voltage and power measurement, crest factor measurement, and measurement of radio frequency (RF) leakage to ensure no hazardous currents are present, return electrode current monitoring, and contact quality monitor (CQM) test. The CQM is the 'watchdog' circuit that

initiates alarms and prevents the ESU from energizing when the high limit threshold for current flowing through the return electrode plate or pad has been exceeded. Some analysers also test for the gas flow and pressure for inert gas outputs, which are used for cleaner incisions.

### Output Power Measurement

The verification of output power of an electrosurgery unit is important to ensure the continuing efficacy of the equipment and to promote consistency in the settings of output level controls. This test can be done with the help of a load consisting of non-inductive resistors and current metre suitable for the frequencies and waveform measured. Electrosurgical devices are currently capable of delivering up to 500 W of power at fundamental output frequencies ranging from 0.3 to 3 MHz. In some units, significant harmonic components exist beyond 5 MHz. At these frequencies, precise measurements of output power require that adequate consideration be given to the RF nature of the output waveforms.

Electrosurgery generator manufacturers generally use RF current measurement as their standard measuring technique for research and development, product manufacturing, testing, and calibration. RF current measurement is inherently more accurate than RF voltage measurement across the test load ranging from  $10\Omega$  to a maximum of  $5000\Omega$ , irrespective of the voltage measured across resistive or capacitive divider network. Current measurement is usually done through the use of a current transformer, capable of accurately measuring high currents. Figure 140.1 shows a representative circuit for measurement of RF current. The simplest method of RF output power measurement is to apply RF current to the test load between the active and dispersive electrodes. A low level voltage is tapped off of a  $5\Omega$  resistive divider network and applied to the thermal converter, generating a DC voltage proportional to the input RF voltage. The DC voltage output of the thermal converter is amplified and measured. The amplified signal can be digitized in an A/D converter and given to a microprocessor, which



**Figure 140.1** RF generator output measuring circuit using variable load.

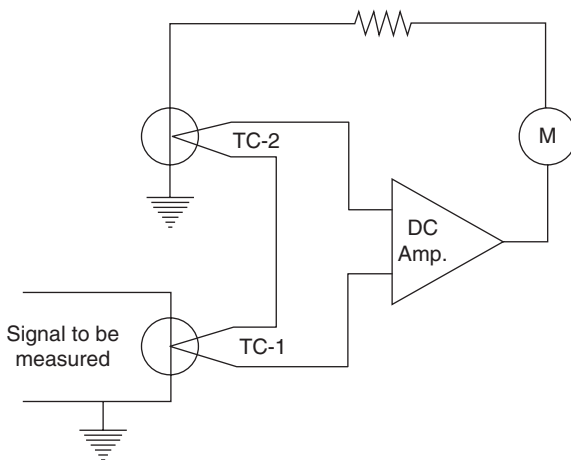
controls all system functions and calculates the various parameters for display through hardware/software functions.

The ESU measurement technology utilizes thermal converter technology and resistive/capacitive voltage divider circuitry. Figure 140.2 shows the principle of operation of the electrosurgical analyser based on this principle.

A thermal converter consisting of a heater element, a thermocouple, and an evacuated glass envelope is used to measure the output power. The heater element varies in temperature as a function of the root mean square (RMS) current through it. The thermocouple is electrically insulated from, but thermally coupled to, the middle of the heater element. It produces a voltage that is a function of the heater temperature. The evacuated glass envelope eliminates the loss of heat by convection and increases the sensitivity of the thermal converter.

The output of the thermal converter is proportional to the square of the applied voltage. This output when applied directly to a metre would give rise to a non-linear scale. Also, the readings are likely to vary with ambient temperature. By using two matched thermal converters, one heated by the signal to be measured and the other heated by DC signal, these problems can be conveniently overcome. The two thermocouple outputs are connected in series opposed. This combined signal is fed to the input of a high-gain DC amplifier. The output of the amplifier is fed back and drives the heater of the second thermal converter. The voltage generated by the second thermocouple subtracts from the voltage of the first thermocouple and reduces the voltage applied to the amplifier. This process continues until the two heaters are at approximately the same temperature and the thermocouples are generating approximately the same voltage, thus balancing the system.

Since the two thermal converters are a matched pair and are at the same temperature, both heaters must have equal RMS currents flowing through them. The DC current flowing through the second thermal converter can be measured easily. Hence, the RMS value of the signal applied to the first thermal converter has also been measured.



**Figure 140.2** Principle of operation of surgical diathermy analyser based on thermal converter.



### ***High Frequency Leakage Test***

IEC 60601-2-2 standard specifies the design criteria of electrosurgical generators with respect to the limit on the amount of capacitive leakage of the high frequency current. At frequencies higher than 400 kHz, the electrical current tends to leakage due to capacitive coupling, which may lead to malfunctioning of the ESU and possible injury to the patient. The RF leakage test measures the RF leakage current in various test configurations and compares the result to a user set pass/fail values, as required by IEC 60601-2-2. The manufactures of ESU analysers usually provide detailed instructional diagrams for each high frequency leakage test set-up on its display so that each high frequency leakage measurement can be automatically initiated through the cut and coagulation control on the analyser.

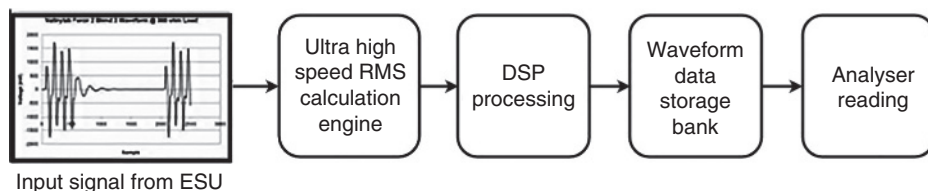
Breakdown of insulation in the surgery leads as a result of high voltages (peak to peak up to 10 kV) is also a consideration when testing the electrosurgical generator. This can be verified by including the surgical leads as part of the test set-up. Beware that this might lead to exposure to conductive parts and possible injury.

### ***Contact Quality Monitoring (CQM) Verification***

To ensure maximum effectiveness of the surgical procedure and to reduce the risk of injury to the patient during electrosurgical procedures, the ground plate must cover an optimum amount of skin surface area and establish a high conductivity contact where the electric current exits the patient. This is monitored by the ESU through impedance measurement (CQM) between the two (split) or more conductive pads within the patient return plate. When there is an extreme variation or very high/low impedance appears, the CQM will initiate an audible and/or visual alarm and deactivate of the output energy to prevent potential patient injury.

The ESU analysers simulate this test by automatic and manual increase or decrease of electrical resistance values in  $1\Omega$  resolution. This allows the testing of CQM systems that are required to get triggered by relative changes in resistance. In the automatic mode, the analyser utilizes a motor-driven potentiometer, which can simulate resistance variations at the desired resolution. This allows the user to trigger the CQM system by simulating fault conditions including very high or very low impedance values or a large variation in impedance, such as a change of 10%.

Figure 140.3 shows a block diagram of a modern electrosurgery analyser. These analysers make RF current measurements taking into consideration the actual frequency of the RF waveform, and it is measured through the actual AC impedance of the test load at the operating frequency of the applied waveform. The application of digital signal processing technology allows digital analysis of the complex RF waveform. The digitization is done at high speed with up to 32 768 discrete data points. This enables to measure accurately even pulsed waveform. Digitization also provides for more measurement parameters. The analyser is suitable with both isolated and earth/ground-referenced types of ESUs. The power distribution test evaluates the output across multiple loads and determine how well the impedance-sensing circuits of new generation electrosurgery generators automatically adjust the output of the ESU so that it is not affected by the presented load. The RF leakage test



**Figure 140.3** Block diagram of an electrosurgical analyser that makes RF current measurements taking into consideration the actual frequency of the RF waveform. It is measured through the actual AC impedance of the test load at the operating frequency of the applied waveform.

displays on screen graphics illustrating correct test connection configurations, complete with user set pass/fail limits. The test is done by measuring the leakage current through  $200\ \Omega$  load.

The newer ESU generators have introduced several special features that require equally sophisticated analysers for their performance. For example, there are generators in the market that operate at 4 MHz as compared with earlier units that worked on 500 kHz–1 MHz. Also, some generators produce pulsed output waveform that cannot be measured with most legacy analysers. These generators incorporate embedded microcomputer controllers that are totally firmware driven. In addition, some units specify 1% accuracy, requiring a highly accurate and versatile analyser. Such requirements are met by the modern ESU analysers that utilize digital signal processing technology to make various measurements.

Modern analysers are provided with wireless port that can communicate with a PC that has an 802.15 (Bluetooth) wireless interface. For PCs without the Bluetooth interface, USB adapter can be used. They have a large memory storage of up to 5000 test records, eliminating the need to download data after the completion of each preventive maintenance or troubleshooting session. All hardware and software necessary to complete preventive maintenance and troubleshooting are built in the unit. Testing of the analysers particularly involves compliance with international standards: (i) IEC 60601-1 (Medical Electrical Equipment – Part 1: General requirements for safety) and (ii) the specific standard IEC 60601-2-2 (Medical Electrical Equipment – Part 2: Particular requirements for the safety of high frequency surgical equipment), American National Standards Institute (ANSI) and Association for the Advancement of Medical Instrumentation (AAMI).

Figure 140.4 shows an electrosurgical analyser, model Uni-Therm from M/s Rigel, United Kingdom, which can make measurements that include high frequency leakage (mA RMS), high power current (W, mA RMS, V peak and crest factor) and power distribution, and patient return plate alarm testing. An ultra-low inductive load bank provides enables performance testing up to 8 A RMS with a duty cycle of up to 100%, making the analyser suitable for calibrating and performance testing of conventional and high power electrosurgical generators. For the power test, an internal array of resistors provides a safe variable load of 0–5115  $\Omega$  in 5  $\Omega$  steps with 1  $\Omega$  resolution, enabling the production of accurate and detailed power distribution curves, with tabular view of test results. The plate security test offers isolated, motor-driven



**Figure 140.4** Electrosurgical analyser model Uni-Therm.  
Source: Image reproduced with courtesy of M/s Rigel, UK.

potentiometer, which provides a continuous swept resistance change, enabling fast testing of alarms, complete with user set pass/fail limits. The automatic mode allows the user to select a test sequence, which will carry out a predetermined set of tests against user definable limits. Bluetooth-enabled technology allows wireless connectivity to PCs and other equipment for the fast and convenient downloading of test data and the uploading of the electrosurgical device's power curves and the manufacturer's test specific programmes.

## Specifications

*Displayed parameters:* Power (W), RF current (mA), and test load ( $\Omega$ )

*Test performed:* Generator output, RF leakage, isolated monopolar or bipolar output

*RF power (W)/resolution:* 1–400 W/resolution (0.1 W)

*RF current range:* 30–2500 mA RMS (resolution: 1 mA)

*Bandwidth/system response:* Flat response at 10 kHz–10 MHz, –3 dB points  
1 kHz–20 MHz

*Test load section:* Selection range of 50–750  $\Omega$ , step size of 50  $\Omega$

*Duty cycle:* 50% at 400 W (maximum 30 seconds)

## Applications

They are used in biomedical equipment maintenance workshop and ESU manufacturing units for test and calibration of electrosurgical machines.

# 141

## Endoscope

### Purpose

An endoscope is a device that enables to look inside the body to examine internal organs. Endoscopes can examine gastrointestinal, respiratory, and urinary tracts, as well as other internal organs just through a small incision. The images of the target organ can be captured through the long tube of the endoscope. Attachments for use with endoscopes for cutting, grasping, and other functions are available that allow minimally invasive procedures, thereby improving patient care and minimizing recovery time. The endoscope can also be used for performing biopsies and retrieving foreign objects from inside the body.

