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Endobronchial Ultrasonography: An Overview

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Introduction

Endobronchial ultrasonography (EBUS) is a diagnostic modality whereby a miniature ultrasonic probe is introduced into the bronchial (tracheal) lumen, providing tomographic images of the peribronchial (peritracheal) tissue. Endoscopic ultrasonography (EUS) is an established, indispensable technique for examining the gastrointestinal tract, particularly the stomach and large intestine. The applications of EUS include assessment of the depth of tumor invasion, detection of lymph node metastases, tumor staging, and fine-needle aspiration (FNA) under EUS guidance.

In 1988, Pandian et al. [1] were the first to report the clinical use of a narrow-gauge ultrasonic probe for intravascular ultrasonography. In 1990, EBUS was first mentioned in the study by Hürter et al. on EBUS of the lung and mediastinum. Since then, research and development in this field have been primarily conducted by Becker (Germany) and us (Japan).

Typically, radial EBUS probes are of the 20 MHz radial type. Therefore, tissue penetration of the ultrasound waves is of the order of approximately 2–3 cm; in other words, EBUS provides a tissue cross-section image with a

radius of approximately 2–3 cm centered on the trachea or bronchus.

Some important EBUS studies are:

- Hürter and Hanarath [2]. Endobronchial sonography in the diagnosis of pulmonary and mediastinal tumors (in German).
- Iizuka et al. [3]: Evaluation of airway smooth muscle contractions in vitro by high-frequency ultrasonic imaging.
- Ono et al. [4]: Bronchoscopic ultrasonography in the diagnosis of lung cancer.
- Goldberg et al. [5]: US-assisted bronchoscopy with use of miniature transducer-containing catheters (delineation of central and peripheral pulmonary lesions).
- Becker [6]: EBUS – a new perspective in bronchology (tracheobronchial wall seven-layer structure).
- Kurimoto et al. [7]: Assessment of usefulness of EBUS in determination of depth of tracheobronchial tumor invasion (tracheobronchial wall five-layer structure).

Based on these studies, the current applications of EBUS are as follows:

- Determination of the depth of tumor invasion of the tracheal/bronchial wall (allocation of patients to localized endobronchial treatments such as photodynamic therapy).

- Identification of the location of a peripheral lung lesion during bronchoscopic examination (more accurate than fluoroscopy in determining contact between lesion and bronchus, thereby reducing abrasions, the time to determine biopsy sites, and duration of fluoroscopy).
- Qualitative diagnosis of peripheral lung lesions and differentiation between benign and malignant lesions.
- Determination of position and shape of peribronchial structures, particularly lymph nodes (at the time of transbronchial needle aspiration).
- Determination of the spatial relationship between bronchus and lesion in the short-axial image of the bronchus (if the bronchus is situated near the center of the lesion, the lesion might have arisen from the bronchus).

Issues arising from the application of EBUS to date and the results of studies include the following:

- Standardization of how the layers in the tracheobronchial wall structure are interpreted (how many layers are seen).
- Changes in the layer structure of the tracheobronchial wall with the use of higher frequencies (e.g. 30 MHz).
- Evaluation of the qualitative diagnosis accuracy and differentiation between benign and malignant lesions from EBUS images of peripheral lung lesions.
- Evaluation of peribronchial lymph node metastases.
- Complications of EBUS-guided transbronchial needle aspiration (TBNA).
- Technique of needle aspiration from the esophagus using the convex bronchoscope.

EBUS facilitates examining the state of the bronchial wall and extramural tissue that cannot be visualized with bronchoscopy alone. This book will present an overview of EBUS with reference to actual clinical cases.

Principles of Ultrasonography

What Is a Sound Wave?

Definition of Ultrasound

Typically, ultrasound refers to sound wavelengths >20 MHz that cannot be heard by the human ear. Because considerable variations exist in the range of frequencies audible to humans, we often define sounds in terms of their purpose. In this case, ultrasound is “sound not intended for humans to hear.”

Frequency and Wavelength

The frequency of a sound tells us whether it is high or low in pitch. The unit of frequency is hertz (Hz), defined as the number of oscillations per second. For example, a sound with a frequency of 20 MHz has 20×10^6 oscillations per second. Medical ultrasonography equipment produces sounds with a frequency range of 2–50 MHz. Wavelength is the length of a soundwave, and it varies inversely with frequency; thus, the higher the frequency, the shorter is the wavelength (Figure 1.1).

Speed of Sound

Sound travels through various materials, such as air and water (hereafter media), and the speed at which it travels through each medium is the speed of sound for that medium. The speed of sound through the human body is generally considered to be 1530 m/s, although the actual speed of passage varies for different organs and tissues.

Production of Ultrasound Images

Transmitting and Receiving Ultrasound Waves

Ultrasonic probes used in medical ultrasonography comprise a sensor that transforms electrical signals into ultrasound and vice versa. When an electrical signal is applied to an electrode of an ultrasonic transducer (also known

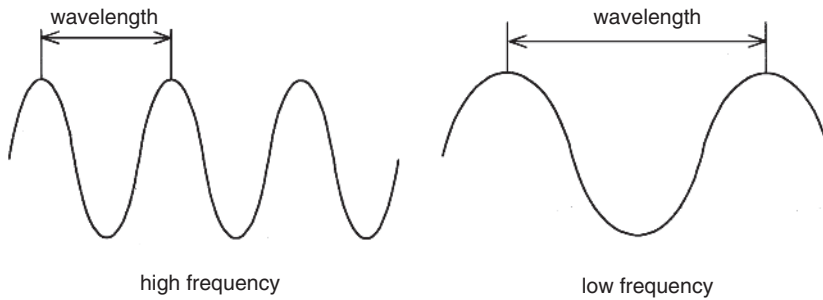


Figure 1.1 Correlation between frequency and wavelength.

