Endobronchial Ultrasonography Using a Guide Sheath Increases the Ability To Diagnose Peripheral Pulmonary Lesions Endoscopically *

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Endobronchial Ultrasonography Using a Guide Sheath Increases the Ability To Diagnose Peripheral Pulmonary Lesions Endoscopically*

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Study objective: **To assess the ability of endobronchial ultrasonography (EBUS) using a guide sheath (EBUS-GS) to diagnose peripheral pulmonary lesions.**
Method: **We devised a technique for EBUS-GS covering a miniature probe, and 150 lesions were evaluated in a prospective open study. In this procedure, the probe covered by a guide sheath is introduced into the lesion via the working channel of a bronchoscope. The probe is withdrawn, while the guide sheath is left *in situ*. A brush or biopsy forceps is introduced through the guide sheath into the lesion.**
Results: **One hundred sixteen of 150 EBUS-GS procedures (77%) were diagnostic. Cases in which the probe was located within the lesion had a significantly higher diagnostic yield (105 of 121 cases, 87%) than when the probe was located adjacent to it (8 of 19 cases, 42%) [$p < 0.0001$, χ^2]. The diagnostic yield from EBUS-GS in lesions ≤ 10 mm (16 of 21 lesions, 76%), >10 to ≤ 15 mm (19 of 25 lesions, 76%; $p = 0.99$, χ^2), >15 to ≤ 20 mm (23 of 35 lesions, 66%; $p = 0.41$, χ^2), and > 20 to ≤ 30 mm (33 of 43 lesions, 77%; $p = 0.96$, χ^2) were similar, demonstrating the efficacy of EBUS-GS even in lesions ≤ 10 mm in diameter. In 54 of 81 lesions ≤ 20 mm, fluoroscopy was not able to confirm whether the forceps reached the lesion. However, the yield was the same with (67%, 18 of 27 lesions) and without (74%, 40 of 54 lesions) successful fluoroscopy ($p = 0.96$, χ^2). Moderate bleeding occurred in two patients (1%); there were no other complications.**
Conclusions: **EBUS-GS is a useful method for collecting samples from peripheral pulmonary lesions, even those too small to be visualized under fluoroscopy.**

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Key words: endobronchial ultrasonography; guide sheath; peripheral pulmonary lesions

Abbreviations: EBUS = endobronchial ultrasonography; EBUS-GS = endobronchial ultrasonography using a guide sheath; TBB = transbronchial biopsy

Endobronchial ultrasonography (EBUS) with a very thin ultrasonic probe inserted through the working channel of a flexible bronchoscope provides cross-sectional images of the tracheobronchial wall and adjacent mediastinal structures. The indications for EBUS include the following: (1) determination of depth of invasion of tracheobronchial tumors,[1,2] (2) delineation of the anatomic relationships between the pulmonary artery and veins and diagnosis of invasion by hilar tumors,[3] (3) visualization of peritracheal and peribronchial lymph nodes and diagnosis of metastases, and (4) localization and qualitative diagnosis of peripheral pulmonary lesions (benign or malignant).[4–6] Bronchial brushing cytology and transbronchial biopsy (TBB) have been used to diagnose peripheral pulmonary lesions. However, fluoroscopy is required in most cases to direct the operator to the site of interest. Still, it is often difficult to confirm whether the forceps has reached the lesion. To increase the reliability of collection

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from peripheral pulmonary lesions, we devised a technique using EBUS with a guide sheath (EBUS-GS). Our experience with 150 patients is reported.

Materials and Methods

Subjects

The study was designed to prospectively evaluate the role of EBUS-GS in the evaluation of patients with a solitary pulmonary lesion detected by chest radiography and CT. One hundred fifty consecutive patients with a peripheral pulmonary lesion who underwent bronchoscopy between May 2001 and November 2002 at National Hiroshima Hospital and Hiroshima City Hospital were enrolled for this study. Informed consent was obtained in all patients prior to the procedure.

Equipment

A miniature ultrasound probe (20 MHz, mechanical-radial type) [UM-S20–20R; Olympus Optical; Tokyo, Japan] with an outer diameter of 1.7 mm was used. The probe was connected to an endoscopic ultrasound system (EU-M30; Olympus Optical). A guide sheath (Olympus Optical) was manufactured especially for this purpose.

