How to increase the yield of transbronchial needle aspiration (TBNA)?

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Abstract: Transbronchial needle aspiration (TBNA) is a relatively sensitive, accurate, and safe technique in the diagnosis and staging of lung cancer. There are many factors influencing the yield of TBNA, such as location and the size of the mediastinal lymphadenopathy (MLN), types of the needle used and the experience of the bronchoscopist. Furthermore, knowledge of anatomy, guidance, availability of rapid on-site evaluation (ROSE) and the number of aspirates, preparation of specimen and interpretations of the cytology and histology of specimens all play important roles. Especially, whether an endobronchial ultrasound (EBUS) is required for TBNA in the diagnosis of mediastinal masses is currently a disputed subject.

Keywords: Transbronchial needle aspiration (TBNA); endobronchial ultrasound (EBUS); lung cancer; mediastinal and hilar lymphadenopathy; yield

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Introduction

Transbronchial needle aspiration (TBNA) was first introduced and performed by the rigid bronchoscope by Schieppati in 1949 and was adapted for use in flexible bronchoscope by Wang in 1983 (1,2). It has become a proven procedure to establish the diagnosis of mediastinal and hilar lymphadenopathy, submucosal disease and peripheral lung nodule.

Available studies have shown a high yield for diagnostic yield, especially, in malignant mediastinal and hilar lesions (3-5). Since conventional TBNA (c-TBNA) uses endobronchial landmarks identified on CT to estimate the location of lymph nodes, many attempts have been made to increase the yield of c-TBNA, of which rapid on-site cytologic evaluation (ROSE) and endobronchial ultrasonography-TBNA (EBUS-TBNA) are the most prominent (6-9). ROSE confirms whether the lesion or lymph node has been reached by the pathologic examination. In contrast, the endpoint with EBUS is confirmation that the needle is in the lesion by ultrasound visualization. In this review, we aim to address these critical issues to many attempts been made to increase the yield of TBNA.

Predictors of positive TBNA yield

According to the analysis of Bonifazi M, which involved fifty-three studies, more than 8,000 patients, major predictors included lymph node size (short axis length >2 cm), presence of abnormal endoscopic findings, subcarinal and right paratracheal location, and the use of histological needle by an experienced bronchoscopist (10). In patients with suspected sarcoidosis, sampling of more than one lymph node stations and stage I were the only predictors of a successful TBNA result (11). Knowledge of factors that predict a positive TBNA result may help optimize the diagnostic success in different clinical settings.

Guidance

TBNA with guidance is a valuable technique to sample abnormal lymph nodes. Originally, fluoroscopy in conjunction with endobronchial visualization was used to guide TBNA. CT scan correlation with endobronchial anatomy was then provided by Wang (12). Recently, several newer approaches, such as EBUS or esophageal US, electromagnetic navigation, and virtual CT bronchoscopic guidance have been used to improve the yield of TBNA.

CT bronchoscopic simulation guidance

CT bronchoscopic simulation extracts relevant information from a CT data and displays it in a way with which the bronchoscopist is familiar. Orientation by using CT bronchoscopic simulation helps improve guidance for TBNA of endobronchial invisible lesions (13,14). It is particularly well suited for setups in which guidance systems are not available, such as electromagnetic navigation or endobronchial/transesophageal US, and may be a helpful tool for less experienced bronchoscopists.

CT fluoroscopy

CT fluoroscopy enabled rapid localization of the position of the bronchoscopic tip. The needle was observed whether it was planted in the airway, to assure that it was directed toward the intended site. The feedback provided by CT fluoroscopy allowed a rapid documentation of needle position, enabling immediate adjustment (15,16).

