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Methodological and Technical Considerations

Evolution of Cardiac Mapping: From Direct Analog to Digital Multi-dimensional Recording

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Summary

Mapping of the electrical activity of the heart started in the late 1870s and has evolved from indirect recordings with a rheotome by Engelmann to highly sophisticated direct recordings of cardiac potentials with multi-terminal electrodes. This chapter mainly focuses on direct recordings from the heart. Developments of cardiac mapping from the rheotome via the string galvanometer and cathode ray tube to computerized digital mapping systems will be followed, and focus will be directed to various aspects that are important for mapping procedures. The advantages and disadvantages of different recording modes will be addressed and the different types of information that are derived from electrograms will be discussed. Ways to obtain three-dimensional information from catheters or multi-electrode arrays will be reviewed, and various other techniques to obtain information about propagation and repolarization of the action potential from the heart are explained.

Introduction

Cardiac mapping involves the recording of electrical activity of the heart at various sites to estimate the electrical status of the heart. The information concerning cardiac conduction and repolarization has both scientific and clinical interest. Earliest systems were only able to record one signal at a time and to obtain information from multiple sites: the recording probe had to be repositioned several times in sequence.

This implies that during its earliest time mapping was only possible in case of a stable rhythm. In the clinical setting, a large number of arrhythmias are indeed monomorphic and sustained and can be mapped in a sequential way using catheter-based systems like the CARTO system (Biosense-Webster, Baldwin Park, CA, USA). However, also for clinical purposes, multi-terminal electrode systems have been developed, allowing mapping of irregular rhythms.

In exceptional cases the display of multiple electrograms, one below the other, can be useful to follow changes in the electrical activity in time. This might be of importance when one is interested in changes induced by rate, drugs or the autonomic nervous system. However, most often data reduction is needed for quick understanding and parameters like activation times or fractionation are derived from the signals. An important hallmark of mapping is the recording mode. Although technically data gathering is not a problem, for analysis the choice of a unipolar or bipolar signal is of importance because certain electrophysiological parameters can only be derived from one or the other (Table 1.1). The type of recording electrode used highly depends on the question to be solved and the spatial resolution needed. A spatial resolution that is too low may result in incorrect information and possibly the wrong decisions for treatment in the clinical setting.

In the following text, developments of mapping are reviewed, characteristics of the different recording modes are discussed, as well as the information that can be derived from electrograms and various recording electrodes, and alternative mapping methods are considered.

Table 1.1 Characteristics of three different recording modes.

Recording mode	Characteristics of electrograms
Unipolar	1 Reveal local + distant activation
	2 Sensitive for 60 Hz interference and remote activation
	3 Accurate activation time estimation
	4 Repolarization time estimation possible
	5 Morphology is direction independent
	6 Interpretation of the morphology is easy
Bipolar	1 Reveal local activation only
	2 Suppresses 60 Hz interference and remote activation
	3 Inaccurate activation time estimation (because of point 5 above)
	4 No information about repolarization
	5 Morphology is direction dependent
	6 Interpretation of the morphology is difficult
Laplacian	1 Reveal local activation only
	2 Suppresses 60 Hz interference and remote activation
	3 Accurate activation time estimation
	4 No information about repolarization
	5 Morphology is direction independent
	6 Interpretation of the morphology is easy

Indirect recordings of the electrical activity from the heart

The first primitive electrocardiogram (ECG) was plotted in 1878 by Theodor Wilhelm Engelmann at the Department of Medical Physiology in Utrecht in the Netherlands with the help of a differential rheotome, an instrument that alternately delivered a stimulus to tissue and measured the resulting current through it (Figure 1.1a) [1–3]. Differential rheotome data obtained by Frederick James Montague Page in the same year were good enough to provide for the first time indirect, global information about the time course of depolarization and repolarization of the myocardium. However, a better instrument was needed, especially a recording one that could provide a direct plot of voltage versus time. Such an instrument, the capillary electrometer, had already been developed a few years earlier by Gabriel Lippman. The function of the capillary electrometer is based on the principle of polarization and surface tension at a mercury–sulfuric acid interface. The mercury column of the electrometer was connected to the patient's chest, whereas the sulfuric acid column was connected to the back. If the potential difference changed, the mercury meniscus moved and its position was observed by a microscope. With this instrument Augustus Desiré Walter recorded the first wave form of heart activity from the body surface (Figure 1.1b). Recordings from the exposed hearts of animals had already been made with

(a)

(b)

