

CT -guided transthoracic biopsy of solitary pulmonary Nodules using automatic biopsy gun.

Mohammed abd kadhim¹ MBChB; FIBMS, Alaa Kassar Salih¹ MBChB; FIBMS, Zaid Khidher ahmed¹ MBChB; FIBMS, Qasim Fawzi Hasan².

Abstract

Background: CT –guided percutaneous transthoracic fine needle aspiration biopsy (TFNAB) has become a widely accepted and effective minimally invasive technique for the diagnosis of a variety of intrathoracic lesions that are not readily accessible with bronchoscopy. It is generally regarded as a safe procedure with limited morbidity and extremely rare mortality. It provides high diagnostic accuracy and has a relatively low complications rate.

Objectives: The aims of our study were to report our experience with regard to the accuracy & pneumothorax rate of percutaneous CT-guided biopsy of solitary pulmonary nodules using automatic biopsy gun.

Patients and methods: Between January 2006 and August 2009, 54 patients (46 men and 8 women) with solitary pulmonary nodule underwent CT guided transthoracic biopsy at Al-Kadhimiya teaching hospital, Baghdad, Iraq. All the lesions could not be diagnosed with fiberoptic bronchoscopy. CT-guided biopsy was performed with an 18-gauge automatic biopsy gun. Chest radiography was done 2-4hr later and 24hr after biopsy for observation of pneumothorax. The overall diagnostic accuracy, pneumothorax rate, and chest tube insertion rate were determined. Diagnostic accuracy and pneumothorax rate were statistically compared according to lesion size & lesion depth (p value of less than 0.05 was considered to be significant).

Results: Forty one patients (76%) diagnosed as malignant (diagnostic accuracy of 87.8%).

Thirteen patients (24%) were diagnosed as benign (diagnostic accuracy of 92.3%). The overall diagnostic accuracy was 89% (48 of 54). The diagnostic accuracy did not differ with respect to the lesions size and lesions depth from the chest wall. Accurate diagnosis was made in 25 of the 29 nodules <20 mm (86%) and in 23 of the 25 nodules ≥20 mm (92%). Similarly accurate diagnosis was made for 36 (90%) of the 40 nodules shallower than 60 mm and for 12 (85.7%) of the 14 nodules ≥60 mm. Pneumothorax occurred in 23 (42%) patients. Pneumothorax occurred more frequently in small sized lesions (16 out of 29 lesions measuring <20 mm) as compared to (7 out of 25 lesions ≥20 mm) (P <0.05). Similarly pneumothorax occurred more frequently in deeper lesions (10 out of 14 lesions ≥60mm in depth) as compared to (13 out of 40 lesions <60 mm in depth) (P <0.05). Only 7 (13%) patients requiring thoracostomy tube placement.

Conclusions: CT- guided biopsy using automatic biopsy gun allowing a specific diagnosis for benign & probably malignant lesions. Diagnostic accuracy was not affected by the size and depth of the lesions. Deeper & small sized lesions have associated with an increased rate of pneumothorax.

Keywords: solitary pulmonary nodule, CT – guided biopsy, automatic biopsy gun.

IRAQI J MED SCI, 2010; VOL.8 (3):34-41

Introduction

CT –guided percutaneous transthoracic fine needle aspiration biopsy (TFNAB) has become a widely

accepted and effective minimally invasive technique for the diagnosis of a variety of intrathoracic lesions that are not readily accessible with bronchoscopy⁽¹⁻³⁾. It is an easy, reliable and safe procedure that obviates the need for exploratory surgery in medically treatable or unresectable cases⁽⁴⁾. It is a relatively accurate method of diagnosing benign and malignant lesions of the chest^(3, 5-7).

¹Dept. Surgery, College of Medicine, Al-Nahrain University, Al-Kadhimiya teaching hospital,² Radiographer - CT operator/ Al-Kadhimiya teaching hospital.

Address Correspondence to: Dr. Mohammed abd kadhim

E- mail: Dr_a_mohammed@yahoo.com

Received: 14th October 2009, Accepted: 2nd May 2010

Haaga and Alfidi ⁽⁸⁾ reported the first computed tomography (CT)-guided biopsy in 1976, and numerous reports since that time have shown TFNAB procedures to be both effective and accurate ^(3, 5-7, 9-11).

