

Original Article

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A comparison of the diagnostic value of 19-gauge histology and 22-gauge cytology needles in bronchoscopy for the evaluation of endobronchial lesions

Elif YILMAZEL UÇAR¹ Mehmet MERAL¹, Metin AKGÜN¹, Sare ŞİPAL², Hasan KAYNAR¹, Leyla SAĞLAM¹, Ali Metin GÖRGÜNER¹

Aim: To prospectively compare the sensitivity of Wang 22-gauge needle aspiration and 19-gauge needle aspiration with bronchial biopsy and determine whether there was difference between 22-gauge and 19-gauge needle aspirations in the diagnosis of endobronchial malignancies.

Materials and methods: All patients (63 patients) in the study underwent fiberoptic bronchoscopy that included 22-gauge needle aspiration and 19-gauge needle aspiration. In 50 patients bronchial biopsy was done. The sensitivities of the individual techniques were compared.

Results: Cancer was diagnosed in 48 patients by 22-gauge needle aspiration and 19-gauge needle aspiration, and in 43 patients by bronchial biopsy. The sensitivity of bronchial biopsy was 0.86. The addition of 22-gauge and 19-gauge needle aspirations to bronchial biopsy increased the sensitivity to 0.90 and 0.88, respectively, but the difference was not statistically significant (P = 1.0). The maximal diagnostic yield was obtained with the combination of needle aspirations and forceps biopsy in the detection of submucosal or peribronchial bronchogenic carcinoma (100%) (P < 0.05).

Conclusion: The combination of forceps biopsy and transbronchial needle aspirations should be used for the highest rate of bronchoscopic diagnostic yield. However, there was no difference for increasing diagnostic yield in patients with visible endobronchial lesions between 22-gauge and 19- gauge needles.

Key words: Bronchoscopy, endobronchial lesions, forceps biopsy, transbronchial needle aspiration

Endobronşiyal lezyonların bronkoskopik incelemesinde 19-gauge histoloji ve 22-gauge sitoloji iğnelerinin tanı değerlerinin karşılaştırılması

Amaç: İleriye dönük olarak yaptığımız bu çalışmada, endobronşiyal malignitelerin tanısında bronşiyal biyopsi ile birlikte Wang 22-gauge ve 19-gauge iğne aspirasyonlarının duyarlılığı ve 22-gauge ve 19-gauge iğne aspirasyonları arasında farklılık olup olmadığını karşılaştırmayı amaçladık.

Yöntem ve gereç: Çalışmaya alınan tüm hastalara (63 hasta) fiberoptik bronkoskopiyle 22-gauge ve 19-gauge iğne aspirasyonları yapıldı. Biyopsi, hastalardan 50'ne uygulandı. Her bir tekniğin duyarlılığı karşılaştırıldı.

Bulgular: Biyopsiyle 43 hastaya, 19-gauge iğne aspirasyonu ve 22-gauge iğne aspirasyonu ile 48 hastaya kanser tanısı konuldu. Bronşiyal biyopsinin duyarlılığı % 86 idi. Biyopsinin, 22-gauge iğne aspirasyonu ile kombinasyonuyla bu duyarlılık % 90'a, 19-gauge iğne aspirasyonu ile kombinasyonuyla % 88'e çıktı. Fakat, istatiksel olarak anlamlı farklılık yoktu (P = 1,0). Submukozal-peribronşiyal bronkojenik karsinomların belirlenmesinde iğne aspirasyonları ve forseps biyopsinin kombinasyonuyla maksimal tanısal oran elde edildi (% 100) (P < 0,05).

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¹ Department of Chest Disease, Faculty of Medicine, Atatürk University, Erzurum - TURKEY

² Department of Pathology, Faculty of Medicine, Atatürk University, Erzurum - TURKEY

Correspondence: Elif YILMAZEL UÇAR, Department of Chest Disease, Faculty of Medicine, Atatürk University, Erzurum - TURKEY E-mail: eucar1979@yahoo.com

Sonuç: En yüksek bronkoskopik tanısal oran için forseps biyopsi ve transbronşiyal iğne aspirasyonları birlikte yapılmalıdır. Endobronşiyal lezyonlarda tanı oranını artırmak için 22-gauge ve 19-gauge iğne aspirasyonları arasında farklılık gözlenmemiştir.

