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CT-guided core needle biopsy of the lung in patients with primary malignancy suspected of lung metastasis: 5-year experience from a single institution

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PURPOSE
We aimed to evaluate the diagnostic accuracy and safety profile of computed tomography (CT)-guided percutaneous transthoracic needle biopsy (PTNB) in patients with primary malignancy suspected of lung metastasis and assess possible factors associated with nondiagnostic results.

METHODS
All PTNBs with core needle performed in our hospital from January 2014 to January 2019 were retrospectively reviewed. Overall, 108 cases were found to have a history of primary malignancy with suspected lung metastasis. Patient demographics, lesion characteristics, procedure techniques and complications were evaluated as predictors of overall diagnosis, final diagnosis of lung metastasis, and nondiagnostic results. Statistical analysis was performed using univariate analysis.

RESULTS
The overall diagnostic accuracy of PTNB was 83.3%. Lung metastasis was found in 52.8% of PTNBs (57 of 108) and nondiagnostic results were present in 27.6% (18 of 108). Of the 18 cases with nondiagnostic results, 11 cases had a final diagnosis of lung metastasis (61.1%), yielding PTNB a sensitivity of 83.8% and specificity of 100% for the detection of lung metastasis. Smaller lesion size ($p = 0.014$), pneumothorax ($p = 0.026$), and hemoptysis ($p = 0.014$) were significantly associated with overall nondiagnostic results. Similarly, smaller lesion size ($p = 0.047$), pneumothorax ($p = 0.019$), high-grade pulmonary hemorrhage ($p = 0.019$), and hemoptysis ($p = 0.012$) were significantly correlated with unsuccessful biopsies in the diagnosis of lung metastasis.

CONCLUSION
CT-guided core needle biopsy of the lung in patients with primary malignancy suspected of lung metastasis has a high diagnostic accuracy with acceptable complication rates. Small lesion size, pneumothorax, high-grade pulmonary hemorrhage, and hemoptysis are significantly associated with nondiagnostic results in the final diagnosis of lung metastasis. Repeat biopsy and clinical/radiological follow-up should be considered in cancer patients with nondiagnostic results due to the high probability of lung metastasis.

Despite recent advances in the systematic treatment of cancer, the incidence of various types of cancer metastases continues to rise (1). Lung is the most common metastatic site for tumors except the liver (2), and about 20%–54% of patients with primary malignancy suffer from lung metastasis (LM) during development of the disease (3). Among them, breast, colon, kidney, head and neck are the most common primary sites of LM (4, 5). The diagnosis and determination of the magnitude and scope of LM is exceedingly important for confirming the stage of tumors for lung cancer and other malignancies, as well as the selection of operation or overall treatment options for patients (1, 3).

Currently, computed tomography (CT) is considered to be an advanced and effective method to detect and diagnose LM. Although typical LM can generally be identified in CT examination, it is necessary to make the definite diagnosis of cancer progression; besides, some imaging features of atypical LM are various and difficult to diagnose, including solitary mass, cavitation, and hemorrhage around the metastatic nodules (6). So the histological

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specimens should confirm the final diagnosis when new nodules appear in the lung in patients with a history of primary malignancy. CT-guided percutaneous transthoracic needle biopsy (PTNB) has been proven to be an accurate, safe, and minimally invasive technique for the diagnosis of pulmonary lesions, particularly pulmonary nodules, including LM (7, 8). The pathological diagnosis of metastasis or primary malignancy after PTNB is usually accurate with low false positivity rates; results without a specific diagnosis are considered nondiagnostic, which may lead to insufficient evidence to guide treatment and patient management; moreover, nondiagnostic results need more attention in biopsy procedure (9). Indeed, according to a recent large multicenter study of 2590 PTNBs with nondiagnostic results (10), the overall proportion of a final diagnosis of malignancy was 40.4%, and some malignancy-associated risk factors in nondiagnostic results were also shown. Moreover, another retrospective analysis found that history of malignancy was an important independent risk factor for the final diagnosis of malignancy in nondiagnostic biopsies (11), indicating the need for further evaluation of nondiagnostic cases of PTNB in patients with a history of primary malignancy.

The purpose of our study was to retrospectively evaluate the diagnostic performance and complications of PTNB of the lung with core needle in patients with primary malignancy and suspected LM and assess possible factors associated with nondiagnostic PTNB results over the past 5 years in our hospital.

