



## Case Report

# Ultrasound-guided pleural biopsy following a non-diagnostic thoracentesis for non-small cell lung cancer

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## ABSTRACT

We report a case of a 65-year-old man with a cavitary lung mass and parietal-based pleural nodules in which a pleural ultrasound-guided approach yielded a definitive diagnosis of stage IV non-small cell lung carcinoma. Computed tomography-guided biopsy is often preferred approach for the majority of United States hospitals for sampling pleural nodules as compared to US. The advantages of an US-guided approach include [1]: increased portability [2]; decreased procedure time [3]; reduced reliance on dedicated ancillary support staff [4]; need for local anesthesia only [5]; lack of ionizing radiation exposure; and [6] cost reduction.

## 1. Introduction

Medical thoracoscopy and video-assisted thoracic surgery are the gold standards for diagnosis of malignant pleural disease, with a diagnostic yield above 90% [1]. Both procedures are invasive and are associated with significant cost and resource utilization, including use of space, time, and staff, and requiring either conscious sedation or general anesthesia. Thoracoscopy is contraindicated in high-risk cardiac patients, high continuous oxygen need, or severe pulmonary hypertension, or if diagnostic yield is limited due to significant pleural adhesions [2]. Image-guided closed biopsies, using Computed Tomography (CT) or Thoracic Ultrasound (TUS), are minimally invasive alternatives with high diagnostic yields. US-guided biopsy offers additional advantages compared to the CT approach [1]. Pulmonologists should consider US-guided transthoracic biopsy as a comparable approach in some cases.

## 2. Case presentation

A 65-year-old man with an extensive smoking history, very severe chronic obstructive lung disease complicated by chronic hypoxic respiratory failure requiring continuous supplemental oxygen support developed new onset non-pleuritic chest pain. A chest x-ray and computed tomography (CT) revealed a cavitated left upper lobe lung (LUL) mass measuring  $3.7 \times 2.6$  cm without pathologic enlarged mediastinal lymphadenopathy (Fig. 1). A position emission tomography-computed tomography (PET-CT) revealed hypermetabolic activity in Ref. [1] LUL mass (SUVmax 17.4) [2]; pleural-based focus, medial aspect of the posterior left lower hemithorax (SUVmax 3.3); and [3] pleural-based focus, more lateral aspect of the posterior left lower hemithorax (SUVmax 5.7) (Fig. 2).

The patient underwent an US-guided thoracentesis, with cytology that resulted negative for malignancy. Three weeks later, the Pulmonary Service was consulted for consideration of performing a diagnostic bronchoscopy. We performed a pleural ultrasound using a generic, portable ultrasound equipped with a phase array 5-1Mhz probe, with the patient seated in an upright position. A

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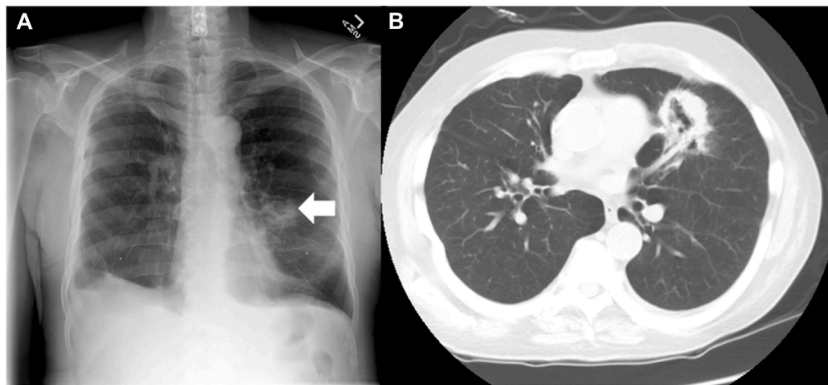


Fig. 1. 1A. Postero-anterior chest x-ray demonstrating the cavitated lung mass in the left upper lobe (white arrow). 1B. Non-contrast Computed Tomography demonstrating cavitated lung mass in the left upper lobe (3.7 × 2.6cm) without enlarged mediastinal or hilar lymphadenopathy.