Anahtar sözcükler: Bronkoskopi, endobronşiyal lezyonlar, forseps biyopsi, transbronşiyal iğne aspirasyonu

Introduction

Fiberoptic bronchoscopy (FOB) is a minimally invasive procedure commonly used in the diagnosis and staging of lung cancer (1). It provides highly valuable information to the physician in determining the treatment strategies for endobronchial lesions by facilitating direct observation of the lesions. FOB also allows biopsy procedures of directly observed endobronchial lesions and transbronchial fine needle aspiration (TBFNA) of tumors with indirect findings, facilitating cytopathological thus evaluations. Although all the benefits and uses of bronchoscopy have been well defined, there has been an increasing tendency to use advanced invasive methods that are relatively more time consuming, costly, and presenting higher mortality and morbidity rates compared to bronchoscopy (1).

However, а well-planned bronchoscopic evaluation has been reported to provide higher diagnostic rates in patients suspected for lung cancer and spare some patients from undergoing advanced invasive methods and redundant thoracotomy (2-6). In consensus reports on bronchoscopy to date, the regular use of biopsy, endobronchial brushing, and isotonic lavage concomitantly has been advocated (7,8), and, according to these reports, the diagnostic accuracy of these 3 procedures has ranged between 71% and 87% based on the results of various studies. As can be deduced from these results, only 15%-20% of patients require a second bronchoscopy procedure or further diagnostic techniques.

Needle aspirations via flexible bronchoscopy (FB) are also used a sampling method for a variety of bronchial, peribronchial, or pulmonary lesions (9). Its ability to establish diagnosis and staging in a single noninvasive intervention has made transbronchial needle aspiration (TBNA) the key technique for the evaluation of patients with suspected lung cancer (10,11). Wang 19-gauge and 22-gauge fine needles have been compared in biopsy procedures of mediastinal lymph nodes (12). However, to best

of our knowledge, no such comparisons have been made for endobronchial lesions so far in the English literature, and therefore data on this subject have remained limited.

We aimed to determine whether endoscopic fine needle aspiration (EFNA) would provide additional benefits to the conventional diagnostic interventions (forceps biopsy, brushing, or lavage) described above in suspected lung cancer patients scheduled for routine bronchoscopy, particularly in endobronchial lesions directly observed during initial bronchoscopy and areas associated with indirect tumoral findings (abnormalities in the mucosal folds such as mucosal thickening, indistinctness or disappearance, mucosal paleness, absence of mucosal surface luster, irregular mucosal surface, increased vascularity, concentric stenosis of the lumen, external compression, etc.). The study also aimed to compare the diagnostic and complication rates of Wang 19-gauge and 22-gauge needles used in this procedure.

Materials and methods

The study population consisted of patients who underwent routine bronchoscopy evaluation for suspected lung cancer for 2 years. The patient and his/ her relatives were informed of the present pathology and the interventions planned. The method of application, the requirement for the procedure, the results, and the potential risks were explained. We sought and obtained ethics approval from Atatürk University Local Ethics Committee.

Before bronchoscopy, chest X-ray and computerized tomography results of the thorax of the patients were available. All the blood values and coagulation tests were monitored. In the bronchoscopic evaluation, endobronchial lesions were categorized as exophytic mass lesions (EML) and submucosal/peribronchial lesions (SPL) according to the characteristics of the lesions. Submucosal disease was described as bronchial narrowing, mucosal thickening, disappearance of mucosal signs, erythema, increase of placation, and marked vascular structure. Peribronchial disease was defined as a secondary narrowing of the lumen against external compression (13).

All the patients underwent fine needle aspiration with both Wang 22-gauge cytology and 19-gauge histology needles followed by routine procedures (brushing, forceps biopsy, lavage, etc.) depending on the characteristics of the endobronchial lesion.