Main points

- CT-guided percutaneous transthoracic needle biopsy (PTNB) in patients with primary malignancy suspected of lung metastasis has a high diagnostic accuracy.
- Small lesion size, pneumothorax, high-grade pulmonary hemorrhage, and hemoptysis are significantly associated with unsuccessful biopsies in the diagnosis of lung metastasis.
- Repeat biopsy and clinical/radiological follow-up should be considered in cancer patients with nondiagnostic biopsy results.

Methods

Study group

Electronic medical records of all CT-guided percutaneous transthoracic core needle biopsies of the lung (n=3120) performed between January 2014 and January 2019 in our hospital were retrospectively searched to select patients with a previous history of primary cancer and suspected lung metastases. Patients who underwent PTNB with a clear history of primary cancer before procedure and lung lesion(s) suspected to be LM by chest CT scan were included. Patients with CT-guided biopsy resulting in pathological diagnosis of LM without confirmed history of primary malignancy before the biopsy were excluded. According to these criteria, 108 PTNBs in 100 cancer patients with suspected LM were included in the analysis (64 male and 44 female patients; mean age, 57.99±12.72 years; age range, 26–82 years). Eight patients had two biopsies and repeated biopsies were considered to be independent cases in the calculations, as variables selected were different in each procedure.

Biopsy procedure

All patients underwent PTNB with CT guidance by using 16-slice spiral CT (Brilliance 16, Philips). The CT scan parameters were as follows: helical scan; tube voltage, 120 kV; tube current, 80 mAs; slice thickness, 5 mm; CT interval, 5 mm. All biopsies were performed using core needle in coaxial cutting needle system with 18-gauge needles (OptiMed 1399-1210, 18G-100/150 mm).

Bleeding profile, including platelet count, clotting time, activated partial thromboplastin time and international normalized ratio were checked and any antiplatelet/anticoagulant agents were discontinued for >1 week before the procedure. All procedures were performed by or under the supervision of a chest radiologist.

Operator reviewed recent chest CT image of the patient before biopsy and chose target lesion according to the location, size, and shape. Patient was placed in a suitable position and routine CT scanning was carried out to locate, determine and mark the biopsy points on the body surface. Operator selected the length of the cutting needle (100 mm or 150 mm) and designed the puncture path in consideration with minimal damage to the lung tissue, while avoiding ribs, blood vessels, interlobar fissures, and intercostal nerves. The nurse routinely disinfected the puncture area and operator performed local infiltration anesthesia with lidocaine at a concentration of 2% and the needle was inserted at an optimal angle. During the procedure, several small-scale scans were performed to determine the position of the needle tip and verify that it reached the edge of the lesion. The tissue was then cut once or twice or more, and the biopsy specimens were fixed with 10% formaldehyde solution and sent for pathological examination. After the operation, the patient underwent a repeat CT scan and short-term clinical monitoring to observe incidence and occurrence of complications.

This retrospective study was approved by our hospital ethics committee (protocol number 2019-KY-056-01) and the need for informed consent was waived.

Data collection and analysis

Two experienced thoracic radiologists and a research fellow evaluated all cases in the image database of our institution and reviewed institutional medical records including clinical data and pathology results.

Patient demographics included age, sex, history of primary malignancy and the number of lung lesions (solitary or multiple). Target lesion variables included size (longest dimension on axial CT images), morphology (solid, part-solid, consolidation or cavity), depth (defined as needle path length: distance from the chest wall to the nearest edge of the lesion along the needle path) and emphysema around the lesion (absent or present). Procedural variables included the biopsy position (supine, prone, lateral), needle-pleura angle (the needle and a line drawn tangential to the pleura with the tangent of the right part as the baseline, and categorized as <90° or ≥90°) and number of needle passes.

Complications associated with PTNB were recorded during or after procedure. Pneumothorax was defined as the presence of free gas in the pleural cavity. Pulmonary hemorrhage was categorized into two groups according to severity, as simplified from a previous hemorrhage grading scheme (7, 12): (a) low-grade hemorrhage, needle tract hemorrhage 2 cm or less in width; (b) high-grade hemorrhage, an area of hemorrhage more than 2 cm around the needle to the entire lobar and hemothorax, with observation and measurement of pulmonary hemorrhage by selecting the widest width on CT axial images. Hemoptysis was defined as any expectoration of blood or fresh blood during or after the procedure. Serious complications were defined as situations requiring intervention or leading to death.