CT-guided TFNAB is generally regarded as a safe procedure with limited morbidity and extremely rare mortality ^(5, 6, 9, 10, 12). It provides high diagnostic accuracy and has a relatively low complications rate ⁽¹³⁻¹⁵⁾.

The management of solitary pulmonary nodule (SPN) depends on many factors including clinical features, results of relevant investigations, population characteristics, and local policy ^(16, 17). The most important first step is to determine the likelihood of the nodule being malignant and then to decide whether the lesion should be removed, observed, or further investigations performed ^(18,19). TFNAB is advocated to improve the precision of management by increasing the confidence with which masses can be categorized as benign or malignant ^(6, 20, 21), and so it has a strong impact on the diagnostic protocol of the solitary pulmonary nodule ⁽²²⁾. CT-guided lung biopsy has found wide-spread acceptance as a principal method of diagnosing SPN ^(5, 11, 23-25).

Most CT-guided lung biopsies described in earlier reports were performed with fine-needle aspiration for cytology and the materials obtained by means of aspiration are usually suitable only for cytological examination and were useful in differentiating malignant from benign lesions, but these have some limitation in certain clinical settings, it does not allow adequate subtyping of carcinoma, seldom yields a specific pathologic diagnosis in cases of benign disease and a negative result does not exclude malignancy ^(6, 26-29). More recently, tissue core biopsy using an

automated cutting needle, which enables the histological evaluation of the obtained samples has been implemented ⁽³⁰⁾, and this may improve the diagnostic yield and increase the chances of obtaining a specific diagnosis ^(31, 32). The automatic biopsy gun has become popular for biopsy of various organs ⁽³³⁾. The advantages of obtaining a core specimen include greater accuracy in allowing a specific diagnosis for benign lesions, the ability to diagnose carcinomas without a trained cytopathologist and greater accuracy in defining cell types of carcinomas ⁽³³⁻³⁵⁾.

To our knowledge this study is the first one done in Iraq to study role of CT-guided biopsy of solitary pulmonary nodule using automatic biopsy gun.

Patients and methods

Between January 2006 and August 2009, a prospective study included 54 patients with solitary pulmonary nodule underwent CT guided biopsy at Al-Kadhimiya teaching hospital, Baghdad, Iraq. The study population included 46 men and 8 women with a mean age of 56 years (range, 34–66 years). All the lesions could not be reached & diagnosed with fiberoptic bronchoscopy. The average lesion size was 2.1 mm (range, 0.5–40mm) and the average depth of lesions from the skin surface was 51 mm (range, 18–82mm).

Examinations were done with the CT unit (Somatom plus4; siemens medical system). Preliminary scans were done without use of contrast medium in either prone or supine position to plan the biopsy approach. Biopsies were performed in the prone, supine or lateral decubitus positions, depending on proximity of the lesion to the chest wall. After the lesion had been localized, depth of the lesion from the skin surface was measured. The chosen entry site was prepared and

draped in a sterile fashion, under the local anesthesia biopsy needle was inserted and biopsy was performed with automatic biopsy gun (Temno, Italy, 18-gauge, 15cm length). The obtained specimen was treated by H & E stain.

All patients were hospitalized. They rested in bed and underwent chest radiography 2-4hr later and 24hr after biopsy. If pneumothorax was not present, the patient was discharged the morning after biopsy. Thoracostomy tubes were inserted if the pneumothorax was moderate to large (>30%) on the basis of the distance from the lung apex to the cupola or on the basis of continued size increase on follow-up radiographs. Thoracostomy tubes were also inserted if the patients experienced substantial pain or shortness of breath in the presence of a small pneumothorax

True positive diagnosis: in cases with surgical confirmation, when biopsy of another site revealed cancer with the same histologic characteristics, or when the lesion increased in size and other proven metastases were found.

True-negative diagnosis: in cases with surgical confirmation, when the lesion disappeared or decreased in size with or without the use of antibiotics, or when the lesion remained stable on follow-up CT for 18-24 months. Follow-up CT was scheduled 3, 6, 12, 18, and 24 months post- biopsy.

False-positive diagnosis: if surgical resection yielded a benign diagnosis, if the lesion disappeared or decreased in size before surgical resection, or if the lesion remained stable on the follow-up CT for at least 18-24 months in patients refusing surgical resection.