To keep the risk of contamination to a minimum, fine needle aspirations were primarily performed. Before the needle aspiration, the secretions from the area where the procedure would be performed were cleaned. The aspirations were done first using a 22-gauge cytology needle and then by using a 19-gauge histology needle. Depending on the characteristics of the lesion, one or more of the penetration methods (Jabbing, Piggy-back, Hub-Against-the-Wall, or Cough) (14) was used. In the submucosal lesions, the penetration was realized at a 45° angle, while in the other lesions direct insertion was made. After making sure that the needle was properly inserted, it was minimally advanced and aspiration was carried out. For aspiration, a 50-mL injector was used. After completion of the aspiration, the needles were withdrawn into their sheaths and removed from the biopsy channel. The material obtained was fixed on slides using fixation solution [Ethanol R:11-S;7-16 (BIO-FIX®)] and sent for pathological evaluation. All the findings were evaluated by an experienced pathologist. The pathology results were classified as positive or negative for malignancy.

Statistical analysis

Statistical analyses were performed using SPSS 11.0. Comparisons of the results obtained with the 2 different needles and their comparisons with the biopsy results were done with McNemar's test. The compatibility of the needles with each other and with the biopsy results was evaluated using the Kappa method. P < 0.05 was considered statistically significant.

Results

The study included 63 patients. The mean age of the patients was 60 \pm 12 years (range: 22-81

years), and 55 (87%) were male and 8 (13%) were female. Of the patients, 60 were diagnosed with malignancy by bronchoscopic methods and 3 by Tru-Cut biopsy. Table 1 summarizes the radiological and bronchoscopic characteristics of the lesions. The lesions were mostly located in the right lung (57%); 62% were exophytic masses and 38% were submucosal/peribronchial in nature.

Table 1. Radiographic and bronchoscopic characteristics of the lesions.

| Characteristics | n (%) |
|---|---------|
| Radiographic location of the lesions | |
| Right | 36 (57) |
| Left | 27 (43) |
| Bronchoscopic location of the lesions | |
| Upper right lobe | 8 (12) |
| Right IMB | 13 (21) |
| Middle right lobe | 4 (6) |
| Lower right lobe | 3 (5) |
| Upper left lobe | 8 (13) |
| Lingula | 2 (3) |
| Lower left lobe | 7 (11) |
| Left main bronchus | 10 (16) |
| Right main bronchus | 6 (10) |
| Main carina | 2 (3) |
| Presence and characteristics of endobronchial l | esions |
| Exophytic mass lesions | 39 (62) |
| Submucosal/peribronchial lesions | 24 (38) |

Fine needle aspiration was performed in all patients. Out of them, 50 patients underwent biopsy, 16 patients brushing cytology, and 58 patients lavage, and post-bronchoscopic sputum was obtained from 47 patients. Cancer was diagnosed in 48 patients by 22-gauge needle aspirations and 19-gauge needle aspiration and 43 patients by biopsy. The sensitivity of bronchial biopsy was 0.86. The addition of 22-gauge and 19-gauge needle aspirations to bronchial biopsy increased the sensitivity to 0.90 and 0.88, respectively, but the difference was not statistically significant (P = 1.0). Table 2 shows the procedures applied and their results. Of the 60 patients who were diagnosed with lung cancer through bronchoscopy, 25 (42%) had small cell lung cancer and 35 (58%) non-small cell lung cancer histopathologically. In 2 patients,

| Procedures | Positive n (%) | Negative n (%) | Total |
|---------------------------|----------------|----------------|-------|
| Biopsy | 43 (86) | 7 (14) | 50 |
| 19-gauge histology needle | 48 (76) | 15 (24) | 63 |
| 22-gauge cytology needle | 48 (76) | 15 (24) | 63 |
| Brushing | 9 (56) | 7 (44) | 16 |
| Bronchoscopic lavage | 33 (57) | 25 (43) | 58 |
| Post-bronchoscopic sputum | 21 (45) | 26 (55) | 47 |

Table 2. The procedures applied and their results.

the small-cell lung cancer diagnosis was established based on 22-gauge needle aspiration findings due to crush artifact in the biopsy.

Table 3 presents the results of biopsy and fine needle aspirations depending on the characteristics of the lesions. In Table 4 the results of the patients in whom biopsy and needle aspiration were performed are summarized, and in Table 5 the results of 19-gauge histology and 22-gauge cytology needles. Table 6 presents the studies on the diagnostic value of transbronchial fine needle aspiration in endobronchial lesions. In our study the sensitivity of a bronchial biopsy was 0.86 and the sensitivity of transbronchial needle aspirations was 0.88. The addition of 22-gauge and 19-gauge needle aspirations to bronchial biopsy increased the sensitivity to 0.90.

