Monaldi Arch Chest Dis
2011; 75: 1, 44-49

Transbronchial Needle Aspiration*

R. Trisolini[1], M. Patelli[1], L. Ceron[2], S. Gasparini[3]

Monaldi Arch Chest Dis 2011; 75: 1, 44-49.

Keywords: Transbronchial needle aspiration, Mediastinal lesions, Hilar lymphoadenopathy, Granulomatous disorders, Transbornchial biopsies.

[1] U.O. Endoscopia Toracica e Pneumologia, Dipartimento di Scienze Oncologiche, Ospedali Maggiore e Bellaria, Bologna,
[2] Divisione di Pneumologia, Dipartimento di Malattie del Torace, Ospedale di Mestre (Venezia),
[3] Divisione di Pneumologia, Dipartimento di Medicina Interna, Malattie Immunologiche e Respiratorie, Azienda Ospedali Riuniti, Ancona, Italy.

Correspondence: Dr. Rocco Trisolini, U.O. Endoscopia Toracica e Pneumologia, Dipartimento di Scienze Oncologiche, Ospedale Maggior, Largo Nigrisoli 2, 40100 Bologna, Italy; e-mail: rocco.trisolini@ausl.bologna.it

Transbronchial needle aspiration (TBNA) is a low cost, minimally invasive bronchoscopic procedure which has been successfully used in the diagnosis of neoplastic, inflammatory, infectious, and developmental disorders [1].

Although it has been developed and predominantly used to sample mediastinal lesions, the technique is extremely versatile, as it can also be used to sample submucosal, peribronchial, and peripheral pulmonary lesions [1].

Technique

Conventional TBNA of hilar and mediastinal lesions was originally thought as a "blind" procedure since target lymph nodes cannot be visualized directly by the operator and the site for aspiration/biopsy is chosen based on the knowledge of a few endobronchial landmarks and prior contrast enhanced CT evaluation [2, 3]. In the last decade, the development of new technologies, especially endobronchial ultrasounds (EBUS) and CT-fluoroscopy, has led to the concept of integration with TBNA to improve the diagnostic yield [4-11]. Initial studies assessing the value of ultrasound-guided TBNA (EBUS-TBNA) compared with conventional TBNA demonstrated the superiority of EBUS-TBNA only for small lymph nodes (<1 cm) or for "difficult-to-reach" lymph node mediastinal areas (2R, 2L, 4L), but these studies were performed with a radial ultrasonic probe which did not allow for a real-time guidance of fine-needle aspiration [7-9]. More recently, a dedicated bronchoscope equipped with a linear array transducer that allows for real-time guidance of TBNA (real-time EBUS-TBNA) has been developed and has been associated with excellent results in the mediastinal staging of lung cancer and sarcoidosis [10]. Even though no other study carried out direct standard vs real-time EBUS-TBNA comparisons, several trials published in the last decade and aimed at evaluating the role of real-time EBUS-TBNA in patients with enlarged hilar/mediastinal adenopathy, obtained average sensitivity and accuracy values close to 90%, certainly superior to those reported for conventional TBNA in most studies [10, 11].

Recommendation

- **EBUS-guided TBNA is superior to conventional TBNA mainly in some specific settings, such as difficult mediastinal LN areas (mainly 2, 3, 4L) and small LN size (<1 cm) (Grade A).**

Specimen handling and preparation methods for cytologic material

As for the handling of TBNA specimens, in those cases in which a histologic core of tissue has been obtained, it is removed gently from the needle's tip and placed in formalin solution before being sent for staining and pathologic analysis [1, 12]. Cytologic material can be managed in two different ways: 1) "smear" ("direct") technique: the aspirate's content material is collected on clean glass slides that are quickly air- or alcohol-fixed before being sent for staining and pathologic analysis. 2) "flush technique": the aspirate's content is deposited in 2 mL 95% alcohol which undergoes cytocentrifugation, cell pellet resuspension and staining [1]. Diacon *and Coll.* recently compared the two preparation methods and concluded that the "direct" technique is associated with a higher yield than the "flush" technique even after stratification for anatomical site and tumour type [13].

It should be noted, however, that alternative or adjunctive preparation methods can be required based on clinicoradiological data or pathologist's preference. In patients with suspected mediastinal infection (especially mycobacterial infection) or lymphoma, the aspirate's content should also be deposited in saline solution for culture or flow cytometric analysis, respectively.