False-negative diagnosis: if surgical resection yielded a malignant diagnosis; if the lesion increased in size; if other proven metastases were

diagnosed on CT or MR imaging and proven by histologic examination of the biopsy specimen or resection.

Final diagnosis of the 54 patients was proved by: formal surgery (36patients), presence malignant liver lesions proved by FNA (3 patients), follow up CT for 20-24months (15 patients)

Statistical analysis

Using the program SPSS (version 15 for Microsoft Windows). The overall diagnostic accuracy, pneumothorax rate, and chest tube insertion rate were determined. The diagnostic accuracy was calculated using the following formula: diagnostic accuracy (%) = (no. true-positive + no. true-negative) / total number of solitary pulmonary nodules. Diagnostic accuracy and pneumothorax rate were statistically compared according to lesion size & lesion depth. A P value of less than 0.05 was considered to be significant.

Results

The study population included 54 patients (46 men and 8 women) with a mean age of 56 years (range, 34–66 years). 29 patients have nodules <20 mm in diameter & 25 patients have nodules \geq 20 mm (20mm is the cutoff value between small & large nodules). Forty patients have lesion <60mm from the chest wall, while 14 patients have lesions \geq 60mm in depth from the chest wall (lesion depth was measured from the pleural puncture site to the edge of the intrapulmonary lesion along the needle path), (60mm is the cutoff value between superficial & deep nodules)

Of 54 pulmonary nodules 41 (76%) diagnosed as malignant (36 true-positive & 5 false negative) with diagnostic accuracy of 87.8% (36 of 41). Thirteen patients (24%) were diagnosed as benign (12 true-negative & 1 false positive) with diagnostic accuracy of 92.3% (12 of 13).

The overall diagnostic accuracy of the procedure was 89% (48 of 54). Table 1 shows the final pathological diagnoses and results of CT -guided biopsy. The diagnostic accuracy did not differ with respect to the lesions size and lesions depth from the chest wall. An accurate diagnosis was made for 25 (86%) of the 29 pulmonary nodules <20 mm and for 23 (92%) of the 25 pulmonary nodules ≥20 mm, a statistically insignificant difference (p = 0.54) as shown in table 2. An accurate diagnosis was made for 36 (90%) of the 40 nodules shallower than 60 mm and for 12 (85.7%) of the 14 nodules deeper than or equal to 60 mm, a statistically insignificant difference(p = 0.52)as shown in table 2.

Pneumothorax occurred in 23 (42%) patients. Pneumothorax occurred more frequently in small sized lesions (16 out of 29 lesions measuring <20 mm) as compared to (7 out of 25 lesions ≥20 mm) (P <0.05). similarly pneumothorax occurred more frequently in deeper lesions (10 out of 14 lesions ≥ 60mm in depth) as compared to shallower lesions (13 out of 40 lesions <60 mm in depth) (P <0.05) as shown in table 3. Only 7 (13%) patients requiring thoracostomy tube placement. Figure 1 shows images of CT –guided biopsy in 2 patients one with malignant lesion & the other with benign lesion.

Table 1: The final pathological diagnoses (no. of patients) and results of CT -guided biopsy (no. of patients & %) of the 54 patients included in the study.

Final pathological Diagnosis	Total No. of patients	Accurate diagnosis by CT-guided biopsy	
		No. of patients	%
Malignant lesions			
Primary carcinoma of bronchus	37	33	89
Secondary metastases	4	3	75
Benign lesions			
Granuloma	4	3	75
Fibrosis	2	2	100
Organizing pneumonia	2	2	100
Hamartoma	5	5	100
Total	54	48	89

Table 2: The diagnostic accuracy of the 48 patients included in the study according to lesion size & lesion depth from the chest wall.

		Accuracy		Total No. of patients	P value
		No.	%		
Lesion size (mm)	nodules <20 mm in size	25	86	48	P =0.54
	nodules ≥20 mm in size	23	92		
Lesion depth (mm)	nodules<60 mm in depth	36	90	48	P =0.52
	nodules ≥60 mm in depth	12	85.7		

Table 3: Cases complicated by pneumothorax compared to lesion size & lesion depth from the chest wall.