Preparation

A bronchial brush (BC-202D-5010; Olympus Optical) or biopsy forceps (BF-19C-1; Olympus Optical) for TBB is introduced into the specially made guide sheath, so that the tip of the forceps reaches the far end of the sheath to facilitate manipulation (Fig 1, *top right*, *1*). The forceps is marked at the near end of the sheath by cellulose tape during bronchoscopy. A miniature probe is introduced into the guide sheath until the tip of the probe juts out of the far end of the sheath (Fig 1, *left*, *2*, and *bottom right*, *3*). Then, the probe and the sheath are bound together at the proximal end of the sheath with cellulose tape so that the tip of the probe remains positioned at the far end of the sheath.

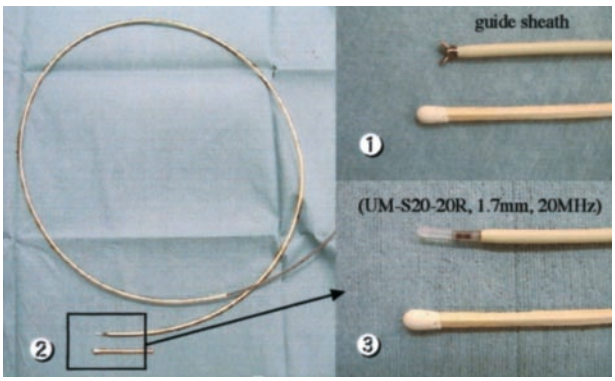


Figure 1. Equipment. *Top right*, *1*: A biopsy forceps for TBB is introduced into the specially made guide sheath, so that the tip of the forceps reaches the far end of the sheath. *Left*, 2, and *bottom right*, *3*: A miniature probe is introduced into the specially made guide sheath until the tip of the probe juts out of the far end of the sheath.

EBUS-GS

Continuous pulse oximetry was performed during bronchoscopy, and BP was measured every 5 min. Oxygen was administered by a nasal cannula, and the flow was adjusted upward from 2 L/min to maintain the pulse oximetric saturation $> 90\%$. A flexible fiberoptic bronchoscope (BF 1T-30, 40, or 240R; Olympus Optical) was used for all procedures.

After the bronchoscope was advanced beyond the vocal cords, all segments of the bronchial tree were visualized. Based on the radiographic findings, the miniature probe with the guide sheath was negotiated into the bronchus of interest.

The probe was advanced until it reached a point where the operator sensed resistance, and then pulled back for scanning (Fig 2, *top left*, *1*). When an EBUS image of the lesion could not be obtained, the probe was withdrawn and a curette was inserted into the guide sheath. While retracting the angulated curette with the guide sheath under fluoroscopy, the tip of the curette was moved into another branch of the bronchus. After the angulated curette was advanced into the bronchus leading to the lesion, the curette was withdrawn and once again the probe was inserted into the guide sheath and another attempt made to obtain an EBUS image. Once the location of the lesion was identified precisely by EBUS, the probe was withdrawn, leaving the guide sheath in place (Fig 2, *top right*, *2*).

A biopsy forceps or bronchial brush was introduced into the sheath until the point marked by the cellulose tape reached the proximal end of the sheath (Fig 2, *bottom right*, *3*). When using the brush, a few vigorous back-and-forth movements were performed to collect the sample on the brush under fluoroscopic guidance.

