# Endobronchial Ultrasound-Guided Transbronchial Biopsy Using Novel Thin Bronchoscope for Diagnosis of Peripheral Pulmonary Lesions

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**Background:** The aim of this study was to evaluate the diagnostic utility of endobronchial ultrasound (EBUS)-guided transbronchial biopsy (TBB) using a novel 3.4-mm thin bronchoscope and a 1.4-mm ultrasonic probe for peripheral pulmonary lesions.

**Methods:** A total of 86 patients with suspected peripheral lesions were included in this prospective study. EBUS-TBBs were performed using a prototype 3.4-mm thin bronchoscope and a 1.4-mm radial ultrasonic probe under fluoroscopic guidance.

**Results:** Twelve patients with endobronchial lesions within the segmental bronchi and three patients who did not return to follow-up were excluded from this analysis. Thus, a total of 71 patients with peripheral pulmonary lesions (mean size, 31.2 ± 12.7 mm) were included in the final analysis. The mean bronchus level reached with the thin bronchoscope was 4.6 generations. Diagnostic histologic specimens were obtained in 49 of 71 patients (69%:80% for malignant lesions and 52% for benign lesions). A definitive diagnosis of malignancy for lesions ≥20 mm and lesions <20 mm was made in 82% (31 of 38) and 67% (four of six), respectively. There were no significant complications.

**Conclusion:** The EBUS-TBB using a 3.4-mm thin bronchoscope and a 1.4-mm radial probe is feasible, accurate, and safe for the diagnosis of peripheral pulmonary lesions.

**Key Words:** Bronchoscopy, Endobronchial ultrasound, Lung cancer, Peripheral pulmonary lesions, Thin bronchoscope.

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In an effort to enhance the diagnostic accuracy of bronchoscopy for peripheral pulmonary lesions, several ancillary technologies have been proposed, such as thin bronchoscopy,[1–4] endobronchial ultrasound (EBUS),[5,6] navigational bronchoscopy,[6–8] and computed tomography (CT) fluoroscopy.[9] Each of them has remarkable features, and the combination of these modalities is likely to be promising for better bronchoscopy.[6]

Innovative technology has permitted the development of a new, thinner, and better-visibility flexible bronchoscope with a working channel, which allows the use of a thin EBUS probe. The aim of this study was to assess the ability of EBUS-guided transbronchial biopsy (TBB) using a 3.4-mm hybrid-bronchofibervideoscope with a 1.7-mm working channel and a 1.4-mm ultrasonic probe to diagnose peripheral pulmonary lesions.

## PATIENTS AND METHODS

### Patients

This prospective study was approved by the institutional review board of our hospital and registered with the University Hospital Medical Information Network-Clinical Trials Registry, UMIN000000509. Informed consent was obtained from all patients. From March 2006 to March 2007, 86 patients were enrolled with localized peripheral pulmonary lesions, such as a solitary pulmonary nodule, a pulmonary mass, or a localized infiltrate, referred for diagnostic bronchoscopy. Patients with diffuse pulmonary lesions were excluded from this study.

### Equipment

A prototype thin bronchoscope (XBF-3B260Y1; Olympus, Tokyo, Japan, 3B260) and a thin ultrasonic probe (XUM-S20-17R; Olympus) were used (Figure 1). The 3B260 is a hybrid bronchofibervideoscope, which incorporates a charge-coupled device in the control section. It has a 3.4-mm distal end diameter, a 1.7-mm working channel diameter, 210° up and 130° down angulation, a 90° field of view, and a 2–50-mm depth of field. The EBUS procedures were performed with an endoscopic ultrasound center (EU-M 30; Olympus) and the XUM-S20-17R, which is a 20-MHz mechanical radial type, reusable, and direct-contact ultrasonic probe with an external diameter of 1.4 mm.

### Procedures

Bronchoscopic procedures were performed using conscious sedation with bolus intravenous midazolam and local

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Disclosure: The prototype thin bronchoscope and thin ultrasonic probe were loaned to the authors by Olympus, Tokyo, Japan for the duration of this study. The authors declare no conflict of interest.