		Pneumothorx rate		Total No. of patients	P value
		No.	%		
Lesion size (mm)	nodules <20 mm in size	16	55	23	P < 0.05
	nodules ≥20 mm in size	7	28		
Lesion depth (mm)	nodules <60 mm in depth	13	32.5	23	P < 0.05
	nodules ≥60 mm in depth	10	71.4		

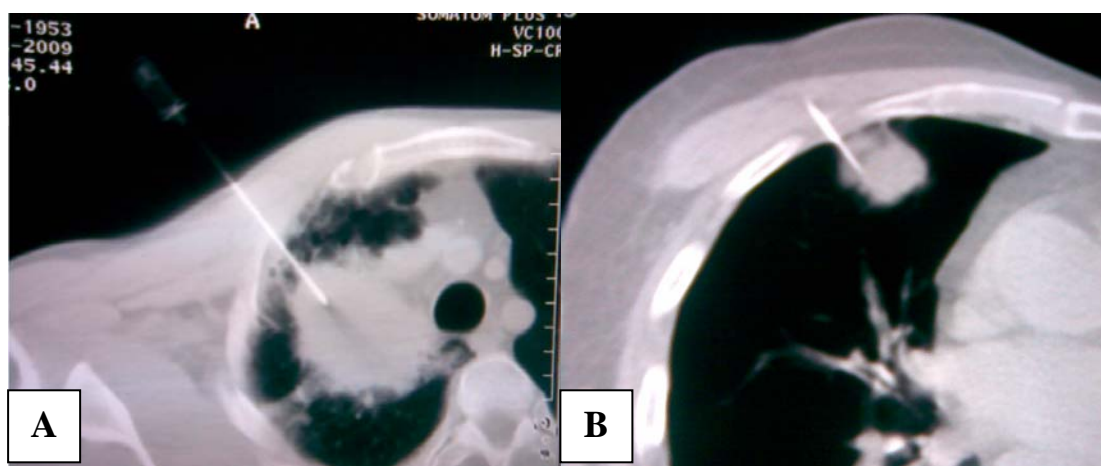


Figure 1: A: 46 year old male with Rt. upper lobe mass, FNAB reveal bronchogenic carcinoma which is proved by sub-sequent surgery & histopathology. B: 35 year old male patient with Rt. Lower lobe mass, FNAB reveal granuloma which was proved by follow up CT for the next 20 months.

Discussion

CT-guided lung biopsy has found wide-spread acceptance as a principal method of diagnosing SPN (5, 11, 23-25). Tissue core biopsy using an automated cutting needle, which enables the histological evaluation of the obtained samples has been implemented (30), and this may improve the diagnostic yield and increase the chances of obtaining a specific diagnosis (31, 32). The advantages of obtaining a core specimen include greater accuracy in allowing a specific diagnosis for benign lesions, the ability to diagnose carcinomas without a trained cytopathologist and greater accuracy in defining cell types of carcinomas (33-35).

In our study diagnostic accuracy for malignant lesions was 87.8% (36 out of 41) and for benign lesions

92.3% (12 of 13), these results were comparable with that reported in the previous studies where the diagnostic accuracy has been reported as greater than 80% for benign disease and greater than 90% for malignant disease (6, 9, 10).

The overall diagnostic accuracy in the current study was 89% (48 of 54) which was comparable with that described in the previously reported studies where the diagnostic accuracy has been described to be high, 81-96% (5, 11, 22, 24, 25, 36-38).

In our study, although the diagnostic accuracy for small pulmonary nodules <20 mm was less (86%) when compared with diagnostic accuracy for larger pulmonary nodules ≥20 mm (92%), this difference is

statistically insignificant ($p = 0.54$), & these results were comparable with that of Lucidarme et al. ⁽²⁵⁾, Westcott et al. ⁽³⁹⁾, and Laurent F. et al. ⁽⁴⁰⁾ where they have shown that the diagnostic accuracy for small nodules is comparable to that for large nodules, but Li et al. ⁽⁶⁾ and Tsukada et al. ⁽³⁰⁾ have reported that diagnostic accuracy for small pulmonary nodules is significantly less than that for large nodules.

Similarly we observed a statistically insignificant difference in diagnostic accuracy between superficial nodules (90%) and deeper nodules (85.7%) ($p = 0.52$) & these results were comparable with that reported in the previous studies ^(38, 40).