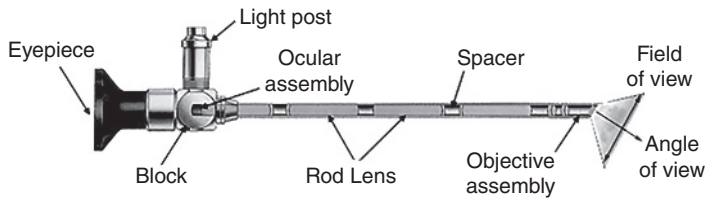
### Principle

Endoscopy allows direct visualization of a diseased area inside the body by using a telescope or a tube that is passed through a natural orifice or through a small incision made in the skin. Endoscopes are optical instruments that may be rigid employing a series of lenses, or flexible employing optical fibres, to carry the illuminating light to target object and to carry back the image to the eyepiece. They are often fitted with one or more extra channels through which operating instruments such as electrosurgery probes, grasping or crushing forceps can be passed. These channels may also be used for delivering fluids or gas, providing suction, or passing sampling catheters or laser light pipes. The whole endoscopy procedure can be recorded so that the images can be studied in detail or for future reference.

### *Rigid Endoscope*

Rigid endoscopes are mostly used to examine various internal organs and structures, especially joints (knee joint) and the external surfaces of organs within the abdominal cavity, such as the ovaries. A rigid endoscope is a straight, narrow metal tubular telescope with an eyepiece at one end to which a camera can be attached. With the camera system, the surgeons can view a greatly magnified image of the target area. A light source is connected to the endoscope that illuminates the structure or organ under examination. Water and air can be pumped down the tube if necessary.

The heart of any rigid endoscope is essentially a collection of lenses that is responsible for collecting and transmitting light from the distal end of the scope to the eyepiece to produce an image. The various parts of the rigid endoscope are shown in Figure 141.1. The core of a rigid endoscope consists of many different lenses and spacers arranged in a very specific order. A field lens and an objective lens assembly are mounted at the distal end of the tube. The field lens is used to determine the size of the image. The



**Figure 141.1** Constructional details of a rigid endoscope.

purpose of the objective lens assembly is to gather and focus light into the rest of the lens system. In endoscopes that provide an angled view, a prism is used to redirect the light gathered by the objective lenses into the lens system.

The lenses are enclosed in a tube and surrounded by a fibre optic light bundle that provides illumination of the working area during procedures. The light fibres run parallel to the inner tubing housing the optical lens assembly. At the distal end, these fibres can be bent to match the direction of view, except for zero degree endoscopes. The light bundle runs from the distal end to a fibre guide attached to the light post on the body of the tube where it can be connected to an external light source. The light from the external light source is focused into the fibre optic light bundle using a light cone, which is enclosed in the light post. All these components are enclosed in a sheath or outer tube, which is composed of more than one layer of tubing to increase rigidity.

All the lenses are held in place by a lens retainer and a tension spring placed at the proximal end. An eyepiece or ocular is placed on the proximal end of the tension spring and is used to provide centring and additional focus to the image. The ocular is enclosed by the eyepiece sleeve that contains the final lens of the scope, the eyepiece cover glass. The eyepiece is used to view the image produced by the scope directly with the naked eye or a camera can be attached to the eyepiece to produce a video image viewable on a monitor. Although the size and arrangement of components may change between different rigid endoscope types, the basic layout and operation is the same.

### ***Flexible Endoscope***

Optical fibres have had a profound effect on advancement of endoscopy and, in this process, dramatically changed the practice of medicine and surgery. These small, flexible light bundles, comprising single fibres, between 50 and 100  $\mu\text{m}$ , allow physicians to direct light into those places in the body where it was not earlier considered possible. The fibre optic bundle carries light from the light source to the point of investigation, keeping the heat of the light source away from the tissue being illuminated. This is referred to as 'cold light source', which provides high intensity light to the endoscope's distal tip. The flexible bundle of thin, multiple optical fibres can be constructed to allow the transmission of images and even to direct laser light to perform microsurgies in regions that are otherwise too delicate or intricate to access.

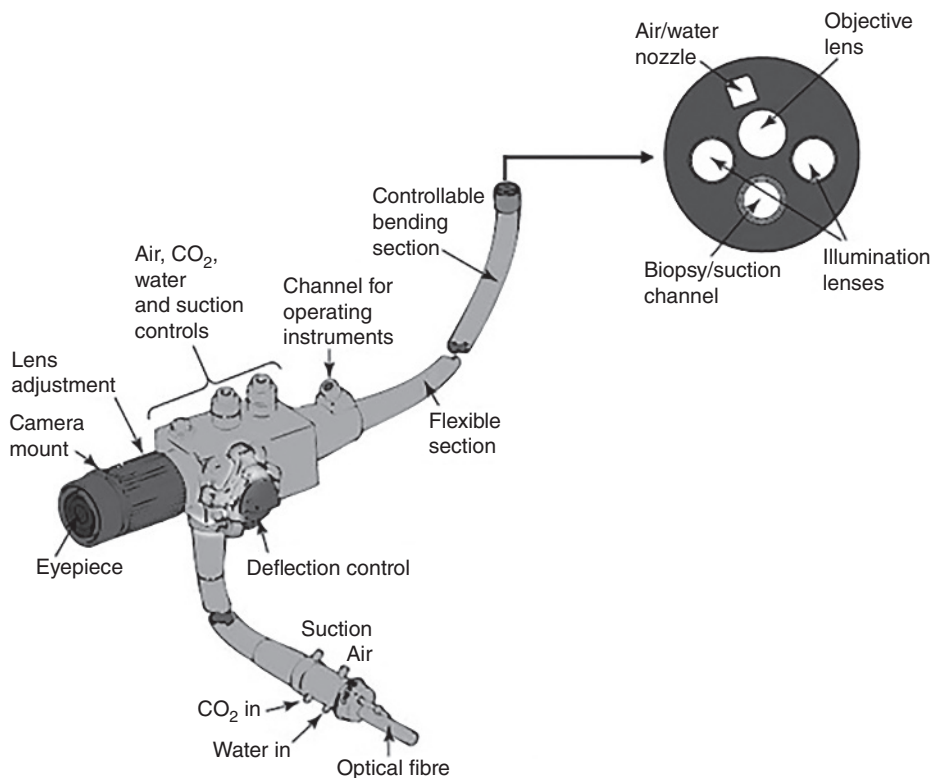
Optical fibres are narrow tubes of glass fibres with a plastic coating that carry light from one end to the other. The light bounces off the walls of the fibre and can even bounce around corners. The light rays travel along the fibres based on total internal reflection. An array of different light delivery devices is now available that can be used with an endoscope. Conventional silica glass fibres transmit wavelengths from the

visible (400 nm) to the mid-infrared (2.5 mm) range. New solid-core fibres are available for the transmission of infrared wavelengths that include fluoride glass, sapphire (up to 5 mm), and silver halide fibres (up to 30 mm). The endoscope comes with a cold light bulb and a flexible optic cable, which allows for a field of vision of up to 80°. The endoscope cable is provided with markings, which allow the user to determine the depth of penetration and to make it easier to locate the observed area. The brightness of the field of vision can be adjusted with the help of an external control.

An endoscope has four basic components:

- *A light source:* For illumination of the object to be studied
- *A tube:* That guides the light to the target object
- *A fibre optic system:* To carry and gather light reflected from the subject
- *An image-capture system:* To capture, process, and store or display the image.

The various mechanical parts of a flexible endoscope are shown in Figure 141.2. It has a shaft, which is only 8–10 mm in diameter and can be up to 1–2 m in length. The whole assembly is flexible and coated in steel and plastic in order to make it waterproof, to prevent chemical damage, and to make it easy to manoeuvre through the body. The flexibility of the insertion tube allows it access to even tight spaces. Under the outer tube, there is a wire mesh that runs along the length and prevents twisting or stretching during use. Below the mesh, a helically shaped steel band helps it to maintain round



**Figure 141.2** Various parts and controls on a flexible endoscope.

shape and provides mechanical protection. The main constituents in the insertion tube are shown in Figure 141.3 and are as follows:

*Fibre optic bundles:* In order to produce a clear image, the shaft contains up to 10000 optical fibres. Light is guided to the area under investigation by this non-coherent fibre optic bundles. The image is transmitted back by a coherent fibre optic bundle, in which the optical fibres are lined up at both ends of the fibre so that an image can be transmitted.

*Air, water, and suction valves:* A set of push buttons and valves are provided at the proximal end of the endoscope to deliver air and water or to suction intraluminal debris. The water is sprayed over the objective lens so to remove debris and provide a clear view. Air is supplied from a pump, which is introduced into the organ such as the colon or stomach to expand the mucosal folds for better visualization.

*Operations channel:* This channel carries accessories to the distal end for surgery.

*Control cable:* The cable provides bending action to the distal end.

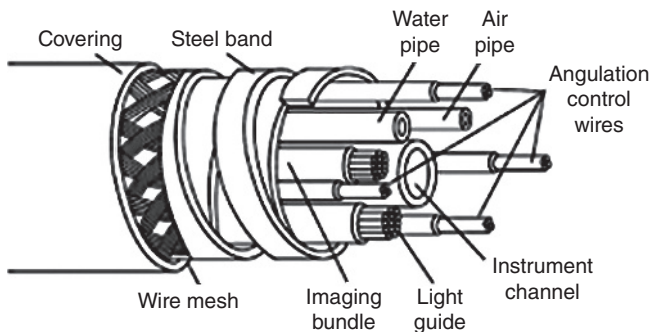
*Additional channel:* This optional channel is required to carry air or carbon dioxide to and from the distal end.

*Distal end:* The distal end is inserted into the patient's body and can be bent in the desired direction with the help of controls on the viewing end. The image is captured and focused by a lens on the end.

*Connection cable:* This 1.5 m cable length provides connection between the endoscope and the light source.

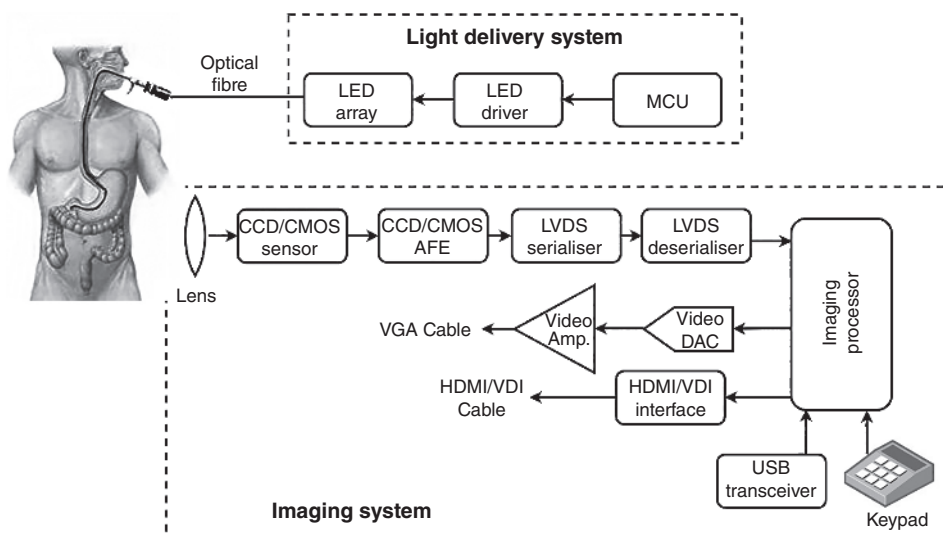
In addition, the insertion tube contains angulation control wires that produce large bending angles that are required for visualization of tissue from different sides. The angulations are provided by a strong set of guide wires that allows to deflect the distal end towards four directions: up, down, left, and right. The wires control is provided at the proximal end and allows to control the viewing angle at the distal end.

