# Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration for the Diagnosis of Intrapulmonary Lesions

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**Background:** The diagnosis of centrally located intrapulmonary tumors not visible on bronchoscopy may be a challenge. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has been shown to be useful for the evaluation of mediastinal lymph nodes. However, there have been no reports of the utility of EBUS-TBNA for the diagnosis of intrapulmonary tumors.

**Objectives:** The purpose of this study was to evaluate the usefulness of EBUS-TBNA for the diagnosis of intrapulmonary tumors located adjacent to the central airway.

**Methods:** From December 2002 to June 2007, 35 patients with pulmonary masses located close to the central airways were accessed by EBUS-TBNA. Conventional bronchoscopic biopsy before EBUS-TBNA was nondiagnostic in 25 of the 35 cases. Patients with endobronchial lesions were excluded from this study.

**Results:** EBUS-TBNA was performed in 19 peritracheal and 16 peribronchial lesions. Cytologic and/or histologic samples were diagnostic in 33 of 35 patients. The final diagnoses of the pulmonary masses were lung cancer in 26 cases (1 small cell lung cancer, 25 non-small cell lung cancer), metastatic lung tumors in 5, and BALT lymphoma in one. The sensitivity and the diagnostic accuracy of EBUS-TBNA for the diagnosis of unknown pulmonary masses was 94.1% and 94.3%, respectively.

**Conclusions:** Intrapulmonary lesions not assessable by conventional bronchoscopic procedures can easily be assessed and diagnosed by EBUS-TBNA as long as it is within the reach of the EBUS-TBNA scope. EBUS-TBNA is a real-time procedure with a high yield which can be applied for the diagnosis of lung tumors.

**Key Words:** Endobronchial ultrasound guided transbronchial needle aspiration, Unknown pulmonary mass, Transbronchial biopsy, Non-small cell lung cancer.

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Although bronchoscopy is widely used for the diagnosis of peripheral pulmonary masses, there are limitations in the yield of conventional bronchoscopic modalities. To improve the diagnostic yield of bronchoscopic biopsies, new modalities have been applied such as computed tomography (CT) guided bronchoscopy,[1] virtual bronchoscopic navigation,[2,3] electromagnetic navigation bronchoscopy,[4,5] endobronchial ultrasound with guide sheath (EBUS-GS),[6,7] and a combination of the different techniques.[8,9] However, due to the anatomy, lesion located in certain areas may be difficult to assess with the present modalities. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive procedure performed under local anesthesia that has enabled mediastinal and hilar lymph node assessment with a high sensitivity.[10–14] In addition to mediastinal and hilar lymph nodes, EBUS-TBNA can assess peritracheal and peribronchial lesions as long as it is within the reach of the EBUS-TBNA scope.[15] Herein, we describe the use of EBUS-TBNA in patients with intrapulmonary lesions located adjacent to the central airway.

## PATIENTS AND METHODS

### Patients

A retrospective chart review of the EBUS-TBNA data base of the Department of Thoracic Surgery, Chiba University was performed to evaluate the yield of EBUS-TBNA in the diagnosis of intrapulmonary lesions. From December 2002 to June 2007, thirty-five patients with intrapulmonary tumors were accessed by EBUS-TBNA. All patients were evaluated by chest CT with contrast single injection and multidetector row CT (Light Speed, GE Medical System, Milwaukee, WI) before the procedure. Pulmonary masses whose drainage bronchus is difficult to be reached such as mediastinal type lung cancer adjacent to the trachea, lesions adjacent to the main bronchus or the segmental bronchus were assessed by EBUS-TBNA. All patients were referred from other centers after a negative conventional bronchoscopic examination or if they were deemed difficult to assess by conventional bronchoscopic methods. Patients with endobronchial findings before EBUS-TBNA were excluded from this study.

