

# Technical Aspects of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration

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Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is becoming a standard method for invasive mediastinal staging and for the diagnosis of paratracheal and peribronchial lesions. It is essential to understand the technical aspects of EBUS-TBNA to ensure safe and efficient procedures. In this review, we discuss the practical aspects to be considered during EBUS-TBNA, including anesthesia, manipulation of equipment, understanding mediastinal ultrasound images, target selection, number of aspirations needed per target, sample handling, and complications.

**Keywords:** Endobronchial Ultrasound; Bronchoscopy; Lung Neoplasms

## Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a bronchoscopic sampling method under ultrasound guidance that enables real-time aspiration of lesions adjacent to the trachea or large bronchi. The use of EBUS-TBNA has rapidly increased, with an accumulation of data on the usefulness of EBUS-TBNA since the first study was published in 2003<sup>1</sup>. According to recent guidelines for invasive mediastinal staging in lung cancer by the American College of Chest Physicians, EBUS-TBNA or endoscopic mediastinal staging is recommended as a best first test over surgical stag-

ing<sup>2</sup>. Use of EBUS-TBNA samples in the molecular analysis of lung cancer is gaining importance. Many studies have been published on the role of EBUS-TBNA in lung cancer staging. Research on the methodology and technical aspects of EBUS-TBNA is also increasing. In this article, we have reviewed the technical and practical aspects of EBUS-TBNA based on the literature and experience from our institute.

## Anesthetic Methods

EBUS-TBNA is usually performed under moderate sedation using narcotics and short-acting benzodiazepines and local anesthesia. EBUS-TBNA also can be performed under general anesthesia, because the procedure is more difficult than routine bronchoscopy due to the size of the scope and longer procedure time. However, the diagnostic advantages of general anesthesia for EBUS-TBNA have not been proved. Patient satisfaction by EBUS-TBNA under conscious sedation was reported to be high<sup>3</sup>. According to one study, 98% of patients reported that they would "definitely return" for EBUS-TBNA in the future if required<sup>3</sup>.

Local anesthesia with lidocaine for EBUS-TBNA is important when the procedure is performed under sedation. It is helpful to use a regular bronchoscope for local anesthesia before EBUS-TBNA because local anesthesia using an ultrasonic bronchoscope is technically more difficult than when using a

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regular bronchoscope. A study was published on methods of local anesthesia. Lee et al.<sup>4</sup> reported that lidocaine delivery via the spray catheter reduced the number of significant coughing episodes compared with standard working channel injection during EBUS-TBNA.

## Manipulation of the EBUS Bronchoscope

White light images by the EBUS bronchoscope show an approximately 30-degree forward oblique view. Therefore, the handling of the EBUS bronchoscope is technically more difficult than a regular bronchoscope. Due to the thickness and limited flexibility of the EBUS bronchoscope, its accessibility to bronchi is more limited than that of regular bronchoscopes, especially when a needle set is applied to the bronchoscope. Insertion of a needle set into the working channel can damage the EBUS bronchoscope when its end is fully flexed. Procedures with an EBUS bronchoscope are easy in the trachea, main stem bronchi, and bronchus intermedius. It is difficult to insert an EBUS bronchoscope into the right and left upper lobes and the narrow right middle lobe. However, in the basal bronchus of lower lobes, EBUS-TBNA can be performed even through the segmental bronchi.

The balloon that covers the ultrasonic probe is inflated with normal saline during EBUS-TBNA. This is helpful to obtain good ultrasound images when the contact of the ultrasonic probe to the bronchial wall is not good due to the bronchial cartilage or angulation of the bronchi. Balloon inflation is not very helpful when the procedure is performed in the narrow bronchus and the contact of the ultrasonic probe to the bronchial wall is good.

## Manipulation of a Needle Set

Inserting the needle into the intercartilagenous space is often difficult. It would be helpful to observe tracheal cartilages on ultrasound images in order to insert the needle into the intercartilagenous space easily. When targeting is difficult, the needle can be inserted into the mediastinal fat space first and then inserted into the target by changing the direction of needle inside the mediastinum. It is necessary to adjust the needle depth before needle insertion to avoid puncturing vessels or cystic lesions in the mediastinum. Pericarditis and infection on a lung mass following EBUS-TBNA that might be related to the full extension of an EBUS-TBNA needle have been reported<sup>5</sup>.

Needle movement in the target lesion has not been studied. Usually, back and forth movement is performed more than 10–20 times. The direction of the needle can be changed inside the target to cover a larger area. Even in the same lymph

node, targeting a more suspicious area of malignancy based on ultrasound images is helpful.

Negative pressure can be applied. However, the use of negative pressure seems not to be related to diagnostic yield. According to a recent random allocation study, sample adequacy and diagnostic yield were similar irrespective of the use of negative pressure<sup>6</sup>. However, more studies are needed regarding the effect of negative pressure on sample amount, and its role in very small nodes.