Electromagnetic navigation-guide (ENB)

ENB is a new technology to increase the diagnostic yield of bronchoscopy for the peripheral lung lesions and MLN. In a pioneering study involving 31 patients with MLN with mean size of 28.1±12.8 mm, diagnostic yield of ENB-guided TBNA (ENB-TBNA) was 100% (17). Recently, in a head-to-head comparison between ENB-TBNA and c-TBNA reported by Diken ÖE (18), the sampling success of ENB-TBNA was significantly higher than c-TBNA in both subgroups (MLN ≤15 mm and >15 mm). It is suggested that the diagnostic yield of ENB-TBNA is irrelevant to the size of MLNs, which was in contrast with other studies.

Endobronchial ultrasonography (EBUS)

There has been renewed interest in TBNA due to the development of an EBUS for TBNA. Whether an EBUS is required for TBNA in the diagnosis of all mediastinal and hilar lymph nodes is currently a disputed subject.

Previous studies have demonstrated that EBUS-TBNA performs better than c-TBNA, as it is capable of sampling with real-time ultrasound visualization. In a retrospective analysis with previously c-TBNA-inadequate or negative results, Cetinkaya E believed that EBUS-TBNA is a more accurate method for the assessment of mediastinal and hilar lymph nodes (19). Yasufuku also reported that EBUS-TBNA had a sensitivity of 94.6%, specificity of 100% and diagnostic accuracy rate of 96.3%, which seemed to be superior to mediastinoscopy or c-TBNA (20). In general, following EBUS guidance, the diagnostic yield of TBNA increased from 71% to 80% (21). In the studies of Herth, the patients were stratified according to the anatomic location of the lymph nodes. It was indicated that EBUS-TBNA performed better in sites other than the subcarinal space. When the lesion was located peripherally, although EBUS-TBNA sampled more accurately and easily, the diagnostic yield was low, but could be improved via combining with other technical (22).

However, some clinicians considered c-TBNA to be sufficient for diagnosis. As reported by Jiang *et al.*, equal numbers of punctures were performed at the target lymph node stations using c-TBNA techniques followed by EBUS-TBNA at the same sites. There was no significant difference in the diagnostic yield of c-TBNA versus EBUS-TBNA. But, when comparing diagnosis of malignancy for each lymph node sampled, there were a significantly greater number of positive lymph nodes sampled by EBUS-TBNA (23).

As authors, we agree that an intimate knowledge of lymph node location in reference to endobronchial anatomy combined with a proper TBNA technique can have a very high diagnostic yield even in the absence of EBUS. However, it is seemed that EBUS-TBNA was especially useful for station 4 L nodes, for sampling lymph nodes less than 10 mm in their short axis, for staging lung cancer in the setting of a negative PET-CT mediastinum, and for re-staging after neoadjuvant therapy.

Rapid on-site evaluation (ROSE)

Commonly, ROSE is used during breast, thyroid and transthoracic needle aspirations. The role of ROSE in TBNA from hilar and mediastinal lymph node is promising, but controversial. Indeed, it does not help to determine the location of the puncture nor does it help in determining the

manner of puncturing.

Some studies have shown that the presence of ROSE is crucial to the determination of material adequacy and reduction of non-diagnostic rate (9,24,25). Despite the lack of statistical significance, ROSE appears to be particularly useful in the diagnostic field of hilo-mediastinal lesions, to increase the diagnostic ability of EBUS-TBNA. It was reported that the diagnostic accuracy of EBUS-TBNA was 91% in ROSE group and 83% in non-ROSE group (26).

Although it is commonly believed that ROSE decreases the percentage of inadequate specimens, this assumption is based on uncontrolled studies or the results of a single study, in which TBNA was used to diagnose peripheral lesions, and in which a subgroup of TBNA from enlarged nodes was not performed. In Trisolini's study, which used a randomized design to limit the occurrence of possible selection biases, it is suggested that ROSE does not increase the diagnostic yield of TBNA (27). The possibility to avoid additional biopsy was the most important benefit of the use of ROSE, as it was associated with a significant reduction of the complication occurrence of TBNA. Additionally, in Baram D' study, ROSE also did not increase TBNA yield, as a high accuracy was seen in TBNA without ROSE (28).