(c)
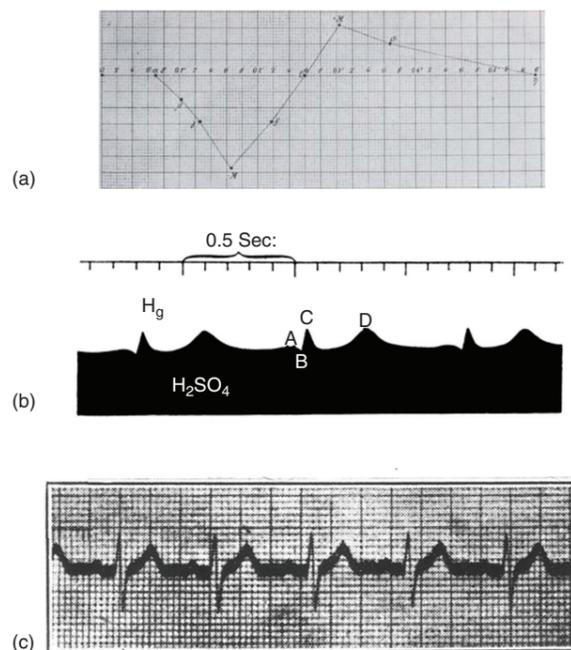
Figure 1.1 (a) The first "electrocardiogram" composed from data recorded with a rheotome and published by T. W. Engelmann in 1878. The potential variations plotted are recorded with a differential rheotome and are an average of 33 measurements. (Adapted from Engelmann TW *Pfluger's Arch Ges Physiol* 1878;**17**:68.) (b) An electrocardiogram recorded with a capillary electrometer by W. Einthoven. (Adapted from Einthoven W *Pfluger's Arch* 1903;**99**:472.) (c) An electrocardiogram recorded by W. Einthoven with a string galvanometer in 1906. (Adapted from Ashikaga H et al. *Circ Res* 2007;**101**:939.)

the capillary electrometer by Engelmann and Page. Electrical sensitivity was sufficient, but mechanics (the inertia of the heavy mercury column) distorted the signal.

Willem Einthoven, who started his research in ophthalmology and respiratory physiology was unsatisfied with the capillary electrometer to study action potentials [4,5]. In contrast to Walter, Einthoven was convinced that the electrogram would be an important aid in the diagnosis of heart disease. He observed how similar the patterns of normal subjects were and how distinctively different the pattern of diseased patients. He therefore felt the need to replace the capillary electrometer by a simpler and more accurate instrument. This led to the use of the string galvanometer, in which a light coil of wire was positioned between the poles of a permanent magnet (Figure 1.1c). Current flow through the coil caused it to be deflected with the flight proportional to the current. The deflections were observed optically. His first design was a huge machine with five people needed to run it. It weighed 250 kg and the electromagnet provided a field strength of 22.000 Gauss and got so hot that it had to be cooled with water. The ECGs he recorded were however of high quality. Apart from devising the instrument, Einthoven

demonstrated the clinical power of the ECG and introduced the equilateral-triangle method (the Einthoven triangle).

The first commercial version of the instrument was made by Sir Horace Darwin, founder of the Cambridge Scientific Instrument Company in England. The first model went to Sir Thomas Lewis at University College Hospital London and was used primarily for research purposes. The principle of string galvanometry and optical amplification to enhance the signal remained in general use for many years until inexpensive cathode-ray oscilloscopes became available in the late 1930s. Until 1932 studies mainly focused on non-arrhythmic abnormalities (bundle branch block, myocardial infarction [MI], the effect of digitalis).

From the instrumentation point of view, the next great advance came in 1920 when vacuum tube amplifiers and oscilloscopes came in more general use. The advantages of electronic amplification and visualization of ECG signals were obvious. Instruments became smaller and transportable. The first commercial instrument in which vacuum tubes and oscilloscopes were used was developed by Siemens and Halske in 1921, but the string galvanometer remained in use in the UK until the 1940s.

Direct recordings of the electrical activity from the heart

Up until the 1950s very few experiments were carried out to obtain an accurate analysis of the activation in the different layers of the ventricular wall, mainly because of the fact that the string galvanometer and direct-writing pen equipment were too slow to allow exact studies of time relationships. To circumvent these problems, Durrer and van der Tweel developed a recording system that was equipped with two pairs of cathode-ray tubes, one pair for photographic registration and the second pair used for continuous visual observation. The system had a bandwidth of about 3 kHz and a noise level of 10 mV rms [6]. Direct recordings were made in canine hearts with needle electrodes consisting of eight terminals and impaled into the left ventricular wall. Recordings were made sequentially with a switch box that allowed every required combination of electrodes onto each of the two recording channels. A similar system with a high fidelity recording system and a fast running film was used by Jouve *et al*. [7] to determine epicardial activation in man. In their classic study about total excitation of the human heart, Durrer *et al*. [8] recorded electrograms on a 14-channel Ampex physiological tape recorder and used an 8-channel oscilloscope for monitoring. For analysis the signals were played back from the tapes at a lower speed and the electrograms were printed out on an Elema ink writer. Final time resolution was better than 1 ms.