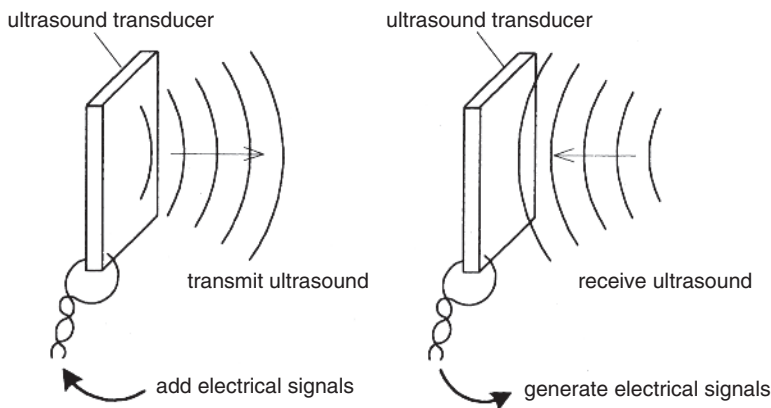


Figure 1.2 Transmitting and receiving ultrasound waves.

as an oscillator/transformer), ultrasound waves are transmitted from the device surface; when ultrasound waves are received by the device surface, an electrical signal is generated (Figure 1.2).

Propagation and Attenuation of Ultrasound Waves

Ultrasound waves produced by an ultrasonic transducer travel through a medium – called propagation. As the soundwave is propagated, the energy of its oscillations is absorbed and scattered, thereby weakening steadily; this phenomenon is called attenuation. Typically, the higher the frequency, the higher is the attenuation rate. Medical ultrasonography equipment uses high frequencies that do not propagate well through the air owing to the high attenuation ratio. Hence, a medium such

as water is required between the ultrasonic transducer and the study object to allow the efficient propagation of ultrasound waves.

Reflection and Penetration

As with light, a proportion of ultrasound waves is reflected at the boundary between different media, and a proportion penetrates the boundary; the ultrasonic processor uses these reflections to construct images.

The ultrasonic transducer emits ultrasound pulses and receives ultrasound pulses reflected from the boundaries between media (Figure 1.3). In addition, the ultrasonic processor evaluates the positions (distance from the probe) of boundaries between media based on the time between transmitting and receiving ultrasound pulses and converts the strength of returning pulses into the brightness of the image.

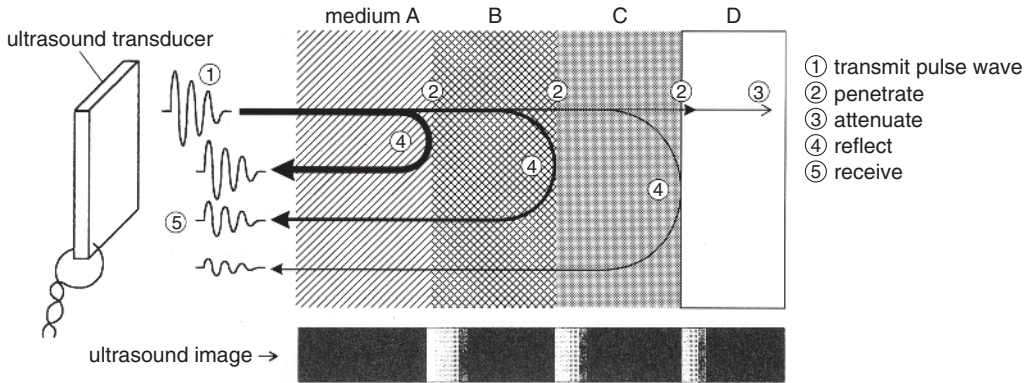


Figure 1.3 How an ultrasound image is made.

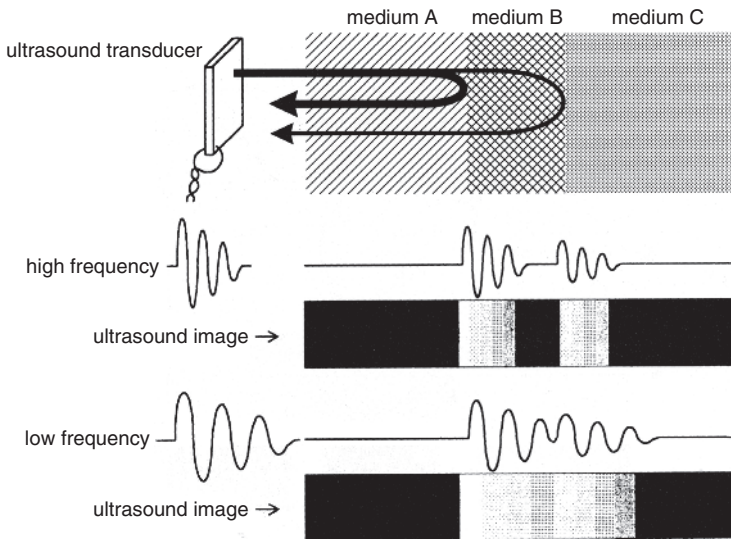


Figure 1.4 Difference in axial resolution between different frequencies.

Following these steps alone offers information about a body along a single line; thus, we obtain a two-dimensional image by moving the ultrasonic transducer (mechanical scanning) or using a linear array of multiple ultrasonic transducers that sequentially emit and receive ultrasound pulses (electronic scanning). This method of ultrasound imaging is called B-mode (B stands for brightness).

Resolution

Axial Resolution

Because an ultrasound pulse wave has a definite length, the boundary between media has a definite width on an ultrasound image. If the

distance between the two boundaries of a medium is decreased, the pulse waves from the two boundaries will overlap, making it difficult to distinguish the two boundaries on the ultrasound image. The ability to distinguish objects on an ultrasound image is called resolution, and the resolution in the direction traveled by the ultrasound pulse is the axial resolution. Typically, higher the frequency, shorter is the ultrasound pulse; thus, distance resolution improves with higher frequencies (Figure 1.4).