So, c-TBNA without ROSE is an efficacious bronchoscopic procedure which should be performed routinely. While ROSE has not been shown to increase diagnostic yield, it does give valuable real-time feedback about the quality of specimen which will likely be more important as molecular testing becomes more routine.

The combination with others bronchoscopic techniques

Dziedzic DA showed (29), the diagnostic yield of the EBUS-TBNA for stage I, and II sarcoidosis is higher than for transbronchial lung biopsy (TBLB) and endoscopic bronchial biopsy (EBB). However, the combination of TBNA with standard bronchoscopic techniques could optimize the diagnostic yield in patients with sarcoidosis and enlarged intrathoracic lymph nodes (30,31).

Aspiration

EBUS-transbronchial needle capillary sampling (TBNCS) (capillary sampling)

Fine needle sampling without suction (capillary sampling) has been studied for biopsies at various body sites and has resulted in similar diagnostic yield. For example, Casal RF found regardless of LN size, no differences in diagnosis, adequacy or quality was found between EBUS-TBNA and EBUS-TBNCS (32). In a study of superficial masses at various body sites, Mair *et al.* also found no difference in diagnostic yield between conventional fine-needle aspiration and fine-needle capillary sampling (33). Recently, Harris K compared the EBUS-TBNA with and without suction, which showed no difference in diagnosing malignant and benign diseases again (34).

However, advocates argue that the cellularity of the samples is greater with suction, whereas opponents believe that suction draws more fluid and blood into the sample, thereby decreasing its quality (35,36). For this, in a prospective randomized study, Puri showed that EUS-guided fine-needle sampling using suction yields a higher number of slides without increasing bloodiness. Although, the proportion of target cells was relatively similar between the suction and non-suction sampling, the sensitivity and negative predictive values of the procedure were significantly higher in suction sampling (37). So, the role of suction in fine-needle sampling remains somewhat controversial.

Auto-aspiration

Traditionally, aspiration with high negative pressure is recommended to obtain a specimen in TBNA. However the assistant experiences difficulty in the precise control of the generation of the negative pressure while performing the TBNA procedure. Theoretically, the auto-aspiration technique provided more adequate sampling than manual aspiration did. Although Larghi *et al.* showed that automatic, continuous and high negative pressure in the fine-needle aspiration and manual aspiration techniques presented the same diagnostic yield (38). However, as Boonsarngsuk V reported, the auto-aspiration was superior to the manual method in obtaining adequate samples in TBNA procedures (39).

Number of aspirates

Little is known about the role of the number of aspirates in the yield of TBNA. Although Chin *et al.* reported a plateau in yield after 7 times of aspirate per nodal site (40), other authors recommend different number of aspirates. For example, Hee Seok Lee determined the optimal number of aspirations per LN station for maximum diagnostic yield during EBUS-TBNA when ROSE is not available.

Maximum diagnostic values included sample adequacy, sensitivity for differentiating malignant from benign LN stations and negative predictive value were achieved in 3 numbers of aspiration (41).

Needle

Twenty-one and 22 G EBUS-TBNA needle

Traditionally, EBUS-TBNA has been performed using a 22-G needle until a larger 21-G needle was introduced in 2011. Theoretically, the 21-G needle is expected to provide a greater amount of sample and resulted in a higher diagnostic yield.

In fact, the inner diameter of the 22-G EBUS-TBNA needle is similar to that of the 21-G needle. As supported, studies from other organ systems showed that sample adequacy may not always correlate with the size of needle. Only a few studies have compared the diagnostic yield of the 21-G needles with the 22-G needles and the results have been inconsistent. In a small investigation, Nakajima et al found no difference in diagnostic yield between 21-G needles and 22-G needles (42). A study by Saji *et al.* found superiority of the 21 G needle regarding cytologic and combined cytologic/histologic diagnostic yield (43). Finally, in a prospective trial involving 60 patients, Oki *et al.* showed no difference in diagnostic yield between 21 and 22 G needles (44). These conflicting results have led to the Lonny B' study, which showed no difference in sample adequacy and diagnostic yield between 21 and 22 G needles (45). Then, Giri S systematically reviewed the existing data, it did not showed differences in the diagnostic yield and sample adequacy between the 21 and 22-G during EBUS-TBNA (46).