Figure 141.4 illustrates a block diagram of an endoscope. It has various components in the image capture and display chain, which include generating light, capturing an image, signal conditioning, and image processing. The light source is a LED that supplies a bright light with controlled directionality. The LEDs can be selected and optimized matching the spectral requirements of the application. The illumination level and timing of LED can be precisely controlled by a pulse width modulator (PWM).



**Figure 141.3** Components contained in the insertion tube of an endoscope.





**Figure 141.4** Block diagram of image processing and display system in an endoscope. CMOS, complementary metal-oxide semiconductor; HDMI, high-definition multimedia interface; MCU, microcontroller unit; VDI, virtual desktop infrastructure; VGA, video graphics array.

The image is captured by a miniaturized charge coupled device (CCD) sensor located directly behind the objective lens that detects reflected light and converts the light to an analog electrical signal. The surface of the CCD is divided into a two-dimensional array of pixels, which may be over a million in number. The signal is transmitted over the light tube's length using low noise line drivers. The final image quality, to a large extent, depends upon the design of the analog front end (AFE). The AFE performs signal conditioning on the analog electrical signal received from the sensor and converts image information to a digitized representation through an analog-to-digital converter.

The digital output of the AFE goes to a low voltage differential signalling (LVDS) circuit that uses differential data transmission. The differential scheme has a significant advantage over single-ended schemes as it is less susceptible to common mode noise. LVDS is a high speed (>155.5 Mbps), low power general-purpose interface standard. After LVDS, the image information is processed in the image processor whose output goes to display circuits, including high definition (HD) display. HD endoscopy uses CCD detector with much higher number of pixels (greater than a million) than conventional endoscopes (pixel number from 0.1 to 0.3 million) to increase resolution by about 10 times. Similarly, high-magnification endoscopes have been introduced, which use optical zoom technology to better visualize the object surface and identify the abnormalities. The image magnification is achieved by using a movable motor driven lens in the optical train. The zoomed magnification achieved is 170 as compared with 35 in standard instruments.

The use of endoscopes is minimally invasive as only a small incision is made in the body, whereas open surgery requires much deeper incisions. After endoscopy, recovery is much quicker as there is less swelling, scarring, and risk of infection. In most of the cases, endoscopy can be performed as an outpatient procedure and may not require hospital stay.

Specialized endoscopes are named depending upon their area of application. For example, cystoscope (bladder), nephroscope (kidney), bronchoscope (bronchi/lungs), laryngoscope (larynx + the voice box), otoscope (ear), arthroscope (joint), laparoscope (abdomen), colonoscopy (colon), enteroscopy (small intestines), hysteroscopy (uterus), ureteroscopy (ureter), and gastrointestinal endoscopes. Endoscopes with forceps (tongs) and scissors can be used to operate or remove tissue for biopsy. The endoscope is inserted through an incision or opening in the body that leads to the area under investigation. Biopsy forceps are then used to take a sample of tissue that can then be analysed by a pathologist.

## Specifications

*Optical system field of view:* 140°

*Depth of field:* 3–100 mm

*Insertion tube outer diameter ( $\phi$ ):* 9 mm

*Working length:* 1030 mm

*Instrument channel inner diameter ( $\phi$ ):* 2.8 mm

*Minimum visible distance:* 3 mm from the distal end

*Air flow rate:* 25 cm<sup>3</sup>/s

*Bending section angulation range:* Up 210°, down 90°, right 100°, left 100°

*Total length:* 1350 mm

## Applications

Endoscopy has had a major impact on the fields of medicine and surgery due to its minimally invasive surgical interventions. The ability to send diagnostic and therapeutic light into the body via minimally invasive procedures has reduced patient discomfort, pain, and length of hospital stay. Endoscopies are commonly used for the diagnosis of cancer. They are used for biopsies to find out whether it is cancerous. Some surgical procedures can be carried out with a modified endoscope, such as the removal of the gallbladder, tying and sealing the fallopian tubes, and taking out small tumours and foreign objects from the lungs or digestive system.

142

## Endoscopic Cyclophotocoagulator

### Purpose

Endoscopic cyclophotocoagulator (ECP) is a device for use as a primary surgery tool for the treatment of glaucoma. Glaucoma is a disease of the eye where excess fluid (aqueous humour), commonly referred to as intraocular pressure (IOP), puts pressure on the

optic nerve and damages vision. The use of ECP technique reduces the amount of this fluid produced in the eye, thereby lowering pressure within the eye. The technique has proved helpful in treating patients suffering from glaucoma.

## Principle

IOP in normal adult population is estimated at 15–16 mmHg with a standard deviation of 3 mmHg. The IOP is measured using a tonometer, which is based on the relationship between the IOP and force necessary to deform the natural shape of the cornea by a given amount. The higher level of IOP is considered as a major risk factor for the development of glaucoma and its progression. IOP is determined by the pressure of aqueous humour that is produced by the epithelium of the ciliary body and enters the anterior chamber of the eye through the opening between the iris and the eye lens. Normally, the fluid gets drained out via trabecular meshwork into the episcleral venous system. If the production of aqueous humour is more than it can be drained out, there would be an increase in IOP. In general, increased IOP is related to higher outflow resistance.

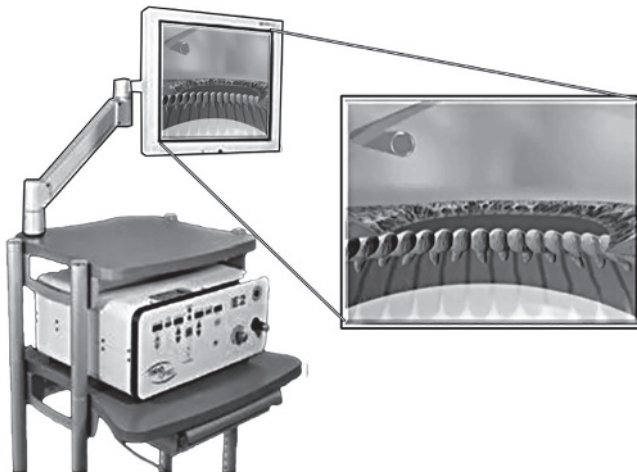
Recent years have seen many techniques and alternatives for the surgical treatment of glaucoma by lowering the IOP. These procedures do so by either improving aqueous outflow or reducing its production. The majority of these techniques with aim of getting increased aqueous drainage for achieving lower IOP are implant based. However, not all eyes respond well to the outflow procedures. The most popular technique that reduces aqueous inflow is known as *cyclophotocoagulation*, which uses laser energy to reduce IOP by selective destruction of the ciliary body.

Cyclophotocoagulator when combined with endoscopy becomes an effective tool for glaucoma management that employs light endoscopy and visualized laser application. As the laser energy is precisely delivered to the ciliary processes, the damage to the underlying ciliary body and surrounding tissue is highly limited. By such selective ablation of pigmented, ciliary epithelium tissue, almost all forms of glaucoma can be effectively treated with this technology. The technique allows continuous, direct observation of the ciliary processes and delivers controlled laser energy to control the aqueous production and resulting in lowering of the IOP. ECP is especially suited for combination with cataract surgery and can treat all forms of glaucoma.

## ECP Technology

The ECP has obviously two parts, i.e. an endoscope for visualization and a laser for photocoagulation. The endoscope is conventionally a tube that includes a lens, a fibre optic cable, and a light source. The laser part contains two lasers: one for aiming at the target and the other for treatment. All these components are housed in a tube that is not bigger than a large hypodermic needle. The combination of these technologies allows the surgeon to view the magnified image of the ciliary processes on a video monitor. With the help of the image, it is possible to choose the areas for treatment and the treatment time. The details of the components of the ECP are as follows:

**Console:** The compact laser and endoscopy console shown in Figure 142.1 contains a xenon light source, a therapeutic laser, and a charge coupled device (CCD) camera.



**Figure 142.1** Typical endoscopic cyclophotocoagulator from M/s Endo Optiks, USA.

Connectivity of the console is provided to any video monitor or video printer. A foot pedal allows hands-free operation.

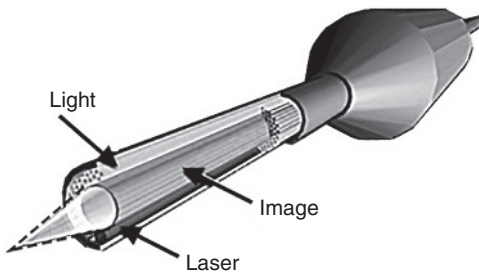
**The laser:** The laser is a semiconductor diode laser that emits continuous wave pulsed energy at a wavelength of 810 nm. This wavelength is optimal for treating the ciliary processes because the pigmented cells absorb the majority of the laser energy at this wavelength. The laser has an up to 2.0 W power output. The laser output, pulse width, light, and aiming beam intensity are controllable from the console, and the parameter values are displayed as digital displays. An emergency shutoff button is provided to ensure safety in operation. Another laser – helium–neon laser (640 nm diode laser) – is provided for aiming the beam of the therapeutic laser at the target.

**Light source:** A 175 W xenon light source is used to provide light to the endoscope. The intensity of output light can be adjusted.

**CCD camera:** The CCD camera is used to process the image obtained by the fibre optic endoscope and displays it on the video display.

**Video display:** The video display is a high resolution monitor and is used for displaying the endoscopic image. The images can be viewed on the video monitor instead of looking through the operating microscope. The video outputs of the endoscopic image can be recorded onto any video recording format. As the procedure can be observed real time on the video monitor, the surgeon can adjust both the amount and duration of laser energy delivered in each application.

The output of all four elements, namely, the diode laser, xenon light source, helium–neon laser aiming beam, and video camera imaging, are transmitted via fibre optics to a 18 or 20 gauge handpiece probe that is inserted intraocularly. The objective lens system creates a 110 field of view, a depth of focus from 1 to 30 mm, and an arrangement of light fibres within the endoscope, which produces a 110 cone of light. The larger-diameter



**Figure 142.2** Endoprobe for endoscopic photocoagulation.

laser endoscope results in giving greater clarity provided by the image bundle and a panoramic field of view. The optimum focus for the laser is 0.75 mm from the probe tip. The unit is compact and portable, with a maximum power output of 1.2 W. A foot pedal controls laser firing for the actual duration of each treatment, which is determined by how long the pedal is depressed.

The endoprobe is a handpiece that connects to the console through a fibre optic cable. It consists of three fibre groupings: the image guide, the light guide, and the semiconductor diode laser guide as shown in Figure 142.2. Images are transmitted through a single probe to allow the surgeon to view and ablate the ciliary epithelium. The endoprobe is connected to the console that contains all of the instrumentation used for endoscopy including the video camera, light source, video monitor, and video recorder. Both straight and curved endoscopic probes are available. To perform the ECP procedure, a tiny fibre optic probe is inserted by the surgeon into the eyeball. This probe is about the same thickness as an ordinary paper clip, but it actually carries a specialized video camera that allows the surgeon to directly see the microscopic structures inside the eye under high magnification. The ECP procedure is painless and typically takes just a few minutes to perform. However, it is an invasive procedure that requires extensive training and practice on the part of the surgeon.

## Specifications

*Laser:* 810 nm diode laser; pulsed; continuous wave (CW); 1.2 W power output

*Laser aiming beam:* 640 nm diode laser

*Laser fibre:* 200  $\mu\text{m}$ , 0.22 NA fibre assembly

*Light:* Xenon light source, 300 W or 175 W

*Camera:* High resolution camera system

*Endoscope beam divergence:* 40°

## Applications

ECP has been utilized to treat a wide variety of glaucoma types. Moreover, it has been increasingly utilized in conjunction with cataract extraction as an initial glaucoma surgery.