The introduction of semiconductor technology has dramatically accelerated the miniaturization of recording sys-

tems, and the rising use of computers made analysis of electrograms easier and more accurate. The development of computer technology made it possible to simultaneously register electrograms from multiple sites with sufficient temporal and spatial resolution to visualize individual activation fronts during propagation and their repolarization patterns.

The first intraoperative cardiac activation mapping was applied by Lewis and Rotschild in 1915 using a roving prove (a single hand-held probe) positioned at several sites in sequence [9]. The drawback of this technique is that it is a time-consuming procedure it is impossible to map non-periodic rhythms such as polymorphic ventricular tachycardias (VTs) and ventricular fibrillation (VF) and that positioning of the electrode at predefined distances is often difficult to perform.

Multi-channel mapping systems

A variety of mapping systems for clinical purposes are available today. The number of channels they can handle is usually less than 100. Although these systems can record multiple channels simultaneously, they usually use one catheter for mapping, meaning that it is a sequential recording technique like, for instance, the CARTO system (Biosense-Webster, Baldwin Park, CA, USA). The newest CARTO systems can however record multiple electrograms simultaneously. Multi-channel systems like the EnSite system (St. Jude Medical, Inc., St. Paul, MN, USA) record 64 signals simultaneously, but use a non-contact mapping catheter. Electrograms at the endocardium are calculated using an inverse procedure.

Several sophisticated electrophysiological mappings systems with more than 200 channels for experimental and clinical use are commercially available nowadays. The UnEmap system (Uni. Services, Ltd, Auckland, New Zealand) has been developed by the Auckland Bioengineering Institute of the University of Auckland in New Zealand. This is a versatile mapping system that allows both electrical mapping and pacing. Although the base unit comprises 448 channels, the number of channels is virtually unlimited. The system has unipolar or true bipolar inputs and a sampling rate of 1–5 kHz. Analog signal conditioning, like gain setting, filter setting and stimulation facility can be set separately for individual channels. The system further includes specialized electrodes and software designed for processing, analysis and display of a large number of data channels.

Another system that is frequently used for cardiac mapping, both from the body surface and directly from the heart is the ActiveTwo system from BioSemi (Amsterdam, the Netherlands). This mapping system has a basic configuration of 256 channels (+ 8 auxiliary channels) all housed in a single ultra-compact box (size $120 \times 150 \times 190$ mm, weight 1.1 kg) and is expandable to 512 channels. The system uses

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a 24 bit A/D converter for each channel, which provides a high dynamic range, allowing true DC measurements. The sample rate ranges from 2 to 16 kHz per channel, depending on the number of channels to be acquired. Acquisition is done with a personal computer via an USB 2.0 interface connected to the mapping system. Special software allows display and acquisition of the signals as well as signal conditioning (unconditioned DC data are however stored). Data analysis might be done by MapLab, an experimental software package for multi-channel ECG-recordings and developed by Mark Potse [10]. The ActiveTwo system is battery operated and can record 256 channels continuously for 5 hours on fully loaded batteries.

A similar system is provided by TMS International. The REFA system from TMSI (Oldenzaal, the Netherlands) can handle up to 272 channels and uses a 22- or 24-bit A/D converter for true DC recordings. The sample frequency ranges from 2 to 20 kHz and the box size is 210 × 360 × 92 mm for 136 channels.

Multi-terminal electrodes

To study the activation pattern of polymorphic tachycardias and fibrillation, a simultaneous recording technique is a prerequisite and multi-terminal electrode systems are needed. Electrode arrays like epicardial sock and plaque electrodes, endocardial balloon electrodes and intramural needles were the first multi-terminal electrodes used for cardiac mapping [11]. These electrodes were custom-made and used to perform epicardial, endocardial or intramural mapping.

A great variety of multi-terminal electrodes have been developed over time by various research groups with form, size and number of electrode terminals depending on the research question to be answered or treatment strategy to be followed (Figure 1.2). Flexible or ridged grid electrodes have been designed for epicardial and endocardial mapping. Flexible electrodes are required if large areas of the heart have to be covered; for small areas ridged electrodes might be sufficient. Flexible electrodes usually consist of a silicon rubber sheet or cast, in which the electrode terminals are embedded.

