Endobronchial Ultrasonography: Current Status and Future Directions

Kazuhiro Yasufuku, MD, PhD, Takahiro Nakajima, MD, Masako Chiyo, MD, PhD, Yasuo Sekine, MD, PhD, Kiyoshi Shibuya, MD, PhD, and Takehiko Fujisawa, MD

Abstract: Endobronchial ultrasonography (EBUS) has emerged as a new diagnostic tool that allows the bronchoscopist to see beyond the airway. The radial probe EBUS was first introduced to evaluate the airway structure, which has been shown to be useful for identifying the extent of tumor invasion in the central airway. With advances in technology, smaller radial probes are now available that are capable of visualizing peripheral lung nodules. EBUS is also used as a tool to assist in a biopsy in respiratory diseases. The radial probe EBUS–guided transbronchial needle aspiration (TBNA) increases the yield of TBNA of mediastinal processes. By the use of the ultra-miniature probe EBUS along with the guide sheath, peripheral lung lesions can be accessed without the exposure to radiation. However, it is still not a real-time procedure with target visualization. The newest development is the convex probe EBUS (CP-EBUS) with a curvilinear electronic transducer on the tip of a flexible bronchovideoscope. CP-EBUS allows real-time EBUS-guided TBNA. Although the main indication for EBUS-TBNA is lymph node staging, it can also be used for diagnosis of intrapulmonary tumors, of unknown hilar and/or mediastinal lymphadenopathy, and of mediastinal tumors. To date, there are no reports of complications related to EBUS-guided TBNA. It is a novel approach that has a good diagnostic yield with excellent potential in assisting safe and accurate diagnostic interventional bronchoscopy. The aim of this review is to highlight the current status of the different EBUS techniques available and to discuss the future direction of EBUS.

Key Words: Bronchoscopy, Endobronchial ultrasonography, Lung cancer, Lymph node metastasis, Mediastinoscopy, Staging, Transbronchial needle aspiration.

Endobronchial ultrasonography (EBUS) is a new tool that allows the bronchoscopist to see beyond the airway. Although bronchoscopic observation only allows visualization of the internal surface of the airway, EBUS allows analysis of the airway structure as well as processes surrounding the airway. After solving technical difficulties for the application of ultrasonography in bronchoscopic practice, the radial probe EBUS was commercially introduced in the early 1990s. EBUS is a new diagnostic tool with great potential for the evaluation of the airway and for the diagnosis of lung cancer and lung cancer staging.

There are two types of EBUS available for clinical use: the radial probe EBUS and the convex probe EBUS. The miniaturized 20-MHz radial probe (UM-BS20-26R, Olympus, Tokyo, Japan) was first introduced for optimal imaging of the bronchial wall. This enables the evaluation of tumor infiltration to the airways, which is useful for the evaluation of early lung cancer and extensive disease. The radial probe EBUS also enables visualization of mediastinal and hilar lymph nodes. Radial EBUS guidance has been shown to increase the yield of transbronchial needle aspiration (TBNA) for lymph node staging of lung cancer. Recently, an even smaller ultra-miniature radial probe (UM-S20-20R, Olympus), which can be introduced into the channel of the bronchoscope like any other forceps, has been used to detect peripheral intrapulmonary nodules. Studies have shown that EBUS can replace fluoroscopy for guiding biopsy procedures on peripheral intrapulmonary lesions by the application of sheath catheters. However, due to the nature of the probe, it is still not a real-time procedure with target visualization.

Although the radial probe EBUS is a useful tool that can broaden the practice of interventional pulmonology, it is still underused. A new endoscope with a built-in linear probe ultrasonography on the tip was developed in collaboration with Olympus Corporation. This new convex probe EBUS (CP-EBUS) enables real-time EBUS-guided TBNA (EBUS-TBNA). The linear ultrasound images are easier to understand. After preliminary studies showing the efficacy of CP-EBUS in surgical lung specimens, we first reported the clinical use of CP-EBUS for the assessment of mediastinal and hilar lymph nodes. The growing number of publications concerning the use of EBUS-TBNA for the evaluation of the mediastinal lymph nodes indicates the effectiveness of the new device.