The most common complication of CT-guided lung biopsy is pneumothorax ⁽¹¹⁾. A higher frequency of pneumothorax is a known disadvantage of CT-guided biopsy when compared to U/S guided biopsy and may be related to the fact that the needle stays across the pleura for a longer time. In addition, all lesions accessible to US-guided biopsy were peripheral and did not require the traversal of aerated lung, whereas it is likely that most difficult, small, deep lesions are sampled at CT-guided biopsy, which also may account for the higher complication rate ⁽⁴¹⁾. Prior studies found pneumothorax rates between 9% and 54% ^(22, 25, 30, 32, 37, 40, 42), in our studies pneumothorax occurred in 42% of the patients. The relatively high rate of pneumothorax in our study may be related to the use of an 18-gauge automatic biopsy gun. Despite the relatively high rate of pneumothorax, we believe that the high yield for benign disease avoids further invasive diagnostic procedures and justifies the risk.

The depth and size of the lesion might have an impact on pneumothorax rate ^(43- 45). Previous

studies have found a strong correlation between lesion size and pneumothorax rate ^(5-7, 43). In our study pneumothorax occurred more frequently in small sized lesions (16 out of 29 lesions measuring <20 mm) as compared to (7 out of 25 lesions ≥ 20 mm) ($P < 0.05$). Cox et al. ⁽⁴³⁾ reported that smaller lesion size correlated with the development of increased pneumothorax rate. They hypothesized that when the lesion is relatively small, the up-and-down movement of the needle tip results in more tearing of adjacent lung parenchyma.

Many authors have reported that greater lesion depth caused the pneumothorax rate to increase ^(5, 7, 42, 45). In our study pneumothorax occurred more frequently in deeper lesions (10 out of 14 lesions ≥ 60 mm in depth) as compared to (13 out of 40 lesions <60 mm in depth) ($P < 0.05$). It would be reasonable to hypothesize that a longer needle path may have a greater chance to tear the pleura and normal lung tissue as patients breathe during the procedure ⁽²⁾. On the other hand, Yeow et al. ⁽⁴⁴⁾ showed that subpleural lesions that were 2 cm from the pleural surface correlated with a higher pneumothorax rate than those farther from the pleura because shallow anchoring made dislodgement of the needle to the pleural cavity easy, causing air ingress. In the present study only 7 patients (13%) requiring thoracostomy tube placement & these results are roughly comparable with that shown by Golfieri R. et al. ⁽²²⁾ which required thoracic drainage in 10% of cases.

In conclusions CT _guided biopsy using automatic biopsy gun allowing a specific diagnosis for benign & probably malignant lesions. Diagnostic accuracy was not affected by the size and depth of the lesions. Deeper & small sized lesions have associated

with an increased rate of pneumothorax.