* Due to the mounting scientific evidence concerning EBUS-TBNA published after 2006, the reference list and some recommendations regarding the present topic have been updated in february 2011 after critical literature review and expert consensus.

Recommendation

- **Cytologic material obtained with TBNA should be prepared with the smear (direct) technique (Grade B).**

Indications

a) Mediastinal lesions

Any lesion involving the middle mediastinum and in close contact with the airway wall is potentially suitable for TBNA sampling.

Bronchogenic carcinoma

TBNA, mainly if performed at the time of initial diagnostic bronchoscopy, can offer the unique opportunity to prevent patients with lymph node extension of primary tumour from being submitted to unnecessary surgical mediastinal exploration. In those cases in which TBNA is performed at the time of initial diagnostic bronchoscopy along with other sampling bronchoscopic procedures aimed at typing the primary tumour, TBNA may be the only positive test in a considerable percentage of cases.

After two decades of use, strengths and limits of TBNA in the mediastinal staging of NSCLC are quite well known and have been thoroughly described in two recent extensive literature reviews. In 2007, Detterbeck *et al*. performed a systematic review on 17 studies where TBNA was used to stage the mediastinum of 1339 patients with NSCLC [14]. The overall sensitivity and specificity were 78% and 99%, respectively. The main limit of TBNA was its high false negative rate (approximately 30%), which suggests that a negative transbronchial aspirate result must not negate further evaluation with more invasive sampling techniques mainly if the clinical-radiological suspect of lymph node metastasis is high. A more recent meta-analysis on the results of TBNA in the mediastinal staging of lung cancer selected, based on rigorous criteria, 13 studies out of 525 initially taken into account [15]. The analysis basically confirmed the very high specificity of the method, but also clearly demonstrated that its yield as well as its positive predictive value largely depend on the prevalence of lymph node metastasis in the population being studied. In particular, the diagnostic yield of TBNA proved high in studies with high prevalence of N2-N3 involvement, and the general implication was that the mediastinal nodes were markedly enlarged in these study populations. On the contrary, TBNA yield was much lower than previously thought in populations with low prevalence of lymph node metastasis. This data suggests that the primary role for TBNA in the mediastinal staging of NSCLC should be that of confirming a neoplastic lymph node involvement which looks likely based on the imaging techniques results, by virtue of its high specificity and sensitivity in this specific setting.

Several studies have evaluated a number of factors to explain the differences seen among the reported diagnostic yields of the procedure in the mediastinal staging of NSCLC, and identified several predictors of a positive TBNA aspirate such as: high prevalence of lymph node metastasis in the study population [14, 15], increasing lymph node size [8, 16], right paratracheal and subcarinal locations [8, 12, 16], use of a histology needle [17], increasing number of needle passes up to 7 [18], experience of the operator [19-20], and small-cell carcinoma histologic type [8, 16, 21-24]. Rapid on-site cytopathologic examination (ROSE) was initially thought to increase both the percentage of adequate samples and diagnostic yield of TBNA [25-27], but more recent data suggests that the main utility of ROSE in the setting of mediastinal TBNA is its capacity to defer additional biopsy and reduce the complication rate of bronchoscopy without compromising its diagnostic success [28-29].

Recommendation

- **TBNA or EBUS-TBNA should be performed in every patient with radiological suspicion of lung cancer and mediastinal involvement, provided that the mediastinal staging is crucial for the therapeutic choice (Grade B).**

Hylar and/or mediastinal lymphadenopathy

Several studies investigated the usefulness of TBNA in an unselected group of patients with hylar and or mediastinal lymphadenopathy. Such a study population is likely to include patients with several different diseases (neoplastic, infectious, inflammatory), and it allows to evaluate the performance of TBNA in patients who are selected almost exclusively based on their imaging findings. The vast majority of these studies concluded that TBNA is safe and effective in this setting and almost uniformly reported a diagnostic yield superior to 60% [30-33].

Recommendation

- **TBNA or EBUS-TBNA should be the initial diagnostic procedure in patients with hylar and/or mediastinal lymphadenopathy, provided that the enlarged nodes are in close contact with the airway wall (Grade B).**

Granulomatous disorders

TBNA has been used with satisfactory results in patients with clinical suspicion of sarcoidosis or mycobacterial infection.