This article reviews the current status of different techniques of EBUS available in the assessment of respiratory diseases. In particular, the utility of EBUS for lung cancer
diagnosis and lymph node staging is reviewed. In addition, the future directions of EBUS are discussed.

DIFFERENT TYPES OF EBUS

Radial Probe EBUS

Two basic types of EBUS radial probes are available. The miniaturized 20-MHz radial probe EBUS (UM-BS20-26R, Olympus) fitted with a catheter that carries a water-inflatable balloon at the tip (Figure 1A and B) is used for the assessment of central airways. The balloon optimizes the contact between the probe and the bronchial wall and allows visualization of detailed images of the bronchial wall structure and surrounding structures. The structure of the cartilaginous portion of the central bronchial wall has been described as a five- or seven-layer structure by different authors. The miniaturized ultrasound probe can be inserted through a 2.8-mm working channel (Figure 1C). The probe rotates 360 degrees to obtain detailed images of the surrounding structures and the bronchial wall structure. The 20-MHz EBUS has a resolution of 1 mm and a penetration of 5 cm. The probe can be used from the trachea to the subsegmental bronchus.

The ultra-miniature radial probe (UM-S20-20R, Olympus) was developed for the detection of peripheral lung nodules. It is also a 20-MHz radial probe, which has an external diameter of 1.4 mm (Figure 1D). The probe is placed into a guide sheath (GS) and the GS-covered probe can be inserted into a 2.0-mm working channel of a regular flexible bronchoscope (Figure 1E). The GS-covered probe is advanced to the peripheral lesion to obtain an EBUS image. After localizing the lesion, the probe is removed, leaving the GS in place. A biopsy forceps and/or a bronchial brush are then introduced into the GS to perform pathologic and cytologic examination.

CP-EBUS

The CP-EBUS is integrated with a convex transducer with a frequency of 7.5 MHz at the tip of a flexible bronchoscope (XBF-UC260F-OL8, Olympus), which scans parallel to the insertion direction of the bronchoscope (Figure 2). The outer diameter of the insertion tube of the flexible bronchoscope is 6.7 mm and that of the tip is 6.9 mm. The angle of view is 90 degrees, and the direction of view is 30 degrees forward oblique. Ultrasound images can be obtained by directly contacting the probe or by attaching a balloon on the tip and inflating with saline (Figure 2B). The ultrasound image is processed in a dedicated ultrasound scanner (EU-C2000, Olympus) and is visualized along with the conventional bronchoscopy image on the same monitor (Figure 3). The ultrasound images can be frozen, and the size of lesions can be measured in two dimensions by the placement of cursors. This system also has the Doppler mode.

The dedicated 22-gauge needle passed through the 2.0-mm instrument channel allows EBUS-TBNA (Figure 2B). The needle is also equipped with an internal sheath that is withdrawn after passing the bronchial wall, avoiding contamination during TBNA. The needle can be visualized through the optics and on the ultrasound image.

Because the endobronchial images obtained by the CP-EBUS scope are not as clear as those obtained with the conventional flexible bronchovideoscope, the authors prefer to examine the tracheobronchial tree using the conventional scope. All procedures can be performed under local anesthesia and conscious sedation (midazolam). Nasal insertion may be difficult due to the probe on tip of the scope. After identifying the lesion of interest with the CP-EBUS, the surrounding structures are also visualized with the use of the Doppler mode to confirm blood vessels. The dedicated TBNA needle is inserted through the working channel of the

FIGURE 1. (A) A 20-MHz miniaturized radial probe (UM-BS20-26R). (B) Balloon sheath (MAJ-643R). (C) A 20-MHz miniature radial probe (UM-BS20-26R) with the balloon sheath (MAJ-643R) on the tip inflated with water, inserted through a 2.8-mm working channel of a flexible bronchoscope. (D) A 20-MHz ultra-miniature radial probe (UM-S20-20R) with a diameter of 1.4 mm, which is used for peripheral intrapulmonary lesions. (E) The probe is placed into a guide sheath and the guide sheath-covered probe can be inserted into a 2.0-mm working channel of a flexible bronchoscope.
bronchoscope, and the lesion is punctured under direct EBUS guidance. The aspirated material is smeared onto glass slides. Smears are air dried as well as fixed in 95% alcohol. Furthermore, Papanicolaou staining and light microscopy are performed by a cytopathologist. Histologic specimens obtained are fixed in formalin before being sent to the pathology department.