After the brushing forceps was withdrawn, the biopsy forceps

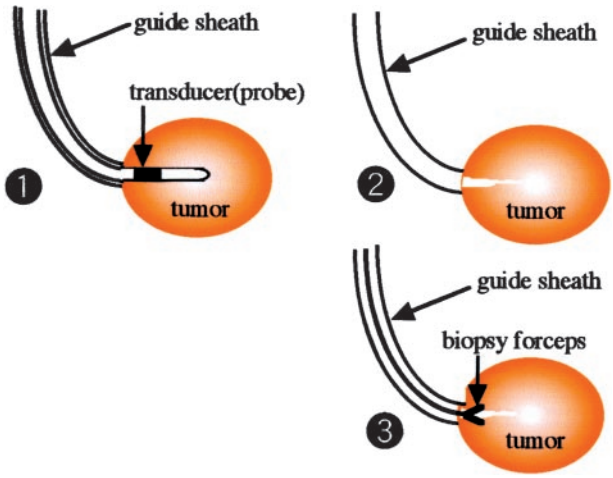


Figure 2. Methods of EBUS-GS. A bronchial brush or biopsy forceps for TBB is introduced into the specially fashioned guide sheath, so that the tip of the forceps reaches the far end of the sheath to facilitate manipulation. The forceps is marked at the near end of the sheath by cellulose tape during bronchoscopy. A miniature probe is introduced into the guide sheath until the tip of the probe barely protrudes from the far end of the sheath. *Left*, *1*: The miniature probe in the guide sheath is negotiated into the bronchus of interest. The probe is advanced until it reaches the lesion. *Top right*, *2*: The probe is then removed with the guide sheath left *in situ* in the lesion. *Bottom right*, *3*: A biopsy forceps or bronchial brush is then introduced into the sheath until the mark with the cellulose tape on the surface of the forceps is at the near end of the sheath. Brushings and/or biopsy specimens are collected.

was once again introduced into the sheath until the mark on the surface of the forceps reached the end of the sheath. The cups of forceps were opened, and the forceps was advanced 2 or 3 mm into the lesion and the cups closed under imaging guidance. One sufficient biopsy specimen was obtained and placed in formalin.

The guide sheath was left in place for approximately 2 min to put pressure on the biopsy to control bleeding. This procedure is concluded after confirming that hemostasis was achieved.

The amount of bleeding that occurs with guide sheath removal was estimated. Bleeding ($\geq$ 60 mL) was considered severe, and $\geq$ 30 mL was considered moderate when there is no danger to the airway.

Size of the Lesion

The largest dimensions in the anteroposterior and mediolateral directions were measured by CT, and the greatest dimension was defined as the size of the lesion when evaluating effect of size on the diagnostic yield.

Time of Procedure

The total time of EBUS-GS was defined as the time from the insertion of the probe to withdrawal of the guide sheath. The EBUS time was the time that was actually performed EBUS. The fluoroscopy time was calculated as the time was actually being performed.

Results

Table 1 shows the diagnoses in the 150 patients established by bronchoscopy, CT-guided transthoracic needle aspiration, thoracotomy, or clinical follow-up. A definitive diagnosis was made by EBUS-GS in 116 patients (77%). Of the 34 patients with nondiagnostic EBUS-GS, the diagnosis was established by transthoracic needle aspiration in 2 patients and by thoracotomy in 24 patients. In two patients, the postbronchoscopic sputum revealed tuberculosis. In six patients, a tissue diagnosis could not be established, but roentgenographic shadows disappeared during follow-up, and these lesions were considered to be inflammatory.

Table 1—*Clinical Diagnosis of Peripheral Pulmonary Lesions in 150 Patients Who Underwent EBUS-GS

Lesions	Data
Benign	
Tuberculosis	9/11
Organizing pneumonia	8/11
Nontuberculous mycobacterosis	7/7
Bronchopneumonia	4/4
Pulmonary abscess	2/2
Sarcoidosis	2/2
Aspergillosis	1/1
Pneumoconiosis	1/1
Inflammatory lesion	0/6
Hamartoma	0/1
Actinomycosis	0/1
Nonspecific interstitial pneumonia	0/1
Tuberculoma	0/1
Total	34/49
Malignant	
Adenocarcinoma	55/72
Squamous cell carcinoma	19/20
Small cell carcinoma	5/5
Large cell carcinoma	1/1
Adenosquamous carcinoma	1/1
Metastasis (malignant fibrous histiocytoma)	0/1
Cancer	1/1
Total	82/101

*Data are presented as No. (total cases).