Conventional TBNA has been shown to increase the diagnostic yield of bronchoscopy in the setting of sarcoidosis when performed along with the other sampling procedures (bronchoaveolar lavage, bronchial and transbronchial biopsy) [34-

38]. The diagnostic yield of TBNA was particularly high (>70%) in stage I, whereas less satisfactory and widely variable results have been reported for the method in stage II [34-38]. More recently, a uniformly higher diagnostic yield has been obtained, both in stage I and in stage II, with ultrasound-guided TBNA [39, 40], and this superiority has been confirmed in a randomised trail comparing EBUS-guided versus conventional TBNA [41].

In the last decade, some groups of investigators reported their experience with the use of TBNA and EBUS-TBNA in the diagnosis of mediastinal/hilar lymph node involvement due to mycobacterial disease both in the setting of immunocompetent and immunocompromised patients [42-44].

Bilaceroglu *et al.* obtained very good results by using a 19-gauge histology needle for diagnosing isolated mediastinal/hilar tuberculosis in a large series of immunocompetent patients [42]. Sensitivity and specificity of the method were 83% and 100% respectively and TBNA was the only means of diagnosis in 68% of patients. Positive culture on TBNA specimens was obtained in 27% of cases. As already observed in the diagnosis and staging of lung cancer, TBNA procedures performed in the right paratracheal and subcarinal areas yielded the best results (91% and 100%, respectively), and the main limit of the method was the unsatisfactory negative predictive value (38%). Hassan *et al.* obtained excellent results (sensitivity 95%, accuracy 79%) by using EBUS-TBNA in a small series (24 patients) of patients with isolated thoracic tuberculous adenopathy [43]. The only possible problem limiting the generalisation of the results of both these studies is the fact that the authors included a cohort of patients with a high pretest probability of tuberculosis, selected based on strong tuberculin skin test, high prevalence of symptoms, and originating from a country with a high prevalence of tuberculosis [42, 43].

Harkin *et al*. reported their experience with TBNA in the diagnosis of mediastinal/hilar adenopathy in patients infected with the acquired immunodeficiency virus [44]. By using a 19-gauge histology needle, the authors were able to diagnose 80% of patients with tuberculosis and 100% of patients with mediastinal lymph node disease due to mycobacteria other than tuberculosis. TBNA was the only means of diagnosis in 48% of cases. Curiously, a positive culture of TBNA specimens was obtained in 61% of cases, a much higher percentage than that usually observed in immunocompetent patients in the same setting [44].

Recommendation

- **TBNA or EBUS-TBNA should integrate the standard bronchoscopic sampling procedures in patients with hylar or mediastinal lymphadenopathy due to suspect sarcoidosis or mycobacterial infection, mainly if endobronchial or parenchimal signs of disease are lacking (Grade B).**

b) Central lesions

Lung cancer may present in the central airway with four different patterns of involvement: 1) exophytic mass lesion; 2) submucosal infiltration; 3) peribronchial pattern with extrinsic compression; 4) peribronchial pattern without signs of extrinsic compression.

Importantly, exophytic lesions cause significant mucosal abnormality, whereas submucosal infiltration and, especially, peribronchial lesions may leave the mucosal surface almost intact. Dasgupta *and coll.* prospectively investigated the diagnostic yield of standard bronchoscopic sampling procedures (bronchial washing, bronchial brushing, endobronchial biopsy) with that obtained with standard procedures plus TBNA [45]. Of the 55 patients with central lung cancer included in the study, 32 had an exophytic mass whereas the remaining 23 patients had either a submucosal pattern or extrinsic compression [45]. The highest yield from any individual bronchoscopic procedure was obtained by TBNA. The combined use of standard bronchoscopic sampling procedures plus TBNA offered a statistically significant advantage as compared to standard procedures alone in patents with submucosal pattern or extrinsic compression (96% vs 65%, p=0.016). The ability of TBNA to penetrate either the submucosal layer or the bronchial wall into the tumour mass is the likely explanation for the above results. In patients with exophytic mass lesion, the combination of standard procedures plus TBNA was also associated with an increase of the diagnostic yield, yet not reaching statistical significance. The extra value of TBNA in exophytic lesions might be explained by its ability to bypass surface necrosis and sample from deep inside the lesion. Moreover, in the specific setting of small cell lung cancer crush artefacts produced during forceps biopsy may be responsible for a non-diagnostic result [45]. The results obtained by Dasgupta *et al.* have been confirmed in several other studies with similar design [46-48].