### EBUS-TBNA

EBUS-TBNA was performed on an outpatient basis under conscious sedation. Local anesthesia was achieved with nebulised 1% lidocaine solution (5 ml) in the pharynx. A bolus dose

of 2 ml of 2% lidocaine was used during the procedure. The bronchoscope was inserted orally with conscious sedation by midazolam. Patients were monitored for Electrocardiogram, pulse oximetry, and blood pressure without the presence of an anesthesiologist. The convex probe-EBUS (CP-EBUS) (BF-UC260F-OL8, Olympus, Tokyo, Japan) was used for EBUS-TBNA. The outer diameter of the linear probe is 6.9 mm and the diameter of the bronchoscope is 6.2 mm. The size of the tip of the bronchoscope limits the reach of the CP-EBUS to the segmental bronchus. The CP-EBUS is integrated with a convex transducer (7.5 MHz) which scans parallel to the insertion direction of the bronchoscope. Images can be obtained by directly contacting the probe or by attaching a balloon on the tip and inflating with saline. The ultrasound image is processed in a dedicated ultrasound scanner (EU-C2000, Olympus, Tokyo, Japan) and is visualized along with the conventional bronchoscopy image on the same monitor. The Power Doppler mode is also available in this system. The dedicated 22-gauge needle (NA-201SX-4022, Olympus, Tokyo, Japan) is used for EBUS-TBNA. The needle is equipped with an internal sheath which is withdrawn after passing the bronchial wall, avoiding contamination during EBUS-TBNA. The needle can be visualized through the optics and on the ultrasound image (Figure 1).

For optimal sampling, the internal sheath is used to clear the tip of the internal lumen clogged with bronchial membrane once the needle is inside the lesion. The internal sheath is removed and negative pressure is applied by a syringe. The needle is moved back and forth inside the tumor. Finally, the needle is retrieved and the internal sheath is used once again to push out the histologic core. The rest of the aspirated material is smeared onto glass slides. Smears are air dried and immediately stained by Diff-Quik staining for rapid on-site cytology to confirm adequate cell material. Furthermore, Papanicolaou staining and light microscopy is carried out by an independent cytopathologist. Histologic cores are fixed with formalin and stained with hematoxylin and eosin (Figure 1). In some cases, immunohistochemistry was performed for additional information. EBUS-TBNA diagnosis was confirmed either by open thoracotomy, thoracoscopy or clinical follow-up for at least 6 months.

## Data Analysis

The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy rate was calculated using the standard definitions.

# RESULTS

## Patient Characteristics

Thirty-five patients with intrapulmonary lesions adjacent to the central airway (19 masses adjacent to the trachea,