References

1. Takuji Yamagami, Shigeharu Iida, Takeharu Kato, Osamu Tanaka and Tsunehiko Nishimura. Combining Fine-Needle Aspiration and Core Biopsy under CT Fluoroscopy Guidance: A Better Way to Treat Patients with Lung Nodules? *AJR* 2003; 180:811-815.
2. Ohno Y, Hatabu H, Takenaka D, et al. CT-guided transthoracic needle aspiration biopsy of small (20 mm) solitary pulmonary nodules. *AJR* 2003; 180:1665 -1669.
3. Moore EH. Technical aspects of needle aspiration lung biopsy: a personal perspective. *Radiology* 1998; 208:303-318.
4. Priola AM, Priola SM, Cataldi A, Ferrero B, Garofalo G, Errico L, Marci V, Fava C. CT-guided percutaneous transthoracic biopsy in the diagnosis of mediastinal masses: evaluation of 73 procedures. *Radiol Med.* 2008 Feb; 113(1):3-15.
5. Kazerooni EA, Lim FT, Mikhail A, Martinez FJ. Risk of pneumothorax in CT-guided transthoracic needle aspiration biopsy of the lung. *Radiology* 1996; 198:371-375.
6. Li H, Boiselle PM, Shepard JO, Trotman-Dickenson B, McCloud TC. Diagnostic accuracy and safety of CT-guided percutaneous needle aspiration biopsy of the lung: comparison of small and large pulmonary nodules. *AJR* 1996; 167:105-109.
7. Laurent F, Michel P, Latrabe V, Tunon de Lara M, Marthan R. Pneumothoraces and chest tube placement after CT-guided transthoracic lung biopsy using a coaxial technique: incidence and risk factors. *AJR* 1999; 172:1049 -1053.
8. Haaga JR, Alfydi RJ. Precise biopsy localization by computed tomography. *Radiology* 1976; 118:603-607.
9. Larscheid RC, Thorpe PE, Scott WJ. Percutaneous transthoracic needle aspiration biopsy: a comprehensive review of its current role in the diagnosis and treatment of lung tumors. *Chest* 1998; 114:704-709.
10. Tsukada H, Satou T, Iwashima A, Souma T. Diagnostic accuracy of CT-guided automated needle biopsy of lung nodules. *AJR* 2000; 175:239-243.
11. Laurent F, Latrabe V, Vergier B, Michel P. Percutaneous CT-guided biopsy of the lung: comparison between aspiration and automated cutting needles using a coaxial technique. *Cardiovasc Intervent Radiol* 2000; 23:266 - 272.
12. Perlmutter LM, Johnston WW, Dunnick NR. Percutaneous transthoracic needle aspiration: a review. *AJR* 1989; 152:451-455.
13. Laspas F, Roussakis A, Efthimiadou R, Papaioannou D, Papadopoulos S, Andreou J. Percutaneous CT-guided fine-needle aspiration of pulmonary lesions: Results and complications in 409 patients. *J Med Imaging Radiat Oncol.* 2008 Oct; 52(5):458-62.
14. Wallace MJ, Krishnamurthy S, Broemeling LD, et al. CT-guided percutaneous fine-needle aspiration biopsy of small (1-cm) pulmonary lesions. *Radiology* 2002; 225:823-828.
15. Arslan S, Yilmaz A, Bayramgürler B, Uzman O, Nver E, Akkaya E. CT- guided transthoracic fine needle aspiration of pulmonary lesions: accuracy and complications in 294 patients. *Med Sci Monit.* 2002 Jul; 8(7):CR493-7
16. Lillington GA. Management of the solitary pulmonary nodule. *Hosp Pract (Office Edn)* 1993; 28:41-8.
17. Midthun DE, Swensen SJ, Jett JR. Approach to the solitary pulmonary nodule. *Mayo Clin Proc* 1993; 68:378-85.
18. Minami H, Yoshimura M, Matsuoka H, et al. Lung cancer treated surgically in patients <50 years of age. *Chest* 2001; 120:32-6.
19. Naruke T, Tsuchiya R, Kondo H, et al. Prognosis and survival after resection for bronchogenic carcinoma based on the 1997 TNM-staging classification: the Japanese experience. *Ann Thorac Surg* 2001; 71:1759-4.
20. Henschke CI, Yankelevitz D, Westcott J, et al. Work-up of the solitary pulmonary nodule. American College of Radiology. ACR appropriateness criteria. *Radiology* 2000; 215:607-9.
21. Van Moore A Jr, Levy JM, Duszak RL Jr, et al. Needle biopsy in the thorax. American College of Radiology. ACR appropriateness criteria. *Radiology* 2000; 215:1029-40
22. Golfieri R, Sbrozzi F, de Santis F, Giampalma E, Cavina M, d'Arienzo P, Gavelli G. Clinical role of CT-guided transthoracic needle biopsy in diagnosis of solitary pulmonary nodules; *Radiol Med.* 1998 Apr; 95(4):329-37.
23. Viggiano RW, Swensen SJ, Rosenow EC 3rd. Evaluation and management of solitary and multiple pulmonary nodules. *Clin Chest Med* 1992; 13:83-95.
24. Hayashi N, Sakai T, Kitagawa M, et al. CT-guided biopsy of pulmonary nodules less than 3 cm: usefulness of the spring-operated core biopsy needle and frozen-section pathologic diagnosis. *AJR* 1998; 170:329 -331.
25. Lucidarme O, Howarth N, Finet JF, Grenier PA. Intrapulmonary lesions: percutaneous automated biopsy with a detachable, 18-gauge, coaxial cutting needle. *Radiology* 1998; 207:759 -765.