The numbers of positive and negative cases with both needles were equal (15 negative, 48 positive). No statistically significant differences were found between the 2 needles for positive and negative cases (P = 1.0). The compatibility rate of the results with both needles was 74%.

Table 3. The results of biopsy and FNA* according to the characteristics of the endobronchial lesions.

| | Exopl | Exophytic Mass | | Submucosal/Peribronchial | |
|--------------|----------|----------------|----------|--------------------------|--|
| | Positive | Negative | Positive | Negative | |
| Biopsy | 29 | 7 | 14 | _ | |
| 19-Gauge FNA | 27 | 12 | 21 | 3 | |
| 22-Gauge FNA | 26 | 13 | 22 | 2 | |

*FNA: Fine needle aspiration

Table 4. The results of the patients who underwent biopsy and FNA.*

| | Positive biopsy | | Negative biopsy | |
|-------------------|-----------------|-----------------|-----------------|-----------------|
| | Needle positive | Needle negative | Needle positive | Needle negative |
| 19-Gauge FNA | 36 | - | - | - |
| 22-Gauge FNA | 33 | - | 1 | - |
| 19-Gauge+22-Gauge | 31 | 5 | 1 | 5 |

*FNA: Fine needle aspiration

| | _ | 22-gauge cytology FNA | | Total |
|------------------------|-------|-----------------------|----|-------|
| | | + | - | Total |
| 19-gauge histology FNA | + | 43 | 5 | 48 |
| | _ | 5 | 10 | 15 |
| | Total | 48 | 15 | 63 |

Table 5. Comparisons of the FNA* results.

*FNA: Fine needle aspiration

| Studies | Biopsy positivity (%) | TBFNA positivity (%) | Biopsy plus TBFNA positivity (%) |
|-------------------------------|-----------------------|----------------------|----------------------------------|
| Lundgren et al. ¹⁵ | 69 | 46 | _ |
| Shure et al. ²² | 55 | 71 | 89 |
| Thida et al. ¹⁶ | 62 | 47 | _ |
| Govert et al. ¹⁷ | 82 | 82.4 | 95 |
| Dasgupta et al. ¹⁴ | 72 | 78 | 96 |
| Kacar et al. ¹⁸ | 72 | 76 | 96 |
| Our study | 86 | 88 | 90 |

Table 6. Studies on the diagnostic value of TBFNA* in endobronchial lesions.

*TBFNA: Transbronchial fine needle aspiration

The results with 19-gauge histology needle and biopsy results were not statistically significantly different (P = 0.36), and the compatibility rate of 19-gauge fine needle aspiration (FNA) and biopsy was 52%. However, the compatibility between 22-gauge cytology needle and biopsy was 37%. The differences between the compatibility rates of 22-gauge cytology needle and 19-gauge histology needle with biopsy results were not statistically significant (P = 0.43)

In 13 patients who underwent FNA only and not biopsy, the results with both needles were positive in 11 patients. In the remaining 2 patients, the results were positive with 22-gauge FNA only. No serious complications developed in any of the patients during the FNA procedure.

Discussion

Our study shows that FNA, either with 19-gauge histology or 22-gauge cytology needle, was a useful

adjunct method in the diagnosis of lung cancer. Although 19-gauge histology provides better compatibility with bronchoscopic biopsy, there was no significant difference between the 2 needles. It is also possible to say that the use of FNA in addition to bronchoscopic biopsy increases the yield of bronchoscopy in the diagnosis of lung cancer.

The literature provides no data on the diagnostic rates of these needles for endobronchial lesions. Schenk et al. have compared the 2 needles in the staging of lung cancer by sampling the mediastinal lymph node (12). In their study, significant results were obtained with 19-gauge FNA. It is reasonable to expect better results with 19-gauge histology needle because of its wide diameter and ability to obtain more material; however, we could not find a significant difference statistically. The 19-gauge needle may be more valuable in sampling from the lymph node but may not be so important in sampling from endobronchial lesions. Fine needle aspiration significantly increases the rate of diagnosis in endobronchial lesions (15-19). Although endobronchial ultrasound (EBUS) (20), computed tomography (CT) guidance (21), and rapid on-site evaluation (ROSE) improve FNA yield (22), these methods require considerable resources and are not universally available. The rate of diagnosis with FNA ranges between 65% and 92% (15-19). In our study, diagnostic rate has been determined as 88%. FNA may be an alternative method in the diagnosis of endobronchial lesions, particularly in cases with a tendency for hemorrhage, and in those with necrosis or in those difficult to diagnose with forceps biopsy due to crush artifact in the biopsy (23,24).