More recently, EBUS-TBNA has shown its ability to localise and sample central malignant lesions growing with a peribronchial pattern, yet not compressing the airways [49, 50]. Tournoy *et al.* performed EBUS-TBNA in 60 patients with peribronchial central lesion, most of whom had had a prior, non diagnostic bronchoscopy. They obtained an 82% sensitivity and could cancel transthoracic needle aspiration in 47% of patients and surgery in 30% of patients [49]. These studies suggest that EBUS-TBNA should be the first-step technique in the diagnostic approach to peribronchial central lung lesions not compressing the airways.

Recommendations

- **In the diagnostic approach to a "central" malignant lesion there is indication to TBNA use when the pattern of airway involvement is either submucosal or peribronchial (extrinsic compression) (Grade B).**

- **In the diagnostic approach to a "central" malignant lesion there is indication to the use of EBUS-TBNA when the pattern of airway involvement is peribronchial, especially if there is no sign of extrinsic compression (Grade B).**

c) Peripheral lesions

Bronchoscopy in patients with peripheral lung lesions may have both staging and diagnostic purposes. The inspection of the airways allows, in fact, to complete the definition of the "T descriptor" of the TNM staging system, and to rule out the existence of synchronous lesions. As for the diagnosis, the yield of standard bronchoscopic sampling procedures (bronchial washing, bronchial brushing, transbronchial biopsy) in this setting depends on several variables such as size of the lesion, presence/absence of the bronchus sign, use of imaging techniques to guide the sampling [49].

In a recent, systematic literature review, Schreiber analysed the 5 studies (793 patients included) in which TBNA had been performed, under fluoroscopy, along with other bronchoscopic sampling procedures, and he demonstrated that the method was associated with a higher yield (67%) than bronchoalveolar lavage (42%), bronchial brushing (52%), and transbronchial biopsy (46%) [51]. Katis *et al.* prospectively investigated the diagnostic yield of standard bronchoscopic sampling procedures (bronchial washing, transbronchial biopsy) with that obtained with standard procedures plus TBNA [52]. The yield of TBNA under fluoroscopic guidance was superior to that of bronchial washing (62% vs 24%, $p<0.005$), bronchial brushing (62% vs 27%, $p<0.005$), and transbronchial biopsy (62% vs 38%, $p<0.005$). The combined use of standard bronchoscopic sampling procedures and TBNA offered a statistically significant advantage as compared to standard procedures alone (70% vs 46%, $p<0.05$).

Interestingly, similar results have been recently reported by Chao *et al.*, who evaluated for the first time, the added value of TBNA guided by endobronchial ultrasound in patients with peripheral pulmonary lesions. The authors, in fact, demonstrated that the sensitivity of TBNA (72%) was higher than that of both transbronchial lung biopsy (50%, $p=0.004$) and bronchial washing (13.5%, $p<0.001$).

In conclusion, there is strong evidence in the literature that TBNA improves the diagnostic yield of bronchoscopy in patients with peripheral lesions, whatever the imaging guide [53-56].

Recommendation

- **In the diagnostic approach to a "peripheral" lesions there is indication to the use of TBNA, whatever the imaging guide, along with other standard bronchoscopic sampling procedures (Grade B).**