Lateral Resolution

Resolution in the direction perpendicular to the direction traveled by the ultrasound pulse, in other words in the direction the probe moves

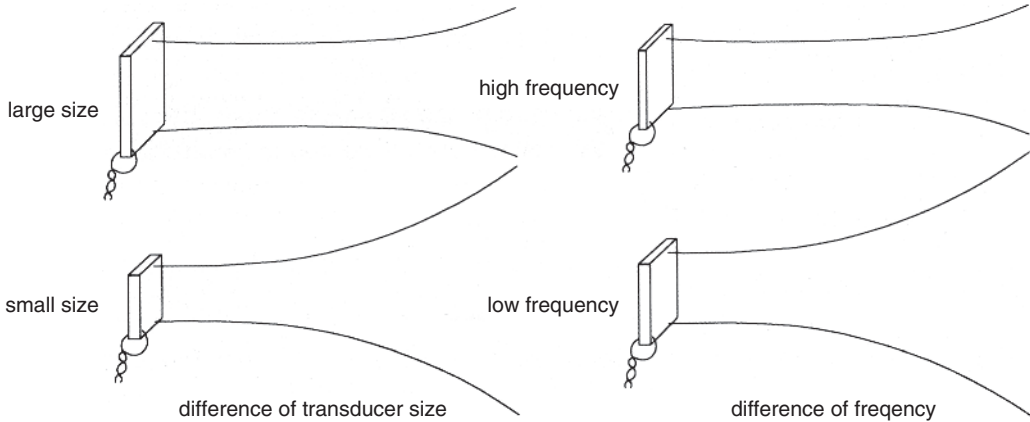


Figure 1.5 Pulse wave spreading.

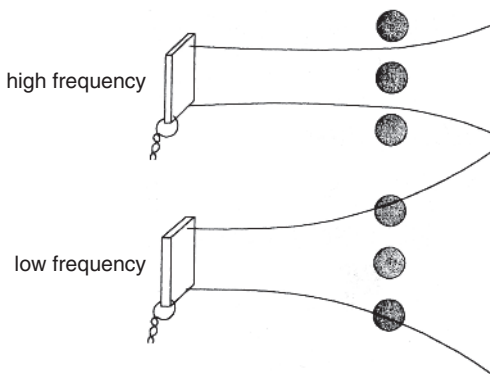


Figure 1.6 Lateral resolution.

or the direction of the array of transducers, is called lateral resolution. The ultrasound pulse wave emitted by a transducer gradually spreads out as it propagates through a medium. The degree of spreading depends on the transducer size (aperture area) and frequency. As the transducer size or frequency increases, the degree of spreading decreases (Figure 1.5). Lateral resolution improves with decreased spread (Figure 1.6).

Depth Penetration

Because ultrasound waves attenuate as they propagate through a medium, they can only reach a certain distance. Hence, ultrasound images can only be attained for a certain distance from the ultrasonic probe; this distance is called the depth penetration (or

penetration). In addition, the depth penetration depends on the frequency and transducer size (aperture area). Because the attenuation rate of an ultrasound wave increases as its frequency increases, the depth penetration improves as the frequency decreases (Figure 1.7). As the aperture area of the ultrasonic transducer increases, it can emit a stronger pulse and can also convert weaker received pulses into electrical signals. Hence, the depth penetration increases as the transducer size increases.

Image Quality Adjustment

Despite using an ultrasonic probe appropriate to the task, its abilities cannot be completely harnessed unless appropriate image quality adjustment is performed. The fundamentals of image quality adjustment are gain, contrast, and sensitivity time control (STC).

Gain

Gain, also called brightness, is the mechanism for adjusting the overall brightness of an ultrasound image. Adjustment of the gain evenly increases or decreases the entire ultrasound signal (the signal from the ultrasonic transducer converted for display on the monitor). Changes in the gain make the entire image brighter or darker, but do not alter the differences in brightness between light and dark sections of the image (Figure 1.8).

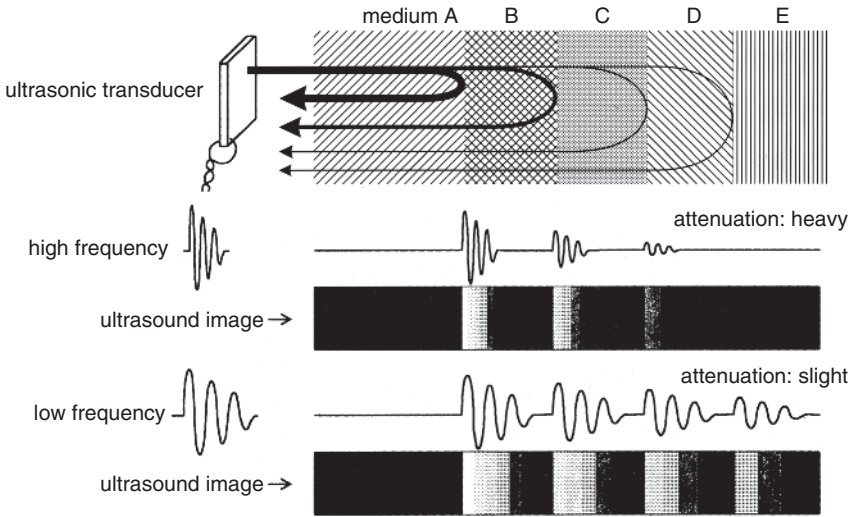


Figure 1.7 Differences in depth penetration at different frequencies.

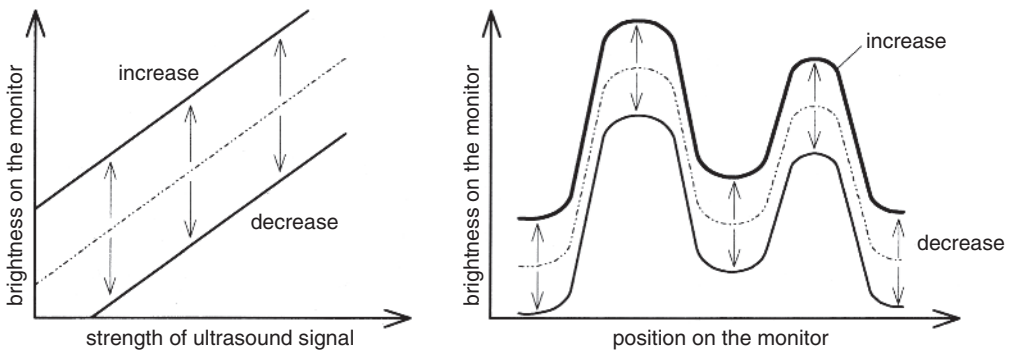


Figure 1.8 Adjustment of gain (brightness).