Classification of biopsy result and final diagnosis

The pathological results after PTNB were divided into the following three groups: malignancy (malignant cells or cells suspected of being malignant), specific benign results (benign neoplasm, benign processes such as organizing pneumonia or inflammatory cells with tuberculosis, bacterial or fungal infection) and nondiagnostic results (insufficient material or presence of nonspecific benign, atypical cells and normal lung tissues).

Cases in the nondiagnostic group received a final diagnosis on the basis of surgical resection, repeated biopsy, therapeutic effect, any other examination, or clinical and radiological follow-up at least one year after PTNB. In particular, the final diagnosis of benign disease without biopsy or surgical resection was made if: 1) the lesion spontaneously resolved without chemotherapy or radiation; 2) the lesion shrunk after only anti-inflammatory therapy or the use of antibiotics; or 3) the size of the lesion remained stable or shrunk after a follow-up of at least one year on CT. The lesion was confirmed to be LM when the clinical course was consistent with obvious malignant processes, such as progression at follow-up CT or other organ's metastasis, according to the comprehensive diagnosis of clinicians. Those with clinical/radiological follow-up less than one year were excluded.

Statistical analysis

Statistical analysis was carried out using the SPSS version 21.0 (IBM SPSS) for Windows. Categorical variables were presented as relative frequencies (percentage). Normal distribution of continuous variables (age, lesion size and needle path length) were checked by Kolmogorov–Smirnov test. Continuous variables with normal distribution were presented as mean ± standard deviation and those with non-normal distribution were presented as median (interquartile range [IQR]). We performed univariate analysis with Pearson chi-square, continuity correction, Fisher exact test and Fisher–Freeman–Halton exact test for categorical variables, where applicable, and the Student t test and the Mann–Whitney U test for continuous variables, where applicable. Statistical significance level was set at $p < 0.05$.

Results

Over a 5-year period, 108 cases in 100 patients with primary malignancy suspected of LM have been evaluated; each patient underwent at least one biopsy and 8 patients had repeated biopsies at the same target. The most common history of primary malignancy in our study was nasopharyngeal carcinoma (17/108, 15.7%), breast cancer (14/108, 14%), and colon adenocarcinoma (9/108, 8.3%). The mean biopsied lesion size was 4.87±2.07 cm. The incidences of overall complication, pneumothorax, pulmonary hemorrhage, and hemoptysis after PTNBs were 54/108 (50%), 16/108 (14.8%), 48/108 (44.4%), and 4/108 (3.7%), respectively. Patients with pneumothorax did not require chest tube placement in our study. Pulmonary hemorrhage was low grade in 31.5% (34/108) and high grade in 13% (14/108). Serious complications that required surgical intervention occurred in 2 of 108 cases (1.86%), both with symptoms of severe hemoptysis, hypotension and unconsciousness; PTNB-related mortality rate was 0.93% (1/108). The other principal characteristics of the analyzed PTNBs are shown in Table 1.

The overall diagnostic accuracy of PTNB was 83.3% (90/108); LM was found in 57 PTNBs (52.8%), primary lung cancer in 16 (14.8%), specific inflammation in 17 (15.7%) (7 cases of inflammatory cells with mycobacterium tuberculosis, 6 cases of organizing pneumonia, 2 cases of inflammatory cells with positive bacterial infection, 1 case each of fungus and hamartoma), 18 (16.67%) PTNBs showed nondiagnostic results. And those 6 cases of organizing pneumonia were also confirmed in the radiological follow-up.

In the nondiagnostic group, pathology results were nonspecific benign (8/18, 44.4%), atypical cells (2/18, 11.1%), normal lung tissue (3/18, 16.67%) and insufficient material (5/18, 27.8%). Of 18 nondiagnostic PTNBs, 11 received a final diagnosis of LM