Summary of Recommendations

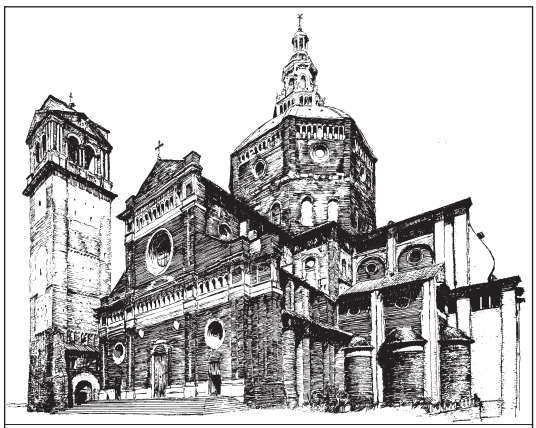
- **EBUS-guided TBNA is superior to conventional TBNA mainly in some specific settings, such as difficult mediastinal LN areas (mainly 2, 3, 4L) and small LN size (<1 cm) (Grade A).**
- **Cytologic material obtained with TBNA should be prepared with the smear (direct) technique (Grade B).**
- **TBNA or EBUS-TBNA should be performed in every patient with radiological suspicion of lung cancer and mediastinal involvement, provided that the mediastinal staging is crucial for the therapeutic choice (Grade B).**
- **TBNA or EBUS-TBNA should be the initial diagnostic procedure in patients with hylar and/or mediastinal lymphadenopathy, provided that the enlarged nodes are in close contact with the airway wall (Grade B).**
- **TBNA or EBUS-TBNA should integrate the standard bronchoscopic sampling procedures in patients with hylar or mediastinal lymphadenopathy due to suspect sarcoidosis or mycobacterial infection, mainly if endobronchial or parenchimal signs of disease are lacking (Grade B).**
- **In the diagnostic approach to a "central" malignant lesion there is indication to TBNA use when the pattern of airway involvement is either submucosal or peribronchial (extrinsic compression) (Grade B).**
- **In the diagnostic approach to a "central" malignant lesion there is indication to the use of EBUS-TBNA when the pattern of airway involvement is peribronchial, especially if there is no sign of extrinsic compression (Grade B).**
- **In the diagnostic approach to a "peripheral" lesions there is indication to the use of TBNA, whatever the imaging guide, along with other standard bronchoscopic sampling procedures (Grade B).**

References

1. Dasgupta A, Mehta AC, Wang KP. Transbronchial needle aspiration. *Seminars Resp Crit Care Med* 1997; 18: 571-81.
2. Wang KP, Terry P, Marsch B. Bronchoscopic needle aspiration in the diagnosis and staging of bronchogenic carcinoma. *Chest* 1983; 84: 571-6.
3. Wang KP. Flexible transbronchial needle aspiration biopsy for histologic specimens. *Chest* 1985; 88: 860-3.
4. White CS, Weiner EA, Patel P, *et al*. Transbronchial needle aspiration: guidance with CT fluoroscopy. *Chest* 2000; 118: 1630-38.