Contrast

Contrast is the mechanism for adjusting the difference in brightness between light and dark sections of an image. Adjustment of the contrast makes the most significant changes in the sections of an image with the strongest ultrasound signal; in other words, changing the contrast primarily alters the brightness of the lighter sections of an image, and the darker sections are changed only relatively little. Increasing the contrast of an ultrasound image yields an image with enhanced differences between light and dark areas, whereas decreasing the contrast yields an image with minimal

differences between light and dark areas (Figure 1.9).

Sensitivity Time Control

STC, also known as time gain compensation, is the mechanism for adjusting the gain according to the distance (depth) from the ultrasonic probe. As shown in Figure 1.7, attenuation of the ultrasound wave increases with the distance from the probe; thus, ultrasound signals from distant (deep) regions are weaker than those from near (shallow) regions. To correct this and make the overall image as even as possible, the ultrasonic processor amplifies the

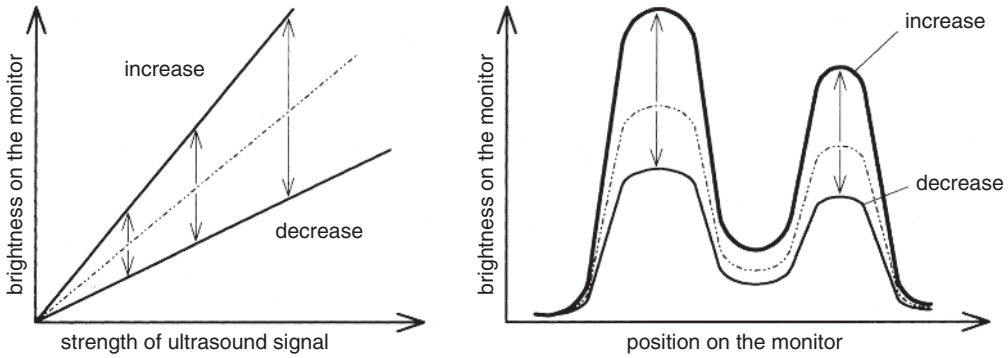


Figure 1.9 Adjustment of contrast.

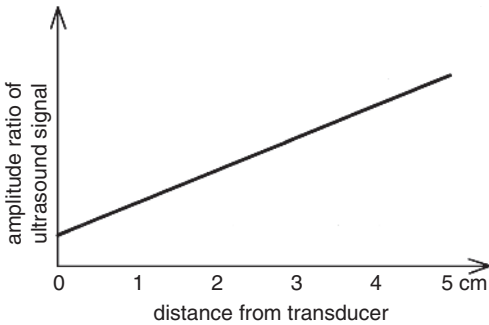


Figure 1.10 Sensitivity time control default settings.

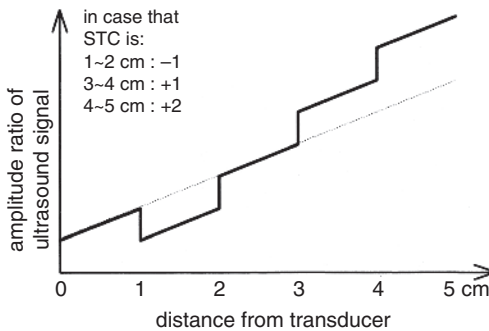


Figure 1.11 Adjustment of sensitivity time control (STC).

ultrasound signal based on the current distance from the probe (the time for the ultrasound pulse to return to the transducer; Figure 1.10). By altering the degree of amplification, adjustment of STC can make the ultrasound image lighter or darker based on the distance from the probe (Figure 1.11).

Equipment

Endoscopic Ultrasonic Probe

This section introduces the equipment (manufactured by Olympus Corporation, Tokyo, Japan) used by the author.

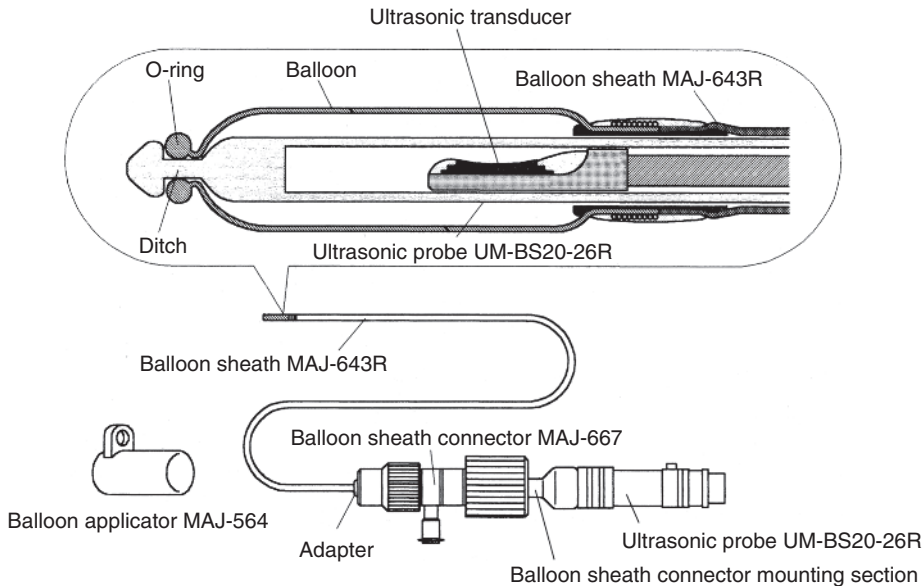
Table 1.1 shows the frequencies and outer diameters of the endoscopic ultrasonic probes used. Because the resolution and depth penetration of an ultrasonic probe depend on the frequency and size of the transducer (as the outer diameter of the probe increases, the size of the ultrasonic transducer increases), the probe needs to be selected to suit the aim of the procedure.

Ultrasound examinations can be performed using either the balloon (the probe contacts the study object through a balloon filled with a medium) or the direct contact method (the probe makes direct contact with the study object). The method is usually selected according to whether the study object is centrally or peripherally situated, and probe selection is also made according to the region being examined.

With the balloon method, the UM-BS20-26R ultrasonic probe (which can be inserted in a bronchoscope instrument channel with a diameter of at least 2.8 mm) is generally used (Figure 1.12). Other probes can also be used in the balloon method in combination with the

Table 1.1 Ultrasonic probes.