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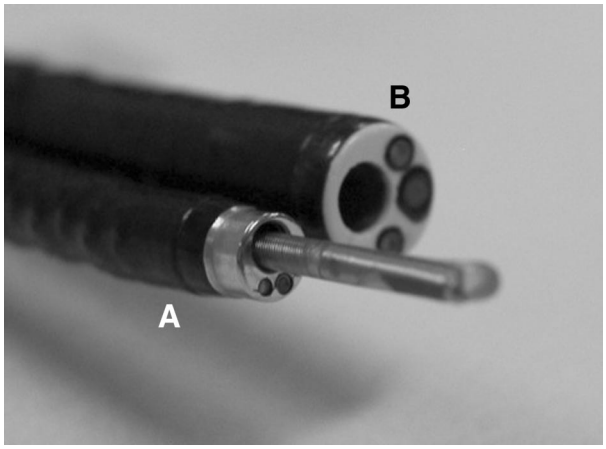


**FIGURE 1.** A comparison of bronchoscopes. *A,* Thin bronchoscope (XBF-3B260Y1, 3.4-mm distal end diameter, Olympus, Tokyo, Japan) and thin ultrasonic probe (XUM-S20-17R; Olympus). *B,* Standard bronchoscope (BF-1T260, 5.9-mm distal end diameter; Olympus).

anesthesia with lidocaine by staff pulmonologists or supervised pulmonary residents of our institution. A 5.0-mm inner diameter endotracheal tube was placed transnasally under thin bronchoscopic control, which facilitated repeated insertion and removal of the bronchoscope, and then the tracheobronchial tree was examined in standard fashion using the 3B260. After examining the endobronchial region, the 3B260 was advanced toward the bronchus most likely leading to the lesion under direct vision. Then, a thin ultrasonic probe was passed through the working channel and advanced to the lesion under bronchoscopic control with fluoroscopic visualization. If the lesion surrounding the probe was clearly visualized by EBUS, the bronchus in which the probe passed through could be the correct route leading to the target lesion. After determining the leading bronchus to the lesion, the 3B260 was further advanced as far as possible using the probe as a guide and wedged into the peripheral bronchus. After that, the probe was removed, and TBB was performed using a 1.5-mm forceps (FB-32D, Olympus) under fluoroscopic guidance. Ten biopsy specimens were taken from each lesion, and each specimen was then transferred into separate containers filled with formalin for histologic examination. After TBB, washing in the corresponding bronchus for cytologic and cultural examination was performed with 10 to 20 mL of saline solution. Other procedures such as brushing, curettage, or needle aspiration biopsy for the target lesion were not performed in the same setting. A chest radiograph was obtained routinely to identify pneumothorax after the procedures.

## Diagnosis

All malignant diagnoses were confirmed pathologically. The benign diagnoses were established by surgical procedure, microbiological analysis including tuberculosis or nontuberculous mycobacteriosis, or clinical follow-up. An inconclusive histologic diagnosis of nonspecific fibrosis or inflammation was considered to be nondiagnostic.

## Statistical Analysis

The lesions located within the segmental bronchi that were defined as central lesions[10] were excluded in this analysis. Means and percentages were presented as appropriate. The accuracies were calculated using the standard definitions. Results were analyzed using Pearson $\chi^2$ test. Statistical analyses were performed using a statistical software program (JMP; SAS Institute, Cary, NC). Results were considered statistically significant when the $p$ value was less than or equal to 0.05.

# RESULTS

An endobronchial lesion within the segmental bronchus that was defined as a central lesion was identified with the 3B260 in 12 patients. Another three patients did not return to follow-up. Thus, a total of 71 patients (45 men and 26 women; mean age, 67.2 years; range, 45–85 years) with peripheral pulmonary lesions (mean ± SD size, 31.2 ± 12.7 mm; range, 8–70 mm) were included in the final analysis.