Although the sampling ability of the needles available now is high, we still expect the development of needles with better ability to sample histologic specimens for ancillary tests, such as immunohistochemistry, molecular analysis, and gene typing.

A new 22 G EBUS-TBNA needle

Recently, a new 22-G EBUS-TBNA needle, GUS-45-18-022, has become available. The tip of the needle is very sharp and has an easy handling design. As reported by Izumo T, the new 22-G needle had a significantly shorter procedure time than the Olympus 22-G needle. Of the 214 punctures by the new 22-G needle, 74.3% were diagnostic, 13.1% were non-diagnostic and 12.6% had no histologic specimen. The 235 punctures by the Olympus 22-G needle were diagnostic in 61.3%, non-diagnostic in 25.5% and had no histologic specimen in 13.2% (47). So, the yield for diagnostic and histologic sample by the new 22-G EBUS-TBNA needle was superior to Olympus 22-G needle.

Histologic needle

TBNA using transbronchial histology (19-gauge) and cytology (21-gauge) needles have demonstrated lower diagnostic yield for benign than for malignant lesions (3). It was also found no difference in the sampling yield of histologic specimens between the 21-gauge and 22-gauge EBUS-TBNA needles (44). At least, increasing sample volume using a 21-gauge needle rather than a 22-gauge needle might contribute to improve diagnostic yield in EBUS-TBNA. Based on it, Saji J did reveal the benefits of using the 21-gauge needle for histologic diagnostic yields (43). However, recently, Wong *et al.* achieved high diagnostic yield for sarcoidosis using EBUS-TBNA by the 22-gauge needle (91.3%) (48).

The newly developed cryo-needle operates in a similar way to the EBUS-TBNA, to obtain specimens for histological evaluation. In a mediastinal lymph node of a pig, Franke KJ successfully performed EBUS-guided cryo-needle biopsies (49), which yielded histological specimens with high quality.

Specimen preparation

Histologic specimens

In most articles, rarely are the histologic and cytologic yields reported separately. Recently, Stratakos *et al.* showed a 35.3% increase in the diagnostic yield for malignancy though histologic examination of TBNA samples, compared with sole cytology (50). Hermens's study also shows that histologic material can reveal additional information in 14% of TBNA samples (51). In view of these data, obtaining a histologic TBNA specimen could increase the diagnostic yield.

Liquid-based cytology (LBC)

The conventional cytological preparation is limited by the presence of air-drying artifacts and obscuring material, such as mucus, necrosis, inflammatory cells and blood. LBC has the advantage of creating preparations with a clean background. It could offer the possibility to divide the samples equally on a number of more or less identical slides. As Qiu T reported, compared to conventional assay, LBC

can improve diagnostic sensitivity of cytological specimens of EBUS-TBNA. So, LBC preparation was regarded as a method of improving diagnostic values of cytological assessment of EBUS-TBNA (52).

Cell blocks

The value of cell-block processing of EBUS-TBNA samples has only been marginally investigated. Sanz-Santos J found that cell-block preparation from EBUS-TBNA samples is a simple way to provide additional information in diagnosis of lung cancer, and increases the diagnostic yield by nearly 7%, and allows for genetic analysis in a 60% of the patients with lung adenocarcinoma (53).