Indications for EBUS-TBNA are assessment of mediastinal and hilar lymph nodes and diagnosis of lung tumors and mediastinal tumors. All the mediastinal lymph nodes except for the subaortic and paraesophageal lymph nodes (levels 5, 6, 8, and 9) are accessible by CP-EBUS. Because the outer diameter of the tip of the CP-EBUS is 6.9 mm, hilar lymph node levels 10 and 11 are approachable. However, part of level 12 is not accessible.

**EBUS FOR EVALUATION OF THE CENTRAL AIRWAY**

Radial probe EBUS was first developed for the evaluation of the central airway. It has been used for the management of patients with early lung cancer. In particular, pre-malignant lesions or small intrabronchial radiographically invisible tumors detected accidentally or by screening in high-risk patients. In these cases, the treatment strategy depends on the extent of tumor invasion within the different layers of the bronchial wall. Conventional radiographic imaging alone is not capable of distinguishing the tumor extent. In contrast, radial probe EBUS can detect the alterations of the multilayer structure of the bronchial wall for such small tumors (Figure 4). A comparison of ultrasonograms and the histologic findings in 24 lung cancer cases revealed that the depth of tumor invasion was accurate in 23 lesions using EBUS (95.8%).2 A smaller study in a series of 15 patients showed a high diagnostic yield of 93% for predicting tumor invasion into the tracheobronchial wall.23 EBUS has also been shown to improve the specificity (from 50% to 90%) for predicting malignancy in small autofluorescence-positive lesions that were negative in white light bronchoscopy.24

Photodynamic therapy is one of the best modalities for early-stage lung cancer treatment as long as it is not an invasive disease. Thus, confirmation of the extent of tumor invasion becomes the most important factor before treatment. A very interesting study looked at 18 biopsy-proven early-stage squamous cell carcinomas for which EBUS was performed to evaluate tumor extent.25 Nine lesions were diagnosed as intracartilaginous by EBUS, and photodynamic therapy was subsequently performed. The other nine patients had extracartilaginous tumors not detected by computed tomography (CT) and were considered candidates for other therapies. Using EBUS, a 100% complete remission rate was achieved in the endoluminal-treated group. At a mean follow-up of 32 months, none of the patients had a recurrence. Other than the use in early-stage lung cancer, EBUS has been demonstrated to be useful for the evaluation of advanced lung cancer. Preoperative assessment of tumor spread in centrally located lung cancer is essential for tumor resectability. One trial showed that EBUS, in contrast to chest CT, was highly accurate in evaluating the question of airway

![FIGURE 2.](image-url)

**FIGURE 2.** (A) Tip of the ultrasound puncture bronchoscope (CP-EBUS, Olympus XBF-UC260F-OL8) with the linear curved array ultrasonic transducer. (B) The balloon attached to the tip of the bronchoscope is inflated with normal saline and a dedicated 22-gauge transbronchial needle aspiration needle is inserted through the working channel to perform EBUS-TBNA.

![FIGURE 3.](image-url)

**FIGURE 3.** The dedicated ultrasound scanner (EU-C2000, Olympus). The ultrasound images can be frozen, and the size of lesions can be measured in two dimensions by the placement of cursors.
EBUS FOR PERIPHERAL INTRAPULMONARY LESIONS

Transbronchial biopsy (TBB) is often performed for the diagnosis of peripheral intrapulmonary lesions. Although the complication rate is generally low, there is radiation exposure and the diagnostic yield varies widely. For lesions that are too small to visualize by fluoroscopy, CT guidance has been reported to increase the yield of TBB. Percutaneous needle aspiration cytology is performed with a high yield, but there is a high occurrence rate of pneumothorax.