26. Austin JH, Cohen MB. Value of having a cytopathologist present during percutaneous fine-needle aspiration biopsy of lung: report of 55 cancer patients and metaanalysis of the literature. *AJR* 1993; 160:175 -177.
27. Wei-Yu Liao, Ming-Zen Chen, Yih-Leong Chang, Heuy-Dong Wu, Chong-Jen Yu, Ping-Hung Kuo, and Pan-Chyr Yang. US-guided Transthoracic Cutting Biopsy for Peripheral Thoracic Lesions Less than 3 cm in Diameter . *Radiology*. 2000; 217:685-691
28. Yu CJ, Yang PC, Chang DB, et al. Evaluation of ultrasonically guided biopsy of mediastinal masses. *Chest* 1991; 100:399-405.
29. Yang PC, Chang DB, Yu CJ, et al. Ultrasound-guided core biopsy of thoracic tumors. *Am Rev Respir Dis* 1992; 146:763-767.
30. Tsukada H, Satou T, Iwashima A, Souma T. Diagnostic accuracy of CT-guided automated needle biopsy of lung nodules. *AJR* 2000; 175:239 -243.
31. Sakai T, Hayashi N, Kimoto T, Maeda M, Ishii Y, Murashima S, et al. CT-guided biopsy of the chest: usefulness of fine-needle core biopsy combined with frozen-section pathological diagnosis. *Radiology* 1994; 190:243-6.
32. Klein JS, Salomon G, Stewart EA. Transthoracic needle biopsy with a coaxially placed 20-gauge automatic cutting needle: results in 122 patients. *Radiology* 1996; 198:715-720.
33. Moulton JS, Moore PT. Coaxial percutaneous biopsy technique with automated biopsy devices: value in improving accuracy and negative predictive value. *Radiology* 1993; 186:515-22.
34. Haramati LB. CT-guided automated needle biopsy of the chest. *AJR* 1995; 165:53-5.
35. Sakai T, Hayashi N, Kimoto T, Maeda M, Ishii Y, Murashima S, et al. CT-guided biopsy of the chest: usefulness of fine-needle core biopsy combined with frozen-section pathological diagnosis. *Radiology* 1994; 190:243-6.
36. Huang Z, Zhang X, Wang W; CT-guided percutaneous transthoracic aspiration biopsy of chest lesions: factors influencing the diagnostic accuracy; *Zhonghua Yi Xue Za Zhi*. 2002 Nov 25; 82(22):1525-8.
37. D'Alessandro V, Parracino T, Stranieri A, Greco A, De Cata A, Sperandeo M, Mazzoccoli G, Maiello E, Vendemiale G. Computed-tomographic-guided biopsy of thoracic nodules: a revision of 583 lesions. *Clin Ter*. 2007 Nov-Dec; 158(6):509-13.
38. Arslan S, Yilmaz A, Bayramgürler B, Uzman O, Nver E, Akkaya E. CT- guided transthoracic fine needle aspiration of pulmonary lesions: accuracy and complications in 294 patients. *Med Sci Monit*. 2002 Jul; 8(7):CR493-7.
39. Westcott JL, Rao N, Colley DP. Transthoracic needle biopsy of small pulmonary nodules. *Radiology* 1997; 202:97-103.
40. Laurent F, Latrabe V, Vergier B, Montaudon M, Vernejoux JM, Dubrez J. CT-guided transthoracic needle biopsy of pulmonary nodules smaller than 20 mm: results with an automated 20-gauge coaxial cutting needle. *Clin Radiol*. 2000 Apr; 55(4):281-7.
41. Sheila Sheth, Ulrike M. Hamper, Deroshia B. Stanley, Jane H. Wheeler, and Patricia A. Smith, US Guidance for Thoracic Biopsy: A Valuable Alternative to CT. *Radiology*. 1999; 210:721-726.
42. Khan MF, Straub R, Moghaddam SR, Maataoui A, Gurung J, Wagner TO, Ackermann H, Thalhammer A, Vogl TJ, Jacobi V. Variables affecting the risk of pneumothorax and intrapulmonal hemorrhage in CT-guided transthoracic biopsy. *Eur Radiol*. 2008 Jul; 18(7):1356-63.
43. Cox JE, Chiles C, McManus CM, Aquino SL, Choplin RH. Transthoracic needle aspiration biopsy: variables that affect risk of pneumothorax. *Radio*. 1999; 212:165-168.
44. Yeow KM, See LC, Lui KW, et al. Risk factors for pneumothorax and bleeding after CT-guided percutaneous coaxial cutting needle biopsy of lung lesions. *J Vasc Interv Radiol* 2001; 12:1305-1312.
45. Topal U, Ediz B. Transthoracic needle biopsy: factors effecting risk of pneumothorax. *Eur J Radiol* 2003; 48:263-267.