Acta Biomed 2023; Vol. 93, N. 4: e2023113 DOI: 10.23750/abm.v94i4.14090

Endobronchial ultrasound: A pictorial essay

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Abstract. *Background and aim:* endobronchial ultrasound has gained widespread popularity in the last decade, becoming the primary technique for minimally invasive evaluation of the mediastinum and staging of lung cancer. Several tertiary and quaternary care institutes use this method, performed by trained and accredited specialists. Its main indications are (I) diagnosis and staging of lung cancer, (II) mediastinal lymphadenopathy diagnosis (III) sampling peripheral pulmonary lesions. *Conclusions:* this manuscript aims to describe the operational potential of both convex endobronchial ultrasound probe and radial endobronchial ultrasound probe technology, focusing on lung cancer. This review is complemented by the description of peculiar clinical cases in which endobronchial ultrasound played a pivotal role in reaching the diagnosis. (www.actabiomedica.it)

Key words: EBUS, CP-EBUS, RP-EBUS, lung nodule, ultrasound, TBNA, TBB

Background

Bronchoscopy allows the visual evaluation of lower airways, helping to diagnose different diseases of the trachea, bronchi, and lung parenchyma.

Thoracic endoscopy has advanced quickly during the past few decades. The introduction of new technologies, such as thin and ultrathin bronchoscopes, specific needles and biopsy tools (i.e., cryoprobes), virtual navigation technologies, and endobronchial ultrasound (EBUS), led to significant diagnostic and therapeutic improvements (1, 2). In particular, EBUS represents a milestone in the field, introducing the capability of seeing outside the tracheal and bronchial lumen. Before the implementation of EBUS, invasive endoscopic procedures such as transbronchial needle aspiration (TBNA) and mass debulking by rigid bronchoscopy needed a visual image of the anatomical structures surrounding the central and distal airways. Routine use of EBUS has allowed a more advanced procedural workflow, reducing the risk of vascular puncture and mediastinal organ injury, introducing new procedural capabilities (e.g., systematic mediastinal lymph node staging) (3).

Available EBUS tools

The first published evidence regarding EBUS appeared in 1992 (4); at that time, only a large-bore EBUS radial probe was available, and, due to its size, the application in clinical practice was limited only to lesions surrounding central airways (trachea and main bronchi). Two further models were introduced after the evolution and miniaturization of the ultrasound probes: the convex probe EBUS (CP-EBUS) (see Figure 1) and the miniaturized radial probe ultrasound (RP-EBUS) (see Figure 2).

Both these tools were designed to provide a real-time EBUS-guided sample of the target lesions. RB-EBUS and CP-EBUS use flexible catheters for radial and convex probes with an inflatable balloon at the

tip to allow circular contact with the airway for the ultrasound. Hence, they provide an optimal image of the airways and the surrounding structures. Both CP-EBUS and RP-EBUS provide a B (brightness) mode view.

CP-EBUS

The CP-EBUS consists of a convex probe capable of using different frequencies (5, 6, 7.5, 10, 12 MHz) with a 65° scanning range. The lower the frequencies are, the better the waves penetrate different tissues. In order to increase the contact area between the instrument and the mucosa, the probe's tip is covered by a saline-filled inflatable balloon. The probe can produce imaging with color doppler, pulsed doppler, and elastography (5, 6).

Figure 1. CP-EBUS with a dedicated needle in the working channel. Copyright by Olympus Corporation. The images have been provided by Olympus Corporation.

The CP-EBUS allows direct observation and a contemporary minimally invasive sampling of anatomical structures beyond the airway walls, employing dedicated needles and a protocolled procedure (6). Briefly, the tip of the CP-EBUS is placed adjacent to the target area, and then the balloon placed at the probe tip of the probe is inflated with saline to improve the ultrasound image quality. Next, a dedicated transbronchial needle system is deployed through the bronchoscope's working channel. Once the needle catheter emerges from the working channel, the tip of the catheter itself is adjusted so that only a tiny part of it exits inside the airway.