EBUS can be used to assist TBB of peripheral intrapulmonary lesions. Because the air content of the lung parenchyma completely reflects the ultrasound signal, pulmonary masses can be precisely located by EBUS. Pulmonary lesions have a hypoechoic texture and a sharply defined border due to strong reflective interface between the aerated lung and the lesion. Focusing on the internal structure of the peripheral lesions, a classification system for distinguishing benign from malignant lesions has been reported. Moreover, EBUS-guided TBB of peripheral pulmonary lesions has been shown to yield a similar success rate as fluoroscopy guidance. A large-scale, prospective, randomized study to compare EBUS-GS even in lesions <3 cm has been performed with good results. In lesions >3 cm, there were no significant differences in the diagnostic ability between the two procedures. However, in lesions <3 cm and <2 cm, a considerable decrease in TBB sensitivity (31% and 23%) was seen, whereas EBUS-guided TBB maintained its sensitivity (75% and 71%) (p = 0.0002 and p < 0.001, respectively).

More recently, studies have shown the efficacy of a new devise, the GS, for sampling of peripheral lesions to increase the diagnostic yield of TBB under EBUS guidance. A miniature probe introduced into the GS is inserted into a working channel of a fiberoptic bronchoscope. The GS-covered probe is advanced to the peripheral lesion to obtain an EBUS image. After localizing the lesion, the probe is removed, leaving the GS in place. A biopsy forceps and a bronchial brush are introduced into the GS to perform pathologic and cytologic examinations. Surprisingly, the diagnostic yield of this new technique was not altered by the tumor size, demonstrating the efficacy of EBUS-GS even in lesions <10 mm in diameter. It is even useful for TBB of fluoroscopically invisible solitary pulmonary nodules. The problem with this technique is the complexity of the procedure.

LYMPH NODE STAGING IN LUNG CANCER

Invasive and Noninvasive Staging Modalities

During the staging process of lung cancer, accurate lymph node staging is one of the important factors that affect patient outcome. Conventional imaging methods available for the evaluation of the mediastinum such as CT are inaccurate in the diagnosis of mediastinal lymph node metastasis. Positron emission tomography (PET) has been reported to increase the diagnostic yield. However, imaging alone is inaccurate. Therefore, tissue confirmation of suspected malignant lymphadenopathy is required, especially before surgical resection. The different methods available for obtaining pathology specimens from the mediastinal lymph nodes includes mediastinoscopy, conventional TBNA, EBUS-guided...
TBNA using a radial probe, CT fluoroscopy-guided TBNA, and endoscopic ultrasonography–guided fine needle aspiration (EUS-FNA) (Table 1). However each of these methods has its limitations.

Conventional bronchoscopic TBNA would be the preferred method for patients with radiographic evidence of enlarged mediastinal lymph nodes that are adjacent to the airways because bronchoscopy is usually performed in lung cancer patients and assessment for endobronchial lesions can be performed during the same procedure. However, conventional TBNA is a blind procedure preventing target visualization and therefore the yield for TBNA varies widely. To overcome these problems, EBUS has been used to increase the yield of TBNA.

Before the availability of the CP-EBUS, the radial probe EBUS was used for TBNA guidance of mediastinal lymph nodes. Although a high diagnostic yield has been reported, it is still not a real-time procedure with target visualization. The introduction of the CP-EBUS has allowed real-time TBNA of mediastinal and hilar lymph nodes (Figure 5).

**EBUS-TBNA for Lymph Node Staging**

The first article to report the diagnostic yield of EBUS-TBNA in a prospective study for lymph node staging of lung cancer not only showed the high yield, but also the impact of this procedure on patient management. CP-EBUS can access all the mediastinal lymph nodes except for the subaortic and paraesophageal lymph nodes (levels 5, 6, 8, and 9). Hilar lymph nodes (levels 10 and 11) are also approachable. In 105 patients, EBUS-TBNA was successfully performed to obtain samples from 163 lymph nodes. With respect to the correct prediction of lymph node stage, EBUS-TBNA had a diagnostic accuracy rate of 96.3%. In the 20 suspected lung cancer cases, a mediastinal lymph node was used for tissue diagnosis of malignancy and staging. In addition, as a result of EBUS-TBNA, 29 mediastinoscopies, eight thoracotomies, four thoracoscopies, and nine CT-guided percutaneous needle biopsies were avoided. EBUS-TBNA spared invasive staging procedures, which had a major impact on patient management in lung cancer.