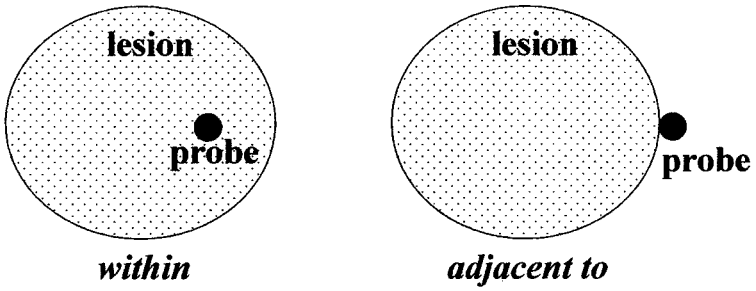
The overall yield of EBUS-GS was 77% (116 of 150 lesions), and the diagnostic yield of EBUS-GS in malignant and benign lesions was 81% (82 of 101 lesions) and 69% (34 of 49 lesions), respectively. Table 2 shows the diagnostic yield of each sampling method. The diagnostic yield from brushing cytology was 60% (90 of 150 lesions), and the yield from TBB was 81% (89 of 110 lesions). Among malignant lesions, the yield by TBB (65 of 75 lesions, 87%) was significantly higher than that of brushing cytology (71 of 100 lesions, 71%) [$p = 0.01$, χ^2], as it was for benign lesions (24 of 35 lesions [69%] and 19 of 50 lesions [38%], respectively) [$p = 0.002$, χ^2]. The lesions in which brushing cytology was negative and TBB was diagnostic included 16 benign lesions and 9 malignant lesions. The 16 benign lesions included 10 cases of organizing pneumonia, each one of abscess, aspergillosis, bronchopneumonia, pneumoconiosis, sarcoidosis, and nonspecific inflammation. The nine malignant lesions included six well-differentiated adenocarcinomas, each one poorly differentiated adenocarcinoma, squamous cell carcinoma, and small cell carcinoma each.

The effect of probe location on the yield is shown in Fig 3. Lesions in which the probe was advanced to within the lesion, as determined from the EBUS image, had a higher diagnostic yield (105 of 121 lesions, 87%) than when the probe was adjacent to the lesion on the EBUS image (8 of 19 lesions, 42%) [$p < 0.0001$, χ^2]. The yield by TBB for lesions in which the probe was located within the lesion (85 of 104 lesions, 82%), was very significantly higher than when the probe was adjacent to it (1 of 15 lesions, 7%) [$p < 0.0001$, χ^2]. Sixteen nondiagnostic procedures in which the probe was located inside the

Table 2—*Diagnostic Yields From Peripheral Lesions by Brushing and TBB With EBUS-GS

Variables	Brushing	TBB	Combined
Positive sample	90/150 (60)	89/110 (81)	116/150 (77)
Benign	19/50 (38)	24/35 (69)	34/49 (69)
Malignant	71/100 (71)	65/75 (87)	82/101 (81)

*Data are presented as No./total (%).



location of the probe	brushing (140)	TBB (110)	total (140)
within (121)	81/121 (67%)	79/96 (82%)	105/121 (87%)
adjacent to (19)	7/19 (37%)	1/14 (7%)	8/19 (42%)

FIGURE 3. Effect of probe location on the yield. Lesions in which the probe was advanced to within the lesion, as determined from the EBUS image, had a higher diagnostic yield (105 of 121, 87%) than when the probe was adjacent to the lesion on the EBUS image (8 of 19, 42%) [$P < 0.0001$, χ^2]. The yield by TBB for lesions in which the probe was located within the lesion (85 of 104, 82%) was very significantly higher than when the probe adjacent to it (1 of 15, 7%) [$P < 0.0001$, χ^2].

lesion consisted of six cases of well-differentiated adenocarcinoma, and two cases each of bronchioloalveolar carcinoma, moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, actinomycosis, and tuberculosis.

Table 3 shows the effect of the size of the lesion on the yield from EBUS-GS. Diagnostic yield from EBUS-GS for lesions defined as a mass (> 30 mm; 24 of 26 lesions, 92%) was significantly higher than that for lesions defined as nodules (≤ 30 mm; 92 of 124 lesions, 74%) [p = 0.04, χ^2]. The diagnostic yield from EBUS-GS for lesions ≤ 10 mm (16 of 21 lesions, 76%), >10 to ≤ 15 mm (19 of 25 lesions, 76%) [p = 0.99, χ^2], >15 to ≤ 20 mm (24 of 35 lesions, 69%) [p = 0.41, χ^2], and > 20 to ≤ 30 mm (33 of 43 lesions, 77%) [p = 0.96, χ^2] were similar. When the lesion was ≤ 30 mm, size did not affect the yield by EBUS-GS. In other words, the yield for lesions ≤ 10 mm did not decrease.