Negative pressure should be removed before retrieval of the needle from the lesion to reduce contamination of bronchial epithelial cells. The needle should be fully retracted into the needle sheath before the needle set is removed from the working channel in order to avoid damage to the bronchoscope.

## Searching for Targets and Understanding Ultrasound Images

Understanding the mediastinal anatomy on ultrasound images is essential for EBUS-TBNA. However, it can be difficult to find targets depending only on ultrasound images. The location of the target on computed tomography images should be understood in relation to bronchial anatomy in order to find the target on ultrasound images. It would be helpful to first localize the part of the bronchus adjacent to the target on white light images. Ultrasound images of major landmarks during EBUS-TBNA such as the superior vena cava, aorta, azygos vein, heart, and thyroid should be understood.

Understanding the typical echo-features of benign and malignant lymph nodes is necessary for selecting target lymph nodes. The typical features of benign nodes include oval shape, size <1 cm, indistinct margin, presence of a central hilar structure, relatively high echogenicity, and homogenous echogenicity. In contrast, common features of malignant nodes are round shape, size >1 cm, distinct margin, absence of the central hilum, eccentric cortical thickening, relatively low echogenicity, heterogenous echogenicity, and presence of necrosis. Fujiwara et al.<sup>7</sup> evaluated 6 echo-features in 1,061 lymph nodes sampled by EBUS-TBNA in a retrospective study. Round shape, distinct margin, heterogeneous echogenicity, and presence of necrosis were independent predictive factors for metastasis. Ninety-six percent of lymph nodes were proven not metastatic when all four categories were determined as benign. In a prospective study that evaluated 100 patients, increased size and round or oval shape were related to metastasis, and other findings were not significantly associated with metastasis<sup>8</sup>. Echo-features cannot provide absolute criteria for metastasis, but they are helpful in selecting target nodes or the target area in a single node.

Doppler mode can be applied to avoid puncturing vascular structures and to observe the vascularity of the target. Nakajima et al.<sup>9</sup> reported that increased vascularity in lymph nodes

was related to metastasis. The vascularity of metastatic lymph nodes observed by EBUS correlates with the mRNA expression of vascular endothelial growth factor-C<sup>10</sup>.

### Number of Lymph Node Stations Sampled by EBUS-TBNA in Lung Cancer Staging

Several lymph node stations are selected during EBUS-TBNA in lung cancer staging. Various factors, such as the size of lymph nodes, positron emission tomography findings, potential pathway of lymphatic metastasis, echo-features of nodes, and impact on treatment decision, are considered in selecting target nodal stations. According to Hwangbo et al.<sup>11</sup>, the mean number of nodal stations having at least one lymph node >5 mm was 3.2 in potentially operable lung cancer patients. Among them, the mean number of accessible nodal stations by EBUS-TBNA was 2.5<sup>11</sup>. In that study, an average of two nodal stations were sampled by EBUS-TBNA. According to a study that compared EBUS-TBNA and mediastinoscopy, an average of 2.8 nodal stations were selected during EBUS-TBNA under general anesthesia<sup>12</sup>. EBUS-TBNA is advantageous compared to mediastinoscopy because target nodes can be selected based on the ultrasound features of lymph nodes. The number of nodal stations needed during mediastinal staging with EBUS-TBNA should be determined considering the factors mentioned above in each patient.

### Number of Aspirations

The number of aspirations needed per lesion can be different depending on the purpose of the procedure. When the purpose of EBUS-TBNA is tissue acquisition and diagnosis of lung cancer, sufficient sample is needed for molecular tests such as epidermal growth factor receptor (*EGFR*) mutation analysis and anaplastic lymphoma receptor tyrosine kinase (*ALK*) gene rearrangement. However, the number of aspirations during EBUS-TBNA for these molecular tests has not been studied. In lung cancer staging, the optimal number of aspirations per nodal station by EBUS-TBNA has been studied when rapid onsite cytopathologic examination (ROSE) is not available. Hwangbo et al. reported that sample adequacy and diagnostic values by EBUS-TBNA increased up to the 3rd aspiration. When at least one tissue core specimen was obtained by the 1st or 2nd aspiration, two aspirations per lymph node station were acceptable<sup>13</sup>. Two or three aspirations per nodal station can be appropriate for EBUS-TBNA for lung cancer staging when ROSE is not available.

### Needle Size and Use of Forceps

EBUS-TBNA is usually performed using a 22-gauge (22G) needle. Larger needles (21G) are available; however, their advantages have not been proved. Yarmus et al.<sup>14</sup> compared 22G and 21G needles in 1,299 patients in a retrospective study. Sample adequacy and diagnostic yield were not statistically different between the groups.