Additional reports have shown the use of EBUS-TBNA in combination with EUS-FNA for the mediastinal lymph node staging of lung cancer. EBUS has better access to anterior and superior mediastinal lymph nodes, whereas EUS has better access to posterior and inferior mediastinal lymph nodes. Theoretically, the whole mediastinum is accessible by combining EBUS and EUS.

**TABLE 1. Comparison of Invasive Staging Modalities of the Mediastinum**

<table>
<thead>
<tr>
<th>Method</th>
<th>Accessible Nodal Stations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard mediastinoscopy</td>
<td>Superior mediastinal, subcarinal</td>
</tr>
<tr>
<td>VATS</td>
<td>Superior mediastinal (right), subcarinal, aortic nodes</td>
</tr>
<tr>
<td>TBNA</td>
<td>Superior mediastinal, subcarinal, N1 nodes</td>
</tr>
<tr>
<td>Conventional EBUS</td>
<td>Subaortic, inferior mediastinal, subcarinal</td>
</tr>
<tr>
<td>Radial EBUS guided</td>
<td></td>
</tr>
<tr>
<td>CT guided</td>
<td></td>
</tr>
<tr>
<td>EBUS-TBNA</td>
<td></td>
</tr>
<tr>
<td>EUS-FNA</td>
<td></td>
</tr>
</tbody>
</table>

EBUS, endobronchial ultrasonography; EUS-FNA, endoscopic ultrasonography–guided fine-needle aspiration; EBUS-TBNA, endobronchial ultrasonography–guided transbronchial needle aspiration; TBNA, transbronchial needle aspiration; VATS, video-assisted thoracoscopic surgery.

**FIGURE 5.** Chest computed tomography (CT) (A), endobronchial ultrasonography (EBUS) (B), and pathology (C, D) performed in a 58-year-old patient with lung cancer of the right upper lobe. (A) A CT scan demonstrates pretracheal lymph node swelling (level 4R lymph node). (B) EBUS demonstrates level 4R lymph node (4R) and SVC. The 22-gauge needle is seen within the lymph node. (C) EBUS-transbronchial needle aspiration (TBNA) revealed adenocarcinoma on cytology. (D) A histologic specimen was also obtained by EBUS-TBNA that revealed adenocarcinoma.
Recently, a study comparing EBUS-TBNA, CT, and PET for lymph node staging of lung cancer showed a high yield using CP-EBUS. One hundred two potentially operable patients with proven (n = 96) or radiographically suspected (n = 6) lung cancer were included in the study. CT, PET, and EBUS-TBNA were performed before surgery for the evaluation of mediastinal and hilar lymph node metastasis. EBUS-TBNA was successfully performed in all 102 patients (mean age, 67.8 years) from 147 mediastinal and 53 hilar lymph nodes. Sensitivity of CT, PET, and EBUS-TBNA for the correct diagnosis of mediastinal and hilar lymph node staging was 76.9%, 80.0%, and 92.3%, and specificity was 55.3%, 70.1%, and 100%, respectively. The diagnostic accuracies were 60.8%, 72.5%, and 98.0%. EBUS-TBNA was proven to have a high sensitivity as well as specificity compared with CT or PET, for mediastinal staging in patients with potentially resectable lung cancer (Figure 6).