While maintaining the real-time ultrasound view, the needle is pushed out of the catheter, passing through the bronchial wall toward the target lesion. Once the target has been reached, the needle stylet is removed, variable suction pressure is applied, and the needle is passed through the lesion several times. At the end of sampling, suction is released, and the needle is pulled back into the catheter. The entire transbronchial needle system is then removed en block from the

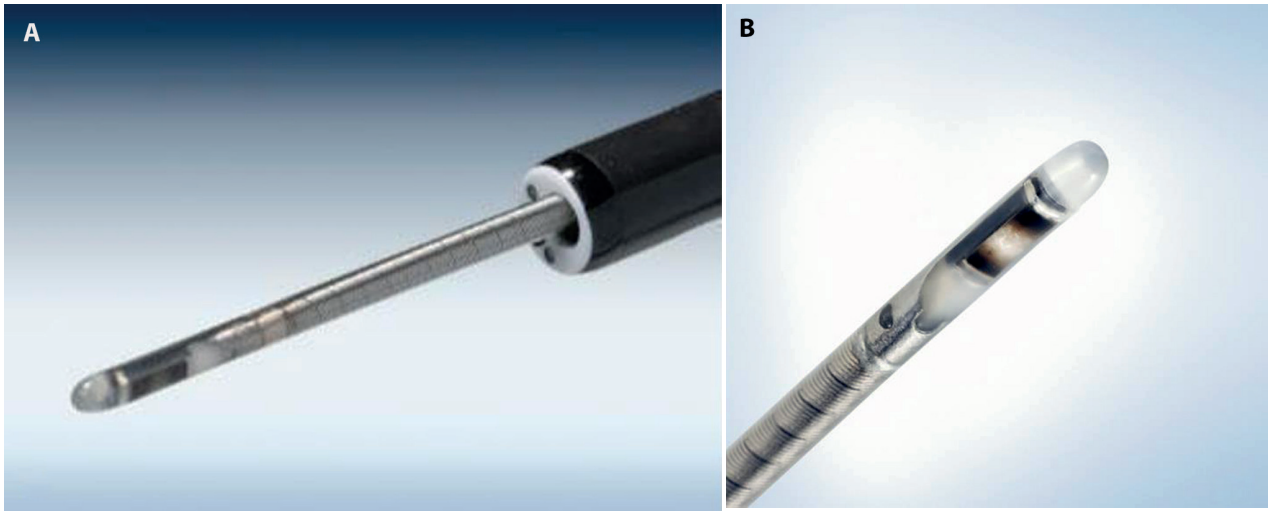

Figure 2. RP-EBUS. A: probe inside the working channel of the bronchoscope. B: Magnification of the distal structure of the probe (UM-S20-17S). Copyright by Olympus Corporation. The images have been provided by Olympus Corporation.

working channel. The sample obtained is then prepared according to local protocols.

The procedures involving CP-EBUS can have both a therapeutic and a diagnostic role (7) (see Table 1).

Lymph node pattern

The bronchoscopist, during a procedure, must annotate the following details related to the lymph node: size, shape (triangular, round, non-defined), presence/absence of the hilum, margins (distinct/indistinct), echogenic pattern (homogenous/non-homogenous), intranodal vascularisation presence/absence. All these morphological parameters are fundamental to predicting malignancy and guiding the decision, during multidisciplinary group discussion, on the patient's disease staging (6, 8). Ultrasonographic characteristics such as morphology, vascularization, echogenicity, and elastographic image pattern (see Figure 3) may correlate with the final diagnosis, although they cannot replace tissue sampling (9-11).

Table 1. Indications for CP-EBUS.

Indications
Main: • Diagnosis and staging of lung cancer • Mediastinal lymphadenopathy diagnosis • Sampling of parenchymal lung nodules (within the airways reachable by the endoscope) • Sampling endobronchial or peribronchial lesions • Sampling mediastinal masses • Guidance of therapeutic interventions (e.g., placement of fiducial markers) • Detection of early airway malignancy • Evaluation of the extent of airway tumor invasion Others: • Diagnosis of a pulmonary artery mass • Diagnosis of pulmonary embolism • Diagnosis of intracardiac masses • Draining infected mediastinal cysts • Staging of thyroid cancer

Vascular patterns

Color Doppler observation of vessels is possible with CP-EBUS. Vascular changes can be easily seen in metastatic lymph nodes (LNs), as the normal vascular structure of the LN is generally distorted by tumor infiltration.