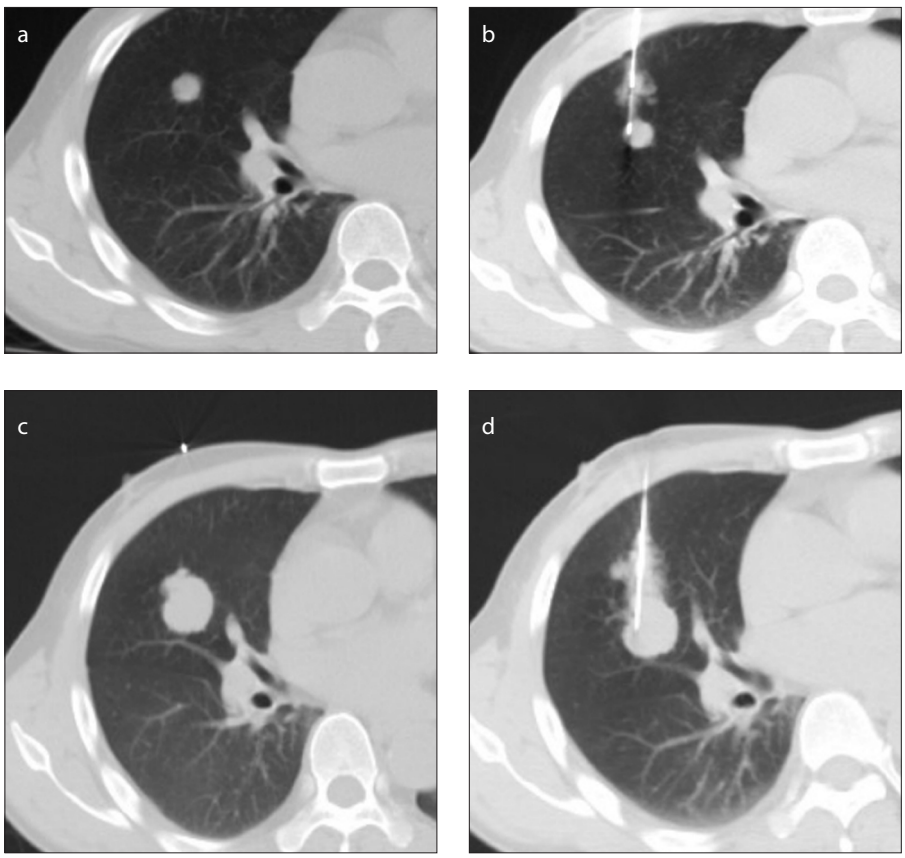

Figure 1. a–d. A nondiagnostic case of CT-guided lung biopsy in a 51-year-old man who had undergone excision of a left submandibular gland mass, which proved to be a submandibular gland carcinoma, 2 months previously. Localizing CT image **(a)** shows a 1.3 cm right middle lobe solitary nodule. CT image **(b)** during lung biopsy revealed pulmonary hemorrhage along the needle tract. Pathologic examination showed nonspecific inflammatory cells. Axial CT image **(c)** taken after 2 months shows increased lesion size. Image **(d)** shows the second lung biopsy, also accompanied by pulmonary hemorrhage around the nodule and along the needle tract; the lesion was confirmed to be lung metastasis at pathologic examination.

Table 1. Patient demographics, lesion characteristics, procedure techniques, complications and biopsy pathology results (n=108)

Variable	n (%)
Demographics	
Age (years), mean±SD	57.99±12.72
Male/female	64 (59.3) /44 (40.7)
Primary malignancy history before CT-guided biopsy	
Nasopharyngeal carcinoma	17 (15.7)
Breast cancer	14 (13.0)
Colon adenocarcinoma	9 (8.3)
Rectal adenocarcinoma	8 (7.4)
Esophageal cancer	7 (6.5)
Hepatic cellular cancer	7 (6.5)
Lymphoma	6 (5.6)
Lung adenocarcinoma	3 (2.8)
Renal cell carcinoma	3 (2.8)
Cervical carcinoma	3 (2.8)
Endometrial carcinoma	3 (2.8)
Submandibular gland carcinoma	2 (1.9)
Laryngocarcinoma	2 (1.9)
Thyroid carcinoma	2 (1.9)
Gastric cancer	2 (1.9)
Pancreatic cancer	2 (1.9)
Bladder cancer	2 (1.9)
Uterus leiomyosarcoma	2 (1.9)
Oligodendroglioma	1 (0.9)
Oral cancer	1 (0.9)
Tongue cancer	1 (0.9)
Lung squamous cell carcinoma	1 (0.9)
Thymoma	1 (0.9)
Yolk tumor of anterior mediastinum	1 (0.9)
Rhabdomyosarcoma of thorax	1 (0.9)
Cholangiocarcinoma	1 (0.9)
Renal pelvic carcinoma	1 (0.9)
Prostatic cancer	1 (0.9)
Ureteral carcinoma	1 (0.9)
Choriocarcinoma	1 (0.9)
Trophoblastic carcinoma	1 (0.9)
Osteosarcoma	1 (0.9)
Number of lung lesions of the patient	
Solitary	40 (37)
Multiple	68 (63)
Lesion characteristics	
Biopsied lesion size (cm), median (IQR)	2.6 (1.8, 4.1)

(61.1%). One case was finally diagnosed as lung adenocarcinoma by surgery (5.6%). Four cases were finally diagnosed as specific inflammation (22.2%): 2 were diagnosed at repeated biopsies, while the other 2 were diagnosed at clinical/radiological follow-up. Two cases had no final diagnosis due to follow-up failure (11.1%).