The construction of large electrode arrays with more than 100 electrode terminals is tedious by using classic techniques and often yields irregular electrode spacing. Modern construction techniques are less time consuming and use, for instance, fine pitch, isolated, copper ribbon cables or flexible printed circuit flat cables that are assembled together, such that the active surface is the cut end of the cable. In this way multi-electrodes with spacings <200 μm have been made with up to 400 electrode terminals [12]. Photolithographic manufacturing processes have been applied as well. Electrodes are present on flexible polyimide foil or printed circuit board foil [13]. For endocardial mapping of the entire endo-
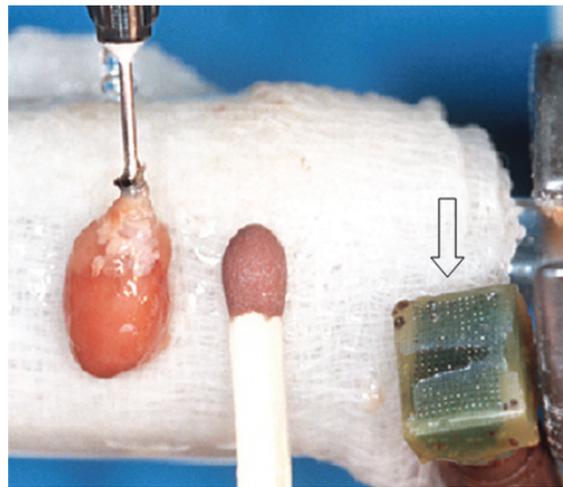
Figure 1.2 High resolution multi-electrode (open arrow) harboring 247 electrode terminals at interelectrode distances of 0.3 mm and used for epicardial mapping of a Langendorff perfused mouse heart (at the left). The electrode has been constructed using conventional techniques and consists of silver wires (diameter 0.1 mm) embedded in epoxy resin and isolated except at the tip.

cardial surface, silicon balloon electrodes and basket electrodes have been developed and applied. The balloon electrode requires an empty cavity and therefore is used only in isolated, Langendorff-perfused hearts or during extracorporal circulation. The balloon electrode has been used frequently in the past during antiarrhythmic surgery in patients with VT due to remote MI [14]. For experimental endocardial mapping of the atria, ridged electrodes can be used, consisting of a cast of the atrial cavity with embedded electrodes. Such electrodes are usually custom-made (Figure 1.3).

Catheter-based multi-electrodes

Several catheter-based multi-electrodes have been developed in the past and are still being developed, usually by industry. The basket is a catheter device harboring eight splines with eight electrode terminals on each spline. The basket is inserted into the cavity in a non-deployed condition using a sheath. If the basket is positioned at the right position in the cavity, the sheath is withdrawn and the basket deployed. This device allows the recording of 64 endocardial electrograms simultaneously and has been used to guide ablation of atrial flutter and to determine the arrhythmogenic area of VTs [15,16]. For the atrium, several special multi-terminal catheters have been developed for the rapid assessment of focal and reentrant arrhythmias and areas with complex fractionated electrical activity. Jones *et al*. [17] describe the use of a high density catheter with 20 poles with a distal spiral configuration (7-F shaft, 4-F spiral ring). The electrode is deployed in the appropriate chamber through a long sheath. An alternative electrode system, especially
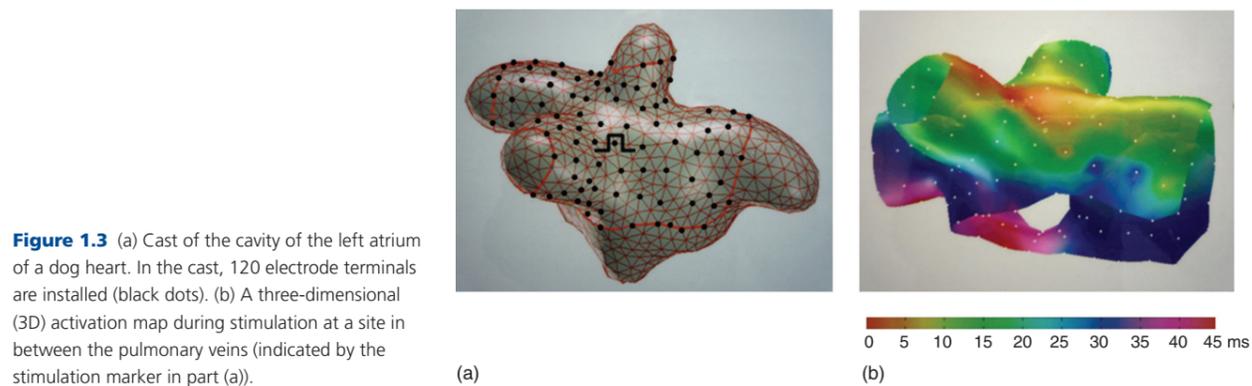
Figure 1.3 (a) Cast of the cavity of the left atrium of a dog heart. In the cast, 120 electrode terminals are installed (black dots). (b) A three-dimensional (3D) activation map during stimulation at a site in between the pulmonary veins (indicated by the stimulation marker in part (a)).