Moreover, several major cervical and mediastinal vessels can be analyzed through the tracheal lumen using CP-EBUS. The aortic branches, innominate vein, aortic arch, descending aorta, pulmonary arteries, left atrial chamber, azygos vein, and superior vena cava are all identifiable and inspectable from the airway lumen. Different pathologic vascular patterns can be observed, and either vascular, pulmonary, or mediastinal pathologies with vascular and cardiac involvement can be diagnosed and staged through direct visualization or by cytological sampling (12-14). In the example proposed in Figure 4, a newly diagnosed pulmonary embolism was detected with CP-EBUS during a primary lung cancer diagnostic procedure.

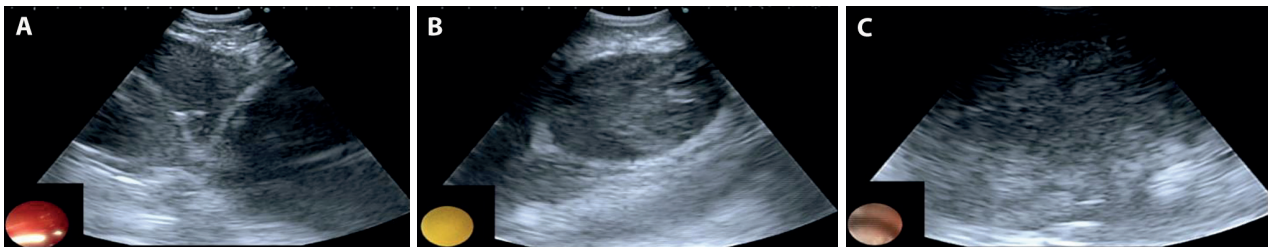

Figure 3. Lymph node pattern. A: normal, triangular lymph node with a conserved hilar structure. B: 12mm adenopathy, round shaped, with distinct margins - metastasis from lung cancer demonstrated on cytological examination. C: 30mm adenopathy with indistinct margins - metastasis from lung cancer demonstrated on cytological examination. The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

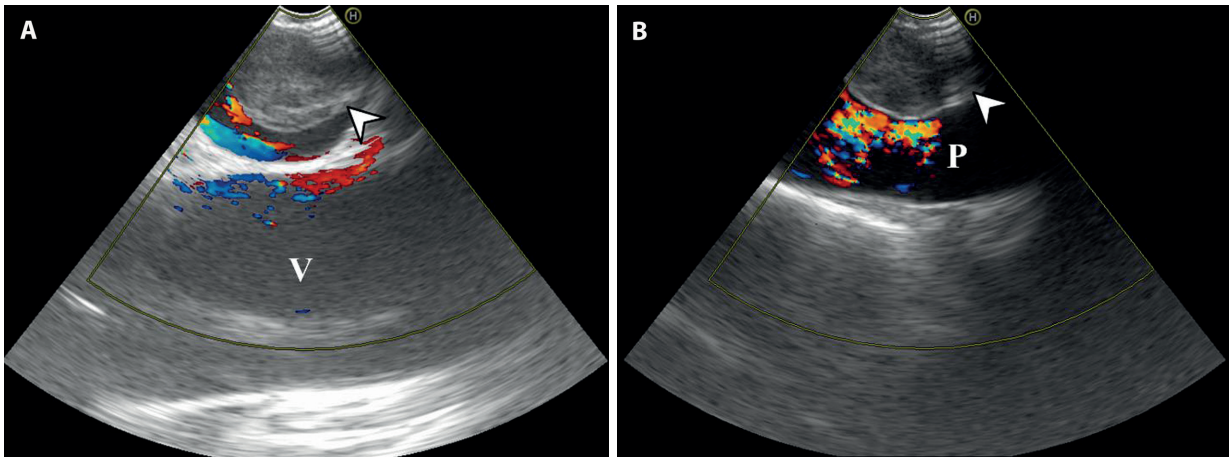

Figure 4. Pulmonary embolism detected during CP-EBUS (white arrowhead). A: embolus in the proximal region of the right pulmonary artery as seen from the right main bronchus. B: same lesion in the median region of the right pulmonary artery as seen from the right main bronchus. (P: pulmonary artery; V: superior vena cava.) The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

Pulmonary and mediastinal lesions

CP-EBUS, especially with small diameter probes, can be applied to sample peripheral lesions (see Figure 5). The more the instrument is inserted through distal airways, the more the probe is in direct contact with the mucosa, reducing the need to use the balloon. In this regard, a new CP-EBUS device aimed at sampling peripheral lesions has been designed without an integrated structure aimed at supporting the balloon. This technology will facilitate sampling lung nodules and distal lesions by having a real-time ultrasound view available (15).