Crush artifact may occur in all pulmonary cancers. Nevertheless, it is encountered more frequently in small cell lung cancer (25). In our study, forceps biopsies of 2 small cell cancer cases were negative, while FNA results of the same cases were positive.

In endobronchial lesions, particularly submucosalperibronchial ones, the combination of TBFNA and forceps biopsy significantly increases the diagnosis rate (15,19). Inability to reach the lesion by forceps biopsy and ability of the fine needle to penetrate the tissue facilitating sampling may be important factors in using the combined approach. Dasgupta et al. attained a significant increase in the diagnosis rate (from 72% to 96%) through combined application of TBFNA with other diagnostic methods (15). In our study, 51.3% of the lesions were submucosalperibronchial. With the addition of FNA to the biopsy procedure, the rate of diagnosis increased to 90%.

The number of FNA procedures may increase the sensitivity and diagnosis rate in endobronchial lesions

References

- Joos L, Patuto N, Chhajed PN, Tamm M. Diagnostic yield of flexible bronchoscopy in current clinical practice. Swiss Med Wkly 2006; 136: 155-159.
- Versteegh RM, Swierenga J. Bronchoscopic evaluation of the operability of pulmonary carcinoma. Acta Otolaryngol 1963; 56: 603-611.
- Robbins HM, Morrison DA, Sweet ME, Solomon DA, Goldman AL. Biopsy of the main carina; staging lung cancer with the fiberoptic bronchoscope. Chest 1979; 75: 484-486.

(18,26). Govert et al. performed FNA using a 22-gauge cytology needle 4 times and achieved a diagnosis rate of 95%. A larger number of FNA procedures did not increase the risk of complications. In our study, aspiration was performed with 2 different needles, once with each of them. The diagnosis rate was 90%, and no serious complications were observed. This has shown that fine needle aspiration is a safe method and that increased number of aspirations may increase sensitivity.

Biopsy is the method of choice because of the high diagnostic value of the material obtained during the diagnostic procedure of lung cancers. When multiple biopsy samples are obtained, the rate of diagnosis can be as high as 90% (27,28). However, in cases with a tendency for hemorrhage and those difficult to obtain multiple samples from, the diagnostic rates of lesions covered with necrosis and undiagnosed lesions because of crush artifact in the biopsy sample increases with combined use of TBFNA. Moreover, in submucosal-peribronchial lesions, TBFNA increases the diagnosis rate significantly compared to forceps biopsy (15,19).

In conclusion, transbronchial fine needle biopsy is a safe method and it increases the diagnosis rate, particularly in submucosal-peribronchial lesions. In cases where sufficient material cannot be obtained by forceps biopsy (necrosis, crush artifact), TBFNA increases the diagnosis rate while decreasing the need for repeated bronchoscopy. TBFNA and biopsy combination is the optimal approach in increasing the diagnosis rate and preventing repeated bronchoscopy procedures. However, there was no difference for increasing diagnostic yield in patients with visible endobronchial lesions between 22-gauge and 19-gauge needles.

- 4. Shure D, Fedullo PF, Plummer M. Carinal forceps biopsy via the fiberoptic bronchoscope in the routine staging of lung cancer. West J Med 1985; 142: 511-513.
- Rabin CB, Selikoff IJ, Kramer R. Paracarinal biopsy in evaluation of operability of carcinoma of the lung. Arch Surg 1952; 65: 822-830.
- Gunen H, Kizkin O, Tahaoglu C, Aktas O. Utility of blind forceps biopsy of the main carina and upper-lobe carina in patients with non-small cell lung cancer. Chest 2001; 119: 632-637