## 143

# Endoscopy Capsule (Radio Pill)

### Purpose

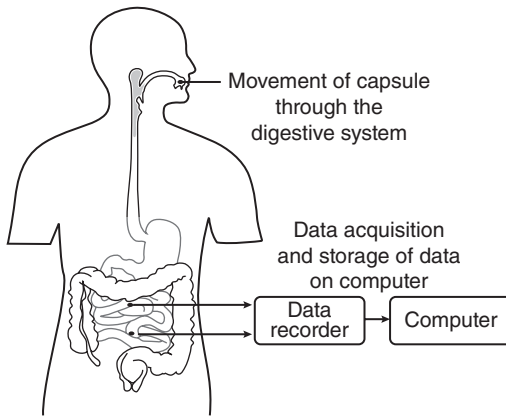
Endoscopy capsule or radio pill is a miniature device that wirelessly sends images of the inside of the stomach and digestive tract, thereby assisting in the diagnosis of the gastrointestinal tract. As the conventional endoscopy involves interventional procedures, though minimally invasive, capsule endoscopy has the potential to rapidly become a viable alternative to the convenience of both doctors and patients. Capsule endoscopy is also capsule enteroscopy or wireless capsule endoscopy.

### Principle

Capsule endoscopy is used to examine those parts of the gastrointestinal tract that cannot be seen with conventional types of endoscopy. Upper endoscopy involves the use of a video camera that is attached to a long flexible tube. It is inserted through the throat and is designed to view the oesophagus, the stomach and the first part of the small intestine called the duodenum. On the other hand, a colonoscope, which is inserted through the rectum, allows to view the colon and the distal portion of the small intestine. With these two types of endoscopy, it is not possible to visualize the majority of the middle portion of the gastrointestinal tract comprising of the small intestine. Capsule endoscopy has proved helpful when disease is suspected in the small intestine, an area that is not easily reachable with traditional endoscopy procedures. The capsule endoscopy technique allows to see the inner surfaces of the gastrointestinal tract and is useful in diagnosing sources of occult bleeding or causes of abdominal pain.

Capsule endoscopy is a procedure that employs a tiny wireless camera to take pictures of the gastrointestinal tract, which can be useful for medical diagnosis. The capsule is similar in shape to a standard vitamin size capsule. It contains a tiny endoscopy camera (one or three chips) and an array of LEDs encased in a clear, smooth shell. The whole assembly is powered by a tiny battery. After the capsule is swallowed by the patient, it travels along the digestive tract taking thousands of pictures per second. The images are transmitted wirelessly to an array of receivers contained in a portable recording device worn on a belt by the patient. The received images are transferred to a computer for diagnosis, review, and display as illustrated in Figure 143.1. A radiofrequency signal, transmitted by the capsule, is used to accurately estimate the location of the capsule and to track it in real time inside the body and gastrointestinal tract. Eventually the capsule will exit the patient when he/she has a bowel motion.

A typical wireless endoscopy imaging capsule is 'the PillCam' (Figure 143.2) from M/s Medtronic. The swallowable capsule measures just 11 mm × 26 mm with cameras on both ends and a flashing light source that enables to take pictures of the entire gastrointestinal tract from the oesophagus to the colon. The capsule has a field of view of 140°. The camera can detect objects as small as 0.1 mm in the oesophagus and 0.5 mm in



**Figure 143.1** Data acquisition and storage of data on a computer as the endoscopy capsule moves through the digestive system.



**Figure 143.2** Endoscopic capsule PillCam. *Source:* With Courtesy of M/s Medtronic, USA.

small bowel. The images are taken by the capsule at 2 Hz, and the information is transmitted to the data recorder via an array of sensors attached to the patient's chest and abdomen. The PillCam produces 57 000 images in an eight hour period without causing any inconvenience to the patient.

The PillCam recorder is small portable recording device that communicates with the capsule as it travels through the gastrointestinal tract. The recorder is attached to the sensor belt, which is worn by the patient around his waist. After the procedure, the data can be downloaded on a PC from the recorder for review. A handheld rapid real-time viewer allows real-time viewing during the procedure. The device software incorporates essential analysis features that help in image interpretation, convenient study management, and network connectivity. A complete capsule endoscopy system is shown in Figure 143.3.

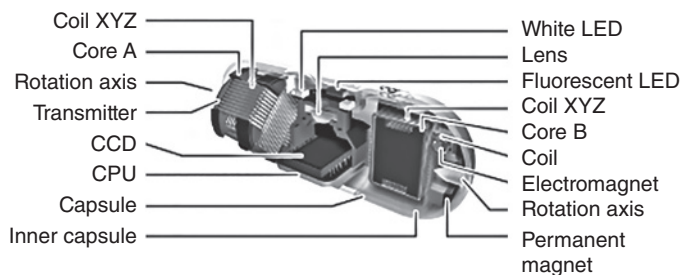
Several versions of PillCam are available to meet requirements of specific applications. PillCam SB is the most widely used version for directly visualizing the small bowel to detect and monitor abnormalities such as lesions, ulcers, tumours, and bleeding within the small bowel. PillCam<sup>®</sup> COLON capsule endoscopy is employed for visualization of the colon, including identifying the occurrence of polyps. PillCam<sup>®</sup> ESO is meant for visualization of the oesophagus.

Another advanced endoscopy imaging capsule under development is from M/s RF SYSTEM lab., Japan. The internal components of this capsule are shown in Figure 143.4. When the capsule is swallowed by the patient and it reaches the intestines, it starts capturing 30 two-megapixel images per second. Fluorescent and white LEDs in the capsule illuminate the tissue walls. The capsule is thus capable of capturing up to 870 000 images at a rate of 30 frames/s during its eight hour stay in the body. The capsule requires about 50 mW of power to run its camera, lights, and computer. Since the batteries can be bulky, the capsule draws its power through induction charging. A vest worn by the





**Figure 143.3** Complete Endoscopic system for PillCam. *Source:* With Courtesy of M/s Medtronic, USA.



**Figure 143.4** Complete capsule endoscopy system, SAYAKA. *Source:* Courtesy of M/s RF SYSTEM lab. Japan.

patient contains a coil that acts as an antenna where they are saved to a standard memory card. The memory card is connected into a PC where the software compiles thousands of overlapping images into a flat map of the intestines. The images can be as large as 1175 megapixels. The video can be replayed and the problem area images magnified up to 75-fold to study details.

Most endoscope capsules have their cameras placed at one end, facing forward. So, the tissue walls are visible only in the periphery of their images. In one system, the camera is mounted in the capsule facing the side and spinning 360° so that it shoots directly at the tissue walls. It is characterized by a double-structured capsule made up of an outer and an inner capsule. While the outer capsule traverses through the gastrointestinal tract, the inner capsule alone spins. This spinning is derived by small permanent magnet and an electromagnet, which causes stepping rotation with a stepping angle of 7.5°. This stepping rotation is necessary in order to prevent fluctuation or blurring in the images. The advantage of this lateral macro photography is clear-cut and high resolution images despite a low light environment. These images are recorded in 2MB/mm<sup>2</sup> pixel resolution, which allows up to around 75-fold enhancement on a 17 in. monitor.

The endoscopic capsule camera is equipped with a lens and an image sensor. The lens should be ideally a wide-angle type to capture as much of the gastrointestinal tract as it can. The endoscopic capsules using a wide-angle lens oriented to and focused on the lateral surface has an intrinsic fault of distortion within that peripheral view. This distortion in the images is generally corrected with the help of software.

## Specifications

*Field of view:* 170°

*Capsule size:* ~26 mm long and 11 mm wide

*Resolution:* 320 × 320 pixels

*Frame rate:* 3 images/s

*Operating time:* 12 hours

*Minimum detectable object:* Minimum size less than 0.1 mm

## Applications

Capsule endoscopy is a powerful technique to diagnose problems in the small intestine, but unlike conventional endoscopy, it cannot treat pathology that may be discovered. Common applications for performing capsule endoscopy include unexplained bleeding, iron deficiency, abdominal pain, and detection of polyps, ulcers, and tumour of the small intestine. Capsule endoscopes are designed to be disposable after use, which eliminates any possibility of in-hospital infection that can be associated with conventional endoscopy.

# 144

## ENT Treatment Unit

### Purpose

The ENT treatment unit is an integrated device comprising of several functional sub-systems, designed for examination and/or therapy of the ear, nose, and throat. The main organs for application of ENT treatment unit are the mouth to the pharynx, the auditory canal to the ear drum, and the nasal cavities. Thus, the doctor can examine the oral and nasal cavities and inside the ears with a single equipment set-up.

### Principle

An ENT treatment unit is equipped with a wide selection of integrated functions designed to accommodate specific requirements of a facility. A typical ENT diagnostic and treatment unit is shown in Figure 144.1. The ENT treatment units primarily create/provide for the following:

- **Suction:** Suction pumps are used to create suction in the desired area. Alternatively, the central vacuum supply system can be used, if available in the clinic. The powerful surgical suction provides sucking up to 70l/min. It has a jar for collecting secretions. Vacuum pump uses oil-less design, so it features low noise non-pollution and low maintenance action.



**Figure 144.1** ENT treatment unit model Micronic Plus. *Source:* Image Courtesy of Entemed BV, Netherlands.

- *Compressed air:* The compressed air module is employed for medication spraying and the Politzer manoeuvre. Compressed air spray gun comes with various spray nozzles for oil, liquid, and powder, characterized by fine spray and adjustable pressure. The spray gun gives out tiny drops. The end of spray head is made by stainless steel, so it is not easily corroded and damaged by medicines and can be easily cleaned and maintained.
- *Ear irrigation:* The ear irrigation system provides up to 500 ml/min water at the right temperature. With the compressed air, the ear irrigation system allows use of heated water at 37°C (Hygrotherm). For the thermal nystagmus stimulation, the auditory canal is irrigated for a limited time with water, having a temperature between 20°C and 47°C (Variotherm).
- *Thermal nystagmus stimulation:* This is warm water module that includes irrigation handle, exchangeable jet connection, and splash protection. The water heating is electronically controlled.
- *Examination microscope:* When the microscope is used, its illumination system is automatically activated. The magnification changer provides for various magnifications for optimum quality of the image as per examination requirements. A beam splitter can be integrated directly in front of the ocular enabling the connection of an ENT camera for display of the image on a LCD. The examination results can be archived with the documentation system on the computer. The objective has magnification of (0, 4/0, 6/1/1, 6/2, 5) with  $f = 250$  mm, eyepiece with 10× magnification.
- *Mirror warmer:* It is controlled with time setting by touch screen for 10–120 seconds.

*Power supply:* The power supply is required for LED light handles and LED headlight. Cordless examination headlight with battery charger is integrated on treatment unit. LED light source has a long LED service life (50 000 hours). The LED light intensity is similar to the usual halogen cold light source of 150 W.

Power supply is also required for light sources (halogen cold light) for use with scopes with light conducting cable integrated in the module. The light of halogen quartz lamp can be adjusted at any angle with the help of a special snake type light hose.

Provision for attaching several optional facilities is also made for an ENT diagnostic and treatment centre. These include the following:

*High-resolution charge coupled device (CCD) camera (1/3) with high light sensitivity and large depth of sharpness:* The camera is with 400 000 pixels integrated light source with fibre optic cable. The camera is integrated into the information and communication technology (ICT) infrastructure of the hospital using the standard interfaces as DICOM or HL7.

*Video endoscopy imaging system connection with video camera:* The treatment unit allows a video image endoscopy function, while a computerized system displays an enlarged image of the processes in the nose, throat, or ear on a monitor. The endoscopy equipment comprises of the cameras and cold light sources. The endoscopy system allows a choice of imaging software and choice of three diagnostic modules with useful feature of ear, nose, and throat images.