Central airway malignancy diagnosis and staging

Malignant diseases located nearby the central airways may be diagnosed, staged, and predisposed for treatment with CP-EBUS. Direct cytological and histological sampling with CP-EBUS is feasible and can be carried out with systematic staging of the ipsilateral and contralateral tracheobronchial lymph nodes in a single procedure (16). In addition, placement of fiducial markers for subsequent stereotactic body radiotherapy may be performed (17).

Elastography

Elastography performed during the endobronchial ultrasound helps characterize various tissues and provides information on the stiffness of the tissue through different colors deriving from compression deformation. Conventionally, blue areas indicate a stiffer part of the sampled lesion, whereas yellow and red represent the soft ones.

Therefore, elastography can facilitate identifying and sampling the most representative area of a solid lesion, avoiding the necrotic areas that can lead to inadequate tissue sampling (18).

In Figure 6, CP-EBUS was used to visualize a paravertebral lesion, which was otherwise difficult to sample by fluoroscopy due to the radiologically overlapping with other anatomical structures. Elastography also allowed us to sample the most solid area (in red) of the lesion, which had an inhomogeneous ultrasound pattern.

Diagnosis and staging of other mediastinal diseases

CP-EBUS can be used to sample every lesion in proximity to the airways: as specified in the

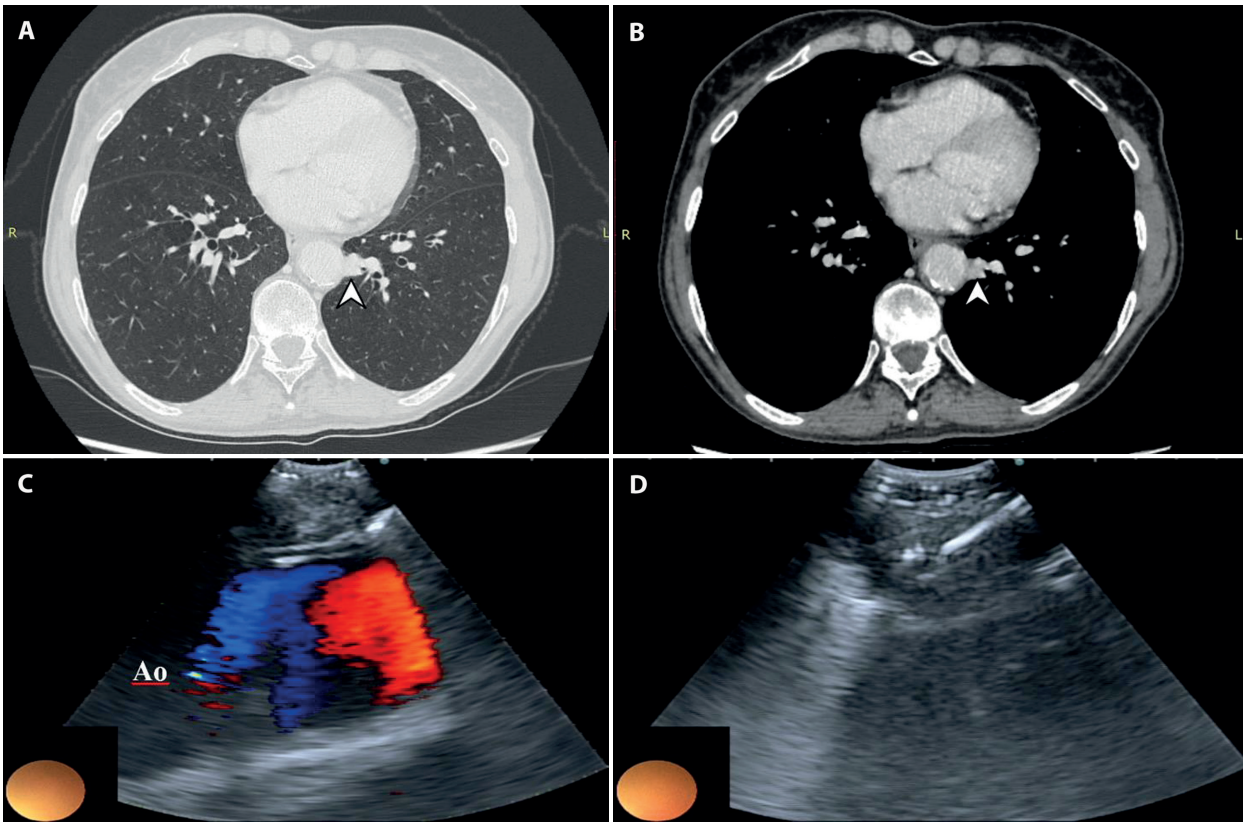

Figure 5. Peripheral lesion of the left lower lobe sampled in real-time with CP-EBUS guidance. A/B: chest CT scan, nodule (white arrowhead). C: color-doppler evaluation (Ao: descending aorta). D: a sampling of the lesion under real-time evaluation (needle-in-lesion). The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