Table 1 details the results of EBUS-TBB with the 3B260. A histologic diagnosis was made in 49 of 71 patients (69%). The diagnostic yields for malignant lesions and benign lesions were 80% (35 of 44) and 52% (14 of 27), respectively ($p$ = 0.02). The sensitivity, specificity, negative predictive value, positive predictive value, and accuracy for diagnosing malignancy were 80%, 100%, 75%, 100%, and 87%, respectively.

Table 2 shows the diagnostic yield of this procedure related to the lesion size, which was determined by measuring the greatest diameter on CT. Diagnostic yield was higher for the lesions ≥20 mm in size (44 of 57, 77%) than <20 mm in size (5 of 14, 36%) ($p$ = 0.003).

**TABLE 1.** Final Diagnoses and Results of EBUS-TBB with Thin Bronchoscope in 71 Patients

| Histologic Findings | Patients (Diagnosis) |
|---|---|
| Malignant | |
| Adenocarcinoma | 14 |
| Squamous cell carcinoma | 14 |
| Small cell carcinoma | 1 |
| Non-small cell carcinoma | 4 |
| Metastatic adenocarcinoma | 1 (Colon) |
| Metastatic squamous cell carcinoma | 1 (Maxillary sinus) |
| Benign | |
| Organizing pneumonia | 6 |
| Epithelioid cell granuloma with or without necrosis | 5 (Three nontuberculous mycobacteriosis, one tuberculosis, and one unspecified) |
| Inflammatory pseudotumor[a] | 1 |
| Pulmonary abscess | 1 |
| Typical carcinoid[a] | 1 |
| Nondiagnostic | |
| Suspected lung cancer | 4 (Four lung cancer) |
| Nonrepresentative samples | 18 (Five lung cancer, one nontuberculous mycobacteriosis,[a] five improved, and seven unchanged with 12–25-mo follow-up) |

Data are presented as *n*.
[a] Surgically confirmed.
EBUS-TBB, endobronchial ultrasound-guided transbronchial biopsy.

**TABLE 2.** Diagnostic Yield of EBUS-TBB with Thin Bronchoscope According to Lesion Size

| | Lesions Diagnosed/Lesions Examined | | |
|---|---|---|---|
| **Lesion Size** | **Malignant** | **Benign** | **Total** |
| <20 mm | 4/6 (67) | 1/8 (13) | 5/14 (36) |
| >20 mm | 31/38 (82) | 13/19 (68) | 44/57 (77) |
| Total | 35/44 (80) | 14/27 (52) | 49/71 (69) |

Data are presented as *n* (%). Diagnostic yield for lesions >20 mm vs. <20 mm; $p = 0.003$ using the $\chi^2$ test. Diagnostic yield for malignant lesions vs. benign lesions; $p = 0.02$ using the $\chi^2$ test.

EBUS-TBB, endobronchial ultrasound-guided transbronchial biopsy.

**TABLE 3.** Diagnostic Yield and Inserted Bronchial Generation of Thin Bronchoscopy in Relation to Bronchopulmonary Segments

| **Segments** | **Bronchial Generation Inserted** | **Lesions Diagnosed/Lesions Examined** |
|---|---|---|
| RUL | 4.8 ± 1.3 | 16/24 (67) |
| RML | 4.6 ± 1.1 | 3/5 (60) |
| RLL | 4.5 ± 1.2 | 14/18 (78) |
| LUL | 4.6 ± 1.5 | 9/14 (64) |
| Lingula | 6.0 | 1/1 (100) |
| LLL | 4.1 ± 0.8 | 6/9 (67) |

Data are presented as mean ± SD or *n* (%). Diagnostic yield in the location of the lesions; $p = 0.91$ using the $\chi^2$ test.

RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

Table 3 shows the diagnostic yield and inserted bronchial generation of thin bronchoscopy according to the bronchopulmonary segments. The 3B260 could be inserted into 4.6-generation bronchi on average (range, 2nd–7th generation). Endobronchial abnormalities such as exophitic endobronchial mass, submucosal spread, or peribronchial tumor causing extrinsic compression that presented beyond the segmental bronchi were visualized with the 3B260 in 14 patients (20%). The diagnostic yield was not affected by the lobar location of the lesions ($p = 0.91$).