Outer sheath method (OSM)

To improve diagnostic yield by avoiding the puncture of cartilage rings, a new method, the OSM was developed to enable identification of a suitable puncture site. While pressing the outer sheath of the needle against the bronchial wall, the hyperechoic line would appear on EBUS image. Basing on the EBUS images, the tip of outer sheath will move to the epithelium above the cartilage to detect the best site for puncturing simultaneously. As Inoue T reported, OSM did enable a suitable puncture site to be identified, improving diagnostic yield by nearly 6% (54).

Training and practice

The European Respiratory Society and American Thoracic Society Joint Statement on Interventional Pulmonology states that trainees should perform at least 40 procedures in a supervised setting, and 25 procedures should be done annually to maintain competency. The American College of Chest Physicians guidelines for interventional pulmonary procedures indicated that trainees should be supervised for 50 EBUS procedures, and a physician should perform 20 procedures per year.

Without formal training

C-TBNA is a bronchoscopic diagnostic technique that lends itself well to the focused acquisition of experiential knowledge and technical skill. Kupeli believed, c-TBNA can be learned by practicing in a model without formal training, and achieve diagnostic yield similar to those published in the literature (55).

Simulator models

Simulator models to teach TBNA include expensive high-fidelity platforms using three-dimensional virtual anatomy with force feedback technology, and low-fidelity models comprised of silicone or animal airways. Both low- and high-fidelity simulators could offer trainees direct experience in the manipulation of a bronchoscope, and an opportunity to acquire procedure-specific skills. Ideally, these two models can be used sequentially, and enhance the learners' experience because of their respective advantages. However, the user preferences promoted us to agree that the low-fidelity model may be better suited to provide trainees with a basic train of skills (56-58).

Learning curve

More successful results are obtained after a certain learning curve, as it is the case for every invasive technical. According to the learning curve analysis, the ability to perform EBUS-TBNA required approximately 37 procedures, which means the diagnostic accuracy did not peak until after 37 procedures (59). In the other study, the number of procedures required to achieve an optimum field was 50 (60). Bizekis *et al.* presented the initial experience with the EBUS procedure for 51 patients. It is shown that the first 25 patients had 72.22% sensitivity and 80% accuracy, whereas the last 26 patients had 95.45% sensitivity and 96.15% accuracy (61). Cordovilla R strongly feels that EBUS-TBNA helped trainees better understand the puncture of the mediastinal lymph nodes, increases the diagnostic yield of c-TBNA by nearly 20% (62).

Summary

TBNA should remain in the armamentarium of every bronchoscopist and on the curriculum of pulmonary fellowship training programs even if EBUS technology is not available. In our opinion, improved accuracy was achieved by the experience gained with the increase in the number of the procedure, especially, the principle of TBNA, puncturing the needle into the lesion through the bronchial wall.