diagnosis and staging section, the probe can identify extra-bronchial anatomical and pathological structures, potentially to be sampled by transbronchial route (19).

In Figure 7, we showed the case of a left paratracheal solid lesion being sampled. The definitive cytological result of TBNA was compatible with a papillary thyroid carcinoma metastasis.

EUS-B

Transesophageal bronchoscopic ultrasound (EUS-B) represents a low-risk procedure alternative to EBUS. In EUS-B, the EBUS bronchoscope is inserted gently through the oesophageal route until it reaches the stomach. This technique allows for the visualization of mediastinal and thoracic para-oesophageal structures. This route does not cause tracheal obstruction by the instrument and takes advantage of the collapsibility of the oesophageal lumen, favoring the probe's contact with the mucosa. This technique is preferred in patients with precarious respiratory conditions, as well as to target difficult-to-reach mediastinal lesions. It provides greater patient comfort and increased diagnostic yield for intrathoracic lesions (20, 21).

RP-EBUS

The RP-EBUS consists of a radial probe with a rotating transducer that can be inserted through the bronchoscope's working channel. RP-EBUS provides a 360° image of the structures surrounding the airway and allows a real-time vision of the target lesion.

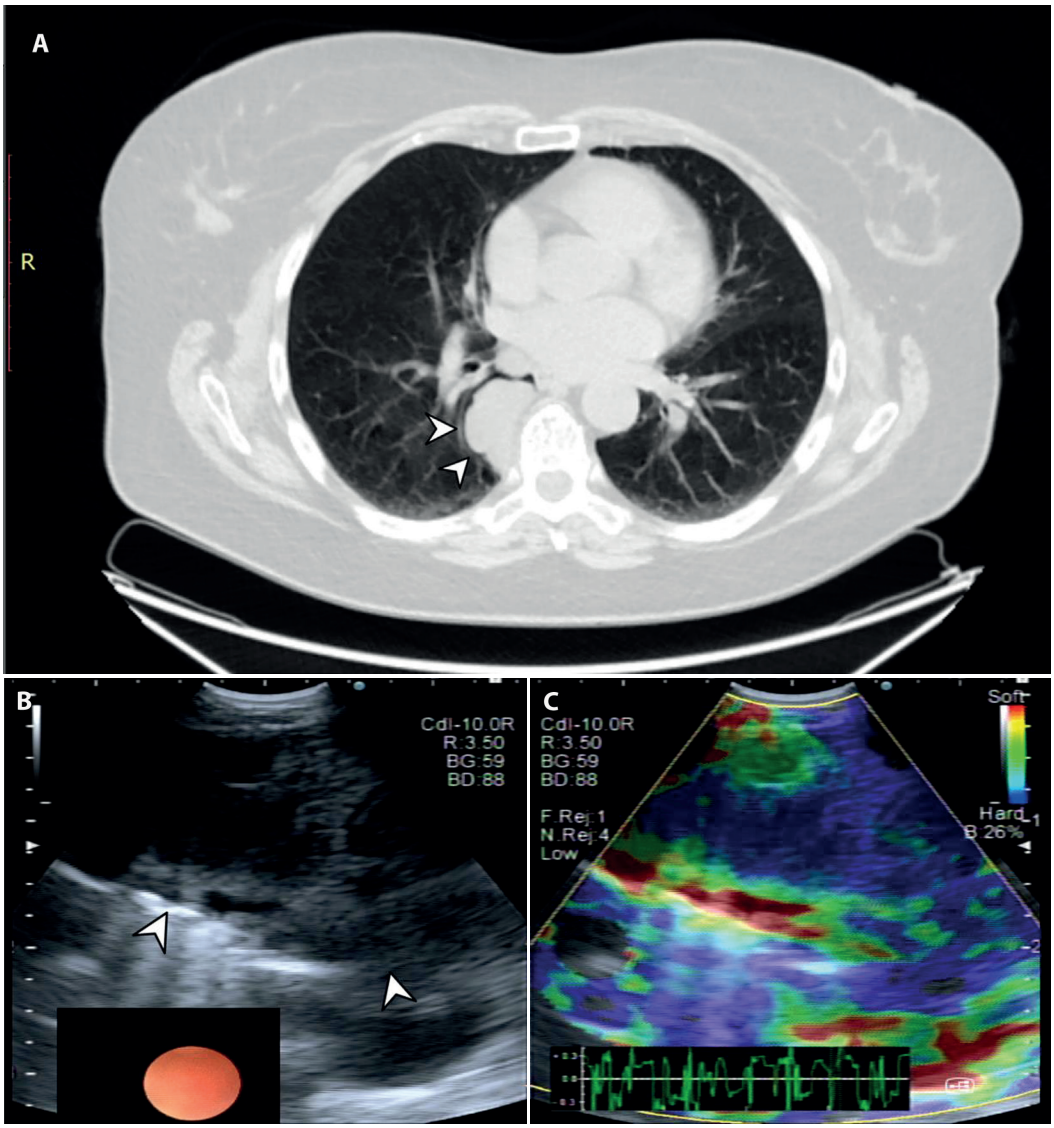

Figure 6. Right paravertebral lesion sampled with CP-EBUS. A: Chest CT showing a right paravertebral mass (white arrowhead). B: EBUS view of the lesion (white arrowhead) showing inhomogeneous hypoechoic areas, compatible with colliquation. C: same lesion, elastographic evaluation showing the different stiffness levels inside the lesion. The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