Model name	Maximum outer diameter	Frequency	Compatible biopsy channel
UM-2R	2.5 mm	12 MHz	2.8 mm or more
UM-3R	2.5 mm	20 MHz	2.8 mm or more
UM-4R	2.4 mm (2.0 mm at proximal side)	20 MHz	2.6 mm or more
UM-S20-20R	1.7 mm (2.0 mm at proximal side)	20 MHz	2.2 mm or more
	2.55 mm (incl. guide sheath SG-201C)		2.6 mm or more
UM-S30-20R	1.7 mm (2.0 mm at proximal side)	30 MHz	2.2 mm or more
	2.55 mm (incl. guide sheath SG-201C)		2.6 mm or more
UM-S30-25R	2.5 mm	30 MHz	2.8 mm or more
UM-BS20-26R	2.6 mm (incl. balloon sheath MAJ-643R)	20 MHz	2.8 mm or more
UM-S20-17S	1.4 mm (1.7 mm at proximal side)	20 MHz	2.0 mm or more
	1.95 mm (incl. guide sheath SG-200C)		2.0 mm or more

**Figure 1.12** Structure of UM-BS20-26R.

balloon sheath MH-246R (outer diameter 3.6 mm); this will need a special bronchoscope, such as the BF-ST49, with an instrument channel and a diameter of at least 3.7 mm, or a rigid bronchoscope with an instrument channel of 11.5Fr or more. Of note is that the direct contact method does not require a balloon; therefore, the probe is passed directly down the bronchoscope instrument channel.

Bronchoscope

Having selected an ultrasonic probe according to the aim of the investigation and the region being examined, it is then essential to select a bronchoscope suitable for use with that probe. In particular, when the balloon method is selected, care must be taken to prepare a bronchoscope with an instrument channel diameter of at least 2.8 mm.

Ultrasonic Processor and Probe Driving Unit

Ultrasound images are obtained by attaching the endoscopic ultrasonic probe to the Endoscopic Ultrasound Center EU-ME1 (Figure 1.13) and EU-ME2 (Figure 1.14) via the Probe Driving Unit MH-240; they are highly compact and fit in the standard endoscopic equipment trolley.

Preparations

Required Equipment

- Ultrasonic probe (sterilized)
- Balloon sheath
- Balloon sheath connector (for attachment of the balloon sheath to the probe)



Figure 1.13 Endoscopic Ultrasound Center (EU-ME1). *Source:* Courtesy of Olympus.



Figure 1.14 Endoscopic Ultrasound Center (EU-ME2). *Source:* Courtesy of Olympus.

- Three-way stopcock with an extension tube
- Physiological saline, 20 ml
- 20 ml syringe

Assembling the Balloon Probe

The advantage of the ultrasonic probe UM-BS20-26R is that it can be used with flexible bronchoscopes with a standard instrument channel with a diameter of at least 2.8 mm (BF-IT260, IT290, and IT240R).

Assemble the balloon probe in accordance with the instructions provided in the manual.

- Pass the balloon sheath connector from the probe tip down, and fix it to the balloon sheath connector attachment on the probe.
- Insert the balloon sheath from the probe tip, and press the balloon sheath clasp into the balloon sheath connector.
- The optimum position for the ultrasonic transducer is not in the center of the balloon, but the transducer should just protrude from the base of the balloon (Figure 1.15); this enables the transducer to rotate within the maximally expanded portion of the balloon when inflated.

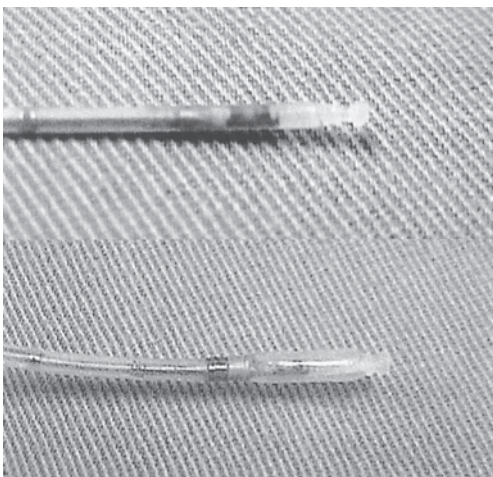


Figure 1.15 Probe (above) and probe inside balloon sheath (below).

- Draw up 15 ml of physiological saline into the syringe, fill the three-way stopcock extension tube with saline, and attach the extension tube to the balloon sheath connector inlet.
- Pull back on the syringe to create negative pressure, drawing out as much air as possible from between the balloon sheath and the probe. After repeating this step three times, slowly release the negative pressure and then slowly inject physiological saline into the balloon.
- Continue pushing the syringe plunger with the balloon tip pointing upward, filling the balloon with saline. Although a small bubble of air will enter the balloon, the tip of the balloon is separate, with a hole in it. Pulling the balloon in the direction of the tip, make a space between the probe tip and the balloon. The air in the tip of the balloon will go out.
- After eliminating all the air in the balloon, fix the probe by hand through the balloon, and push the O-ring on the balloon tip into the groove in the probe tip, either by hand or using a balloon applicator. Once the balloon has been filled with saline and checked for leaks and air bubbles, preparation is complete (Figure 1.16).

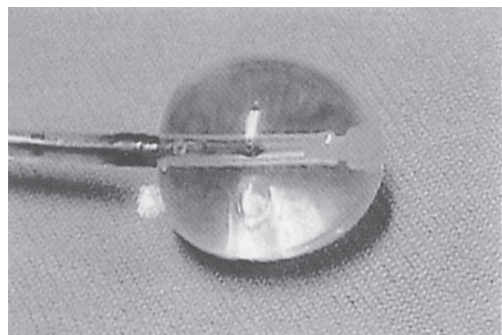


Figure 1.16 Balloon inflated with saline.

Connecting the Probe to the Driving Unit

Insert the connection of the ultrasonic probe into the connector on the driving unit, pointing the pin at the 12 o'clock position.

Connecting the Power and Data Entry

Only turn on the power to the Ultrasound Center after connecting the probe. The ultrasonic probe will be damaged if it is connected when the power is on. After the probe has been connected, switch the monitor to the ultrasound input, and enter the patient's identity number, age, and name.