Mini-forceps can be applied in EBUS guided sampling. Herth et al.<sup>15</sup> evaluated the role of mini-forceps in 75 patients without known or suspected non-small cell lung cancer (NSCLC), and showed a higher diagnostic yield using miniforceps than with the 21G needle (88% vs. 36%). Chrissian et al.<sup>16</sup> also reported higher diagnostic yield using miniforceps than with needle aspiration (91% vs. 81%) in patients presenting with mediastinal or hilar lymphadenopathy and a low likelihood of NSCLC. Mini-forceps can be useful when histological samples are important for diagnoses such as lymphoma. More studies are needed on this issue.

### Sample Handling and ROSE

EBUS-TBNA samples are handled by various methods according to the purpose of the procedures. Smearing on glass slides is a method that can minimize sample loss. However, the use of cytological slides is technically more difficult than tissue core or cell-block samples in molecular analyses such as *EGFR* studies. Histological tissue cores obtained by EBUS-TBNA can be handled like biopsy samples. According to a study by Lee et al.<sup>13</sup>, approximately 75% of EBUS-TBNA samples contained histologic tissue cores. Tissue core samples are easily used for molecular tests such as *EGFR* or *ALK* mutation analysis<sup>17,18</sup>. Cell-block samples processed into paraffin blocks are also easily used for molecular tests. Navani et al.<sup>19</sup> reported that *EGFR* mutation analysis was possible using cell-block samples in 90% of patients in whom mutation analysis was requested. EBUS-TBNA samples in normal saline are used for microbiological tests, flow cytometry, etc.

ROSE is used during EBUS-TBNA. Nakajima et al.<sup>20</sup> reported that the concordance rate for staging between ROSE and the final pathological diagnosis was 94.3%. Oki et al.<sup>21</sup> reported that ROSE during EBUS-TBNA was not associated with diagnostic yield and is associated with a lower need for additional bronchoscopic procedures and puncture number. More studies on the role of ROSE during EBUS-TBNA are needed.

### Prevention of Complications

EBUS-TBNA is a safe procedure with a very low complication rate. A meta-analysis reported a complication rate of 0.15%<sup>22</sup>. In a registry study that evaluated 1,317 cases, 1.44% of

the cases had complications (bleeding requiring intervention, 3; pneumothorax, 7; sustained hypoxia, 4; respiratory failure within 24 hours, 3; clinically significant airway injury, 1; hypotension, 1) were reported<sup>23</sup>. Transbronchial lung biopsy performed in the same bronchoscopic session with EBUS-TBNA was a risk factor for complications.

The rate of infectious complications is not high. Mediastinitis, pericarditis, and infection on the primary tumor have been reported in case series<sup>5,24</sup>. Infectious complications were reported following EBUS-TBNA on cystic or necrotic lesions<sup>5,24</sup>. A consensus on the use of prophylactic antibiotics for EBUS-TBNA has not been established. According to guidelines for endoscopic ultrasound-guided fine needle aspiration (EUS-FNA), prophylactic antibiotics are recommended for EUS-FNA on cystic lesions<sup>25</sup>. We believe that prophylactic antibiotics should be considered when EBUS-TBNA is performed on cystic or necrotic lesions. EBUS-TBNA should be carefully performed so as not to puncture the pericardial space or cystic structures.

The risk of bleeding complication is not high. In a case series, EBUS-TBNA was safely performed in 12 patients taking clopidogrel<sup>26</sup>. However, medications that increase bleeding risk should be stopped if possible.

## Learning Curve and Education

The learning curve is different for different individuals. In one study, 96% sensitivity was reported following 10 cases of EBUS-TBNA<sup>27</sup>. In another study, markedly increased diagnostic values were observed following the first 25–50 cases<sup>28</sup>. Kemp et al.<sup>29</sup> compared the learning curves of 5 bronchoscopists. They showed that there was a wide range of time over which EBUS-TBNA competence was attained<sup>29</sup>.

Computer-based EBUS-TBNA simulators are used for EBUS-TBNA training. Skills learned using an EBUS-TBNA simulator are transferable to clinical EBUS-TBNA performance<sup>30</sup>. The Endobronchial Ultrasound Skills and Tasks Assessment Tool (EBUS-STAT) was created as an objective competency-oriented assessment tool of EBUS-TBNA skills and knowledge. The score is correlated with procedure experiences<sup>31</sup>. Such objective assessment tools for EBUS-TBNA skills would be helpful for EBUS-TBNA training.

## Conclusion

EBUS-TBNA is becoming the standard for the sampling of mediastinal lesions<sup>2</sup>. It is important to possess knowledge of its technical aspects to obtain good diagnostic yield and ensure safe procedures. EBUS-TBNA can be safely performed under local anesthesia and sedation. Understanding equipment handling and ultrasound images are essential for EBUS-

TBNA. Although the risk of complications is low, one should possess knowledge of possible complications and try to avoid them.

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