The lesion was localized with EBUS in 65 patients (92%). On the EBUS image, the ultrasonic probe could be inserted into the target lesion in 51 patients (72%), the probe could not be inserted into the target lesion but reached the margin of the lesion in 14 patients (20%), and the lesion could not be visualized in six patients (8%). The diagnostic yield related to the location of the probe in relation to the target lesion was 82% (42 of 51), 42% (6 of 14), and 17% (one of six) ($p < 0.001$).

A representative case with a successfully diagnosed peripheral pulmonary lesion (adenocarcinoma; measuring 18 mm in diameter) is shown in Figures 2 and 3.

There were no significant procedure-related complications, such as major bleeding or pneumothorax.

## DISCUSSION

To our knowledge, this is the first report on the utility of EBUS-TBB using a thin bronchoscope for making a pathologic diagnosis of localized peripheral pulmonary lesions. Using this method, a diagnostic histologic specimen was obtained in 69% of patients with peripheral pulmonary lesions. The diagnostic yield for malignant lesions was as high as 80% (35 of 44), even excluding 9% (4 of 44) of suspicious results for malignancy.

With the progress of technologies, thinner bronchoscopes with a working channel and dedicated biopsy instruments have been developed, and several investigators[1–3,11,12] have reported its utility for evaluating peripheral pulmonary lesions. Nevertheless, the clinical application of thin bronchoscopy for investigating peripheral pulmonary lesions has been quite limited because of the limitations of the small

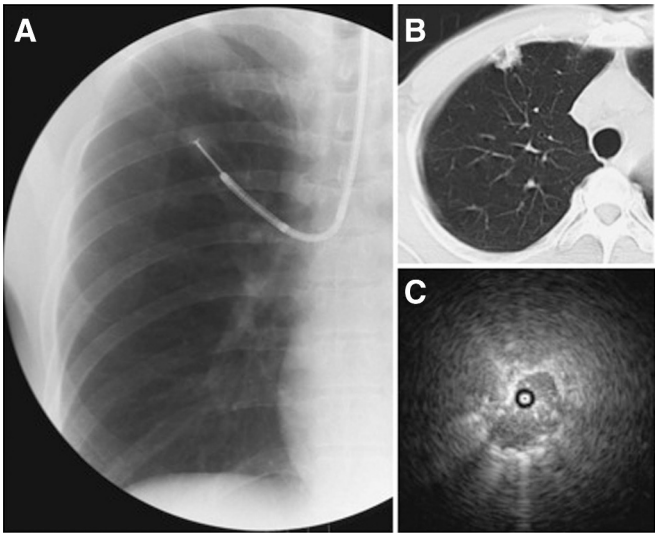


**FIGURE 2.** Lung cancer (adenocarcinoma) measuring 18 mm in the right upper lobe. *A,* Fluoroscopic images of transbronchial biopsy using XBF-3B260Y1. *B,* Computed tomography (CT) image. *C,* Ultrasonic image.