*17 in. thin film transistor (TFT) monitor* or touch screen TFT monitor for the above, with digital online zooming of images

*Rhinomanometer:* PC-based module

*Tympanometer:* The integrated tympanometer acts as a diagnostic device for objective measurement of the tympanic membrane and the Eustachian tube.

*Sinus echography:* PC-based module

Besides, the equipment is equipped with spray gun, suction gun, blowing gun, laryngoscope preheating device, film viewer, adjustable seat, and warm water rinsing system.

The ENT system is microprocessor controlled with embedded software. The system allows to access useful information via the touch screen menus on LCD display. This enables to select diagnostic modules and digital imaging components. The display includes counters for total use of suction, fibre optic light, compressed air, endoscopy, and total use time counter. In addition, there is a fault diagnosis program and service due indicator. The system incorporates an articulated arm that can be positioned for convenient accessibility to the handpieces. Certain integrated functions are automatically triggered by means of infrared sensors when the handpieces are removed from their holders. The position of the chair can be adjusted from a touch screen 7 in. monitor mounted on an articulated arm. Imaging/patient management software packages are available for connection to the hospital's information system (HIS) or picture archival and communication system (PACS) via HL7 interface (DICOM compatible).

## Specifications

*Suction:* At 40 l/min/760 hPa, or 55 l/min/920 hPa

*Ear rinsing:* With  $37 \pm 1^\circ\text{C}$ , maximum 500 ml/min or at  $37 \pm 2^\circ\text{C}$  with compressed air

*Thermal control:*  $20\text{--}47^\circ\text{C}$  water for nystagmus stimulation

*Compressed air:* Maximum 2 bar

*Electric power supply for LED:* 700 mA

*LED cold light source:* 210 klux  $\pm$  10%

## Applications

The ENT treatment units assist the surgeon in performing various kinds of ENT, outpatient department (OPD) procedures from one single unit. Application sites are clinics of doctors and hospitals.

# 145

## Enteral Feeding Pump

### Purpose

The enteral feeding pump is a simple-to-use precision device that provides patients with either continuous or intermittent feeding and automatic flushing. The device accurately delivers programmed doses of enteral nutrition, allowing patients to comply with prescribed feeding schedule. The devices are available both for paediatric and adult patients to maintain a normal lifestyle.

### Principle

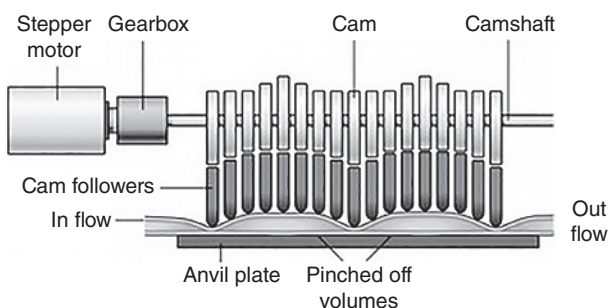
An enteral feeding system consists of a disposable administration feeding set that works in conjunction with a flow control pump, for supplying fluid to a patient at a controlled delivery rate. The feeding set includes an inlet tube that is connected to a source of fluid at one end and a drip chamber at the other end. The device is a micro-computer controlled pump that provides accurate, controlled enteral feeding in a safe manner. The pump is a volumetric pump that uses a specially designed feeding set, which includes a cassette that delivers measured amounts of enteral product. As an optional feature, the pump can flush the feeding set and indwelling feeding tube each hour with a 25 ml flush. The enteral pumps are designed to deliver only liquid enteral feeding products.

The heart of the system is the peristaltic pump, which is functionally very simple. The working of the peristaltic pump is similar to the human body, which uses 'peristalsis' action to move food through the digestive tract. The wave-like muscle contractions progressively squeeze the digestive tract, essentially 'pushing' the food through. The various means for achieving peristaltic action are as follows: cam-operated fingers pressing the tubing in succession; a rotor on an eccentric shaft that

squeezes an eccentric cylindrical liner; and a row of eccentric cams that moves a cam follower, producing a clamping effect and imparting a squeezing action to plastic tubing, among others. They are self-priming, as no valves or seals are required, and the accuracy rate is high. Peristaltic pumps use speed control of the drive motor to control the rate at which feeding is done. The peristaltic pumps as illustrated in Figure 145.1 achieves this action by utilizing a circular pump 'head' and simple rotating roller. The roller is designed to pinch the tubing and gently squeeze the fluid through specially designed tubing. The major components of a peristaltic pump are the pump tube, pump head and roller, driving motor, and control electronics. The control electronics may comprise of variable frequency drive, motor starter, programmable logic controller (PLC), etc. that are generally housed in a separate enclosure.

The peristaltic pump may have anywhere from one to six or more individual rollers that squeeze the tube, pinching off the captured fluid and delivering it to the discharge end of the pump tube. Multiple rollers provide slightly smaller volumes of fluid per revolution, less pulsation, and therefore a longer roller life. Unlike many types of pumps, peristaltic pumps are capable of operating at very low revolutions per minute while maintaining very high accuracy, repeatability, and priming capability. The factors that affect the amount of squeeze required for a particular application include system pressure, suction lift, fluid viscosity, and tube material.

The peristaltic pump usually makes use of DC powered gear motor with a gear ratio of 100 : 1 or a stepper motor. The rate of fluid delivery is controlled in the software by varying the pause between the revolutions. Each revolution takes about four seconds. A slower rate results in longer pauses. Rotor rotation is determined with three equally spaced magnets mounted on the rotor, which are detected by a sensor in the pump. The motor operates under the control of the microcontroller. The flow of fluid is monitored by a drop detector circuit. The circuit consists of an infrared emitting diode (IED) and a phototransistor sensor pair. When a drop falls between the IED and the sensor, a pulse gets generated. The software is designed to look for the presence of at least one drop every two revolutions of the rotor. If this does not occur, a flow error is indicated.



**Figure 145.1** Principle of peristaltic pump.



**Figure 145.2** Typical enteral feeding pump.

When the pump has delivered the desired amount of fluid set by the operator, the pump will stop and give out a beep and light indication. There are a number of operating situations when the pump is on, and alarm conditions are activated. These could be empty feeding container, an occlusion causing delivery to stop, overfilled or dislodged drip chamber, dirty sensors, or improperly placed drip chamber. Using appropriate key, after the alarm condition is corrected, will cancel the alarm and return pump to hold mode. A typical enteral pump is shown in Figure 145.2.

The foremost consideration in the design of enteral pumps is the patient safety. Apart from providing an accurate volume flow, pumps and their associated devices must ensure patient safety even in the presence of misuse or equipment malfunction. Alarms that detect air in the infusion line, depletion of the infusate, or malfunction of the pump itself are usually integral parts of infusion systems. The maximum pressure that a pump can generate should be limited in order to avoid tissue infiltration or trying to pump into an occluded line.

## Specifications

*Flow rate/volume mode:* Flow rate: 1–600 ml/h, volume limit: 1–9999 ml/h

*Accuracy:*  $\pm 5\%$

*Flow pressure:* 15 psi

*Alarms:* Tubing not loaded, delivery not started, tubing dislodged, delivery error, delivery complete, low battery

*Battery:* Built-in rechargeable lithium battery

*Occlusion pressure:* 5.8–23.2 psi

## Applications

The enteral feeding pumps are usually designed for both hospital and alternate care applications.



## 146

## Ergometer, Bicycle

### Purpose

A bicycle ergometer is a fixed cycling machine used to evaluate the fitness level of an individual or athlete by measuring the work done by the exerciser. Bicycle ergometry serves as an alternative to treadmill testing for those patients who suffer from some physical limitations restricting weight bearing such as orthopaedic, peripheral vascular, or neurological conditions. The machine is also less expensive as compared with a treadmill and much easier to work out.

### Principle

The two most common types of formal exercise testing are the treadmill walking and bicycle ergometry. The latter employs exercise bikes, which allow low-impact movement when operated and do not put much stress on joints. The exerciser or test subject rides the bicycle while connected to monitoring equipment for measurement of heart rate, pulse, metabolic changes, and respiratory effects of exercise. The desired work intensity can be adjusted by variations in resistance and cycling rate. Although work load or exercise capacity is usually measured in watts, it is possible to translate watts to oxygen uptake in millilitres per minute. *Metabolic equivalent* (MET) can then be calculated by dividing oxygen uptake per minute with the product of  $3.5 \times$  body weight (kg). MET is a unit of measure of the rate at which the body expends energy that is based on the energy expenditure while sitting at rest and is equal to 3.5 ml of oxygen per kilogram of body weight per minute.

A bicycle ergometer comprises pedals and a seat similar to a traditional bicycle. It includes handle bars and a seat height adjustment arrangement. The special ergonomic construction promotes seating position for all heights. Some machines are equipped with an electrical seat height adjustment that simplifies getting onto the ergometer, especially for older patients or those with a walking disability. Upper body position and leg-to-foot pedal angle can be optimally set by adjusting the height and inclination from the handlebars. The saddle height can be adjusted for patient heights from 120 to 210 cm.

At the ideal seat height, the knee should be slightly flexed at full extension. For safety purposes, adaptable pedal grips are included. In addition, metres, dials, or digital displays are appropriately placed for easy reading. The power, which is absorbed directly by friction, is transmitted to the pedals by the patient, or the mechanical power is converted by means of a dynamo into electric power, which is then in turn dissipated by a resistance. Exercise bicycles typically use a crankshaft and bottom bracket, which turns a flywheel by means of a belt or chain.

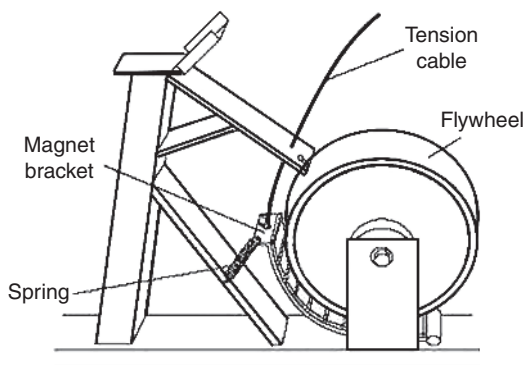
Modern bicycle ergometer machines are quite sophisticated and computer-controlled precision electronic trainers that measure the body's workload efficiency and provides for

continuous monitoring of physiological effects. They allow the user to simulate real cycling conditions such as hill climbing and also to vary resistance to pedalling via a mechanism attached to the bicycle gears. Measuring blood pressure and recording electrocardiogram (ECG) is easier with bicycle as fewer artefacts are observed as compared with the treadmill. The machines generally provide five predefined stress test programs, in addition to 10 user-definable programs. The LCD shows dynamic values for load, blood pressure, heart rate, and revolutions per minute (rpm). Most machines have ECG/pulse sensors that work by detecting the ECG through the metallic conducting palm sensors and then relaying the signal back to the computer where the heart rate can be calculated and sent to the display. A typical bicycle ergometer is shown in Figure 146.1.

A typical bicycle ergometer test consists in riding of the subject at a constant speed of about 50 rotations/min for a set amount of time. The bicycle ergometer usually operates on the principle that a variable resistor, usually a friction wheel or an eddy current brake, is provided, and simply the duration of the exercise and possibly the speed of movement of the shaft is detected. From these values, the services performed by the user work can then be estimated. During the test, resistance is applied to the bike in small increments, which increase the intensity of the exercise. Resistance mechanisms that are usually incorporated are of the following types:

*Friction resistance:* Friction-based resistance gets applied when the rear wheel of the bicycle comes in contact with two parallel rollers, which rotate when the user pedals. The resistance provided by the rolling friction of the bicycle tyre against these rollers simulates the resistance the subject experiences in actual conditions at the same speed. The limitation of this technique is that it cannot simulate the resistance that may be due to varying terrain or blowing of window.