It was impossible to confirm that the forceps reached the lesion under fluoroscopy in 54 of 81 lesions that were ≤ 20 mm in size. The yield in these lesions was 74% (40 of 54 lesions), and was similar to the yield when it was possible to determine whether the forceps reached to the lesion by fluoroscopy (18 of 27 lesions, 67%) [p = 0.96, χ^2].

Yield was affected by the location of the lesion (Fig 4). The yield from the left upper apical posterior

Table 3—*Effect of Lesion Size on Diagnostic Yield by EBUS-GS of Peripheral Pulmonary Lesions*

Lesion Size, mm	No./Total (%)
≤ 10	16/21 (76)
> 10 to ≤ 15	19/25 (76)
> 15 to ≤ 20	24/35 (69)
> 20 to ≤ 30	33/43 (77)
> 30	24/26 (92)

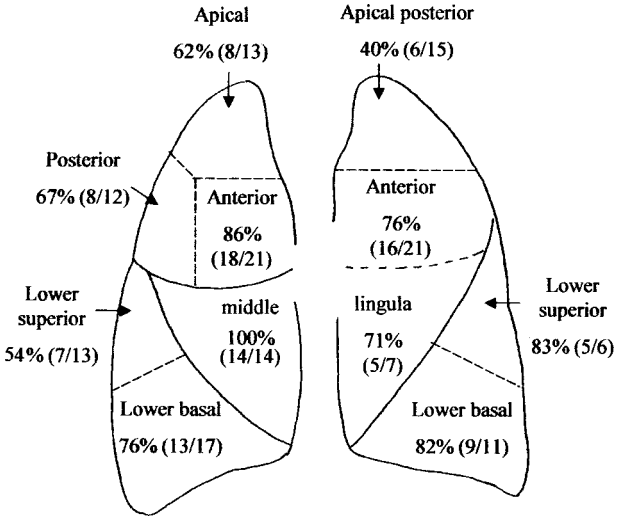


FIGURE 4. Diagnostic yield affected the location of the lesion. Positive yields were as follows: right upper lobe apical segment (8 of 13 lesions, 62%), right upper lobe posterior segment (8 of 12 lesions, 67%), left upper apical posterior segment (6 of 15 lesions, 40%), upper lobe anterior segment (34 of 42 lesions, 81%), lingula (5 of 7 lesions, 71%), right middle lobe (14 of 14 lesions, 100%), lower lobe superior segment (12 of 19 lesions, 63%), and lower lobe basal segment (22 of 28 lesions, 79%). The yield from the left upper apical posterior segment (6 of 15 lesions, 40%) was significantly lower than that from other locations (p = 0.003, χ^2).

segment (6 of 15 lesions, 40%) was significantly lower than that from other locations ($p = 0.003$, χ^2).

Ten lesions could not be imaged by EBUS. In these cases, we withdrew the probe and inserted the curette. After searching for the lesion by curettage, the probe was again inserted in these cases, and EBUS-GS was diagnostic in 3 of 10 cases. Moderate bleeding was noted in two patients (1%). None of the patients required bronchial intubation. There was no death, pneumothorax, or other clinically significant morbidity. The overall time of EBUS-GS was 8.83 ± 0.77 min, the mean scanning time was 61.5 ± 23 s, and the mean fluoroscopy time was 59.0 ± 45.2 s ($\pm$ SD). The procedures and images of EBUS-GS will be described in a representative case.

Representative Case

A 74-year-old man had a 10×8-mm nodular lesion in segment B5b of the right lung (Fig 5). Bronchoscopy was performed to confirm the diagnosis of the nodular lesion. A miniature probe covered by the guide sheath was introduced into B5b of the right lung, and pulled back to obtain EBUS images. EBUS revealed heterogeneous internal echoes and a lesion with an irregular margin that contained almost no vessels or bronchi. These findings were suggestive of a solid tumor with a high cell density. The guide sheath was left at the site of the lesion identified by EBUS, and the probe was withdrawn. A bronchial brush and biopsy forceps were introduced into the bronchus. Cytology of the bronchial brushings revealed adenocarcinoma, and TBB confirmed the diagnosis of poorly differentiated adenocarcinoma.