(a)

(b)

0 5 10 15 20 25 30 35 40 45 ms

for the atrium is the 20-polar PentaRay catheter (Biosense-Webster, Baldwin Park, CA, USA). This mapping catheter has five soft radiating splines, with four 1 mm electrode terminals per spline and a 4 mm inter-electrode spacing. The electrodes cover an area of approximately 9.6 cm^2 [18,19].

Unipolar versus bipolar recordings

One common problem in all mapping systems is the choice of the recording mode, which, in its simplest form is unipolar or bipolar [20]. In the unipolar mode, the recording (different) electrode is located at the site of interest on the heart and connected to the positive input of a differential amplifier, whereas the indifferent electrode is located far away from the heart (theoretically at infinity). This electrode is connected to the negative input of the differential amplifier. In bipolar mode, the different and indifferent poles of the electrode are positioned close together (usually the distance between the poles is in the millimeter range). If the poles are close together, the bipolar signal approximates the first derivative of the unipolar signal, which takes into consideration that there are important differences between the unipolar and bipolar mode. The derivative of a signal results in a reduction of the low frequency components in the signal. A wave front distant from the recording site will generate low frequency components in the unipolar signal, because the signal will change only marginally if the front moves. If the distance between an activation front and the recording site is small, the recorded signal will change rapidly, resulting in high frequency components in the signal. Thus, for unipolar recordings, low frequency components refer to remote wave fronts, whereas high frequency components refer to local wave fronts. The bipolar mode will filter out the low (remote) frequency components and retain the high frequency (local) components. Thus, a major difference between the two recording modes is that unipolar electrograms contain information of both local and distant activation, whereas bipolar electrograms mainly reflect local activation. Because we are frequently interested in the (local)

activation time at the recording site, the bipolar recording seems to be preferable. However, bipolar recordings have several disadvantages: (i) the signal is dependent on the direction of the wave front and activation fronts running parallel to the line between the poles do not generate a signal; (ii) deriving activation times from bipolar signals is problematic because of the direction dependence and the differentiating nature of the electrode; (iii) interpretation of the configuration of the bipolar electrogram is difficult, in contrast to the unipolar electrogram, where a biphasic deflection refers to a passing wave front, a negative deflection to a site where activation is initiated and a negative deflection to a site where activation comes to an end [21].

The dilemma of the choice between unipolar and bipolar mode can best be solved by recording them both simultaneously, which is not a problem with current technology. Unipolar and bipolar recordings provide independent information (Table 1.1): unipolar recordings provide local and remote activation as well as accurate activation times, whereas bipolar recordings provide accurate local activation. Thus, the bipolar signal shows you which part of the unipolar signal is local and that allows an accurate determination of the activation time (Figure 1.4a). If grid electrodes are used with fixed distances between the poles, bipolar signals can easily be constructed mathematically from the recorded unipolar electrograms. Combined unipolar and bipolar electrogram criteria have also been used to evaluate the transmurality of atrial ablation lesions [22]. In addition, unipolar electrograms allow determination of (local) repolarization times.

The Laplacian recording mode

A modification/extension of the bipolar recording mode is the Laplacian mode [23]. The Laplacian signal is calculated as the difference between the signal at the target electrode and the weighted sum of surrounding electrodes at equidistant. In a regular grid, this can easily be done mathematically for all terminals (except at the rim of the electrode) if

(a)