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Footnote

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References

1. Wang KP, Terry P, Marsh B. Bronchoscopic needle aspiration biopsy and paratracheal tumors. Am Rev Respir Dis 1978;118:17-21.
2. Wang KP, Terry P. Transbronchial needle aspiration in the diagnosis and staging of bronchogenic carcinoma. Am Rev Respir Dis 1983;127:344-7.
3. Sharafkhaneh A, Baaklini W, Gorin AB, et al. Yield of Transbronchial needle aspiration in diagnosis of mediastinal lesions. Chest 2003;124:2131-5.
4. Selçuk ZT, Firat P. The diagnostic yield of transbronchial needle aspiration in superior vena cava syndrome. Lung Cancer 2003;42:183-8.
5. Goussard P, Gie RP, Kling S, et al. The diagnostic value and safety of transbronchial needle aspiration biopsy in children with mediastinal lymphadenopathy. Pediatr Pulmonol 2010;45:1173-9.
6. Zhu T, Zhang X, Xu J, et al. Endobronchial ultrasound guided-transbronchial needle aspiration vs. conventional transbronchial needle aspiration in the diagnosis of mediastinal masses: A meta-analysis. Mol Clin Oncol 2014;2:151-5.
7. Khan A, Agarwal R, Aggarwal AN, et al. Blind transbronchial needle aspiration without an on-site cytopathologist: Experience of 473 procedures. Natl Med J India 2011;24:136-9.
8. Jeffus SK, Joiner AK, Siegel ER, et al. Rapid on-site evaluation of EBUS-TBNA specimens of lymph nodes: comparative analysis and recommendations for standardization. Cancer Cytopathol 2015;123:362-72.
9. Sindhwani G, Rawat J, Chandra S, et al. Transbronchial needle aspiration with rapid on-site evaluation: A prospective study on efficacy, feasibility and cost effectiveness. Indian J Chest Dis Allied Sci 2013;55:141-4.
10. Bonifazi M, Zuccatosta L, Trisolini R, et al. Transbronchial needle aspiration: a systematic review on predictors of a successful aspirate. Respiration 2013;86:123-34.
11. Sun J, Yang H, Teng J, et al. Determining factors in diagnosing pulmonary sarcoidosis byendobronchial ultrasound-guided transbronchial needle aspiration. Ann Thorac Surg 2015;99:441-5.
12. Wang KP. Staging of bronchogenic carcinoma by bronchoscopy. Chest 1994;106:588-593.
13. Weiner GM, Schulze K, Geiger B, et al. CT Bronchoscopic simulation for guiding transbronchial needle aspiration of extramural mediastinal and hilar lesions: initial clinical results. Radiology 2009;250:923-31.
14. Weiner GM, Geiger B, Schulze K, et al. Computed tomography-bronchoscopicsimulationfor guiding transbronchial fine needle aspiration of extramural targets: a phantom study. Invest Radiol 2007;42:807-14.
15. White CS, Weiner EA, Patel P, et al. Transbronchial needle aspiration: guidance with CT Fluoroscopy. Chest 2000;118:1630-8.
16. Garpestad E, Goldberg S, Herth F, et al. CT fluoroscopy guidance for transbronchial needle aspiration: an experience in 35 patients. Chest 2001;119:329-32.
17. Gildea TR, Mazzone PJ, Karnak D, et al. Electromagnetic navigation diagnostic bronchoscopy: aprospective study. Am J Respir Crit Care Med 2006;174:982-9.
18. Diken ÖE, Karnak D, Çiledağ A, et al. Electromagnetic navigation-guided TBNA vs conventional TBNA in the diagnosis of mediastinal lymphadenopathy. Clin Respir J 2015;9:214-20.
19. Cetinkaya E, Ozgül MA, Tutar N, et al. The diagnostic utility of real-time EBUS-TBNA for hilar and mediastinal lymph nodes in conventional TBNA negative patients. Ann Thorac Cardiovasc Surg 2014;20:106-12.
20. Herth FJ, Morgan RK, Eberhardt R, et al. Endobronchial ultrasound-guided miniforceps biopsy in the biopsy of subcarinal masses in patients with low likelihood of non-small cell lung cancer. Ann Thorac Surg 2008;85:1874-8.
21. Yasufuku K, Nakajima T, Fujiwara T, et al. Utility of endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of mediastinal masses of unknown etiology. Ann Thorac Surg 2011;91:831-6.
22. Yasufuku K, Chiyo M, Sekine Y, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. Chest 2004;126:122-8.
23. Jiang J, Browning R, Lechtzin N, et al. TBNA with and without EBUS: a comparative efficacy study for the diagnosis and staging of lung cancer. J Thorac Dis 2014;6:416-20.