Checking the Image

Unfreeze and rotate the ultrasonic probe. If it is working properly, multiple echoes with five to seven layers will be observed centered on the probe. If multiple echoes are not observed, the probe may be disconnected or there may be air bubbles in the medium in contact with the transducer of the probe.

Inverting the Image

Next, press the "Image Direction" switch to change the monitor image from Normal to Inverse; this inverts the ultrasound image, so that left and right are the same as the bronchoscopic image, to an image viewed from the proximal site (oral side). In gastrointestinal EUS, a normal ultrasound image is viewed from the caudal direction for easy comparison with computed tomography (CT) scans; however, in EBUS, it is desirable for the directions in the ultrasound image to coincide with those in the image from the bronchoscope. Of note is that the normal mode is only used in special situations, such as for comparison with CT images.

Operation

Anesthesia Application

In principle, anesthesia for EBUS is the same as that for regular bronchoscopic examinations. It should be kept in mind, however, that until the operator becomes more experienced, procedures will tend to be somewhat longer in duration. When EBUS is performed in conjunction with another procedure, such as laser-induced fluorescence bronchoscopy, intravenous anesthesia might be used, allowing spontaneous respiration. An important consideration for the anesthetist is to confirm, under direct observation using a laryngoscope, that local anesthetic spray is applied directly to the pharynx and larynx, particularly the vocal chords. After bronchoscopic examination of the trachea and bronchi, a local anesthetic is further applied to the bronchus (bronchi) into which the balloon probe will be introduced.

Inserting the Probe

Apply xylocaine jelly liberally to the distal end of the balloon probe, and slowly insert it into the instrument channel of the bronchoscope. During the insertion process, hold the probe at a point 2 or 3 cm away from the instrument port. Be aware that there are two places with high resistance in the instrument channel between the instrument port and the distal end of the bronchoscope. The first site is 4–5 cm from the instrument port, where the suction and instrument channels join, whereas the second is 2–3 cm from the bronchoscope tip, where the instrument bends. When resistance is high at either site and it is difficult to pass the probe, remove the probe and reapply jelly, and if that fails, remove the bronchoscope from the patient and reinsert the probe.

Operating the Probe

Advance the probe to a point slightly distal to the site of interest. Inject 1–3 ml of physiological

saline, inflating the balloon while scanning so that it contacts the bronchial wall circumferentially. The optimum volume of saline is that which just enables circumferential contact of the balloon with the bronchial wall. Of note is that overinflation can cause bronchial wall structures to compress or the balloon to burst.

Then, while scanning and capturing images (always ensure video-recording), retract the probe from the distal to the proximal site. It is important to remember to retract the probe very slowly. If necessary, ask the patient to hold their breath while scanning. Advancing the probe from the proximal to the distal site can damage the probe and should be avoided.

Tips for Achieving Optimum Ultrasound Images

To obtain clear, easily understandable images, note the following:

- Rotate the ultrasound image so that it corresponds to the endoscopic images.
 - To assess the depth of tumor invasion, the ultrasound pulse must penetrate the tracheal/bronchial wall perpendicularly.
- Rotate the ultrasound image so that it corresponds to the bronchoscopic images:
 - At a bifurcation (e.g. the opening of the right upper lobe bronchus), we can line up the direction that the balloon is not in contact with the bronchial lumen on the bronchoscopic image with the direction with no echo on the EBUS image. For example (Figure 1.17), in the left ultrasound image below, the direction with no echo, because the balloon is not in contact with the bronchial lumen, is from 4 to 6 o'clock. In the right bronchoscopic image, the direction that the balloon is not in contact with the bronchial lumen is from 2 to 4 o'clock. To match up the images, we need to rotate the EBUS image anticlockwise by about 45°.
 - Rotate the EBUS image according to the relative positions of the bronchial tree and the esophagus and great vessels. When scanning from the left main bronchus to the lower part of the trachea, the esophagus is located at the 6 o'clock direction (Figure 1.18, left). The right pulmonary artery runs anteriorly to the right intermediate trunk from 10 to 2 o'clock (Figure 1.18,

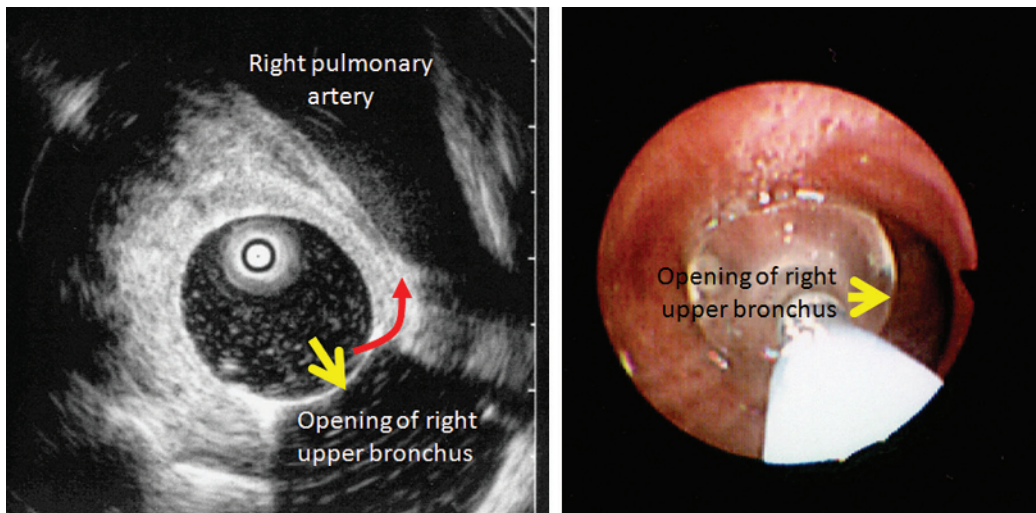


Figure 1.17 Tips for obtaining optimum ultrasound images: Rotation of the ultrasound image so that it corresponds to the bronchoscopic image. The arrows indicate a highly echogenic first layer, with a clearly lined layer structure in that region.