5. Garpestad E, Goldberg SN, Herth F, *et al*. CT fluoroscopy guidance for transbronchial needle aspiration: an experience in 35 patients. *Chest* 2001; 119: 329-32.
6. Goldberg SN, Raptopulos V, Boiselle PM, *et al*. Mediastinal lymphadenopathy: Diagnostic yield of transbronchial mediastinal lymph node biopsy using CT-fluoroscopic guidance: initial experience. *Radiology* 2000; 216: 764-7.
7. Shannon JJ, Bude RO, Orens JB, *et al*. Endobronchial ultrasound-guided aspiration of mediastinal adenopathy. *Am J Resp Crit Care Med* 1996; 153: 1424-30.
8. Herth F, Becker HD, Ernst A. Conventional vs endobronchial ultrasound-guided transbronchial needle aspiration. A randomized trial. *Chest* 2004; 125: 322-25.
9. Trisolini R, Lazzari Agli L, Patelli M. Conventional versus EBUS-guided transbronchial needle aspiration of the mediastinum. *Chest* 2004; 126: 1005-6.
10. 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: 795-8.
11. Adams K, Shah PL, Edmonds L, *et al*. Test performance of endobronchial ultrasound and transbronchial needle aspiration biopsy for mediastinal staging in patients with lung cancer: systematic review and meta-analysis. *Thorax* 2009; 64: 757-62.
12. Patelli M, Lazzari Agli L, Poletti V, *et al*. The role of fiberscopic transbronchial needle aspiration in the staging of N2 disease due to non small cell lung cancer. *Ann Thorac Surg* 2002; 73; 407-411.
13. Diacon AH, Shuurmans M, Theron J, *et al*. Transbronchial needle aspiration. Comparison of two preparation methods. *Chest* 2005; 127: 2015-18.
14. Detterbeck F, Janz MC, Wallace M, Vansteenkiste J, Silvestri GA. Invasive mediastinal staging of non-small cell lung cancer. ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007; 132: 202-220.
15. Holty JC, Kushner WG, Gould MK. Accuracy of transbronchial needle aspiration for mediastinal staging of non-smal cell lung cancer: a meta-analysis. *Thorax* 2005; 60: 949-55.
16. Harrow EM, Abi-Saleh W, Blum J, Harkin T, *et al*. The utility of transbronchial needle aspiration in the staging of bronchogenic carcinoma. *Am J Respir Crit Care Med* 2000; 161: 601-07.
17. 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.
18. Chin R, McCain TW, Lucia MA, *et al*. Transbronchial needle aspiration in diagnosing and staging lung cancer. How many aspirates are needed? *Am J Resp Crit Care Med* 2002; 166: 377-81.
19. Haponik EF, Cappellari JO, Chin R, *et al*. Education and experience improve transbronchial needle aspiration performance. *Am J Resp Crit Care Med* 1995; 151: 1998-2002.
20. Hsu LH, Liu CC, Ko JS. Education and experience improve the perfromance of transbronchial needle aspiration. A learning curve at a cancer center. *Chest* 2004; 125: 532-40.
21. Bilaceroglu S, Cagiotariotaciota U, Gunel O, *et al*. Comparison of rigid and flexible transbronchial needle aspiration in the staging of bronchogenic carcinoma. *Respiration* 1998; 65: 441-49.
22. Vansteenkiste J, Lacquet LM, Demedts M, *et al*. Transcarinal needle aspiration biopsy in the staging of lung cancer. *Eur Resp J* 1994; 7: 265-68.
23. Utz JP, Patel AM, Edell ES. The role of transcarinal needle aspiration in the staging of bronchogenic carcinoma. *Chest* 1993; 104: 1012-6.
24. Chin R, Cappellari JO, McCain TW, Case LD, Haponik EF. Increasing use of bronchoscopic needle aspiration to diagnose small cell lung cancer. *Majo Clin Proc* 2000; 75: 796-801.
25. Davenport RD. Rapid on-site evaluation of transbronchial aspirates. *Chest* 1990; 98: 59-61.
26. Diette GB, White P, Terry P, Jenckens M, Rosenthal D, Rubin HR. Utility of rapid on-site citopathology assessment for bronchoscopic evaluation of lung masses and adenopathy. *Chest* 2000; 117: 1186-90.
27. Diacon AH, Schuurmans MM, Theron J, *et al*. Utility of rapid on-site evaluation of transbronchial needle aspirates. *Respiration* 2005; 72: 182-8.
28. Baram D, Garcia RB, Richman PS. Impact of rapid on-site cytological evaluation during transbronchial needle aspiration. *Chest* 2005; 128: 869-75.
29. Trisolini R, Cancellieri A, Tinelli C, *et al*. Rapid on-site evaluation of transbronchial aspirates in the diagnosis of hilar and mediastinal adenopathy: a randomised trial. *Chest* 2011; 139: 395-401.
30. Sharafkhaneh A, Baaklini W, Gorin AB, Green L. Yield of transbronchial needle aspiration in diagnosis of mediastinal lesions. *Chest* 2003; 124: 2131-2135.
31. Cetinkaya E, Yildiz P, Altin S, Yilmaz V. Diagnostic value of transbronchial needle aspiration by Wang 22-gauge cytology needle in intrathoracic lymphadenopathy. *Chest* 2004; 125: 527-31.
32. Cetinkaya E, Yildiz P, Kadakal F, *et al*. Transbronchial needle aspiration in the diagnosis of intrathoracic lymphadenopathy. *Respiration* 2002; 69: 335-38.
33. Hermens FH, Van Engelenburg TC, Visser FJ, Thunnissen FB, Termeer R, Janssen JP. Diagnostic yield of transbronchial histology needle aspiration in patients with mediastinal lymph node enlargement. *Respiration* 2003; 70: 631-5.
34. Trisolini R, Lazzari Agli L, Cancellieri A, *et al*. The value of flexible transbronchial needle aspiration in the diagnosis of stage I sarcoidosis. *Chest* 2003; 124: 2126-30.
35. Wang KP, Johns CJ, Fuenning C, *et al*. Flexible transbronchial needle aspiration for the diagnosis of sarcoidosis. *Ann Otol Rhinol Laryngol* 1989; 98: 298-300.
36. Morales MCF, Patefield AJ, Strollo PJ, *et al*. Flexible transbronchial needle aspiration in the diagnosis of sarcoidosis. *Chest* 1994; 106: 709-711.
37. Bilaceroglu S, Perim K, Gunel O, *et al*. Combining transbronchial aspiration with endobronchial and transbronchial biopsy in sarcoidosis. *Monaldi Arch Chest Dis* 1999; 54: 217-23.
38. Trisolini R, Tinelli C, Cancellieri A, *et al*. Transbronchial needle aspiration in sarcoidosis: yield and predictors of a positive aspirate. *J Thorac Cardiovasc Surg* 2008; 135: 837-42.
39. Wong M, Yasufuku K, Nakajima T, *et al*. Endobronchial ultrasound: new insight for the diagnosis of sarcoidosis. *Eur Resp J* 2007; 29: 1182-86.
40. Garwood S, Judson MA, Silvestri G, Hoda R, Fraig M, Doelken P. Endobronchial ultrasound for the diagnosis of pulmonary sarcoidosis. *Chest* 2007; 132: 1298-304.
41. Tremblay A, Stather DR, Maceachern P, Khalil M, Field SK. A randomized controlled trial of standard versus endobronchial ultrasonography-guided transbronchial needle aspiration in patients with suspected sarcoidosis. *Chest* 2009; 136: 340-6.
42. Bilaceroglu S, Gunel O, Eris N, Cagirici U, Mehta AC. Transbronchial needle aspiration in diagnosing intrathoracic tuberculous lymphadenitis. *Chest* 2004; 126: 259-67.
43. Hassan T, McLaughlin AM, Gibbons N, Nicholson S, Keane J. EBUS-TBNA performs well in the diagnosis of isolated thoracic tuberculous lymphadenopathy. *Am J Resp Crit Care Med* 2011; 183: 136-137.
44. Harkin TJ, Ciotoli C, Addrizzo-Harris DJ, Naidich DP, Jagirdar J, Rom WN. Transbronchial needle aspiration