(b)
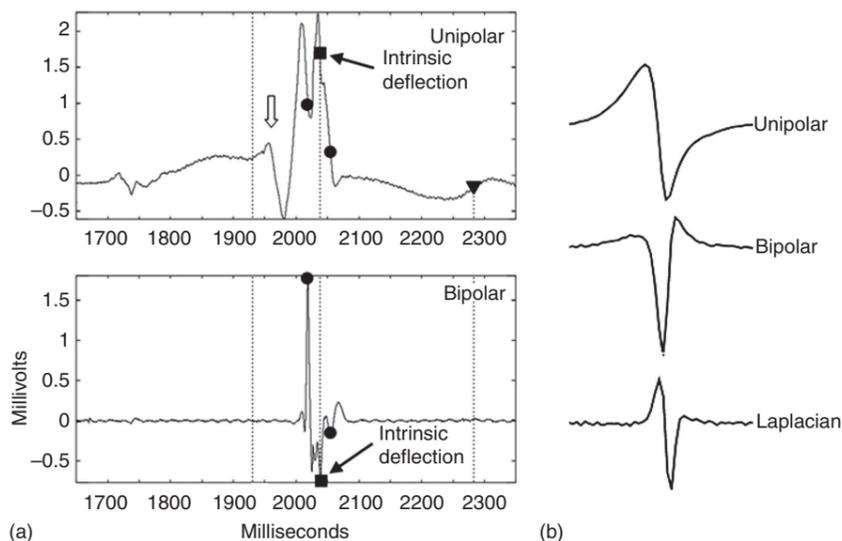
Figure 1.4 (a) Simultaneous recording of a unipolar (upper tracing) and bipolar (lower tracing) endocardial electrogram from the human right ventricle. The black square in the upper panel is the activation time in the unipolar electrogram and corresponds with a sharp (local) deflection in the bipolar electrogram (black square). Black dots in the unipolar recording are local deflections as verified by the bipolar deflections. The deflection marked by the open arrow in the unipolar recording is remote (not present in the bipolar recording). The deflection marked by the black triangle is the T-wave which consists of low frequency components and therefore is not visible in the bipolar recording. (b) Morphology of a unipolar, bipolar and Laplacian recording at the same location.

unipolar signals are recorded. It can be shown that the Laplacian is the second derivative of the unipolar signal and reflects the local (at the center electrode) transmembrane current. The morphology resembles that of the unipolar electrogram, but the deflection is sharper because of the second derivative (Figure 1.4b). The signal is independent of the direction of the wave front in the plane of the electrode; only wave fronts that proceed perpendicular to that plane do not generate a signal. To be independent of the wave front in all directions, a configuration with needle electrodes is required. A comparable recording mode is obtained by the coaxial electrode, which consists of a central electrode surround by a circular one [24]. The ring serves as the reference electrode and is connected to the negative pole of the amplifier. As with the Laplacian, the ring gives the mean of the signals around the central electrode and therefore cancels the dependence of the direction effect of the electrode.

Information extracted from extracellular electrograms

Although the display of a large number of electrograms, one below the other, can provide some insight into the activation process (Figure 1.5), crucial information, like spatial information, will be lost. Therefore, special features are usually derived from the electrograms.

Signal morphology: mono- and biphasic, double potentials, fractionation

Interpretation of the morphology of unipolar electrograms is usually straightforward in contrast to bipolar electrograms. An activation front that approaches the recording site will generate a positive deflection if unipolar signals

(a)

(b)
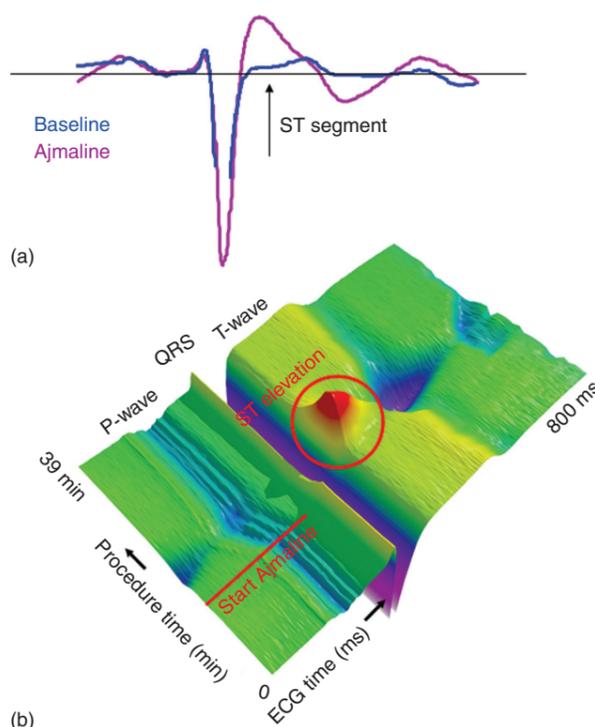
Figure 1.5 (a) Electrocardiogram during base line (blue tracing) and peak ajmaline (purple tracing). (b) Electrocardiogram map of a Brugada syndrome patient before and after application of ajmaline, a sodium channel blocker. After application of the drug, ST-segment elevation occurs (marked by red circle). Electrocardiogram sections of 800 ms are plotted one behind the other and clearly illustrate the increase and decrease of the ST segment following ajmaline application.

