



ORIGINAL ARTICLE

Marked safety and high diagnostic yield of freehand ultrasound-guided core-needle biopsies performed by pulmonologists

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Abstract

Background: Adequate tissue sampling is fundamental for establishing a definitive diagnosis, assessing prognosis and tailoring therapy. Each of the methods for obtaining tissue (e.g., endoscopic, image guidance and surgical biopsies) results in a different diagnostic yield and complication rate profile.

Objectives: Present feasibility, and assess safety and efficacy of freehand transthoracic ultrasound-guided core-needle biopsies (USGNB) of thoracic lesions performed by pulmonologist.

Methods: A retrospective analysis study of ultrasound-guided core-needle biopsies of thoracic lesions performed at the Pulmonary Institute of Rabin Medical Center was conducted from September 2020 to October 2021. All core-needle biopsies were performed under local anesthesia with guidance of Mindray TE7 2019 US system. Procedural variables including complications and pathological diagnostic yield were the primary end point. IRB 0671-21-RMC.

Results: In total 91 biopsy procedures were analyzed in 38 females and 53 males, average age 71.1 years. Twenty-three (25.3%) cases were lung lesions, 7 (7.7%) – mediastinal, 13 (14.3%) – chest wall, 27 (29.7%) – pleural, and 21 (23.1%) supraclavicular lesions. Average lesion size was 51.6 mm, the largest in the mediastinum and the smallest in supraclavicular locations (97.7 mm and 28.0 mm, respectively). Overall pathological diagnostic yield was 90%, highest success in chest wall (100%) and lowest in mediastinal biopsies (71.4%). We had only one complication – hemothorax resolved by chest tube drainage – accounting for only 1.1% complication rate.

Conclusion: Safety and efficacy were demonstrated in freehand US-guided core-needle biopsy of thoracic lesions performed by pulmonologists. We suggest thoracic ultrasound and USG-CNB be part of training and clinical practice in interventional pulmonology.

KEYWORDS

core needle biopsy, pulmonologist, thoracic lesions, ultrasound

INTRODUCTION

Thoracic malignancies are one of the most prevalent and aggressive types of cancer worldwide.^{1,2} Adequate tissue sampling is fundamental for establishing a definitive diagnosis, in order to assess prognosis and tailor therapy.¹⁻³

Each of the methods for obtaining tissue in the clinical setting (i.e., endoscopic, image guidance and surgical biopsies) results in a different diagnostic yield and complication rate profile. Current, common nonsurgical biopsy methods in use, such as computed tomography (CT)-guided transthoracic needle biopsy and transbronchial biopsy, also retain potential

significant risks of complications, in addition to radiation exposure.^{4,5} As such, a need for a safer, less invasive, non-surgical biopsy method to provide satisfactory results, sensitivity, accuracy, and negative predictive value is warranted.

Ultrasound-guided needle biopsy (USG-NB) is an effective and less invasive diagnostic method than surgical biopsy.⁶⁻⁸ USG-NB is also an accurate and inexpensive technique, with a short examination time, which allows real-time bedside monitoring.^{7,8} Using this method for sampling thoracic lesions also exhibited several advantages over the CT-guided procedure.^{9,10} While CT-guidance exposes patients to high radiation for extended periods of time, US-guidance involves minimal radiation exposure and can be performed in a shorter examination with real-time monitoring of needle placement in the target lesion, as well as providing safety measures by employing Doppler imaging, and thus aids in avoidance of vessel damage.^{9,10}

In this study, we aimed to use freehand US-guided thoracic biopsies to present the technical aspects of the procedure, highlight the feasibility, and most importantly assess safety and efficacy of this diagnostic method.

METHODS

We prospectively collected and retrospectively analyzed data from transthoracic ultrasound guided core-needle biopsies (USG-CNB) of thoracic lesions from patients referred to the Pulmonary Institute of Rabin Medical Center from August 2020 to October 2021.

Demographic and clinical characteristics included age, gender, anatomical locations of the lesion, maximal lesion size on chest CT or positron emission tomography-computed tomography (PET-CT), and parietal pleural contact length, for lung lesions, exclusively. Procedural variables including complications and pathological diagnostic yield were the primary endpoint. For each procedure, the size of the core-needle biopsy was recorded.

Patients referred to undergo USG-CN biopsies had newly discovered thoracic lesions which included: peripheral lung masses, chest wall lesions, pleural lesions, mediastinal tumors, and supraclavicular lymph nodes.