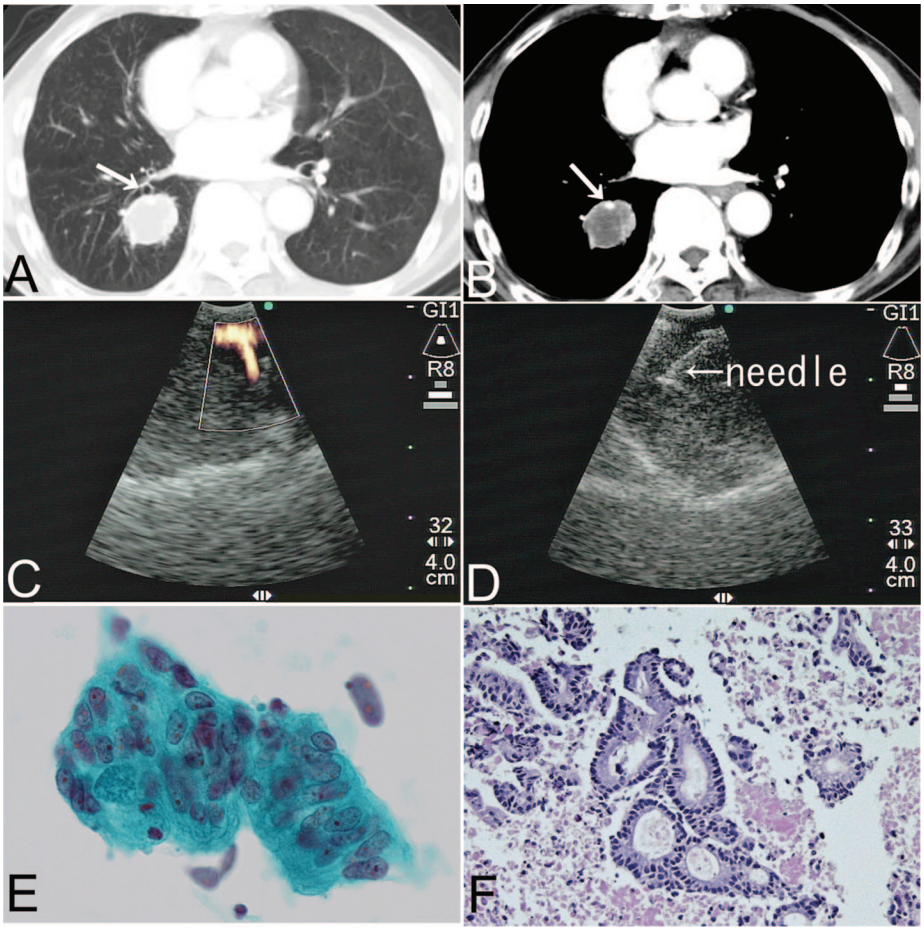


**FIGURE 1.** *A*, Chest CT revealed an abnormal shadow 30 mm in diameter located adjacent to the right B8 bronchus. *B*, Segmental pulmonary artery running beside the tumor close to the right B8 bronchus on mediastinal window. *C*, Doppler mode EBUS image showed the segmental pulmonary artery inside of the tumor. *D*, EBUS-TBNA of the lesion showing the needle within the tumor. *E*, Cytologic examination revealed adenocarcinoma from known colon cancer. *F*, Histologic diagnosis was metastatic lung tumor from colon cancer.

5 adjacent to the intermediate bronchus, 3 adjacent to the right lobar bronchus, 6 adjacent to the right segmental bronchus, and 2 adjacent to the left segmental bronchus) were evaluated in this study. There were 29 male and the average age was 63.2 years (range, 37–86). Conventional transbronchial biopsies were performed in 26 of 35 patients (74.3%) before EBUS-TBNA and were nondiagnostic in all 26 patients. The other 9 cases were judged to be nonaccessible by conventional transbronchial biopsies based on CT and bronchoscopic findings.

## EBUS-TBNA Results

The size of pulmonary lesions on CT varied from 10 to 70 mm in short axis with an average of 30.0 mm (19 lesions were less than 3 cm and 16 were larger than 3 cm). Histologic specimens were available in 23 of 35 patients (65.7%). Pathologic diagnosis was achieved in 33 patients (94.3%, 10 patients by cytology alone, 23 patients by both cytology and histology) and malignant cells were detected in 32 patients. Two false negative patients were diagnosed based on cytology alone. The final diagnosis was lung cancer in 26 patients (1 small cell lung cancer, 25 non-small cell lung cancer), metastatic lung tumors in five, BALT lymphoma in one and focal fibrosis in one. Out of the 32 cases of malignancy, TBNA positive results were confirmed by thoracotomy in 9 cases, thoracoscopy in one case and course observation in 22 cases. Nonsurgical treatment was performed in course observation cases. EBUS-TBNA was nondiagnostic in 2 patients: one patient had a tumor located adjacent to the trachea which was diagnosed as adenocarcinoma by thoracotomy. The other was a metastatic lung tumor from renal cell carcinoma diagnosed also by thoracotomy. The sensitivity, specificity, negative predictive value, positive predictive value, and diagnostic accuracy rate of EBUS-TBNA for the diagnosis of intrapulmonary masses was 94.1%, 100%, 33.3%, 100%, and 94.3%, respectively (Table 1). We did not experience any complications related to EBUS-TBNA.

# DISCUSSION

EBUS-TBNA is a real-time transbronchial needle aspiration technique that was developed mainly for the assessment of mediastinal lymph nodes. Although most of the mediastinal and hilar lymph nodes can be assessed (stations 2, 4, 7, 10, 11, 12), because of the size of the CP-EBUS there is a limit in the reach. From our experience, CP-EBUS can access down to the segmental bronchus in most of the cases.

**TABLE 1.** Comparison of EBUS-TBNA Results of Unknown Pulmonary Nodules with Final Diagnosis

| | EBUS-TBNA Results | | |
|---|---|---|---|
| **Final Diagnosis** | **Malignant** | **Benign** | **Total** |
| Malignant | 32 | 2 | 34 |
| Benign | 0 | 1 | 1 |
| Total | 32 | 3 | 35 |

The sensitivity, specificity, and diagnostic accuracy rate of EBUS-TBNA for diagnosis of intrapulmonary lesions was 94.1%, 100%, and 94.3%, respectively.

Past reports on EBUS-TBNA have focused on sampling of mediastinal and hilar lymph nodes.[10–14] From our experience in over 1600 procedures, we have come across cases, where CP-EBUS was effective for the diagnosis of intrapulmonary lesions located adjacent to the central airway. This study was a retrospective chart review of such cases in our practice. Under real-time ultrasound control and by using the Doppler mode, vessels usually running along the central airway can be avoided during EBUS-TBNA. This resulted in the safety and high yield in this case series with the sensitivity and diagnostic accuracy rate of 94.1% and 94.3%, respectively. We did not encounter any complications related to the procedure.