In friction type bicycle ergometer, the subject is made to work against friction created on ergometer flywheel. Its blades can be adjusted to increase or decrease resistance on the pedals that accurately mimic different gears and generate forces for the cyclist based on their individual load and the track on which they are riding. As the subject pedals the bicycle, the flywheel rotates against the brake belt around its rim. The brake belt is tensioned by the addition of weights on one end, while the other end is attached to a spring balance. The difference between the weight added and the spring balance reading when cycling gives the resistance or the frictional force on the flywheel.



**Figure 146.1** Typical bicycle ergometer showing the mechanism of applying resistance.

*Wind resistance:* The wind resistance consists of a fan device that is placed in contact with the rear wheel of the bicycle. When the user pedals, the wheel rotates, which in turn rotates the fan device. It provides the same resistance as the user will experience when cycling on the road at the same speed. The resistance is higher at the higher speed of the cycle. The disadvantage of this method is that it cannot simulate the varying resistances encountered during changing terrain.

*Hydraulic resistance:* The resistance of the rear tyre can be varied by using a resistance fluid (oil). The fluid is pumped into and out of a cylinder with an enclosed rotating impeller. The resistance encountered by the impeller can be thus controlled and hence the tyre resistance. The advantage of this technique is that it can offer progressive resistance to the user with gradual change.

*Eddy-current resistance:* In this system, permanent magnets are arranged on both sides of a conductive disk. As the magnet rotates, it induces eddy currents in the rotating disk, which then produce electromagnetic fields that interact with the magnetic field of the magnet. It is this interaction that generates a resistance to rotation of the disk and thus of the rear wheel. Newer systems make use of electromagnets instead of permanent magnets. The advantage of this technique is that it maintains constant power output even if the cycling speed changes. The eddy-current brake system is quiet and enables an exact load control.

Modern bicycle ergometers do not depend upon rotational speed. These are usually equipped with computer controlled eddy-current brake system in which only the output to be achieved is predefined. The braking action is constantly compared with the rotational speed, the force expended, and the predefined stress. Deviations are continuously corrected electronically by increasing or decreasing the brake force. For example, if the pedalling frequency is increased, the resistance decreases proportionally.

The mechanically braked ergometers require that a specified cycling rate should be maintained to keep the work rate constant, whereas electronically braked ergometers automatically adjust internal resistance to maintain specified work rates according to the cycling rate. Regardless of the type of bicycle used, it should be possible to adjust the work rate in increments either automatically or manually. Also, the energy received by the ergometer should be independent of the rotary speed within a certain range because it is often quite difficult particularly for elderly or sick people to maintain the speed constant at a specific value.

## Specifications

*Saddle height adjustment:* Continuous, for patients between 120 and 210 cm, with digital readout

*Handlebar:* Continuous handlebar adjustment over 360°

*Crank length:* 170 mm

*Braking:* Computer-controlled eddy current brake

*Load range:* 6–999 W, speed independent

*Speed range:* 30–130 rpm

*Load increments:* User programmable

## Applications

Exercise bikes are used for exercise, to increase general fitness, and for physical therapy because of the low-impact and safe cardiovascular exercise. Modified versions have been used in space to counter cardiovascular reconditioning in the microgravity environment. Athletes and sports centres use bicycle ergometers as a training tool to plan training programs. Bicycle ergometers find applications in universities, sports science labs, bicycle coaching, and testing centres and to study human biomechanics of locomotion and fitness.

147

## Ethylene Oxide Analyser

### Purpose

Ethylene oxide (EtO) analyser is used for in situ measurement of EtO concentration during sterilization. EtO is one of the most commonly used sterilization methods in the healthcare industry because it does not damage delicate instruments and devices requiring sterilization. Accurate monitoring of EtO levels throughout the sterilization process is necessary to facilitate validation and results in more cost-efficient operation.

### Principle

The effectiveness of EtO sterilization systems depends upon several factors that include EtO gas concentration, diffusion rate, temperature, and humidity. Each of these parameters can either directly or indirectly influence the system's level of microbial lethality. Therefore, it is a usual practice to perform accurate and reliable in situ measurements of EtO concentration during sterilization process. The preferred method of EtO measurement is by using non-dispersive infrared (IR) analysers that allow to perform continuous analysis of EtO.

The sensing of EtO by the IR detection method is based upon the ability of the ethylene gas to absorb IR radiation at specific wavelength as it passes through a volume of gas. The IR detection technology utilizes a light source and a light detector that measures the intensity of two different wavelengths, one at the absorption wavelength and one outside the absorption wavelength. The presence of gas between the source and the detector reduces the level of radiation falling on the detector due to absorption that is continuously monitored. Gas concentration is determined by comparing the relative values between the two wavelengths.

The IR absorption method for EtO measurement is based on the spectrophotometric principle that the amount of light absorption that occurs is dependent on the number of molecules present in the absorbing material. Therefore, the intensity of the radiation

leaving the substance may be used as an indication of the concentration of the material. Let us suppose  $P_0$  is the incident radiant energy and  $P$  is the energy, which is transmitted. The ratio of the radiant power transmitted by a sample to the radiant power incident on the sample is known as the transmittance.

$$\text{Transmittance } T = P / P_0$$

The logarithm to the base 10 of the reciprocal of the transmittance is known as absorbance.

$$\text{Absorbance} = \log_{10}(P_0 / P)$$

According to the Beer–Lambert law,

$$P = P_0 10^{-\varepsilon bc}$$

where  $c$  is the concentration,  $b$  the path length of light, and  $\varepsilon$  the extinction coefficient. The concentration  $c$  of the substance is calculated from the absorbance, also called the extinction  $E$ , as follows:

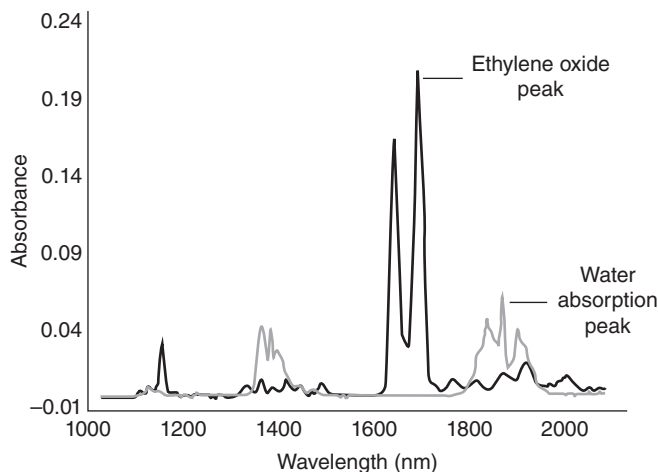
$$\text{Absorbance}(E) = \log P_0 / P = \varepsilon bc$$

In spectrophotometric measurements,  $\varepsilon$  (coefficient of EtO absorption) and  $b$  are nearly constant so that for a particular determination, absorbance varies only with concentration ( $c$ ). Therefore, if absorbance is plotted graphically against concentration, a straight line is obtained. In IR analysers, there is a fixed path length between the IR source and the IR detector. The path length is typically short, just a few centimetres, and the gas concentration is assumed uniform across the path. With a fixed path length, the measurement of IR beam absorption by the gas being measured can be expressed directly in terms of concentration.

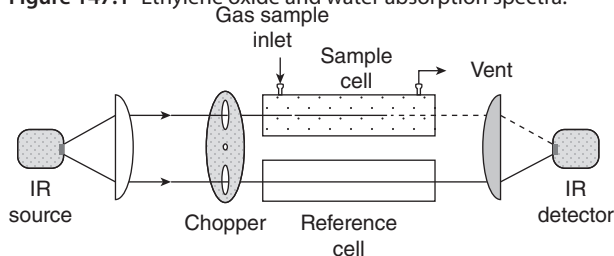
Since spectral absorption is a function of the molecular structure of a particular gas, it implies that every gas has its own spectral signature. By fine-tuning the sensor to the wavelengths absorbed by EtO and comparing them with wavelengths not absorbed by EtO, the sensor allows to measure EtO concentrations in sterilization chambers with high accuracy.

For effective sterilization, it is necessary that the EtO concentration should be of sufficient concentration for an adequate length of time. The presence of water vapour or humidity in the sterilization chamber makes the process more efficient. The instrument, therefore, must have the ability to measure the EtO and water vapour concentrations during the sterilization cycle. This will ensure that the necessary sterilization conditions have been duly met. Figure 147.1 illustrates a typical absorption spectra of EtO and water vapour. EtO gas has two absorbance peaks at 1643 and 1693 nm, whereas water vapour peaks are at 1362 and 1871 nm. Thus EtO and water vapour peaks are quite distinct and do not interfere with each other.

Figure 147.2 illustrates the principle of IR based EtO analyser. In this device, the IR energy passes through two identical tubes and then falls on an IR detector through optical system. One tube acts as a reference cell and is filled with a non-IR absorbing gas such as nitrogen. The other tube is the measuring cell and contains the gas to be analysed. The IR



**Figure 147.1** Ethylene oxide and water absorption spectra.



**Figure 147.2** Principle of infrared ethylene oxide analyser.

source continuously emits IR waves through the two gas tubes, while the detector measures the intensity of two wavelengths. One wavelength relates to the sample and the other to the reference gas absorption wavelength. As the reference gas usually contains nitrogen, the signal received at the detector would correspond to 100%. If the sample gas has EtO gas present in it, the detector will receive attenuated signal. The difference between the two signals will be proportional to the amount of absorbing gas (EtO) in the sample cell. Eventually, it is the difference in the absorption of IR radiation that gives a measure of the concentration of EtO.

The signal conditioning is done by both analog and digital processing techniques. Major analog signal levels are periodically adjusted to keep signals in an optimal measuring range thereby greatly reducing measurement error resulting from varying conditions and simplify the digital signal processing. A microcontroller executes the signal conditioning algorithms and performs a set of diagnostic functions. The calibration is done by issuing two commands, namely, zero and span, which are sent to the device over the digital link. A digital link is used to monitor internal operating parameters as well as gas levels on continuous basis. The output provides an accurate linear response curve over a wide range of operating conditions.

The IR-based EtO analysers have several advantages. They exhibit immunity to contamination and are able to operate continuously in the presence of gas. With the newer sophisticated optical designs, IR detectors are factory calibrated and are virtually

maintenance free. In spite of advantages, there are still some practical problems, mainly due to condensation of water vapour on the sensor's optical surfaces. Some sensors monitor frequencies unaffected by water vapour. This action is similar to camera haze filters that allow the film see through mist and rain, even though the viewer's own vision is obscured. Another approach is to heat its optical surfaces to avoid condensation.

## Specifications

*Detector:* IR

*Output (analog):* 4–20 mA

*Response time:* T50 < 5 seconds, T90 < 10 seconds

*Range:* EtO: 0–2000 mg/l

*Accuracy:*  $\pm 5\%$  of reading

*Repeatability:*  $\pm 2\%$

## Applications

EtO analyser is commonly used in the healthcare and pharmaceutical industries for measurement during sterilization process.

148

## Event Recorder: Cardiac

### Purpose

A cardiac event recorder is used to diagnose and evaluate cardiac arrhythmias of a person during normal activity. The device is very similar to Holter monitoring and is often prescribed for the same reasons, but it monitors the cardiac activity over a longer period, say, up to 30 days. These recorders are particularly useful in recording arrhythmia that might not be detected on a routine electrocardiogram (ECG) or the arrhythmias that occur so infrequently that they are not detected during a 24 hour period by a conventional Holter monitor.