are recorded, whereas a receding front induces a negative deflection. This feature of the unipolar mode results in a single negative deflection at sites where activation is generated (origin of activation), a biphasic deflections (positive followed by negative) at sites where an activation front passes and a positive deflection only if activation comes to an end. These characteristics are valid for normal myocardium; heart disease may make the signals more complex. Nevertheless, morphologic changes may be helpful to derive important information. As shown already by Durrer and co-workers in 1964 [25], electrograms recorded from transmural chronic MI have a characteristic unipolar morphology consisting of QS complexes of which the size depends on the transmurality of MI.

The ST-segment is of interest because an elevation or depression may refer to ischemia. However, sites where activation is blocked but current flow is still possible, as is the case at sites with current to load mismatch, ST-segment elevation may occur as well. This has been suggested as a mechanism for the ST-segment elevation as it occurs in Brugada syndrome [26]. Asynchronous activation may give rise to double or fractionated potentials. If activation proceeds out of phase at two sites of an electrical barrier, double potentials will arise [27]. If multiple electrical barriers are present and activation proceeds asynchronously between the barriers, electrograms may become fractionated, meaning that the signal consists of multiple deflections. Histologically, fractionation refers to abnormal myocardial tissue consisting of an intermingling of fibrotic and myocardial strands. Areas of abnormal slow conduction induced by cardiac remodeling may generate deflections occurring late after the QRS complex. These defections are called late, diastolic or isolated (late) potentials.

Activation maps

Activation maps are most widely used to characterize the electrical status of myocardium and are constructed from activation times. As explained before, these are most accurately derived from unipolar electrograms, although a simultaneously recorded bipolar electrogram can be helpful to select the local deflection in the unipolar electrogram. Two- or three-dimensional (3D) activation maps can be constructed from activation times if the spatial distribution of the electrode terminals is known. For multi-terminal electrode systems the terminal distribution is fixed, whereas catheter systems are frequently equipped with a catheter tracking system providing the 3D coordinates of the different recording sites (LocaLisa, St. Jude Medical, Inc., St. Paul, MN, USA; CARTO, Biosense-Webster, Baldwin Park, CA, USA) [28,29].

Potential mapping

Activation maps provide a powerful tool to detect important characteristics of cardiac arrhythmias, like the site of origin or areas of conduction delay/block, which may be of relevance in the clinical setting to combat the arrhythmias by ablation. However, the construction of activation maps requires the induction of the arrhythmia, which is often not tolerated hemodynamically by the patient. Because of this, potential mapping has been introduced, which involves mapping of the myocardium during sinus rhythm. Recordings are made in bipolar mode to detect local deflections only. Amplitudes of the signals are displayed to detect areas with low voltage amplitudes, which are considered potentially arrhythmogenic. In addition, late potentials during sinus rhythm are important targets as they may refer to sites with impaired conduction. [20].

Activation recovery interval

Action potential duration is another parameter that might be of importance for arrhythmogenicity. Prolonged action potential duration and heterogeneity in the duration has been associated with increased vulnerability for arrhythmias. Estimation of action potential duration requires intracellular measurements, which are difficult to obtain in the clinical setting. As a substitute, the activation recovery interval has been proposed that can be derived from unipolar extracellular electrograms. This interval comprises the distance from the activation time till the time of repolarization. There has been much debate about the way the time of repolarization has to be measured. Theoretical considerations and experiments indicate that the point of fastest upstroke in the T-wave is the time that marks the time of local repolarization [30]. The down-stroke of the T-wave refers in fact to remote repolarization and should therefore not be used. In practice this means that a number of recordings, those with a positive T-wave or no distinguishable T-wave at all, cannot be used for analysis and must be discarded. An alternative methodology is the application of the monophasic action potential catheter.