Comparison of EBUS-TBNA With Mediastinoscopy

Currently the best means to assess lymph node involvement is by direct lymph node sampling. The current gold standard method to obtain such direct sampling is by mediastinoscopy. Mediastinoscopy has the ability to access samples of the paratracheal lymph node stations (levels 2R, 2L, 3, 4R, 4L) as well as the anterior subcarinal lymph node station (level 7). Given the invasive and costly nature of a surgical mediastinoscopy, there has been considerable interest recently in the development of techniques that allow minimally invasive investigation and sampling of mediastinal lymph nodes. EBUS-TBNA allows access to the paratracheal lymph node stations (levels 2R, 2L, 3, 4R, 4L), subcarinal lymph node (level 7), and the hilar lymph node (levels 10, 11, and 12).

Although case series using EBUS-TBNA have reported sensitivities of approximately 90% for detecting malignant disease, there have been no studies directly comparing mediastinoscopy and EBUS-TBNA. An ongoing study comparing the yield of mediastinoscopy and EBUS-TBNA for mediastinal lymph node staging in patients with confirmed or suspected lung cancer show promising results. All patients underwent EBUS-TBNA followed by mediastinoscopy under general anesthesia.

Of 45 patients enrolled in the study, the diagnostic accuracy of EBUS-TBNA and mediastinoscopy for analysis of each lymph node station was 95.6% and 96.6%, respectively. The sensitivity, specificity, and diagnostic accuracy for the correct mediastinal lymph node staging for EBUS-TBNA and mediastinoscopy were 76.9%, 100%, 90.9%, and 84.6%, 100%, and 93.9%, respectively. EBUS-TBNA was uneventful, and there were no complications. These preliminary results show that EBUS-TBNA may reduce the number of mediastinoscopies needed for the staging of the mediasti-
num in non-small cell lung cancer. However, due to the possibility of micrometastases, it is not clear that EBUS-TBNA will completely replace mediastinoscopy for mediastinal staging.

OTHER POTENTIAL USES OF EBUS

EBUS-TBNA for Biopsy of Lung Tumors

The radial probe EBUS has been shown to be effective in the evaluation of peripheral intrapulmonary nodules. In addition, EBUS-guided biopsy of peripheral nodules using the radial probe has been shown to have a good yield without the exposure of radiation. However, these procedures are not real-time biopsies.

Although EBUS-TBNA has been shown to be a useful tool for the assessment and biopsy of mediastinal lymph nodes, its role in the diagnosis of lung tumors has not been identified. The reach of CP-EBUS depends on the size of the bronchus. The outer diameter of the insertion tube of the flexible bronchoscope is 6.7 mm and that of the tip is 6.9 mm. Usually the CP-EBUS can be inserted down to the lobar bronchus. For lower lobes, it can be inserted into the basal segmental bronchus. Lung tumors that are located adjacent to the airway within the reach of CP-EBUS can be diagnosed with EBUS-TBNA. We have experienced many cases in which tumors are located adjacent to the bronchus, but conventional bronchoscopic biopsy procedures produced inconclusive results. As shown in Figure 7, tumors not assessable by conventional bronchoscopy can easily be detected by CP-EBUS, and a firm diagnosis can be obtained by EBUS-TBNA. Lung tumors located in the apex adjacent to the trachea usually difficult to diagnose by conventional bronchoscopic biopsies can also be easily diagnosed by EBUS-TBNA (Figure 8).

Diagnosis of Mediastinal Tumors

Mediastinal processes can be located precisely using radial probe EBUS. This is performed by careful attention to the relation to other mediastinal structures. Studies show that EBUS is more suitable for the detection of infiltration of mediastinal organs by tumor compared with conventional radiographic imaging procedures. In case of compression of airways, EBUS clearly differentiates between vascular abnormalities, fluid, and solid structures. Although EBUS has been shown to be a valuable imaging modality for the mediastinum, there are few reports concerning the actual biopsy of mediastinal tumors under EBUS guidance.