Demographic and clinical data analyzed and compared included: age, gender, core needle gauge size (14–20), maximum lesion diameter on patient's CT/PET-CT scans, maximum pleural contact (measured for lung biopsies), pathological diagnostic yield or nondiagnostic sample and complications (pneumothorax, hemothorax, air embolism, infection, post-procedure hospitalization or death).

Procedure

Ultrasound guidance was performed using the Mindray TE7 2019 US system (Mindray Bio-Medical Electronics Co.). Patient position (supine or prone) was decided in advance based on the location of the lesion using the shortest and safest approach to visualize the movement of the US probe. The US

probe was cleaned with a 0.45% didecyl-diethyl ammonium chloride solution for at least 5 min to ensure disinfection and was covered by sterile disposable cover. Real-time color Doppler imaging was used to avoid vessels. The skin was prepared and draped in a standard fashion with chlorhexidine and sterile draping. For local anesthesia, the skin and subcutaneous tissues were thoroughly anesthetized with 2% lidocaine buffered with sodium bicarbonate under sterile conditions with US guidance. For an easier procedure and to minimize intraprocedural complications, we performed a minimal scalpel cut at the decided location for needle insertion. Following administration of local antiseptics, anesthetics, and the scalpel cut, the biopsy needle was inserted. Real-time sonographic guidance was used to confirm appropriate needle placement throughout the sampling period. If the lesion was positioned superficially or closer to the subcutaneous surface than the pleura, we used a linear ultrasound probe (L12-4S Linear Array ultrasound transducer, TE7; Mindray). For lesions deeper than the pleura, we used an abdominal ultrasound transducer (c5-2s Convex Array ultrasound transducer, TE7; Mindray).

Core biopsies were performed with different size needles: 14, 16, 18 or 20-gauge (Achieve, or Temno; Merit Medical), according to lesion size and location, at the discretion of the pulmonologist performing the procedure.

The core needle device was advanced into the lesion, and core samples were obtained utilizing an appropriate throw length. For small lesions, the needle was advanced into the superficial portion of the lesion, to minimize the possibility of coring through the pleura, and the shortest possible throw length core sample was obtained. Core samples were assessed visually for adequacy.

Post-procedure chest X-ray was obtained to identify any complications. All patients were monitored for 2 h post-procedure.

All biopsy samples were placed in formaldehyde in sterile containers and transferred to the pathology department for histological examination and immunohistochemical analyses.

All cases were followed clinically in our Pulmonary Institute and with recommendation for further evaluation of a suspicious lesion or a USG-CNB nondiagnostic sample, in which case the patient was referred to repeat biopsy with a different modality to achieve definite diagnosis.

Approval of the Helsinki Committee: IRB number: 0671-21-RMC.

Statistical analysis

Descriptive statistics are expressed as numbers and percentages or mean. Demographic and clinical data analyzed and compared including: age, gender, core needle gauge size (14–20), maximum lesion diameter on patient's CT/PET-CT scans, maximum pleural contact (measured for lung biopsies), pathological diagnostic yield or nondiagnostic sample and complications (pneumothorax, hemothorax, air embolism, infection, post-procedure hospitalization or death). For further analysis of the various biopsy samples, we divided

TABLE 1 Patient demographic characteristics and biopsy pathology (*n* = 91)

	Total n = 91	lungs n = 23	mediastinum n = 7	chest wall n = 13	pleura n = 27	supraclavicular n = 21
Age (mean)	71.1	75.8	41.4	65.8	76.4	72.5
Gender (F/M)	38\52	15\8	2\5	3\10	11\16	7\14
Size on CT (mm)	51.6	59.5	97.7	51.4	not applicable	28.0
Trucut needle						
14G	23	2	0	3	16	2
16G	49	16	6	8	5	14
18G	18	5	1	1	6	5
20G	1	0	0	1	0	0
Path diagnosis (%)	91.1	95.7	71.4	100	84.6	95.2
Carcinoma n (%)	52 (57.8)	16	1	9	12	14
Lymphoma n (%)	11 (12.2)	2	3	2	0	4
Inflammatory n (%)	9(10)	0	0	0	9	0
Mesothelioma n (%)	3 (3.3)	2	0	0	1	0
Sarcoma n (%)	2 (2.2)	0	0	1	0	1
Malignancy n (%)	2 (2.2)	1	0	1	0	0
Fibrous tumor n (%)	1 (1.1)	1	0	0	0	0
Thymoma n (%)	1 (1.1)	0	1	0	0	0
Infectious n (%)	1 (1.1)	0	0	0	0	1
Non diagnostic n (%)	8(8.9)	1(4.3)	2(28.6)	0	4(15.4)	1(4.8)
Complications (%)	1(1.1)	1(4.3)	0	0	0	0

Abbreviation: CT, computed tomography.

the cases into the following six categories, according to anatomical location of the extracted biopsy: lungs, mediastinum, chest wall, pleura, and supraclavicular. The baseline characteristics and secondary outcomes were compared with the Student *t* test, χ^2 test, and the Mann–Whitney U test, as appropriate. *p* < 0.05 was considered statistically significant. Statistical analysis was performed using SAS software, version 9.2 (SAS Institute, Inc).