24. Chin R Jr. On-site cytopathologic analysis of bronchoscopic needle aspirates. Pro: On-site analysis is indicated. J Bronchl 2003;10:150-1.
25. Boyan W. On-site cytopathologic analysis of bronchoscopic needle aspiration: con; on-site analysis in not indicated. J Bronchol 2003;10:152-4.
26. Cardoso AV, Neves I, Magalhães A, et al. The value of rapid on-site evaluation during EBUS-TBNA. Rev Port Pneumol (2006) 2015;21:253-8.
27. Trisolini R, Cancellieri A, Tinelli C, et al. Rapid on-site evaluation of transbronchial aspirates in the diagnosis of hilar and mediastinal adenopathy: a randomized trial. Chest 2011;139:395-401.
28. Baram D, Garcia RB, Richman PS. Impact of rapid on-site cytologic evaluation during transbronchial needle aspiration. Chest 2005;128:869-75.
29. Dziedzic DA, Peryt A, Orlowski T. The role of EBUS-TBNA and standard bronchoscopic modalities in the diagnosis of sarcoidosis. Clin Respir J 2015. [Epub ahead of print].
30. Agarwal R, Aggarwal AN, Gupta D. Efficacy and safety of conventional transbronchial needle aspiration in sarcoidosis: a systematic review and meta-analysis. Respir Care 2013;58:683-93.
31. Gupta D, Dadhwal DS, Agarwal R, et al. Endobronchial ultrasound-guided transbronchial needle aspiration vsconventional transbronchial needle aspiration in the diagnosis of sarcoidosis. Chest 2014;146:547-56.
32. Casal RF, Staerkel GA, Ost D, et al. Randomized clinical trial of endobronchial ultrasound needle biopsy with and without aspiration. Chest 2012;142:568-73.
33. Mair S, Dunbar F, Becker PJ, et al. Fine needle cytology--is aspiration suction necessary? A study of 100 masses in various sites. Acta Cytol 1989;33:809-13.
34. Harris K, Maroun R, Attwood K, et al. Comparison of cytologic accuracy of endobronchial ultrasound transbronchial needle aspiration using needle suction versus no suction. Endosc Ultrasound 2015;4:115-9.
35. Wallace MB, Kennedy T, Durkalski V, et al. Randomized controlled trial of EUS-guided fine needle aspiration techniques for the detection of malignant lymphadenopathy. Gastrointest Endosc 2001;54:441-7.
36. Eto H, Suga H, Matsumoto D, et al. Characterization of structure and cellular components of aspirated and excised adipose tissue. Plast Reconstr Surg 2009;124:1087-97.
37. Puri R, Vilmann P, Săftoiu A, et al. Randomized controlled trial of endoscopic ultrasound-guided fine-needle sampling with or without suction for better cytological diagnosis. Scand J Gastroenterol 2009;44:499-504.
38. Larghi A, Noffsinger A, Dye CE, et al. EUS-guided fine needle tissue acquisition by using high negative pressure suction for the evaluation of solid masses: a pilot study. Gastrointest Endosc 2005;62:768-74.
39. Boonsarngsuk V, Pongtippan A, Juthakarn S, et al. Autoaspiration versus manual aspiration in transbronchial needle aspiration in diagnosis of intrathoracic lymphadenopathy. J Bronchology Interv Pulmonol 2009;16:236-40.
40. Chin R Jr, McCain TW, Lucia MA, et al. Transbronchial needle aspiration in diagnosing and staging lung cancer: how many aspirates are needed? Am J Respir Crit Care Med 2002;166:377-81.
41. Lee HS, Lee GK, Lee HS, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration in mediastinal staging of non-small cell lung cancer: how many aspirations per target lymph node station? Chest 2008;134:368-74.
42. Nakajima T, Yasufuku K, Takahashi R, et al. Comparison of 21-gauge and 22-gauge aspiration needle during endobronchial ultrasound-guided transbronchial needle aspiration. Respirology 2011;16:90-4.
43. Saji J, Kurimoto N, Morita K, et al. Comparison of 21-gauge and 22-gauge needles for endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. J Bronchology Interv Pulmonol 2011;18:239-46.
44. Oki M, Saka H, Kitagawa C, et al. Randomized study of 21-gauge versus 22-gauge endobronchial ultrasound-guided transbronchial needle aspiration needles for sampling histology specimens. J Bronchology Interv Pulmonol 2011;18:306-10.
45. Yarmus LB, Akulian J, Lechtzin N, et al. Comparison of 21-gauge and 22-gauge aspiration needle in endobronchial ultrasound-guided transbronchial needle aspiration: results of the American College of Chest Physicians Quality Improvement Registry, Education, and Evaluation Registry. Chest 2013;143:1036-43.
46. Giri S, Pathak R, Yarlagadda V, et al. Meta-analysis of 21- versus 22-G aspiration needle during endobronchial ultrasound-guided transbronchial needle aspiration. J Bronchology Interv Pulmonol 2015;22:107-13.
47. Izumo T, Sasada S, Watanabe J, et al. Comparison of two 22 G aspiration needles for histologic sampling during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). Jpn J Clin Oncol 2014;44:841-5.
48. Wong M, Yasufuku K, Nakajima T, et al. Endobronchial