Discussion

EBUS-GS increases the reliability of specimen collection via bronchoscopy. Diagnostic yields of bronchoscopy for peripheral pulmonary lesions < 2 cm in published reports[7–16] have been varied from 5 to 28%. The diagnostic yield in this study was far superior, and was similar to the overall yield, even when the lesion was undetectable under fluoroscopy. When an undetectable lesion under fluoroscopy is in contact to the probe inserted inside the bronchus, the lesion is visualized by EBUS, and EBUS-GS is particularly useful for lesions ≤ 20 mm that are undetectable by fluoroscopy. Although we used EBUS-GS as the procedure for guiding the biopsy procedure instead of fluoroscopy, fluoroscopy was used to search for lesions while manipulating a curette and during the brush biopsy procedure. While 44 lesions were not visible under fluoroscopy, 10 lesions were not imaged by EBUS. We expect

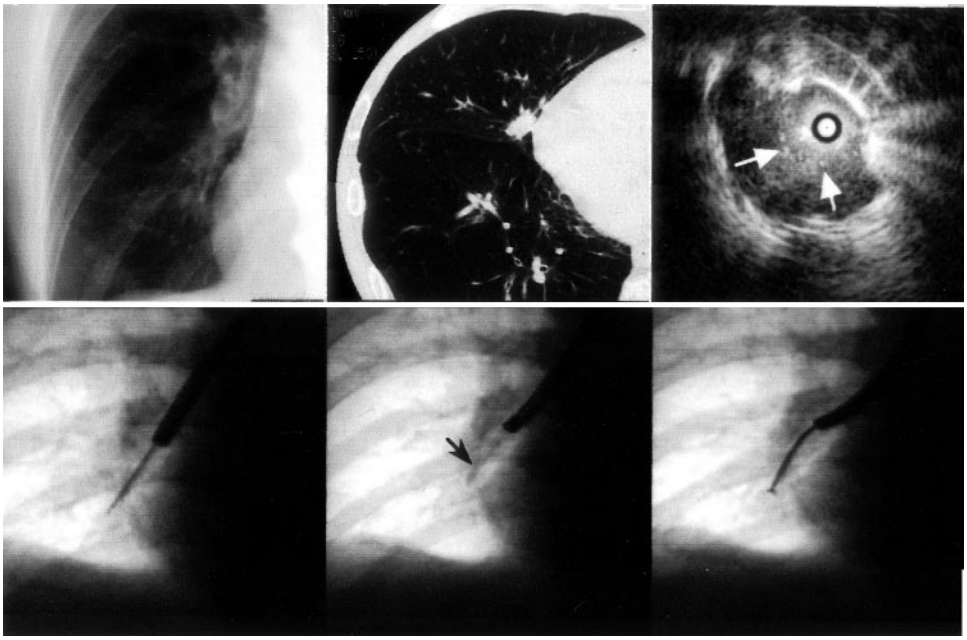


Figure 5. A poorly differentiated adenocarcinoma in the right middle lobe. *Top left*: A lesion is difficult to identify on a plain chest radiograph. *Top center*: Chest CT revealed a nodular lesion, 10×8 mm in size in segment B5b of the right lung. *Top right*: The EBUS image revealed heterogeneous internal echoes (arrow) and an irregular margin of the lesion, with almost no vessels or bronchi within the lesion. *Bottom left*: A miniature probe covered by the guide sheath was introduced into B5b of the right lung. *Bottom center*: A guide sheath (arrow) was left at the site of the lesion. *Bottom right*: A bronchial biopsy forceps was introduced into the lesion.

EBUS-GS to largely replace fluoroscopy in determining the precise site for bronchoscopic tissue sampling.

EBUS-GS was most successful when the probe could be placed within the lesion. The yield of TBB when the probe was adjacent to the lesion was very low (1 of 15 lesions, 7%). This suggests that the lesions visualized as adjacent to the probe may only be in contact with outer surface of the bronchus, and therefore sampling is unlikely to be diagnostic. In this circumstance, the operator should attempt to identify the lesion via another bronchial branch. Nevertheless even when the probe was located within the lesion, 16 lesions could not be diagnosed. Six of these lesions were well-differentiated adenocarcinoma. Here, tumor may not have penetrated the bronchus transmurally. In these cases, the addition of transbronchial needle aspiration might increase the yield.