With the introduction of CP-EBUS, real-time transbronchial needle biopsy of the mediastinum is now possible. We have used EBUS-TBNA of mediastinal tumors suspected of malignancy in various patients (Figure 9). Mediastinal processes diagnosed by EBUS-TBNA include bronchogenic cyst, malignant lymphoma, thymic cancer, mediastinal goiter, and chondrosarcoma. EBUS-TBNA for the diagnosis of sarcoidosis has also been reported to have a very high yield. Compared with diagnosis of lymph node metastasis in lung cancer patients, cytologic diagnosis of mediastinal tumors is often more difficult. Histologic diagnosis is the preferred choice. Although the current 22-gauge needle is capable of obtaining a specimen suitable for histologic examination, a larger needle that will allow us to sample better tissue is needed.
The EBUS-TBNA scope has been shown by several trials to have a high diagnostic yield for lymph node staging of lung cancer. It is a minimally invasive procedure that...

FIGURE 8. Chest computed tomography (CT) (A) and endobronchial ultrasonography (EBUS) (B, C) performed in a 56-year-old patient with suspected lung cancer in the left apical lesion. (A) CT scan demonstrates a tumor in the left apex adjacent to the trachea (arrow). (B) EBUS demonstrates the tumor 2.54 x 2.39 cm in diameter (markers at 1-cm intervals). (C) EBUS-transbronchial needle aspiration was performed. A 22-gauge needle is seen within the tumor. Cytologic results demonstrated adenocarcinoma.

FIGURE 9. Chest computed tomography (CT) (A) and endobronchial ultrasonography (EBUS) (B, C) performed in a 29-year-old patient with anterior mediastinal tumor suspected of malignancy. (A) CT scan demonstrates an anterior mediastinal tumor invading mediastinal structures (arrow). (B) EBUS demonstrates the tumor in back of the brachiocephalic vein (BCV). (C) EBUS-transbronchial needle aspiration resulted in the diagnosis of malignant lymphoma. A 22-gauge needle is seen within the lymph node.

FUTURE DIRECTIONS OF EBUS

The EBUS-TBNA scope has been shown by several trials to have a high diagnostic yield for lymph node staging of lung cancer. It is a minimally invasive procedure that...
spares many invasive procedures. To date, there have been no reports of complications related to EBUS-TBNA. Although the present data on EBUS-TBNA are promising, there is always the possibility of false-negative results. To increase the yield, a larger needle is necessary.

Conversely, the availability of multiple histologic cores from the present 22-gauge needle raises the possibility of looking at molecular diagnosis from EBUS-TBNA obtained specimens.46 Our preliminary experience in lung cancer patients with N2 or N3 disease proven by EBUS-TBNA has shown that DNA can be extracted from paraffin-embedded samples obtained by EBUS-TBNA. The ability to perform biological analysis using nonsurgical biopsy samples using EBUS-TBNA will become very important for the future of lung cancer treatment. EBUS-TBNA samples will possibly provide other molecular biological information that will be useful for the treatment of lung cancer.

Restaging of the mediastinum is another area of growing interest for the treatment strategy of lung cancer. In cases of advanced lymph node stage lung cancer, induction chemotherapy before surgical resection is an option. The current restaging modalities either have a low diagnostic accuracy (CT and PET) or are invasive. Mediastinoscopy is considered the gold standard in staging the mediastinum. However, repeat mediastinoscopy can be technically difficult and is therefore not commonly performed. The ability to perform multiple, repeat biopsies using EBUS-TBNA allows restaging of the mediastinum after the introduction of chemotherapy. Preliminary studies looking at the utility of EBUS-TBNA for mediastinal restaging show promising results.

The reach of EBUS-TBNA and EUS-FNA for tissue sampling of the mediastinum is complementary. EUS-FNA can reach mediastinal lymph nodes not adjacent to the airways and not accessible by EBUS-TBNA such as paraesophageal (level 8), pulmonary ligament (level 9), and subaortic (level 5). Theoretically, by combining EBUS and EUS, a complete and accurate evaluation of the whole mediastinum is possible. Preliminary studies have shown a high diagnostic yield for complete staging of the mediastinum.17,18,21 However, the transesophageal approach is usually unfamiliar to most pulmonologists, and therefore a referral to a specialist is needed, whereas EBUS-TBNA can be performed during bronchoscopy. Further studies will need to prove the efficacy of combining the two modalities in clinical practice.