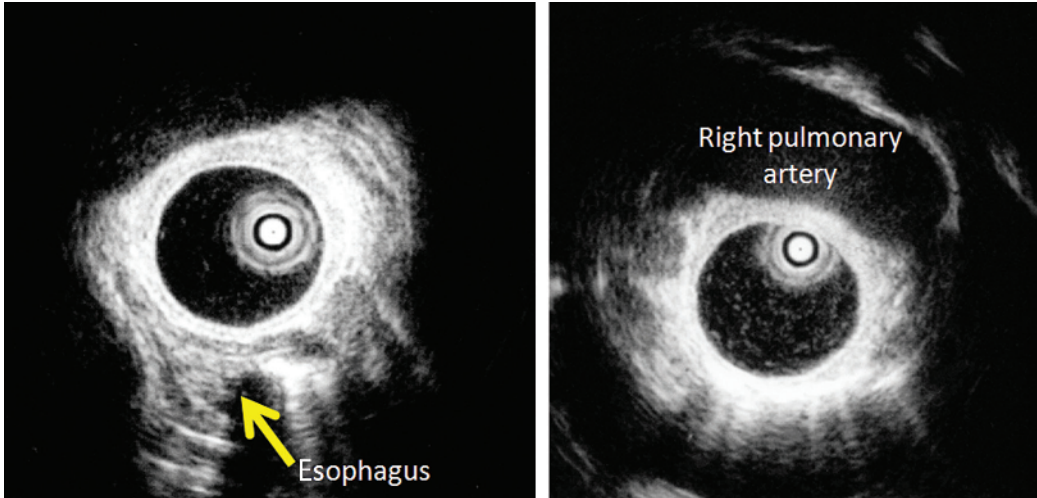


Figure 1.18 Tips for obtaining optimum ultrasound images: Rotation of the endobronchial ultrasonography image according to the relative positions of the bronchial tree and the esophagus and great vessels.

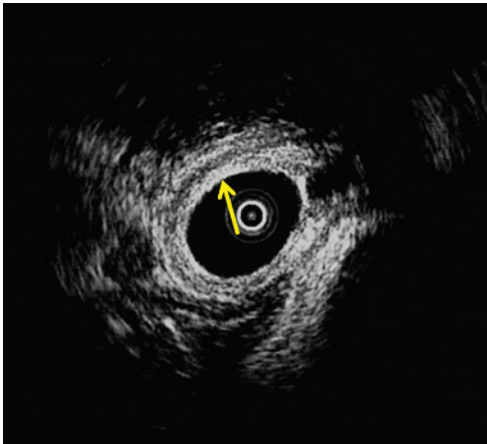


Figure 1.19 Tips for obtaining optimum ultrasound images: To assess the depth of tumor invasion, obtain images with the ultrasound pulse penetrating the tracheal/bronchial wall perpendicularly. The arrow indicates a highly echogenic first layer, with a clearly lined layer structure in that region.

right). Identify the position of these structures, and rotate the EBUS image accordingly.

- To assess the depth of tumor invasion, obtain images with the ultrasound pulse penetrat-

ing the tracheal/bronchial wall perpendicularly. If the first layer (marginal echo, reflected at the boundary between tissues) is highly echogenic, the image can be said to be derived from an ultrasound pulse penetrating the tracheal/bronchial wall nearly perpendicularly (Figure 1.19).

Equipment for EBUS-Guided TBNA

A curved array transducer is combined at the tip of the bronchoscope for EBUS-TBNA (Figure 1.20; BF-UC290F, Olympus) [8–10]. This convex bronchoscope comprises an oblique forward viewing with a convex transducer mounted in front of the lens. This convex transducer is 5–12 MHz and covered with a balloon. In addition, this bronchoscope has a working channel with a diameter of 2.0 mm; we can insert the disposable biopsy instrument with a 22 G needle (Figure 1.21; Vizishot2, Olympus) through the working channel (Figure 1.22). After the convex-type probe is covered by the balloon, saline is



Figure 1.20 Ultrasonic bronchoscope (BF-UC290F). *Source:* Courtesy of Olympus.

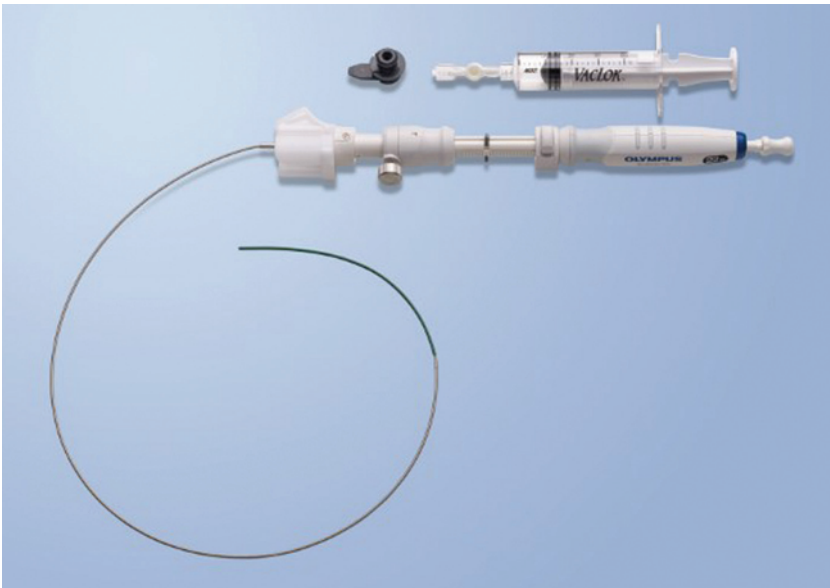


Figure 1.21 Aspiration needle (ViziShot 2). *Source:* Courtesy of Olympus.

injected into the balloon for filling its inner space. This bronchoscope is connected to the ultrasound unit, and the power switch should be turned on.

Because this convex bronchoscope has an oblique forward viewing, there is little difficulty in inserting this scope through the vocal cord. Watching the 12 o'clock direction

of the vocal cord, the tip of this scope is straight, and it is easy to go into the trachea. The bronchoscope reveals the target lesion for TBNA beyond the bronchial wall; this transducer provides longitudinal planes of peribronchial areas, and the ultrasonographic image reveals the real-time movement of the TBNA needle.