in patients infected with HIV. *Am J Resp Crit Care Med* 1998; 157: 1913-18.
45. Dasgupta A, Prasoon J, Minai OA, *et al*. Utility of transbronchial needle aspiration in the diagnosis of endobronchial lesions. *Chest* 1999; 115: 1237-41.
46. Caglayan B, Akturk UA, Fidan A, *et al*. Transbronchial needle aspiration in diagnosis of malignant endobronchial lesions. *Chest* 2005; 128: 704-8.
47. Kacar N, Tuksavul F, Edipoglu O, Ermete S, Guclu SZ. Effectiveness of transbronchial needle aspiration in the diagnosis of exophytic endobronchial lesions and submucosal/peribronchial diseases of the lung. *Lung Cancer* 2005; 50: 221-6.
48. Bilaceroglu S, Gunel O, Cagirici U, *et al*. Comparison of endobronchial needle aspiration with forceps and brush biopsy in the diagnosis of lung cancer. *Monaldi Arch Chest Dis* 1997; 52: 13-17.
49. Tournoy KG, Rintoul RC, van Meerbeeck JP, *et al*. EBUS-TBNA for the diagnosis of central parenchymal lung lesions not visible at routine bronchoscopy. *Lung Cancer* 2009; 63: 45-9.
50. Nakajima T, Yasufuku K, Fujiwara T, *et al*. Endobronchial ultrasound-guided transbronchial needle aspiration for the diagnosis of intrapulmonary lesions. *J Thorac Oncol* 2008; 3: 985-8.
51. Schreiber G, McCrory DC. Performance characteristics of different modalities for diagnosis of suspected lung cancer. *Chest* 2003; 123: 115S-128S.
52. Katis K, Inglesos E, Zacharidiadis E, *et al*. The role of transbronchial needle aspiration in the diagnosis of peripheral lung masses or nodules. *Eur Resp J* 1995; 8: 963-66.
53. Gasparini S, Ferretti M, Secchi EB, Baldelli S, Zuccatosta L, Gusella P. Integration of transbronchial and percutaneous approach in the diagnosis of peripheral pulmonary nodules or masses. Experience with 1,027 consecutive cases. *Chest* 1995; 108: 131-37.
54. Wang KP, Haponik E, Britt J, *et al*. Transbronchial needle aspiration of peripheral pulmonary nodule. *Chest* 1984; 86: 819-23.
55. Reichenberger F, Weber J, Tamm M, *et al*. The value of transbronchial needle aspiration in the diagnosis of peripheral pulmonary lesions. *Chest* 1999; 116: 704-8.
56. Chao TY, Chien MT, Lie CH, Chung YH, Wang JL, Lin MC. Endobronchial ultrasonography-guided transbronchial needle aspiration increases the diagnostic yield of peripheral pulmonary lesions. *Chest* 2009; 136: 229-36.



Pavia - Piazza Duomo