Of the nondiagnostic cases, 8 underwent the second biopsy of the same lesion. The pathological results of the second PTNB were LM (4/8), specific inflammation (2/8) and nondiagnostic (2/8); thus, the second PTNB was concordant with the final diagnosis in 75% (6/8) of cases. The rates of pneumothorax, pulmonary hemorrhage, and hemoptysis in the second PTNB were 12.5% (1/8), 37.5% (3/8), and 12.5% (1/8), respectively, indicating complication rates similar with the overall group.

Nondiagnostic results were significantly more likely to occur with smaller lesion size (p = 0.014), and in the presence of pneumothorax (p = 0.026) and hemoptysis (p = 0.014). The occurrence of high-grade pulmonary hemorrhage tended toward but did not reach significance. Other parameters were not significantly different between the PTNBs yielding diagnostic and nondiagnostic results, as shown in Table 3.

Unsuccessful biopsy was defined as nondiagnostic cases finally diagnosed with LM. Of the 108 PTNBs in patients with history of primary malignancy, 68 were finally diagnosed as LM; 57 of 68 cases were diagnosed successfully by PTNB, while 11 cases were nondiagnostic, yielding a sensitivity of 83.8% and specificity of 100% for diagnosis of LM by PTNB. In 11 cases of LM that could not be initially diagnosed with PTNB, the final diagnosis was made at open surgical resection in 1 case, repeated biopsy in 4 cases (Fig. 1), and clinical/radiological follow-up in 6 cases (Fig. 2). The initial pathological results of PTNB in these cases were nonspecific benign (5/11, 45.5%), atypical cells (2/11, 18.2%), normal lung tissue (2/11, 18.2%) and insufficient material (2/11, 18.2%). Among LM cases, the most common history of primary malignancy was colon adenocarcinoma (9/68, 13.2%). Biopsied lesion size was significantly different between patients with unsuccessful PTNBs and those with successful PTNB (p = 0.047). Pneumothorax, high-grade pulmonary hemorrhage and hemoptysis were associated with a higher number of unsuccessful PTNBs (45.5%, 45.5%, and 27.3% in the presence of pneumothorax, high-grade pulmonary hemorrhage, and hemoptysis vs. 12.3%, 12.3%, and 1.8% in the

Table 1. Patient demographics, lesion characteristics, procedure techniques, complications and biopsy pathology results (n=108) (Cont'd)

Variable	n (%)
Biopsied lesion morphology	
Solid	91 (84.3)
Part-solid	9 (8.3)
Consolidation	6 (5.6)
Cavity	2 (1.9)
Location of biopsied lesion	
Right upper lobe	26 (24.1)
Right middle lobe	9 (8.3)
Right lower lobe	28 (25.9)
Left upper lobe	23 (21.3)
Left lower lobe	22 (20.4)
Emphysema around biopsied lesion	18 (16.67)
Needle path length (cm), mean±SD	4.87±2.07
Procedure techniques	
Patient position	
Supine	47 (43.5)
Prone	39 (36.1)
Lateral	22 (20.4)
Needle-pleura angle (°)	
<90°	60 (55.6)
≥90°	48 (44.4)
Number of needle passes	
1	40 (37)
2	67 (62)
3	1 (0.09)
Complication	54 (50%)
Pneumothorax	16 (14.8)
Pulmonary hemorrhage	48 (44.4)
Low-grade	34 (31.5)
High-grade	14 (13)
Hemoptysis	4 (3.7)
Required intervention	2 (1.86)

SD, standard deviation; IQR, interquartile range.