Three-dimensional patterns

Because the heart is a 3D structure, activation in 3D is often needed. To obtain a 3D pattern, electrograms need to be obtained from epicardial endocardial and intramural sites. This requires the use of needle electrodes. The technique of intramural recording was already used by Durrer and coworkers in 1953 [6]. However, their recording technique was a sequential one, requiring a constant rhythm, whereas a simultaneous recording is needed to study ectopic beats, polymorphic VTs and fibrillation. The number of electrode terminals increases, however, when going from two-dimensions to 3D with a factor of n, if n is the number of intramural planes to record from. Not counting the costs, the number of channels is no real limitation today to make 3D presentations of heart activity.
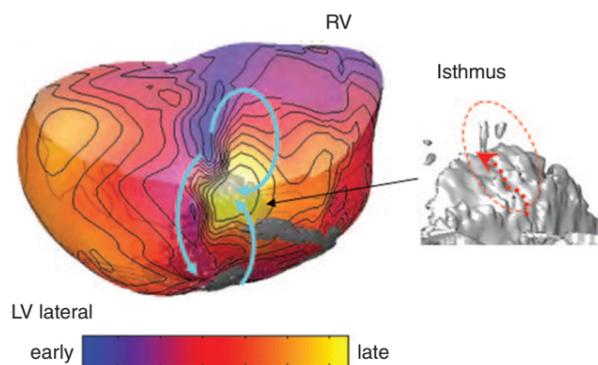
Figure 1.6 Epicardial reentry through scar tissue in a dog heart. Infarcted myocardium was determined by gadolinium-enhanced magnetic resonance imaging (MRI). The possible tract of the reentry circuit in the infarcted area is indicated by the red arrow in the inset at the right. (Adapted from Ashikaga H, *et al. Circ Res* 2007;**101**:939–47.)

Integrative approaches

Current technology allows the combination of different techniques to obtain various types of information from the same patient, simultaneously or sequentially. Electroanatomic mapping is one of the earliest developments in which anatomy of the heart and electrical activity are determined simultaneously [31,32]. Three-dimensional electrophysiological data derived from local or calculated electrograms is integrated with anatomic information derived from the electrode locations at the endo- or epicardium. Electrophysiological data comprises activation maps, voltage distribution and fractionation of electrograms. In addition local and remote components can be derived from unipolar electrograms. Combination of this technique with magnetic resonance imaging (MRI), computed tomography (CT) or high-quality 3D ultrasound images may help to correlate electrophysiological data with visualized scar tissue and fiber orientation (diffusion MRI) [33,34]. Gadolinium-enhanced MRI is a powerful tool to estimate areas with collagen and, together with electrical data, might be helpful to assess arrhythmogenic areas. Magnetic resonance-based visualization of scar morphology may be helpful to facilitate ablation procedures (Figure 1.6) [35,36]. In addition, MRI offers the possibility to determine ventricular dyssynchrony and its relation to electrical activity.

Alternative mapping techniques

Although mapping of the electrical activity using electrodes on or in the heart is most widely used, there are several other techniques to obtain information about the electrical status of the heart.

These include *optical mapping*, which uses potential sensitive dyes that are incorporated in the membrane of the cardiomyocytes and vary the intensity of fluorescence in dependence of the value of the membrane potential. However, this technique is only applicable in the experimental setting on animals and is often restricted to epicardial and/or endocardial mapping [37]. Creating a wedge allows for transmural information of a selected region.

Magnetic imaging is another technique that determines the magnetic field generated by the activation currents using a superconducting quantum interference device (SQUID). This device, which is able to detect magnetic fields lower than 0.1 pT, can detect the activity at the epicardium of the heart and is sensitive enough to detect the magnetic field at the body surface [38]. This technique is not easily applicable in the clinical setting for direct mapping of the heart because magnetic-shielded rooms are required. Recently developed techniques try to determine the electric field generated by the heart using *electric potential sensor* (EPS) technology [39]. This technology is capable of monitoring the electric field outside the heart without a contact electrode. The EPS consists of an electrometer grade operational amplifier with external bias circuitry designed so that it does not compromise the input impedance of the sensor. It records the displacement current only through weak capacitive coupling. The capacitive coupling may take the form of either an air gap or a dielectric spacer.

Conclusion

In this chapter, we followed the development of the recording of the electrical activity of the heart from indirect techniques, such as the rheotome, to highly sophisticated 3D computerized mapping systems. From a technical point of view there are no limitations with regard to the number of electrodes to be used. Computerized mapping systems are able to handle an unlimited number of channels and modern technology makes electrode constructions for large electrode arrays possible. Along with activation times, a variety of other parameters for the analysis of electrograms have been developed, although the exact interpretation is still debatable in a number of cases. Fractionation of electrograms is often used and, although fractionation points to abnormal myocardium, the role for induction or perpetuation of AF is still not completely clarified. Although other mapping techniques are being developed and might be interesting and applicable in the experimental situation, the combination of electrophysiological mapping with structural and functional parameters is the greatest challenge in the clinical setting.

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