RESULTS

We enrolled a total of 91 biopsy cases of US-guided biopsies. The demographic, clinical and pathological characteristics are shown in Table 1. Patients are categorized according to the anatomical location of the extracted biopsy (lungs, mediastinum, chest wall, pleura, and supraclavicular).

The average age in all our patients was 71.1 years; 69.6 in women and 70.8 in men.

The average age of the patients by biopsy group was 75.8 years in the lung of which 65% were female (15/23), 41.4 years in the mediastinum of which 72% were male (5/7), 65.8 years in the chest wall of which 77% were female (10/13), 76.4 years in the pleura of which 59.2% were female (16/27) and 72.1 years in the supraclavicular of which 67% were male (14/21).

The average lesion size excluding the pleural biopsy group was 51.6 mm with 59.5 mm, 97.7, 51.4 and 28 mm in the lung, mediastinum, chest wall and supraclavicular biopsy

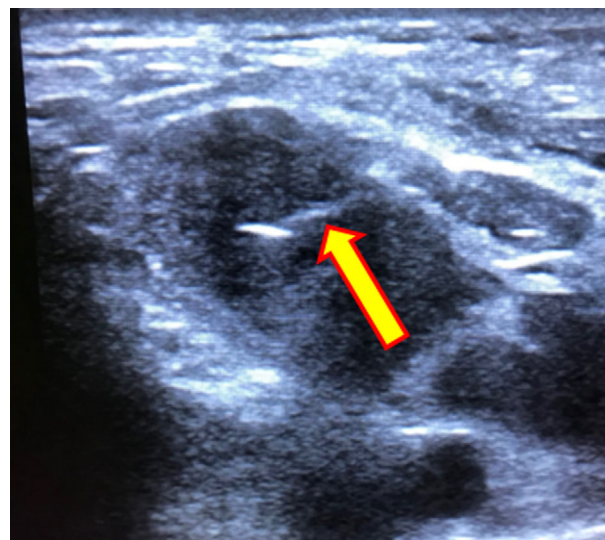


FIGURE 1 Linear ultrasound of 75-year-old male heavy smoker with a previous diagnosis of prostate cancer. The arrow shows a 16G needle biopsy of a right-sided supraclavicular lymph node. A final diagnosis of non-small cell lung cancer was made

groups, respectively. In the lung biopsy group (Figures 1 and 2) the average pleural contact length was 80 mm. We used 14G, 16G, 18G and 20G needles in 22.9%, 54.2%, 21.7% and 1.2% in total, respectively.

The overall pathological diagnostic yield was 90.1% with 95.7%, 71.4%, 100%, 81.5% and 95.2% in the lung,