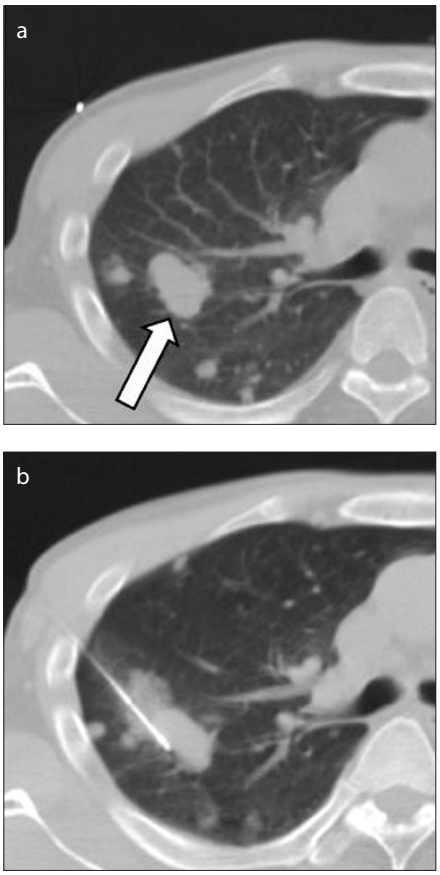

Figure 2. a, b. A nondiagnostic case of CT-guided lung biopsy in a 51-year-old man with hepatocellular cancer and lung metastases. Transverse CT image **(a)** obtained with lung window settings shows multiple nodules in the right lung. A 2.7 cm nodule *(arrow)* was chosen for biopsy. CT image **(b)** taken during lung biopsy revealed minimal pneumothorax and high-grade pulmonary hemorrhage around the lesion and along the needle tract. Subsequently hemoptysis occurred. Pathologic examination showed insufficient specimen. Final diagnosis was made by clinical/radiological follow-up.

absence of those, respectively; $p = 0.019$, $p = 0.019$, and $p = 0.012$, respectively). Other patient-, lesion-, and technique-related variables were not significantly associated with unsuccessful biopsy (Table 4).

Discussion

The lung is one of the most common target organs for various cancers that cause hematogenous metastasis; patients with pulmonary metastasis usually have poor prognosis and decreased survival (3). CT-guided PTNB has proven to be a useful and safe procedure for the diagnosis of lung lesions (7, 13), as it avoids open biopsy in most cases. Early diagnosis of LM in patients with known malignancy may be critical in the planning of effective therapies, such as thermal ablation (14, 15), pulmonary metastasectomy (3, 16, 17), and stereotactic body radiation therapy (18).

In our study, the overall diagnostic accuracy of PTNB was 83.3%. Particularly, PTNB had 83.8% sensitivity and 100% specificity for the diagnosis of LM. Smaller lesion size, pneumothorax, and hemoptysis remained significantly associated with an overall nondiagnostic result. Similarly, smaller lesion size, pneumothorax, high-grade pulmonary hemorrhage, and hemoptysis were significantly correlated with unsuccessful biopsies in the diagnosis of LM. Finally, our results highlight the importance of second PTNB and follow-up of nondiagnostic results in cancer patients with suspected LM.

Our results on the diagnostic performance of PTNB for LM suggested a similar

Table 2. Association between diagnosis obtained from biopsy pathology result and final diagnosis (n=108)

	Final diagnosis				
Biopsy pathology result	Lung metastasis	Primary lung cancer	Specific inflammation	Nondiagnostic result	Total
Lung metastasis	57	0	0	0	57
Primary lung cancer	0	16	0	0	16
Specific inflammation	0	0	17	0	17
Nondiagnostic result	11	1	4	2	18
Total	68	17	21	2	108

Data are numbers of biopsies.

Table 3. Comparison between PTNBs with overall diagnostic and nondiagnostic results

Variable	Diagnostic results (n=90)	Nondiagnostic results (n=18)	*p*
Age (years), mean±SD[a]	57.88±13.34	58.56±9.28	0.838
Sex[b]			
Male	51 (56.7)	13 (72.2)	0.335
female	39 (43.3)	5 (27.8)	
Number of lung lesions of the patient[b]			
Solitary	31 (34.4)	9 (50)	0.327
Multiple	59 (65.6)	9 (50)	
Biopsied lesion size (cm)c, median (IQR)	2.7 (1.9, 4.6)	2.3 (1.5, 2.8)	0.014*
Biopsied lesion morphology[d]			
Solid	77 (85.6)	14 (77.8)	0.653
Part-solid	7 (7.8)	2 (11.1)	
Consolidation and cavity	6 (6.7)	2 (11.1)	
Emphysema around biopsied lesion[e]			
Absent	76 (84.4)	14 (77.8)	0.496
Present	14 (15.6)	4 (22.2)	
Patient position[f]			
Supine	36 (40)	11 (61.1)	0.142
Prone	33 (36.7)	6 (33.3)	
Lateral	21 (23.3)	1 (5.6)	
Needle path length (cm), mean±SD[a]	4.83±2.18	5.05±2.09	0.683
Needle-pleura angle (°)[b]			
<90°	49 (54.4)	11 (61.1)	0.795
≥90°	41 (45.6)	7 (38.9)	
Number of needle passes[b]			
1	30 (33.3)	10 (55.6)	0.130
2 and 3	60 (66.7)	8 (44.4)	
Complication[b]	45 (50)	9 (50)	1.000
Pneumothorax[e]	10 (11.1)	6 (33.3)	0.026*
Pulmonary hemorrhage[b]	41 (45.6)	7 (38.9)	0.795
High-grade pulmonary hemorrhage[e]	9 (10)	5 (27.8)	0.056
Hemoptysis[e]	1 (1.1)	3 (16.7)	0.014*