- British Thoracic Society Bronchoscopy Guidelines Committee, a Subcommittee of Standards of Care Committee of British Thoracic Society. British Thoracic Society guidelines on diagnostic flexible bronchoscopy. Thorax 2001; 56 Suppl 1: i1-21.
- Rivera MP, Detterbeck F, Mehta AC; American College of Chest Physicians. Diagnosis of lung cancer: the guidelines. Chest 2003; 123(1 Suppl): 129-136.
- Mazzano P, Jain P, Arroliga AC, Matthay RA. Bronchoscopy and needle biopsy techniques for diagnosis and staging of lung cancer. Clin Chest Med 2002; 23: 137-158.
- Gasparini S, Silvestri GA. Usefulness of transbronchial needle aspiration in evaluating patients with lung cancer. Thorax 2005; 60: 890-891.
- Minai OA, Dasgupta A, Mehta AC. Transbronchial needle aspiration of central and peripheral lesions. In: Bolliger CT, Mathur PN, eds. Interventional Bronchoscopy. Basel, Karger, 2000; pp. 66-79.
- Schenk DA, Chambers SL, Derdak S, Komadina KH, Pickard JS, Strollo PJ et al. Comparison of the Wang 19-gauge and 22-gauge needles in the mediastinal staging of lung cancer. Am Rev Respir Dis 1993; 147: 1251-1258.
- Shure D, Fedullo PF. Transbronchial needle aspiration in the diagnosis of submucosal and peribronchial bronchogenic carcinoma. Chest 1985; 88: 49-51.
- 14. Dasgupta A, Mehta AC. Transbronchial needle aspiration. Clin Chest Med 1999; 20: 139-151.
- Dasgupta A, Jain P, Minai OA, Sandur S, Meli Y, Arroliga AC et al. Utility of transbronchial needle aspiration in the diagnosis of endobronchial lesions. Chest 1999; 115: 1237-1241.
- Lundgren R. A flexible thin needle for transbronchial aspiration biopsy through the flexible fiberoptic bronchoscope. Endoscopy 1980; 12: 180-182.
- 17. Win T, Stewart S, Groves AM, Pepke-Zaba J, Laroche CM. The role of transbronchial needle aspiration in the diagnosis of bronhogenic carcinoma. Respiratory Care 2003; 48: 602-605.

- Govert JA, Dodd LG, Kussin PS, Samuelson WM. A prospective comparison of fiberoptic transbronchial needle aspiration and bronchial biopsy for bronchoscopically visible lung carcinoma. Cancer 1999; 87: 129-134.
- 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: 221-226.
- 20. Tournoy KG, Rintoul RC, van Meerbeeck JP, Carroll NR, Praet M, Buttery RC et al. EBUS-TBNA for the diagnosis of central parenchymal lung lesions not visible at routine bronchoscopy. Lung Cancer 2009; 63: 45-49.
- 21. Geraghty PR, Kee ST, McFarlane G, Razavi MK, Sze DY, Dake MD. CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: needle size and pneumothorax rate. Radiology 2003; 229: 475-481.
- Diacon AH, Schuurmans MM, Theron J, Louw M, Wright CA, Brundyn K et al. Utility of rapid on-site evaluation of transbronchial needle aspirates. Respiration 2005; 72: 182-188.
- 23. Shure D. Transbronchial biopsy and needle aspiration. Chest 1989; 95: 1130-1138
- 24. Jones DF, Chin R, Capellari JO, Haponik EF. Endobronchial needle aspiration in the diagnosis of small cell carcinoma. Chest 1994; 105: 1151-1154.
- Davenport RD. Diagnostic value of crush artifact in cytologic specimens: occurrence in small cell carcinoma of the lung. Acta Cytol 1990; 34: 502-504.
- Diacon AH, Schuurmans MM, Theron J, Brundyn K, Louw M, Wright CA et al. Transbronchial needle aspirates: how many passes per target site. Eur Respir J 2007; 29: 112-116.
- 27. Gellert Ar, Rudd RM, Sinha G, Geddes DM. Fiberoptic bronchoscopy: effect of multiple biopsies on diagnostic yield in bronchial carcinoma. Thorax 1982; 37: 684-687.
- Popovich J, Kvale PA, Eichenhorn MS, Radke JR, Ohorodnik JM, Fine G. Diagnostic accuracy of multiple biopsies from flexible fiberoptic bronchoscopy: a comparison of centralversus peripheral carcinoma. Am Rev Respir Dis 1982; 125: 521-523.