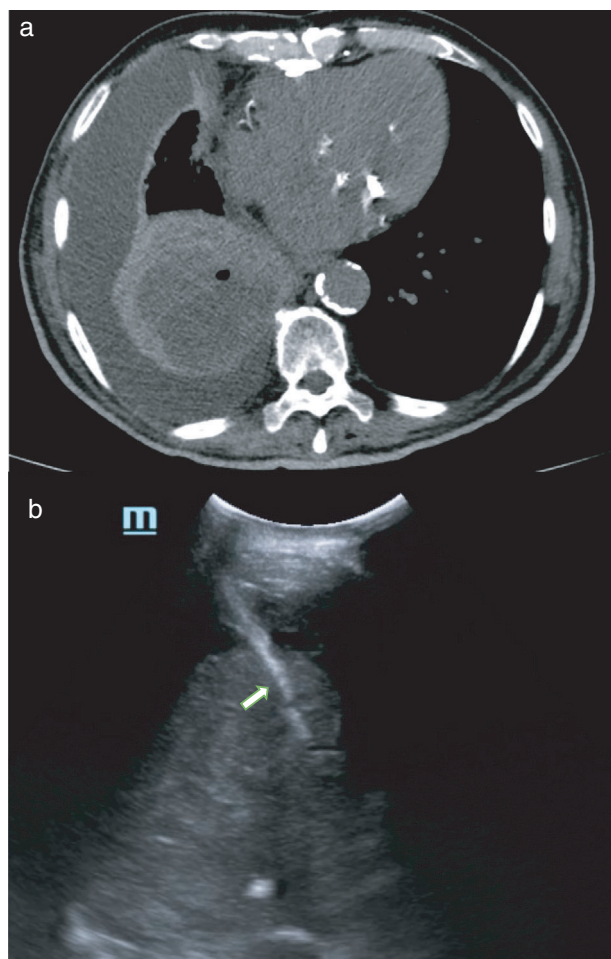


FIGURE 2 Imaging studies of an 82-year-old patient with pleural effusion and right lower lobe lung mass. (a) Axial CT image of the mass surrounded by effusion. (b) Transverse grayscale US image with convex probe showing biopsy needle throw (arrow). CT, computed tomography; US, ultrasound

mediastinum, chest wall, pleural and supraclavicular biopsy groups, respectively. Carcinomas were diagnosed in 59.3% of all biopsies. In the lung group, 17 (73%) cases were diagnosed with carcinoma, two with lymphoma, two with mesotheliomas and one was nondiagnostic. In the mediastinal lesion groups three cases were lymphoma, one thymoma, one carcinoma and two were nondiagnostic. In the pleural group, 12 (44.4%) cases were malignant and nine were (33.3%) inflammatory.

In total, 52/90 (57.8%) of biopsies were positive for carcinoma, 11/90 (12.2%) for lymphoma, 9/90 (10%) inflammatory process, 3/90 (3.3%) mesothelioma, 2/90 (2.2%) sarcoma and fibrous tumor with thymoma constituted one case (1.1%) each. There were 8/90 (8.9%) nondiagnostic cases and as such the total diagnostic yield was high 82/90 (91.1%).

In the lung group, 17/23 (73%) cases were diagnosed as carcinoma, two (8.6%) cases as lymphoma, two (8.7%) as mesotheliomas and one (4.3%) was nondiagnostic. The latter patient was a 78-year-old female referred for CT-guided

lung biopsy, which was positive for adenocarcinoma. In this group of lung lesions, the diagnostic yield was 22/23 (95.7%). We encountered one case of hemothorax in the lung biopsy group which required insertion of a chest tube, administration of blood doses, and hospitalization. After 2 days, the patient was released from the hospital without further clinical consequences.

In the mediastinal lesion groups, there were three cases of lymphoma, one of thymoma, one of carcinoma and two were nondiagnostic. Both nondiagnostic mediastinal cases were referred for surgical biopsy and in both a Hodgkin's lymphoma diagnosis was made. Thus, the diagnostic yield in this group was 5/7 (71.4%) without immediate or late complications.

All USG-NB of chest wall lesions were diagnostic for malignancy and no complications were encountered.

In the pleural group, 12/26 (46.1%) cases were malignant and 9/26 (34.6%) inflammatory. There were four nondiagnostic cases. Two of these cases also had lung masses and diagnosis of non-small cell lung cancer (NSCLC) was made by bronchoscopy. Two other cases were referred for thoracoscopy with a diagnosis of pleural NSCLC.

In the supraclavicular group, most cases were diagnosed as carcinoma 14/21 (67.7%), lymphoma 4/21 (19%) and sarcoma 1/21 (4.7%) and only one case was nondiagnostic. In the case of a 67-year-old woman, a final diagnosis of sarcoidosis was achieved by bronchoscopy. There were no immediate or late complications in this group.

DISCUSSION

The present prospective data analysis study presents an acceptable efficacy and safety of ultrasound-guided thoracic and lung biopsies, demonstrating an overall high diagnostic yield of 90.1% with a low complication rate (1.1%) in the hands of interventional pulmonologists. These findings are remarkable also considering real-time guidance utilizing ultrasound allows for shorter procedural time, it is free of ionizing radiation, and less expensive compared to other image guidance biopsy modalities, such as CT-guided biopsy.^{8,10} All procedures were performed using a standard ultrasound, either with a linear or abdominal probe, for free hand core needle biopsy guidance.

Previous series showed that pulmonologists perform US guided fine needle aspiration safely from thoracic lesions with high diagnostic yield.^{11,12} In this study we evaluated data on the use of USG-NB by interventional pulmonologists and analyzed the diagnostic outcomes of thoracic lesions categorized according to their different locations.