Data are presented as n (%) unless otherwise noted.
PTNB, percutaneous transthoracic needle biopsy; SD, standard deviation; IQR, interquartile range.
[a] Student t test; [b] Continuity correction test; [c] Mann–Whitney U test; [d] Fisher–Freeman–Halton exact test; [e] Fisher exact test; [f] Mann–Whitney U test.
* p <0.05.

rate for the diagnosis of malignant lung lesions as described in previous studies (10, 11, 19). Anna et al. (8) conducted a small-sample study in patients with suspected LM and found the rate of correct diagnosis of metastasis with specific histological typing to be 87%. Additionally, our nondiagnostic biopsy rate within the overall group and among those with a final diagnosis of LM were 16.67% and 16.2%, respectively, consistent with previously reported rates of 1.3%–27.6% in the literature (10, 20, 21). We believe that the nonspecific benign results should also be considered as nondiagnostic, because clinicians still remain confused about planning the next treatment, with LM remaining as a possibility. In our study, 8 patients had second biopsies of the same target when their first biopsy showed nondiagnostic results and 4 of them (50%) were finally diagnosed as LM; there was no increase in the incidence of complications, which is consistent with a prior report (19). If further intervention can be performed, we suggest that a re-biopsy should be considered in all nondiagnostic cases with a history of primary cancer. Furthermore, clinical/radiological follow-up is also important for patients who have small lung lesions that are not suitable for re-biopsy and surgical resection, as many previous studies have acknowledged the importance of follow-up in the final diagnosis of lung malignancy (10, 22, 23).

We found that smaller lesion size was significantly associated with overall nondiagnostic result and unsuccessful biopsies in the diagnosis of LM, which is consistent with findings of previous studies in the diagnosis of lung malignancy (10, 11, 23, 24). It may be more difficult to locate and reach small lesions, the specimen yielding normal lung tissue around the target lesion or inadequate tissue for pathological analysis. In one study, small lesion size (≤20 mm) was an independent risk factor for diagnostic

Table 4. Characteristics in diagnostic successful and unsuccessful biopsies of final diagnosis of lung metastasis

Variable	Successful (n=57)	Unsuccessful (n=11)	*p*
Age (years), mean±SD[a]	56.09±13.16	59.09±10.01	0.476
Sex[b]			
Male	30 (52.6)	9 (81.8)	0.100
Female	27 (47.4)	2 (18.2)	
Number of lung lesions of the patient[b]			
Solitary	19 (33.3)	6 (54.5)	0.305
Multiple	38 (66.7)	5 (45.5)	
Biopsied lesion size (cm)c, median (IQR)	2.9 (1.9, 5.5)	2.3 (1.8, 2.8)	0.047*
Biopsied lesion morphology[d]			
Solid	52 (91.2)	10 (90.9)	0.668
Part-solid	2 (3.5)	1 (9.1)	
Consolidation and cavity	3 (5.3)	0 (0)	
Emphysema around biopsied lesion[b]			
Absent	50 (87.7)	8 (72.7)	0.347
Present	7 (12.3)	3 (27.3)	
Patient position[d]			
Supine	25 (43.9)	6 (54.5)	0.214
Prone	19 (33.3)	5 (45.5)	
Lateral	13 (22.8)	0 (0)	
Needle path length (cm), mean±SD[a]	5.0±2.18	5.10±1.92	0.886
Needle-pleura angle (°)[e]			
<90°	28 (49.1)	8 (72.7)	0.269
≥90°	29 (50.9)	3 (27.3)	
Number of needle passes[b]			
1	19 (33.3)	5 (45.5)	0.500
2 and 3	38 (66.7)	6 (54.5)	
Complication[e]	29 (50.9)	6 (54.5)	1.000
Pneumothorax[b]	7 (12.3)	5 (45.5)	0.019*
Pulmonary hemorrhage[e]	26 (45.6)	5 (45.5)	1.000
High-grade pulmonary hemorrhage[b]	7 (12.3)	5 (45.5)	0.019*
Hemoptysis[b]	1 (1.8)	3 (27.3)	0.012*