Doppler Mode

The Doppler effect is that the frequency of sound increases while the source of sound moves to the ultrasound transducer, and the frequency of sound decreases while the source of sound removes from the ultrasound transducer. Using this effect, the Doppler mode of the Ultrasound Processor enables the visualization

of vessels on EBUS images. The color Doppler mode reveals vessels based on the speed of the bloodstream, vessels coming up to the ultrasound probe as red and vessels removing from the ultrasound probe as blue (Figure 1.23). The power Doppler mode reveals vessels based on the amount of blood in the bloodstream.



Figure 1.22 Ultrasonic bronchoscope with the needle. *Source:* Courtesy of Olympus.

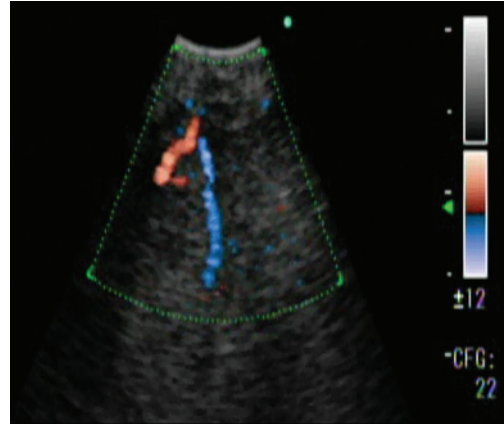


Figure 1.23 Doppler image of a representative case. The color Doppler mode shows vessels according to the speed of the bloodstream, vessels coming up to the ultrasound probe as red, and vessels removing from the ultrasound probe as blue.

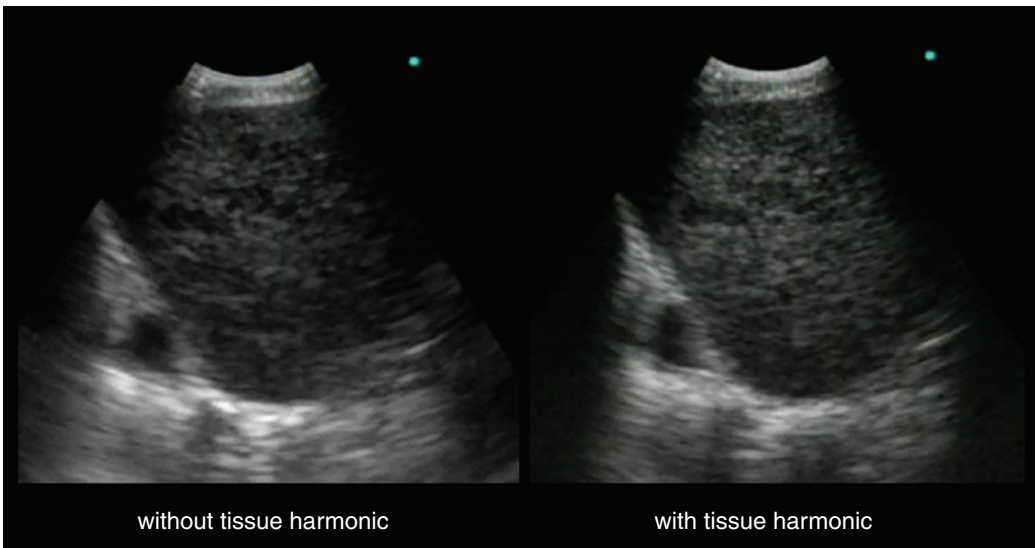


Figure 1.24 Tissue harmonic image of a representative case. The tissue harmonic image (right) is a fine image compared with the normal B-mode image.

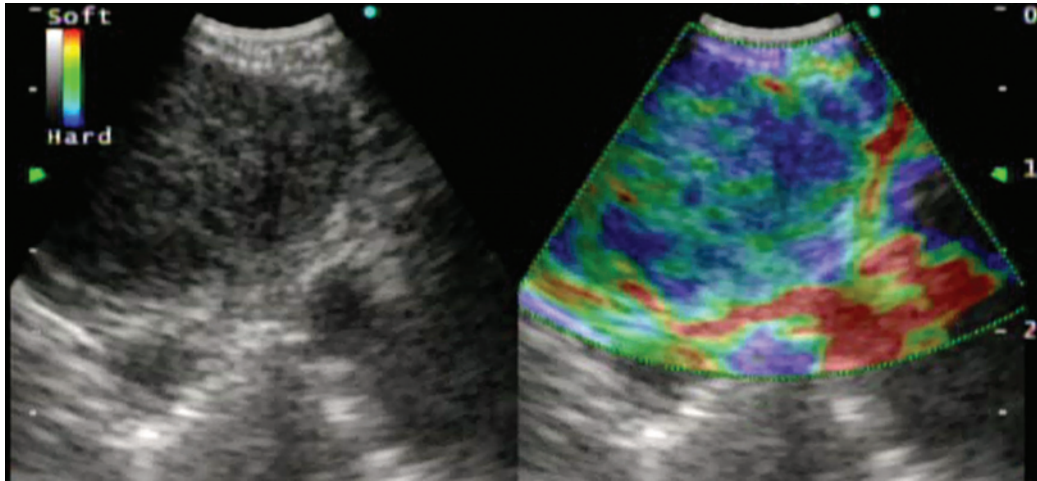


Figure 1.25 Elastography of a representative case. This lymph node shows mixed blue and green areas and is suspected of having heterogeneous internal structures.

New Functions of the Ultrasound Processor

The Ultrasound Processor (EU-ME2, premier; Olympus) provides some improvements.

Tissue Harmonic Echo

Some strains and harmonic components occur while the ultrasound wave is transmitting through organs. Harmonic components are produced from main lobes; then, harmonic components reduce artifacts from side lobes. Tissue harmonic echo visualizes these harmonic

components of ultrasound waves and provides fine EBUS images with reduced artifacts (Figure 1.24).

Elastography

Elastography is an imaging technology for visualizing and assessing the elasticity when an external force compresses an elastic body. On the colored ultrasound strain image, which is superimposed on the B-mode image, each area is colored according to the amount of strain. While blue shows a relatively hard area, green and red show relatively soft areas (Figure 1.25).

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