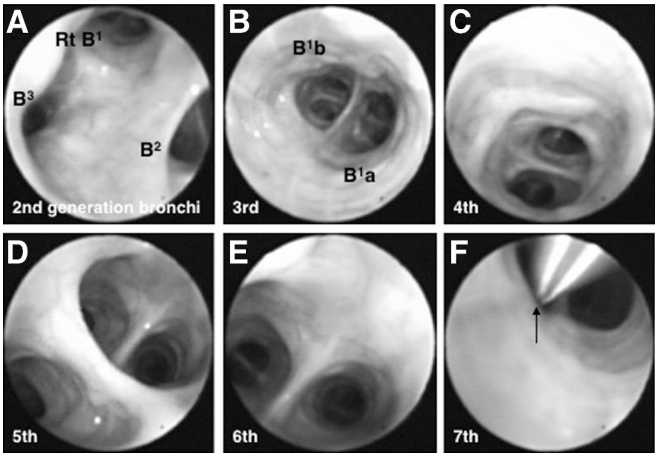


**FIGURE 3.** Thin bronchoscopic views: (*A*) 2nd, (*B*) 3rd, (*C*) 4th, (*D*) 5th, (*E*) 6th, and (*F*) 7th generation bronchi visualized by the thin bronchoscope are shown. *F,* Thin bronchoscope could be inserted as far as the 6th generation bronchus and ultrasonic probe (arrow) was inserted into the 7th generation bronchus under direct vision.

1.2-mm working channel including its limited ability to sample specimens or poor suction capability.[1,2,8] The development of an even thinner bronchoscope with greater visual range, improved visibility, and a larger working channel would assure more effective clinical application.

In a former study,[4] we demonstrated the utility of an exprototype thin fiberoptic bronchoscope with a 1.7-mm working channel (XBF-3B40Y1, 3.5-mm distal end diameter; Olympus) for the examination of peripheral pulmonary lesions. The thin bronchoscope could enter a further two distal generations of bronchi from the bronchi reached by a standard bronchoscope, and it revealed 14% of lesions that could not be visualized with the standard bronchoscope. A diagnostic histologic specimen with TBB using the thin bronchoscope under fluoroscopic guidance was obtained in 65% of patients (72% for malignant lesions and 50% for benign lesions). The new 1.7-mm channel can accommodate a wider variety of bronchoscopic instruments including a larger biopsy forceps in comparison with the conventional 1.2-mm channel of thin bronchoscopes. Additionally, it has enabled thin bronchoscopic EBUS-TBB using a thin ultrasonic probe. Comparison with our former study was not the purpose of this study. Although the enhancement of the diagnostic yield seems to be limited, we prefer to use the EBUS in thin bronchoscopy, because it provides some valuable information at the time of the procedure. In this study, as reported by the other investigator,[5] the locational relationship between the examining bronchus and the target lesion on EBUS image was a good predictor of the adequacy of the procedure. It also provides the bronchologist with immediate feedback to modify the technique or biopsy site accordingly. Furthermore, it might be possible to determine whether or not the lesion is malignant from the ultrasonic features.[13] The overall diagnostic yield is likely to depend on the prevalence of disease. In this investigation, the diagnostic yield of thin bronchoscopic EBUS-TBB in benign lesions, especially small benign lesions, was significantly lower than the yield in malignant lesions. The difficulty to establish a specific benign diagnosis is a common problem for biopsy procedures including bronchoscopy and CT-guided transthoracic needle aspiration. A recent review article[14] reported nondiagnostic biopsy results of CT-guided transthoracic needle biopsy in 44% of patients with benign nodules. Nonspecific benign results should be interpreted carefully considering the pretest probability of malignancy.

Several investigators[6–8] have reported the utility of navigational bronchoscopy in the diagnosis of peripheral pulmonary lesions. The combination of a thin bronchoscope and navigational bronchoscopy seems reasonable. The bronchial map provided by a navigational device may be useless if the bronchoscope or a biopsy instrument cannot follow the indicated route. The good bronchial selectivity and smooth maneuverability of a thin bronchoscope in the peripheral airway provide a surer means to follow the indicated bronchial route correctly. The combination of the present method and navigational technology can thus make the best of mutual abilities, and it may lead to enhanced diagnostic yield.

The safety and good tolerability of thin bronchoscopy with a 1.7-mm channel have been reported in our previous study.[4,15] This study further demonstrated the safety of the procedures with a thin bronchoscope with a 1.7-mm channel.

In conclusion, EBUS-TBB using a 3.4-mm thin bronchoscope and a 1.4-mm radial probe is feasible, accurate, and safe for the diagnosis of peripheral pulmonary lesions, especially malignant lesions. To elucidate in more detail the usefulness of this procedure, prospective comparison with EBUS-TBB using a conventional bronchoscope may be needed.

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