The RP-EBUS probe is provided with a 20 MHz ultrasonic frequency and can be introduced in working channels of different sizes (1.7, 2.0, 2.6, and 2.8 mm). Likewise, CP-EBUS and RP-EBUS basic views give a concentric B-mode image without additional features.

Generally, these probes are used with dedicated guide sheats and addressed to identify small peripheral lesions (22-24). Indeed, the radial probe allows the concentric evaluation of the bronchial wall, lung parenchyma, and the structures surrounding the bronchi.

This technology represents a cornerstone in the pipeline of diagnostic tools for lung cancer and peripheral pulmonary lesions (25, 26).

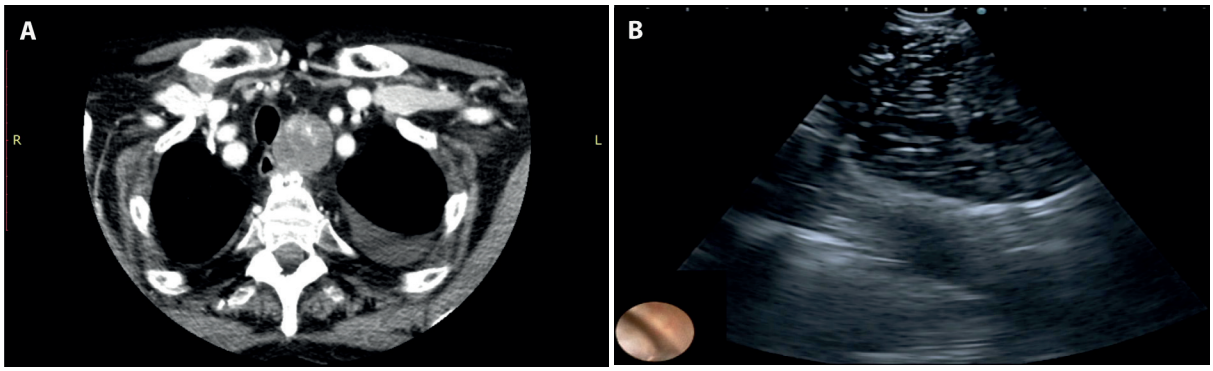

Figure 7. Left paratracheal lesion sampled by EBUS. A: chest CT shows a left paratracheal mass. B: the ultrasonographic appearance of the lesion. The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

Lung patterns

During the procedure with RP-EBUS, lung parenchyma has a dynamic appearance due to the progressive development of atelectasis caused by the insertion of the instrument into the more and more distal airways. Especially for more lengthy procedures, dedicated ventilatory protocols have been proposed, and even lateral decubitus or pronation may be considered (27-30). In addition, RP-EBUS allows for real-time visualization of atelectasis development during endoscopic procedures, as demonstrated by Sagar et al. (31).