### Principle

Cardiac event recorder is designed for the diagnostic evaluation of transient cardiac symptoms. The small, portable battery-powered device is capable of storing up to 10 minutes of electrogastrogram (EGG) recording in solid state non-volatile memory. Recently, cardiac event monitors with expanded memory capabilities have been developed, extending



memory from approximately 20–30 minutes. The single channel ECG is recorded by using a two-wire lead set. These devices are event, time-activated, or patient-initiated recorders that are not conventional, continuous Holter recorders, but systems that can provide limited monitoring for a specific type of cardiac event, such as ST segment analysis. These recorders can capture data both during and preceding the symptoms when a patient activates the unit by pressing a button.

Event recorders document and record abnormal beats but provide no analysis. In order to document the abnormal rhythm that precedes the symptomatology, a memory loop can document the abnormal event prior to activation of the system at the time of the symptom. The major advantage of these devices compared with a traditional Holter monitor is that they are small, allow ECG monitoring for longer time periods, and can provide nearly real-time data analysis when the patient transmits a recording related to the symptomatic event.

The event recorders are of two types as follows:

- *Loop memory monitor:* A looping memory recorder (pre-symptom) that is programmed to record the ECG for a preset period of time, such as 5 or 10 minutes. The device captures ECG data; before, during, and after the patient experiences a cardiac symptom through auto-recording, or manually after the patient presses the *Record* button. An auto-trigger event monitor is particularly useful for recording rhythms when symptoms are rare or suspected to occur during sleep. If the person faints and activates the *Record* button after recovery, the ECG will be stored for the time the patient fainted and right after the button is activated. It is a small device about the size of a pager.
- *Symptom event monitor:* The second type of device is a symptom event monitor (post-symptom) that can be either a handheld device or worn on the wrist. These devices do not have chest electrodes for acquiring ECG signal. When a patient feels a symptom such as chest pain, dizziness, palpitations, or irregular heartbeat, the monitor is placed on the chest and the recording button is activated. Two metal discs fixed on the back of the device function as the electrodes. If the monitor is worn on a wrist, activating the *Record* button will store the ECG in memory. Unlike the looping memory monitor, the symptom based devices do not store ECG before it is activated. A typical symptom based event recorder is shown in Figure 148.1.



**Figure 148.1** Cardiac event recorder from OMRON, which can pick up ECG signals by slightly pressing it on the abdomen.

Both types of devices are designed to send recorded ECG in FM-modulated acoustic mode by telephone to a transmission or receiving centre in a hospital or doctor's office or to a central monitoring centre. This normally involves placing the telephone mouthpiece over the microphone on the front of the monitor. The ECG can also be sent wirelessly using a cell phone. Newer cardiac event monitors allow ECG results to be transmitted via e-mail over the Internet. If the ECG shows a serious abnormality, the patient is suitably advised.

Another type of cardiac event recorder is shown in Figure 148.2. This device comprises of an ECG recorder with a two-wire ECG cable and electrodes. The pre-gelled self-adhesive electrodes are attached on the chest of the patient, and the sensed signal is carried to the recorder by using the ECG cable. The device records the ECG data and analyses it for arrhythmias. Usually, the device is programmed to automatically detect arrhythmias such as tachycardia, bradycardia, and atrial fibrillation. The simplest automatic trigger cardiac event monitors detect a single type of arrhythmia, whereas more sophisticated monitors are capable of detecting several types of arrhythmias. The device can be operated for recording ECG manually by pressing the *Record* button. The ECG data is stored in a flash memory. When an event triggers the recorder, either automatically or manually, the ECG data prior to the time until the post-event time is sent to the buffer circuit. The buffer has a capacity to hold up to 16 events with total time of up to 10 minutes of ECG data. The device can then send the ECG data and associated non-clinical information via telephone using FM modulation technique.

An essential function of event recorder is to reliably detect QRS complex, which forms the most important part in ECG signal processing. R wave is one of the main constituent of QRS complex, which helps in determining and diagnosing heart rhythm irregularities and heart rate variability. In fact, the temporal information of each beat and QRS morphology information forms the basis of development of algorithm for arrhythmia detection. Several methods have been reported in literature for reliable detection of QRS complex. These are mostly based on filtering and non-linear transformation and decision rules, as well as using template matching method. Recently, wavelet transform and neural network based algorithms have been developed.

Wearing and using a cardiac event recorder carry no risk and do not cause any pain. However, wearing the patch electrodes over long periods may result in irritation of the skin. The skin irritation generally disappears when the electrodes are removed.

Mobile cardiovascular telemetry (MCT) has been introduced as a noninvasive ambulatory cardiac event monitor with extended memory that is capable of continuous measurement of heart rate and rhythm over several days, with transmission of results to a remote



**Figure 148.2** Cardiac loop recorder (from M/s Vitaphone GmbH, Germany) that uses ECG electrodes to acquire ECG signal.

monitoring centre. MCT is similar to standard cardiac telemetry used in the hospital setting. The ECG results are sent over standard telephone lines to the remote monitoring centre at the end of each day. The physician evaluates both daily and urgent reports. There is evidence that MCT is superior to patient-activated external loop recorders for diagnosing cardiac arrhythmias as well as to auto-triggered external loop recorders.

## Specifications

*ECG channels:* Single channel

*Input dynamic range:* 10 mV

*Input impedance:* 10 M $\Omega$  minimum

*CMRR:* >70 dB

*Frequency response:* 0.05–40 Hz

*Total recording time:* 30 minutes

*Maximum event time:* 5 minutes (300 seconds)

*Data retention:* 10 years minimum

*Transmission:* Via telephone

*Dimensions:* 90 mm  $\times$  54 mm  $\times$  16 mm

*Weight with batteries:* 3.5 oz

## Applications

Event recorder is indicated for diagnostic evaluation of patients who experience transient symptoms such as dizziness, palpitations, syncope, or chest pain to record cardiac activity associated with these infrequent and transient symptoms.

The main purpose of the device is to record cardiac activity during an event or abnormal symptom.

# 149

## Exercise Stress Testing System

### Purpose

Exercise stress test or simply stress test is intended to determine the effect of physical activity on the working of the heart. Since exercise makes the heart pump harder and faster than it would do normally, the exercise stress test can detect problems within the heart that might not be otherwise noticeable during the routine activities. The test can reveal if there is a lack of blood supply through the arteries that supply blood to the heart. Cardiovascular exercise stress testing involving electrocardiogram (ECG) and blood pressure measurements is today considered as one of the most popular tools in the diagnosis and prognosis of cardiovascular disease, particularly coronary artery disease (CAD), and to assess the effects of therapy.

## Principle

Cardiovascular disease is the leading cause of death in most of the countries. So, it is considered advisable to assess the functioning of the heart and examine the seriousness of the CAD. This assessment is made by conducting exercise stress test, which measures the ability of the heart to respond to externally applied stress in a controlled clinical environment. The test is dynamic and involves progressively increasing the exercise intensity and simultaneously measuring the response of the heart in terms of electrocardiography and blood pressure monitoring. There are other parameters, such as echocardiography, radionuclide imaging, and metabolic gas analysis, which can provide additional information that may be required in certain cases.

There are several protocols for conducting the exercise stress test. Two types of exercise stress tests are commonly performed, and they are for assessment of cardiovascular system and cardiopulmonary system. The cardiac stress test can be done by either exercise on a treadmill or pedalling a stationary exercise bicycle ergometer.

### Treadmill Test

A treadmill is an electrically driven machine that allows a wide range of speeds, varying from 1.6 km/h to about 12.8 km/h. It is designed to accommodate a wide range of body weights, at least up to at least 160 kg. Elevation of the moving platform is controlled electronically to provide a variety of settings in about 10 steps, from zero elevation to 20% elevation. The length of the treadmill platform is at least 125 cm and width around 40 cm. Side rails on both sides of the platform are provided for patient safety and stability. In case of emergency, an emergency stop button can be operated readily by the patient or the staff.

When the exercise stress test is conducted, the level of mechanical stress is progressively increased by adjusting the difficulty in terms of speed and steepness of the slope. There are basically two types of exercise protocols used in treadmill tests as follows:

- *The Balke–Ware protocol:* Under this protocol, a constant speed of 3.3 mph (5.3 km/h) is employed with progressive increments in the load every two minutes. This is achieved by increasing the grade or incline of the motor-driven treadmill. The exercising subject therefore walks ‘uphill’ and his own body weight serves as the load.
- *The Bruce protocol:* It uses simultaneous increments in both speed and treadmill grades at intervals of three minutes. The modified Bruce protocol has two warm up stages, each lasting three minutes. The first is at 1.7 mph (2.7 km/h) and a 0% grade, and the second is at 1.7 mph and a 5% grade. This protocol is mostly used in older individuals or in those who have limited exercise capacity due to cardiac disease.

Both the protocols are satisfactory for most clinical purposes as the basic objective is to study as to how well the heart responds to the stress of different levels of exercise. However, they may have to be sometimes modified to suit the condition of the individual being subjected to exercise testing.

The usefulness of the exercise stress test lies in assessing the extent and severity of the cardiovascular disease, and it remains a useful tool in providing the important prognostic information. For cardiovascular assessment, the heart’s electrical rhythms are continuously monitored by displaying and recording ECG. For recording the heart’s electrical signals, pre-gelled electrodes are applied on the chest, legs, and arms. A cuff is placed around the arm to monitor the blood pressure during the test. Simultaneously, the doctor

keeps a watch as to whether the person has symptoms like chest discomfort or fatigue. The person continues exercising until the heart rate (HR) reaches a set target or until the person develops symptoms that do not allow him to continue. Abnormalities in blood pressure, heart rate, or ECG or worsening physical symptoms could point to CAD.

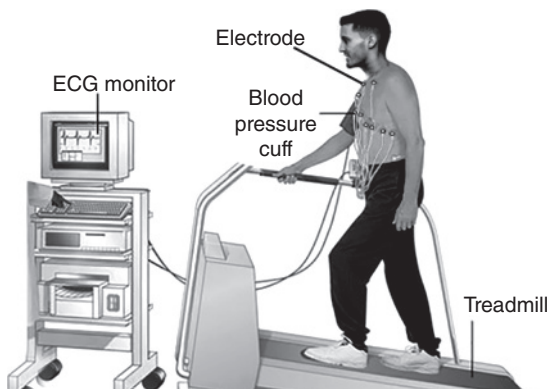
### ***Bicycle Test***

Bicycle ergometer is also popular in some countries for conducting exercise stress test. The speed of the stationary bicycle is usually kept constant, but the resistance is progressively increased. This is achieved mechanically by using a friction belt or brake pads to heavy flywheel. This can also be done electrically by using an alternator or frictionless magnetic system. People who cannot use their legs may exercise with a bicycle-like crank that they turn with their arms. The advantages of bicycle ergometer are that it requires much less space, is quieter, and is generally safer because the risk of falling from the machine is lower than a treadmill. Also, the ECG recording can be done without much motion artefacts.

### ***Instrumentation***

The stress test laboratory is equipped with an exercise device, a PC-based ECG display and recording system, a blood pressure measuring instrument (sphygmomanometer), and a defibrillator. The dynamic exercise is performed by the patient who walks on a treadmill of which the speed and elevation can be adjusted, manually or automatically, to suit a variety of graded exercise protocols. A typical treadmill set up is shown in Figure 149.1. Alternatively, the patient may be asked to pedal an electrically braked bicycle ergometer. Both the treadmill and ergometer are suitable as stand-alone devices for testing purposes. The instrumentation is designed to evaluate the total physiological response of the subject and to ascertain the cardiovascular, respiratory, and muscular fitness status.