Conventional bronchoscopic diagnostic modalities including transbronchial biopsy, transbronchial needle aspiration, and brushing are used for the diagnosis of unknown pulmonary nodules.[16,17] Fluoroscopy guidance increases the sensitivity of bronchoscopic biopsies.[17–19] The reported overall sensitivity in the diagnosis of peripheral lesion under fluoroscopy guidance is 78% and the sensitivity tends to improve when the bronchus is extended to the tumor. On the other hand, the sensitivity of conventional TBNA is 65%.[17] To further increase the yield of transbronchial biopsy, new diagnostic modalities such as CT guided bronchoscopy, virtual bronchoscopic navigation, electromagnetic navigation bronchoscopy, and endobronchial ultrasound with guide sheath (EBUS-GS) have been introduced.[1–9] However, there are limitations in each technique. CT guided bronchoscopy is a real time procedure, but is costly, requires the CT suite and, hence there are only limited reports on its effectiveness.[1] Virtual bronchoscopic navigation has been reported to increase the yield for diagnosis of peripheral nodules from specialized centers in Japan,[2,3] but is still not available in the market. It uses virtual images reconstructed from CT obtained before the procedure. Therefore it is not a real-time procedure. Electromagnetic navigation bronchoscopy also uses CT images for guidance.[4,5] EBUS-GS uses the radial probe EBUS in combination with the guide sheath for biopsy of peripheral lesions.[6,7] Its application is peripheral lesions and due to the nature of the sheath and probe, EBUS-GS cannot be used for the diagnosis of centrally located tumors. EBUS-TBNA can be performed under real-time ultrasound control without the use of the CT or other costly devices.

CT guided transthoracic needle aspiration is the most commonly used modality by interventional radiologists and pulmonologists for tissue diagnosis of pulmonary nodules when the lesion is not visible on bronchoscopy. The reported yield is high and thus being performed routinely.[17,20,21] However, compared with transbronchial biopsies, complications including pneumothorax are seen at a fairly high rate[21,22] with possible tumor seeding in some cases.[23,24] The yield is lower for centrally located tumors compared with peripheral lesions.[25,26] A bronchoscopic real-time procedure that can access centrally located tumors not visible on bronchoscopy (EBUS-TBNA) would solve most of these problems.

It should be noted that there are several limitations that apply to this case study. Firstly, this was a retrospective case study looking at patients with centrally located lesions with no bronchoscopic visible lesions. This constitutes only a part of the population of patients with suspected lung cancer.

 

EBUS-TBNA cannot be used for peripheral lesions that are beyond the reach of the CP-EBUS. Therefore, the results cannot be directly compared with other modalities. Secondly, patients enrolled had a very high suspicion of lung cancer. This is one of the reasons why the negative predictive value (33.3%) was lower than what has been previously reported. Nevertheless, EBUS-TBNA may be used as an alternative to the more invasive CT guided needle aspiration for centrally located tumors. It should be noted that it is complementary to other diagnostic modalities.

In conclusion, EBUS-TBNA is a real-time bronchoscopic procedure that can be used for the diagnosis of centrally located lesions not visible on bronchoscopy with a high yield. It is a minimal invasive procedure that can be performed safely in an outpatient setting by bronchoscopists.