Peripheral lesions

In recent years, the reduction in the incidence of ultra-central and central neoplastic lesions was contraposed to an increase in the detection of peripheral lung lesions with solid and non-solid patterns (32, 33). In light of the implementation of low-dose HRTC screening for lung cancer, the trend is set to increase further (34-36).

The currently available technologies in interventional pulmonology to reach the lung periphery can be categorized into real-time and non-real-time guidance systems (37-40). The only real-time guidance currently available is fluoroscopy, both standard and augmented. Nevertheless, RP-EBUS, with or without additional guidance, is considered the gold standard to confirm the positioning of the bronchoscope relative to the target lesion (41-44). However, the RP-EBUS probe must be removed from the operative channel to insert the sampling instrumentation; hence, it cannot provide a real-time image of the lesion while it is being sampled. The availability of a device allowing the simultaneous presence of the ultrasound probe and the instrumentation for tissue sampling inside the airway is a significant unmet need in thoracic endoscopy (1).

Dedicated guidelines for lesion sampling and tissue sample management have been developed for the RP-EBUS workflow (45). The anatomical relationship between the probe and the lesion can be categorized according to three patterns (Figure 8). The greyscale texture analyses of these patterns correlate with the malignancy risk for the lesion (46).

The precision guaranteed by the miniaturized ultrasound instrumentation allows its application in critical settings (e.g., in the case of patients requiring rapid procedures due to high anesthesiologic risk).

In Figure 9, we showed a peripheral lung lesion sampled with transbronchial needle aspiration (TBNA) and transbronchial biopsy (TBB) in a single lung patient. The TBNA/TBB procedure without ultrasound guidance carries a significant risk of iatrogenic pneumothorax, mainly if performed in the upper lobes. However, RP-EBUS allows for locating the ideal area to maximize the sample quality and reduce the risk of pneumothorax (47-49).

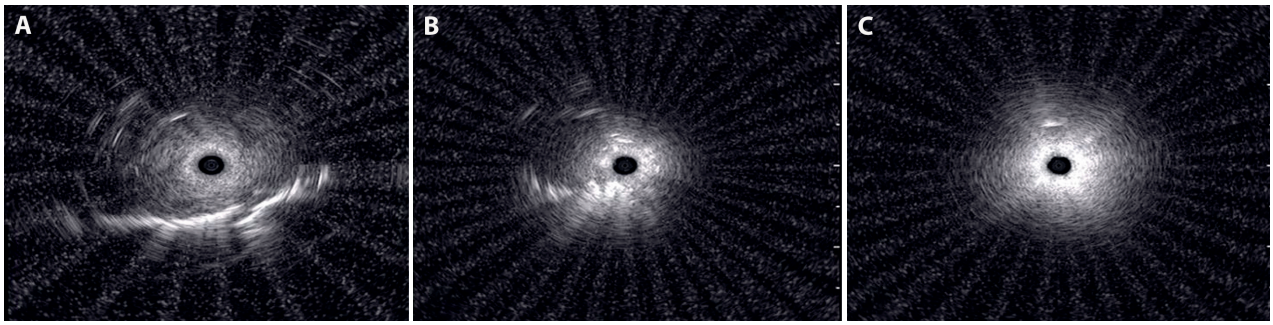

Figure 8. Image patterns of RP-EBUS. A: concentric pattern. B: eccentric pattern. C: no contact with the lesion. The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