ultrasound: new insight for the diagnosis of sarcoidosis. Eur Respir J 2007;29:1182-6.
49. Franke KJ, Nilius G, Ruehle KH, et al. The cryo-needle: a new tool for histological biopsies. A feasibility study. Lung 2013;191:611-7.
50. Stratakos G, Porfyridis I, Papas V, et al. Exclusive diagnostic contribution of the histology specimens obtained by 19-gauge transbronchial aspiration needle in suspected malignant intrathoracic lymphadenopathy. Chest 2008;133:131-6.
51. Hermens FH, Limonard GJ, Hoevenaars BM, et al. Diagnostic value of histology compared with cytology in transbronchial aspiration samples obtained by histology needle. J Bronchology Interv Pulmonol 2010;17:19-21.
52. Qiu T, Zhu H, Cai M, et al. Liquid-Based Cytology Preparation Can Improve Cytological Assessment of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration. Acta Cytol 2015;59:139-43.
53. Sanz-Santos J, Serra P, Andreo F, et al. Contribution of cell blocks obtained through endobronchial ultrasound-guided transbronchial needle aspiration to the diagnosis of lung cancer. BMC Cancer 2012;12:34.
54. Inoue T, Kurimoto N, Furuya N, et al. New technique for endobronchial ultrasound-guided transbronchial needle aspiration to improve diagnostic yield. J Bronchology Interv Pulmonol 2013;20:28-32.
55. Kupeli E, Memis L, Ozdemirel TS, et al. Transbronchial needle aspiration "by the books". Ann Thorac Med 2011;6:85-90.
56. Davoudi M, Wahidi MM, Zamanian Rohani N, et al. Comparative effectiveness of low- and high-fidelity bronchoscopy simulation for training in conventional transbronchial needle aspiration and user preferences. Respiration 2010;80:327-34.
57. Stather DR, MacEachern P, Chee A, et al. Wet laboratory versus computer simulation for learning endobronchial ultrasound: a randomized trial. Can Respir J 2012;19:325-30.
58. Goldberg R, Colt HG, Davoudi M, et al. Realistic and affordable lo-fidelity model for learning bronchoscopic transbronchial needle aspiration. Surg Endosc 2009;23:2047-52.
59. Usluer O, Kaya SO. Endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal lymphadenopathy: effect of the learning curve. Interact Cardiovasc Thorac Surg 2014;19:693-5.
60. Rodríguez de Castro F, Díaz López F, Serdà GJ, et al. Relevance of training intransbronchial fine-needle aspiration technique. Chest 1997;111:103-5.
61. Bizekis CS, Santo TJ, Parker KL, et al. Initial experience with endobronchial ultrasound in an academic thoracic surgery program. Clin Lung Cancer 2010;11:25-9.
62. Cordovilla R, Torracchi AM, García-Macías MC. Enhancement of conventional TBNA outcome after EBUS Training. J Bronchology Interv Pulmonol 2014;21:322-6.

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