Chechani[17] reported fluoroscopic localization to be most difficult when the lesion is small (< 2 cm) and located in the lower lobe basal segment or the upper lobe apical segment. The diagnostic yield for lesions in these two segments (58%) was lower than yields from all other locations (83%). Fletcher and Levin[9] reported the worst yields were from the lower lobe basal segment (2 of 7 lesions, 28%) and superior segment (5 of 19 lesions, 26%). In our EBUS-GS study, the worst yield was noted for lesions in the left upper lobe apical posterior segment (6 of 15 lesions, 40%) [$p = 0.003$, χ^2] when compared with yield from all other locations (103 of 135 lesions, 76%). The reason for lower diagnostic yield in the left upper lobe apical posterior segment is thought to be due to the difficulty inserting the probe into B1 + 2. The yield from the lower lobe basal segments was satisfactory (22 of 27 lesions, 81%). Thus, EBUS-GS appears superior to fluoroscopy for localizing lesions in the lower lobe basal segments.

One advantage of EBUS-GS lies in the repeatability of access to the bronchial lesion for sampling. Without a guide sheath, it can be difficult at times to be certain that the forceps are being inserted into the same bronchial branch for the second biopsy. Further, the bronchial mucosa becomes edematous after several attempts at manipulation, and it can be difficult to insert the forceps into the bronchus. Another advantage of EBUS-GS lies in its ability to protect against bleeding into proximal bronchus from the biopsy site. Although massive hemorrhage following TBB is not frequent ($< 2\%$) into the bronchus,[18,19] excessive bleeding may require hemostasis by wedging the tip of the bronchoscope. If bleeding occurs during EBUS-GS, blood drains through the sheath, because the outer surface of the sheath is snug against the internal surface of the bronchus. In this series of 150 patients, the guide sheath was left *in situ* for approximately 2 min after completion of the biopsy, and only 2 patients (1%) had moderate bleeding following removal. The final advantage of EBUS-GS is the ability to obtain short-axis bronchial views of peripheral pulmonary lesions. Several investigators have reported the use of a miniature probe. Hürter and Hanarath[4] were able to image a peripheral lesion in 19 of 26 patients. In 25 patients, Goldberg and colleagues[5] visualized peripheral lung lesions in 6 patients and hilar lesions in 19 patients; they reported that EBUS provided information that could not be obtained by other diagnostic imaging modalities in 18 of 25 patients. Our method of EBUS using a 20-MHz probe allowed visualization of the inner structures of peripheral lesions, including vessels, bronchi, calcifications, necrosis, hemorrhage, and bronchial dilatation.[6] We previously reported that peripheral pulmonary lesions could be classified as benign or malignant by EBUS.[6] In the representative case, EBUS revealed avascularity and slightly linear or patchy hyperechogenicity. The internal echoes were heterogeneous, with mixed high echoes. These findings identified the lesion as a proliferative solid tumor of high cell density.

Other investigators have described CT-guided bronchoscopy and electromagnetic navigation as new modalities for guiding bronchoscopic biopsies. Asano and colleagues[20] reported a diagnostic rate for small peripheral pulmonary lesions (≤ 2 cm) of 78.3% using CT-guided fiberbronchoscopic transbronchial biopsy. Compared with CT-guided fiberbronchoscopic TBB, EBUS-GS offers advantages including simplicity, lack of radiation exposure for patients and staff, and relatively inexpensive equipment. Drawbacks of EBUS-GS include difficulty in selecting the bronchial branch and incapability of visualizing lesions evident as ground-glass attenuation on CT. Schwarz and colleagues[21] reported an average registration accuracy for real-time electromagnetic navigation of 4.5 mm; their method represents an accurate technology able to localize peripheral pulmonary lesions. Further studies are needed to determine the yield of transbronchial needle aspiration under EBUS-GS, the feasibility of EBUS-GS without fluoroscopy, and the usefulness of a curette through the guide sheath.

Conclusion

EBUS-GS permits samples to be collected precisely from peripheral pulmonary lesions than other methods. It allows biopsies from the same site, protects against bleeding into the proximal bronchus from the biopsy site, and can delineate the inner structure of peripheral pulmonary lesions.

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