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## REFERENCES

1. Shinagawa N, Yamazaki K, Onodera Y, et al. CT-guided transbronchial biopsy using an ultrathin bronchoscope with virtual bronchoscopic navigation. *Chest* 2004;125:1138–1143.
2. Asano F, Matsuno Y, Shinagawa N, et al. A virtual bronchoscopic navigation system for pulmonary peripheral lesions. *Chest* 2006;130: 559–566.
3. Tachihara M, Ishida T, Kanazawa K, et al. A virtual bronchoscopic navigation system under X-ray fluoroscopy for transbronchial diagnosis of small peripheral pulmonary lesions. *Lung Cancer* 2007;57:322–327.
4. Eberhardt R, Anantham D, Herth F, et al. Electromagnetic navigation diagnostic bronchoscopy in peripheral lung lesions. *Chest* 2007;131: 1800–1805.
5. Gildea TR, Mazzone PJ, Karnak D, Meziane M, Mehta AC. Electromagnetic navigation diagnostic bronchoscopy: a prospective study. *Am J Respir Crit Care Med* 2006;174:982–989.
6. Yamada N, Yamazaki K, Kurimoto N, et al. Diagnostic value of endobronchial ultrasonography with a guide sheath for peripheral pulmonary lesions without X-ray fluoroscopy. *Chest* 2007;131:1788–1793.
7. Kurimoto N, Miyazawa T, Okimasa S, et al. Endobronchial ultrasonography using a guide sheath increases the ability to diagnose peripheral pulmonary lesions endoscopically. *Chest* 2004;126:959–965.
8. Asano F, Matsuno Y, Tsuzuku A, et al. Diagnosis of peripheral pulmonary lesions using a bronchoscope insertion guidance system combined with endobronchial ultrasonography with a guide sheath. *Lung Cancer* 2008; 60:366–373.
9. Eberhardt R, Anantham D, Ernst A, Feller-Kopman D, Herth F. Multimodality bronchoscopic diagnosis of peripheral lung lesions: a randomized controlled trial. *Am J Respir Crit Care Med* 2007;176:36–41.
10. Yasufuku K, Chiyo M, Koh E, et al. Endobronchial ultrasound guided transbronchial needle aspiration for staging of lung cancer. *Lung Cancer* 2005;50:347–354.
11. Rintoul RC, Skwarski KM, Murchison JT, et al. Endobronchial and endoscopic ultrasound-guided real-time fine-needle aspiration for mediastinal staging. *Eur Respir J* 2005;25:416–421.
12. Herth FJ, Eberhardt R, Vilmann P, Krasnik M, Ernst A. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes. *Thorax* 2006;61:795–798.
13. Yasufuku K, Nakajima T, Motoori K, et al. Comparison of endobronchial ultrasound, positron emission tomography, and CT for lymph node staging of lung cancer. *Chest* 2006;130:710–718.
14. Herth FJ, Ernst A, Eberhardt R, et al. Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum. *Eur Respir J* 2006;28:910–914.
15. Yasufuku K, Nakajima T, Chiyo M, et al. Endobronchial ultrasonography: current status and future directions. *J Thorac Oncol* 2007;2:970–979.
16. Iyoda A, Baba M, Shibuya K, et al. Transbronchial fine needle aspiration cytological examination: a useful tool for diagnosing primary lung cancer. *Thorac Cardiovasc Surg* 2006;54:117–119.
17. Rivera MP, Mehta AC. American College of Chest Physicians. Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007;132:131S–148S.
18. Baaklini WA, Reinoso MA, Gorin AB, Sharafkaneh A, Manian P. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. *Chest* 2000;117:1049–1054.
19. Schreiber G, McCrory DC. Performance characteristics of different modalities for diagnosis of suspected lung cancer: summary of published evidence. *Chest* 2003;123:115S–128S.
20. Lacasse Y, Wong E, Guyatt GH, Cook DJ. Transthoracic needle aspiration biopsy for the diagnosis of localized pulmonary lesions: a meta-analysis. *Thorax* 1999;54:884–893.
21. Geraghty PR, Kee ST, McFarlane G, et al. CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: needle size and pneumothorax rate. *Radiology* 2003;229:475–481.
22. Yeow KM, See LC, Lui KW, et al. Risk factors for pneumothorax and bleeding after CT-guided percutaneous coaxial cutting needle biopsy of lung lesions. *J Vasc Interv Radiol* 2001;12:1305–1312.
23. Voravud N, Shin DM, Dekmezian RH, et al. Implantation metastasis of carcinoma after percutaneous fine-needle aspiration biopsy. *Chest* 1992; 102:313–315.
24. Kim JH, Kim YT, Lim HK, Kim YH, Sung SW. Management for chest wall implantation of non-small cell lung cancer after fine-needle aspiration biopsy. *Eur J Cardiothorac Surg* 2003;23:828–832.
25. Arslan S, Yilmaz A, Bayramgürler B, et al. CT- guided transthoracic fine needle aspiration of pulmonary lesions: accuracy and complications in 294 patients. *Med Sci Monit* 2002;8:CR493–CR497.
26. Yung RC. Tissue diagnosis of suspected lung cancer: selecting between bronchoscopy, transthoracic needle aspiration, and resectional biopsy. *Respir Care Clin N Am* 2003;9:51–76.