***Electrocardiogram*** The changes in the ECG induced as a result of exercise is an important parameter for the diagnosis of CAD. The test involves the recording of the ECG during exercise. Sophisticated algorithms including digital filters and programs



**Figure 149.1** Treadmill exercise testing system for measuring blood pressure and ECG.

for the morphologic recognition have been developed in order to obtain stabilized artefact-free ECG tracings from a moving subject. The system displays in real time three user selectable leads, a reference ECG complex (template), and the current mean beat on which the system detects stress-induced changes. Most treadmills can store and display activity data, transfer it to a PC, and download patient data from the PC.

The principal ECG abnormalities that appear due to exercise that are indicative of ischemic heart that manifests themselves are ST segment depression and ST segment elevation. Automatic measurements of ST level and slope, current, and maximum heart rate are displayed in real time and can be printed as alphanumeric data or as trends.

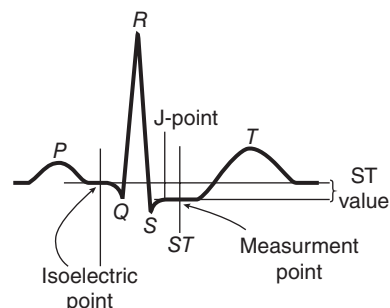
The current standard of determining the ST segment measurement is by measuring the voltage difference between the value at a point 60–80 ms after the J point and the isoelectric baseline. The isoelectric baseline is either between the *P* and *Q* waves (the *P–R* interval) or in front of the *P* wave (the *T–P* interval) as shown in Figure 149.2. It has been observed that the slope of the ST segment significantly influences the abnormal ST shift. Figure 149.3 illustrates normal and abnormal shifts observed in the ST segment. The algorithm used for ST segment monitoring is based on beat detection and classification information provided by multi-lead arrhythmia algorithm. The additional functions performed by the software on the ECG waveforms include filtering the signals, measuring ST values, and generating ST alarms.

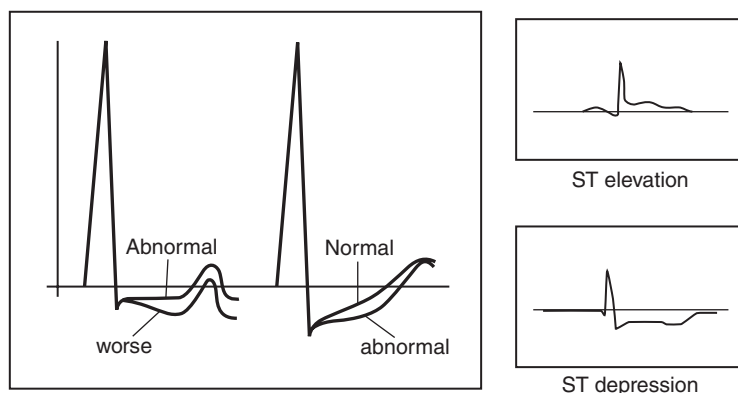
The ST segment is a signal of low amplitude and low frequency content. Therefore, a sampling rate of 250 samples/s is considered adequate. To ensure that the ST segment can be measured accurately, the incoming ECG signals must have a low-end bandwidth of 0.05 Hz to ensure that no signal distortion is introduced in the ST segment. A special ST filter with a higher low-end bandwidth of 0.67 Hz is used to further remove unwanted baseline noise. Since ST segment values do not change very rapidly, every single beat need not be measured. Instead, reliable ST measurement can be extracted using signal averaging techniques. Generally, all QRS complexes detected by the arrhythmia algorithm within a discrete 15 second period are saved and used for ST segment analysis. Statistical analysis techniques are used, and the largest deviation in the value of the ST segment from the reference is selected and displayed.

**Heart Rate** Heart rate is derived from the ECG signal. Significantly slow or rapid changes in heart rate in response to a defined work load imply abnormalities of cardiac function and status of the cardiovascular system.

**Blood Pressure** Blood pressure readings taken before and during the test are important to assist the doctor to determine the state of the subject's heart. The manual method of

**Figure 149.2** ST segment parameter measurement.





**Figure 149.3** ST segment slope evaluation.

measurement of blood pressure is still used in practice. The use is made of a mercury or aneroid sphygmomanometer, although some facilities do have automated blood pressure measuring equipment. Measurements are made prior to exercise and at predetermined intervals thereafter. The readings are usually taken at each level of or grade of exercise.

### **Cardio Pulmonary Exercise Testing**

Cardio pulmonary exercise testing (CPET) is used to evaluate both cardiac and respiratory function. CPET is becoming a routine test in the preoperative assessment of the patients who have to undergo major surgical procedures. The results of CPET assist to assess an individual's risk of perioperative morbidity and mortality and better plan their post-operative care. The test is also advocated in the assessment of fitness level of athletes.

CPET systems involve the analysis of gas exchange at rest, during exercise, and recovery in combination with physiological variables such as heart rate, blood pressure, and ECG monitoring. The integrated results of these test parameters provide a comprehensive assessment of exercise tolerance in respect of ventricular, respiratory, and cellular function, which assists in evaluating cardiovascular and respiratory pathophysiology.

The ability of a subject to perform exercise is directly related to the ability of the cardiopulmonary system to supply oxygen and remove carbon dioxide. These processes depend upon the adequacy of the pulmonary ventilation and gas exchange, gas transport in the blood, and uptake and utilization at a cellular level. CPET evaluates these mechanisms that help in detecting abnormalities that are not apparent at rest. The ventilatory variables that are measured by CPET include oxygen consumption, carbon dioxide excretion, and minute ventilation. By combining these values heart rate and elapsed time, a number of other variables can be deduced. Diagnosis and prognosis of certain abnormalities are determined by comparing the measured values with predicted values of primary and deduced values for different age and sex groups.

$\text{VO}_2 \text{ max}$  ( $V$  – volume,  $\text{O}_2$  – oxygen, max – maximum) testing is employed to measure exercise capacity of a subject, which serves as a monitor for fitness. It is the product of the heart rate, the amount of blood ejected from the left chamber of the heart in a single beat, and the oxygen difference in the arteries and veins. It implies that the ability of the working muscles of a person to use the oxygen in the blood is dependent on the speed and volume of

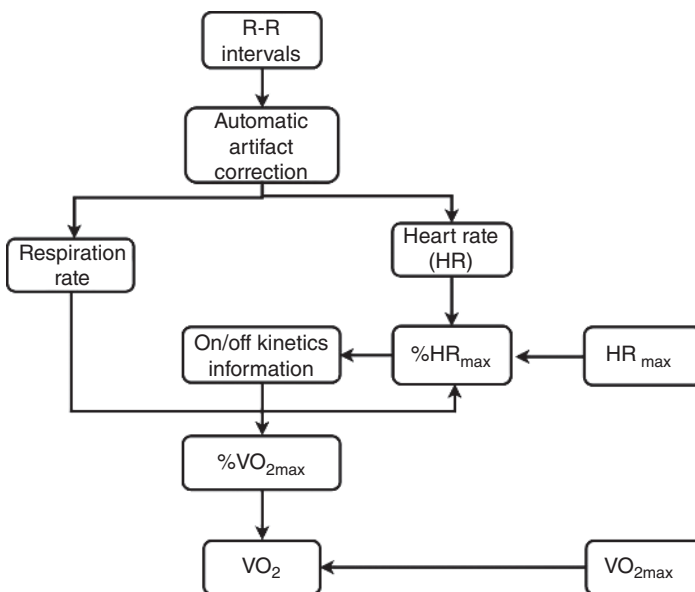


blood pumped by the heart in one minute.  $\text{VO}_2$  max is an objective measure of fitness just as blood pressure and cholesterol numbers are helpful for to identify cardiovascular risk.  $\text{VO}_2$  max is expressed either as an absolute rate in litres of oxygen per minute (l/min) or as a relative rate in millilitres of oxygen per kilogram of body mass per minute (ml/[kg/min]).

It is calculated by the amount of oxygen consumption/minute during an exercise protocol. Oxygen consumption normally rises linearly with the intensity of exercise until a certain point. Gradually, the consumption of oxygen reaches a plateau. This number when the oxygen consumption has reached a maximum is termed as the  $\text{VO}_2$  max. Besides being directly related to the general health status of the cardiovascular system of an individual,  $\text{VO}_2$  max also depends on age, gender, genetics, level, and type of physical training.

CPET is carried out as an outpatient procedure just like in a cardiovascular exercise testing laboratory. Oxygen and carbon dioxide analysers, bicycle ergometer or treadmill on which workload may be modified and heart rate monitor, are essential equipment in the CPET laboratory. The patient walks on a treadmill or sits on a bicycle ergometer and is connected to a 12 lead ECG monitor, blood pressure cuff, and pulse oximeter. For measuring oxygen consumption and carbon dioxide excretion, inspired and expired gases are sampled via a mouthpiece or face mask. The testing begins when the patient starts walking on the treadmill while speed and gradient are increased gradually or when pedalling on the bicycle while the resistance is increased gradually. Oxygen is measured using paramagnetic technology or galvanic fuel cell, while  $\text{CO}_2$  is monitored with non-dispersive infrared technique.

Figure 149.4 shows a block diagram of a system for estimating  $\text{VO}_2$  max, developed by Firstbeat Technologies Ltd. The estimation is based on measurement of HR, beat-by-beat R-R-derived respiration rate, and on/off-response information derived from heart beat data. As a first step, the resting heart rate is determined when the subject is not put



**Figure 149.4** Flow chart of HR-derived  $\text{VO}_2$  estimation. HR(max) = (maximal) heart rate.

to exercise. Then the maximum heart rate is calculated by subtracting the age of the patient from 220. For example, if the age is 40 years, the  $HR_{\max} = 220 - 40 = 180$  bpm. Then calculate the  $VO_2$  max by applying the following formula:

$$VO_2 \max \approx 15.3 \times \frac{HR_{\max}}{HR_{\text{rest}}}$$

Supposing the resting rate is 75 bpm, and the max heart rate is 180 bpm, the  $VO_2$  max =  $15.3 \times 180/75 = 36.72$  ml/kg/min.

Respiration rate and  $VO_2$  have been found to be strongly correlated as respiration rate can distinguish between metabolic from non-metabolic changes in heart rate. Consequently, respiration rate and on/off-response information have been added in the circuit.

## Specifications

*ECG system:* Analysis and display of 12 simultaneous leads

*Storage capacity:* ECG data for at least 500 patients

*Monitor:* Display protocol, stage, clocks for elapsed time, total time, target HR, treadmill speed and grade, premature ventricular contraction (PVC) counts per minute, warning messages and prompts, lead check

*Protocol:* Standard programmable exercise protocols

*Arrhythmia detection:* Automatic arrhythmia detection and documentation

*Treadmill:* Load capacity 160 kg; speed range 0–13.5 mph; elevation 0–25°; minimum 60 in. walking surface with at least 18 in. width

*$VO_2$  measurement:* Oxygen consumption ( $VO_2$  max.), percentage error –3%

$O_2$  measurement accuracy  $\pm 0.2\%$ , range 0–30%

*$CO_2$  measurement:* Range 0–76 mmHg, accuracy  $\pm 2$  mmHg plus  $\pm 5\%$  of reading, flow rate: 50 ml/min  $\pm 10$  ml/min

Breath-by-breath (B  $\times$  B) sampling technique (with face mask) either during exercise or at rest

## Applications

Exercise stress test is performed when the diagnosis of coronary arterial disease is suspected or to determine the physical performance characteristics of a patient. The American Heart Association recommends ECG treadmill testing as the first choice for patients with medium risk of coronary heart disease according to risk factors of smoking, family history of coronary artery stenosis, hypertension, diabetes, and high cholesterol. In addition, oxygen consumption is one of the most commonly assessed variables in the study of exercise physiology and functional assessment of cardiorespiratory performance. It has clinical applications in diagnosis, assessment of adequacy of treatment, and preoperative risk stratification of patients.