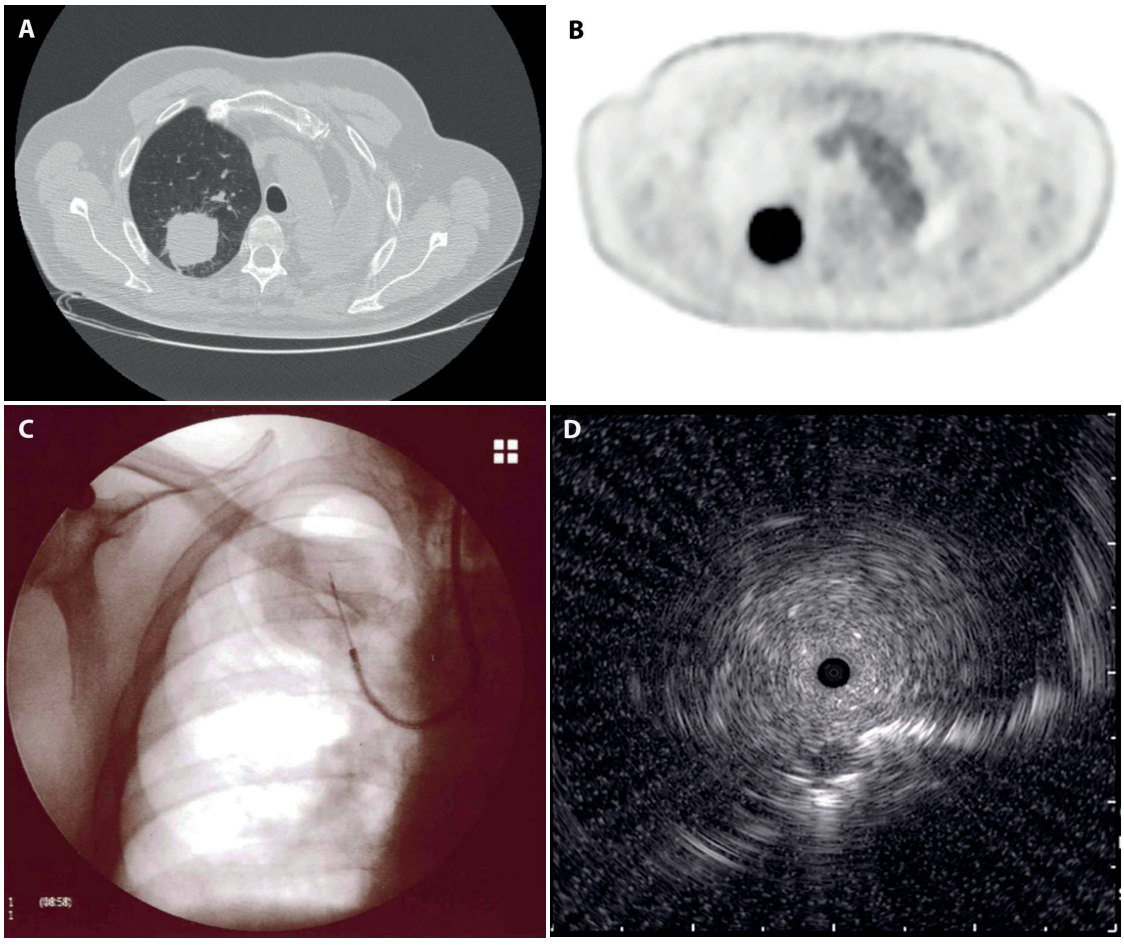

Figure 9. A sampling of a peripheral lesion in a single lung patient. A: chest CT shows a lesion in the right upper lobe. B: PET-CT showing a PET-avid lesion. C: fluoroscopic image with RP-EBUS probe overlapping with the lesion. D: RP-EBUS imaging of the lesion. The images are owned by the Department of Pulmonology, S. Maria della Misericordia University Hospital, Udine, Italy. Informed consent was obtained from the patients for the publication of the images in anonymised format.

Conclusion

EBUS technology improvement in clinical practice has revolutionized the world of interventional pulmonology, allowing the evaluation of what is beyond the tracheal and bronchial wall, leading to the possibility of sampling thoracic lesions with a precision never known before. However, many of the possibilities offered by this technology are yet to be discovered. In the future, research efforts will focus on the definition of procedural quality endpoints, the protocols for sampling large quantities of tissue, and the attempt to implement this technology for therapeutic purposes.

List of abbreviations: B mode: brightness mode; CP-EBUS: convex probe - endobronchial ultrasound; EBUS: endobronchial ultrasound; EUS-B: transoesophageal bronchoscopic ultrasound; RP-EBUS: radial probe - endobronchial ultrasound; TBNA: transbronchial needle aspiration; TBB: Transbronchial biopsy.

Ethics Committee: for isolated case reports and for retrospective case series, approval by the regional Ethics Committee of the authors is not required.

Acknowledgments: No acknowledgments are expressed concerning this document.

Funding: No funding was necessary for the production of this document.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article.

Authors' Contribution: All the co-authors participated in the collection of the iconography, in the drafting of the document, and the final collegial re-evaluation of the manuscript.

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Received: 19 December 2022
Accepted: 13 March 2023
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