Until now, the focus of using EBUS in respiratory disease has been for diagnostic purposes. In the future, the therapeutic use of EBUS will probably change the practice of interventional pulmonology. Further advances in technology will be important to meet these needs.

**CONCLUSION**

EBUS has emerged as a new tool to see beyond what bronchoscopists are used to seeing. The radial probe EBUS allows high-resolution imaging of the multilayer structures of the bronchial wall as well as the evaluation of the surrounding structures. The ultra-miniature radial probe can aid and increase the diagnostic yield of peripheral intrapulmonary lesions. EBUS-TBNA using the new ultrasonic puncture bronchoscope allows real-time needle puncture of the mediastinum and the hilum. It is a minimally invasive procedure that is safe with a high diagnostic yield. The EBUS will be a valuable addition to many bronchoscopic practices in pulmonary medicine in the near future. Further prospective data describing the diagnostic yield of EBUS-TBNA compared with conventional tools will be needed to support the value of this new modality. However, based on our current experience, we believe that the value of CP-EBUS as a diagnostic tool for the staging of lung cancer as well as mediastinal abnormalities will be established in the near future.

**REFERENCES**

transbronchial needle aspiration of lymph nodes in the radiologically
ultrasound guided transbronchial needle aspiration for sampling medi-
21. Herth FJ, RabeKF, Gasparini S, et al. Transbronchial and transesoph-
geal (ultrasound-guided) needle aspirations for the analysis of medias-
wall invasion using transbronchial ultrasonography (TBUS). Eur J Car-
2003;10:249.
25. Miyazu Y, Miyazawa T, Kurimoto N, et al. Endobronchial ultrasonog-
raphy in the assessment of centrally located early-stage lung cancer
before photodynamic therapy. Am J Respir Crit Care Med 2002;165:
832–837.
endobronchial ultrasound for airway invasion around the trachea: esoph-
27. Irani S, Hess T, Hofer M, et al. Endobronchial ultrasonography for the
quantitative assessment of bronchial mural structures in lung transplant
fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest
29. Torrington KG, Kern JD. The utility of fiberbronchoscopy in the eval-
31. Larscheid RC, Thorpe PE, Scott WJ. Percutaneous transthoracic needle
aspiration biopsy: a comprehensive review of its current role in the
32. Herth FJ, Ernst A, Becker HD. Endobronchial ultrasound-guided trans-
bronchial lung biopsy in solitary pulmonary nodules and peripheral
33. Shirakawa T, Inamura F, Hamamoto J, et al. Usefulness of endobron-
chial ultrasonography for transbronchial lung biopsies of peripheral lung
driven biopsy in the diagnosis of peripheral lung lesions. Chest 2005;
128:3551–3557.
35. Spiro SG, Porter JC. Lung cancer – where are we today? Current
advances in staging and nonsurgical treatment. Am J Respir Crit Care
37. Hammoud ZT, Anderson RC, Meyers BF, et al. The current role of
mediastinoscopy in the evaluation of thoracic disease. J Thorac Cardio-
38. Bolliger CT, Mathur PN, Beaminis JF, et al. ERS/ATS statement on
interventional pulmonology. European Respiratory Society/American
aspiration for staging of bronchogenic carcinoma. Chest 1983;84:571–
576.
41. Mehta AC, Kavuru MS, Meeker DP, et al. Transbronchial needle
42. Garpestad E, Goldberg S, Herth F, et al. CT fluoroscopy guidance for
transbronchial needle aspiration: an experience in 35 patients. Chest
43. Lloyd G, Silvestri GA. Mediastinal staging of non small-cell lung
44. Yasufuku K, Quadri M, de Perrot M, et al. A prospective controlled trial
of endobronchial ultrasound guided transbronchial needle aspiration
compared to mediastinoscopy for mediastinal lymph node staging of
lung cancer. Presented at the Western Thoracic Surgical Association
45. Herth F, Becker HD. Endobronchial ultrasound of the airways and the
spinal chondrosarcoma by endobronchial ultrasound-guided transbron-
ultrasound guided transbronchial needle aspiration in the diagnosis of