In our study, the average patient age was 71.1 years, which correlates with published data on patient age, range between 61 and 73 years.^{10–14} On average, patients in the mediastinal group were younger, 41.4 years, which can be expected, as the nature of masses in this location are histologically different from other thoracic sites thus also have a different age distribution.⁸

Our preference was to using a 16G caliber biopsy needle in all groups, except in the pleural biopsy group where we preferred to use a 14G. Most pleural biopsies were performed in the context of suspicious pleural effusion investigation. In our assessment, using a 14G needle for pleural biopsy had several advantages: first the target is not a rounded or ellipsoid lesion, rather it is a layer, which lies perpendicular or oblique to the needle trajectory. As such, it might require a larger biopsy sample to be obtained in order to examine a larger section of the pleural layer.

The overall success rate for ultrasound-guided biopsies in this study was 91.1%, which is a highly diagnostic value that correlates with similar reports on CT guided biopsies.^{8–10,14–16} In our study, the average lesion size was 51.6 mm, with the largest lesion in the mediastinum measuring 97.7 mm and the smallest was a supraclavicular lymph node measuring 27.3 mm. We achieved a very high diagnostic yield of 95.7% in the lung mass group, which is in the top tier of previous reported US and CT guided lung biopsies using GNB.^{13–16} The average lesion size was 59.5 mm, and the average pleural contact length was 80 mm. Previous studies presented a mean size of lesions ranging from 41.5–70 mm.^{11,12} We assume that lesions with extensive plural contact significantly influenced diagnostic accuracy, hence the rather sizeable pleural-lesion contact in our series improved the diagnostic value in our study.

In mediastinal biopsies, in our series, we achieved a 71.4% diagnostic yield. Recognizably, the mediastinum, unlike other thoracic regions, is technically a rather difficult target, being located behind the sternum and the rib cage. Additionally, two nondiagnostic cases, were eventually referred for surgical biopsy. Thus, the meaning of this diagnostic value is that in 5/7 (71.4%) the definitive diagnostic USG-NB procedure had no post-procedure complications, moreover it obviated the need for CT-guided or surgical biopsies. Therefore, this group of patients should possibly be referred to USG-NB as the first step in the diagnosis.

All chest wall US-GNB biopsies performed by our team were diagnostic, without complications, thus obviating the need for CT-guided biopsies in this group of patients.

A well-established method of closed pleural biopsy is by using an Abram's needle. In a study comparing US-GNB with Abram's needle biopsy, for suspicious pleural effusion investigations, the diagnostic accuracy was 81.3% and 74.4%, respectively.¹⁸ In our study we reached a diagnostic yield of 84.6%, with 22/26 pleural US-GNBs. Moreover, we encountered no immediate or late complications. As such, US-GNB can be recommended as the first modality in the investigation of suspicious effusion investigation, prior to thoracoscopic biopsy.

In our study we encountered only one serious procedure related complication (hemothorax), which stands for 1.1% complication rate, in general, and 4.3% in the lung mass group. Notwithstanding, our complication rate is lower than previous studies which report 2.7%–12.8% using US guided percutaneous biopsy (UG-PNB).^{13–17} Moreover, in previous studies comparing US- and CT guided biopsies of lung and

pleural lesions, US was associated with a lower complication rate and improved safety.^{14,17}

Although these data are compelling, our study had several limitations. First, the inherent limitations of a retrospective data analysis study design with small sample sizes across the subgroups weaken our statistical analysis power. Second, procedures were selected by the respiratory physician, and patients were not randomly selected, which may result in selection bias. Third, procedures were performed by a single physician with advanced interventional training. As such, this method of biopsy might not be suitable for general implementation before proper training. Finally, there was no correlation or comparison to an alternative method or imaging modality of thoracic biopsy.

In conclusion, USG-CNB of thoracic lesions performed freehand by pulmonologists is a highly diagnostic method with an excellent safety profile. In the presence of an adequate acoustic window, US guidance can be valuable for the diagnosis of peripheral lung, chest wall, supraclavicular, pleural and mediastinal lesions. Avoiding radiation exposure, real-time bedside use, repeatability, and evasion of vessels with color Doppler imaging make USG-CNB an appealing method. Moreover, the procedure can be performed at the bedside of critically ill patients and even those situated in different positions, such as patients with dyspnea who cannot tolerate prone or supine positioning. Thus, we suggest that US use for thoracic biopsies should be part of the training for interventional pulmonologists and integrated into clinical pulmonary practice.

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CONFLICT OF INTEREST

All authors state they have no conflicts of interest to disclose, nor any relevant financial interests or relationships or affiliations.

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