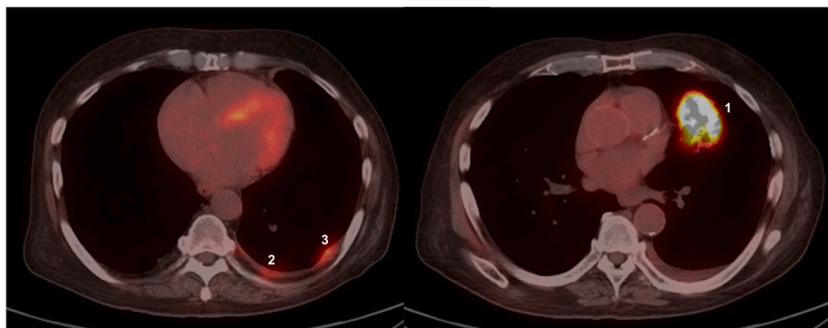


Fig. 2. Positron emission tomography-computed tomography. Three areas with hypermetabolic activity [1]: Lung mass in the left upper lobe [2]; posterior FDG-avid nodule [3]; posterolateral FDG-avid nodule.

pleural-based nodule and a small anechoic pleural effusion were identified. Color Doppler revealed no evidence of a pleural-based arteriovenous malformation. Using a “free-hand” technique, a BioPince™ needle (18Gx10 cm; Argon Medical Devices, Inc, USA) was passed four times at the same angle of the US probe (Fig. 3). A thoracentesis was subsequently performed, with a total of 20mL pleural fluid drained. Pleural fluid analysis was consistent with a lymphocyte-predominant exudate, negative for malignancy. The core biopsy was satisfactory and showed non-small cell lung carcinoma, p40 positive and TTF-1 negative, consistent with stage IV squamous cell carcinoma.

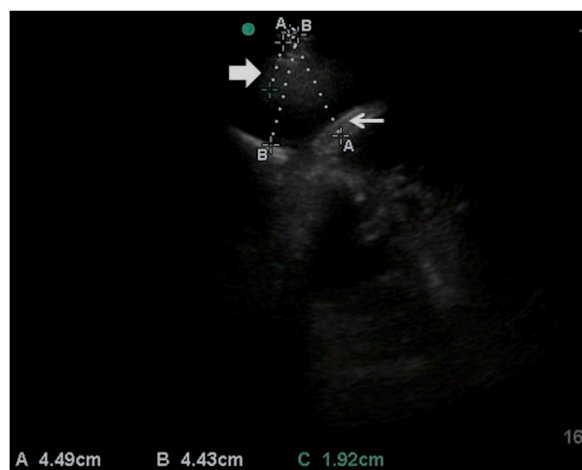


Fig. 3. Lung ultrasound. Diaphragm (narrow white arrow), pleural nodule (thick white arrow). Distance measurements are represented by the dotted lines: (A) skin to diaphragm, (B) skin to lung, (C) size of lung nodule. Diaphragm thickness is > 1 cm, which has a high diagnostic sensitivity for the presence of a malignant pleural effusion regardless of if cytology is negative.

### 3. Discussion

Image-guided closed biopsies are minimally invasive, fast, and associated with lower cost [1]. Disadvantages of CT-guided biopsies include increased cost (time, utilization of radiology department resources, requirement of necessary ancillary staff, etc), and exposure to ionizing radiation. US machines are portable, allowing inpatient and outpatient procedures to be performed with local anesthesia only. Furthermore, US is superior to CT at quantifying pleural fluid volume, identifying complexity in the pleural space, pleural thickening, pleural nodules and tumors [1]. Both techniques can help guide the needle insertion while preventing inadvertent lung and sub-diaphragmatic organ puncture [3]. The procedure can be done using a “free hand” technique or with biopsy needles mounted on the ultrasound probe. The latter ensures the needle moves in the same US plane [4].