Data are presented as n (%) unless otherwise noted.
PTNB, percutaneous transthoracic needle biopsy; SD, standard deviation; IQR, interquartile range.
[a] Student t test; [b] Fisher exact test; [c] Mann–Whitney U test; [d] Fisher–Freeman–Halton exact test; [e] Continuity correction test.
* $p < 0.05$.

failure (20). Moreover, Huang et al. (25) reported diagnostic accuracy of 83.7% for small nodules (≤15 mm) and 96.8% for larger nodules, with high accuracy rates partially attributed to the presence of a bed-side pathologist (26). In our study, diagnostic accuracy of LM was 84.2% for lesions measuring 1.0–2.0 cm without on-site pathologists, which is still a high rate. Some studies (23, 24) suggested that lung lesion size larger than 3 cm or 5 cm could affect diagnostic accuracy, due to a higher necrosis rate. In general, LM is less necrotic, but it should be noted that we should try to sample the solid part of the lesion as much as possible.

PTNB-related complications that were significantly associated with unsuccessful biopsies in the diagnosis of LM included pneumothorax, high-grade pulmonary hemorrhage, and hemoptysis. Pneumothorax during the procedure can cause displacement of the lesion and make needle insertion into the target more difficult, particularly in small lesions. Moreover, unsuccessful biopsies may occur, possibly due to termination of the biopsy procedure, in cases with moderate and severe pneumothorax (27). Takeshita et al. (20) performed CT-guided lung biopsies in 750 patients and found that the presence of pneumothorax during the procedure was an independent risk factor for diagnostic failure. We did not discuss the influence of the severity of pneumothorax because in our study all pneumothorax cases were mild. When there was low-grade hemorrhage during the procedure, which was generally considered to be minor and self-limited, the process could be continued to obtain a specimen in most cases. However, when severe pulmonary hemorrhage or hemoptysis occurred, the hemorrhage obscured the lesion and prevented the needle from being accurately inserted into the lesion, or the operator stopped the process immediately. The alveolar hemorrhage during biopsy significantly increased the likelihood of nondiagnostic results as reported (11). Fontaine-Delaruelle et al. (19) also found that the occurrence of a complication during PTNB remained significantly associated with a false-negative result. Thus, we emphasize the importance of the relationship between complications and nondiagnostic results, and observation of these cases. This study found a significant correlation between high-grade pulmonary hemorrhage and nondiagnostic results; however, very few previous studies have pointed this out.

In our 5-year experience of PTNB, the most common primary malignancies with confirmed LM were colon adenocarcinoma, and pulmonary hemorrhage was the most common complication occurring in 45.6% of our patients with a final diagnosis of LM (31/68), which is reported in the range of 2.9%–54.5% in the literature for core needle biopsies (28). In addition, a large retrospective study reported that the presence of atypical cells in the biopsy sample have a high likelihood of malignancy after nondiagnostic lung biopsies (10). However, in our nondiagnostic cases, the final diagnosis of LM was more often found in patients with nonspecific benign reported on pathology probably due to low number of cases, but also increased attention to such pathological results.

We acknowledge the limitations of our study, the first of which is its retrospective design. Second, possible confounding variables such as technical failure and procedure time were not systematically recorded and therefore not evaluated. Moreover, additional factors (e.g., CT slice thickness, breath-hold or free breathing, difficult location of lesion, operator skill, biopsy type, or needle gauge) that are difficult to assess were not considered in the analysis. Finally, the pathologists did not perform a blind evaluation of the specimen; they were aware of the patient's history of primary malignancy and this may affected the final diagnosis.

In conclusion, CT-guided core needle biopsy of the lung in patients with primary malignancy suspected of lung metastasis has a high diagnostic accuracy, with acceptable PTNB-related complication rates. Smaller lesion size, pneumothorax, high-grade pulmonary hemorrhage, and hemoptysis are significant predictors of unsuccessful biopsies in the diagnosis of LM. We also emphasize the importance of repeat biopsy and follow-up of nondiagnostic results in cancer patients with lung lesion due to the high probability of LM.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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