The traditional reversed-bevel closed needles, I.e. the Abrams and Cope needle, has reasonable diagnostic yield when the pleural disease is diffuse, with tuberculous pleuritis being the classic example. In a randomized, controlled trial comparing diagnostic sensitivity and safety of ultrasound-guided cutting-needle pleural biopsy versus thorascopic pleural biopsy was studied in 196 patients with suspected tuberculous pleuritis where the pleural fluid was non-diagnostic. Both modalities showed similar and statistically similar and strong sensitivities (>80%) in detecting tuberculous pleuritis [5].

Several core biopsy needles are available, with function based on three mechanical principles. The SURECUT needle (TSK Laboratory, Japan) requires a rapid, forward advancement of the needle, with the specimen then being maintained within the needle lumen via application of negative pressure. The yield of this needle system has been demonstrated as inferior to other designs [6]. The Tru-Cut® needle (Merit Medical, USA), obtains a smaller specimen than the SURECUT needle, though the sample is secured in a biopsy chamber. The BioPince™ needle system combines advantages of the SURECUT and the Tru-Cut® needles. It obtains a large biopsy specimen, while maintaining the biopsy secured with a special fixation wire [5]. Similar to Tru-Cut® needles, the depth of the puncture can be pre-set when biopsies are performed. The 18-gauge BioPince™ needle has shown to have an excellent diagnostic yield and low risk of complications [7]. Preferable needle size for pleural biopsy is 16- or 18-gauge to ensure adequate tissue such that mutational analysis and NextGen sequencing of the tumor can be performed.

The diagnostic yield of an image-guided biopsy depends on several factors, including the operator's experience, the use of a systematic approach, and a careful pre-procedural scanning phase. First, proper US gain is needed because pleural-based nodules and masses are relatively hypoechoic and may not otherwise be easily visualized. Second, once the lesion is identified, it is critical to carefully measure the distances to ensure adequate sample of the lesion while avoiding lung or sub-diaphragmatic organ puncture. Third, it is important to account for a few additional millimeters of cutting needle depth to ensure the needle slightly enters the pleural space. This will ensure the parietal pleura is sampled, since tissue deformation will occur with firing of the needle pushing the lesion away. In the above case, the distance from the top of the rib to the lesion was 19 mm and the BioPince™ needle was set at 23 mm. Finally, utilize the Color Doppler setting prior to needle insertion to ensure any vascular anomalies and aberrant intercostal vessels are identified and avoided.

The yield of pleural and peripheral lung nodule biopsy guided through either CT and US are similar with rates of 70–94% [8–12]. US-guided biopsy can be an alternative in cases where thoracoscopy failed or is contraindicated [10]. In a retrospective cohort of 50 cases of US-guided pleural biopsies performed by pulmonologists, the diagnostic yield was 94%, and 26% were performed after a non-diagnostic thoracoscopy [11]. Furthermore, US- compared to CT-guided biopsy reduced procedure time (42%; 295 vs 588 seconds) and pneumothorax rate (5.8% vs 14.7%) [10]. One retrospective study of 13 patients who failed thoracoscopy due to adhesions, and another 37 patients who were deemed too high risk; the diagnostic yield was 94% of the 47 patients and 85% who failed thoracoscopy [11]. A meta-analysis of 10 studies evaluating closed pleural biopsies in the diagnosis of unexplained pleural exudates had a pooled sensitivity of 77% [12]. Finally, another meta-analysis published by Lin and colleagues reviewing ultrasound-guided pleural biopsies in both malignant and non-malignant pleural yielded a pooled sensitivity of 83% and specificity of 100% [13].

### 4. Conclusion

Multiple studies report that US-guided biopsy has a similar diagnostic yield to CT-guided approach, with certain notable advantages [1]: increased portability [2]; decreased procedure time [3]; reduced reliance on dedicated ancillary support staff [4]; need for local anesthesia only [5]; lack of ionizing radiation exposure; and [6] cost reduction. Therefore, we suggest US-guided transthoracic biopsy for certain pleural-based lesions can be considered as a first-line diagnostic approach in carefully selected patients.

### Declaration of competing interest

JH: Consultant/Advisory Boards: IBIOS [IPF]; Roche/Genentech [IPF (Nintedanib)]; Boehringer Ingelheim [IPF (Pirfenidone)]. The remaining authors have no disclosures or any potential conflicts of interest.

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