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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Pre-procedure ^{18}F-FDG PET/CT imaging improves the performance of CT-guided transthoracic biopsy

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PURPOSE

To compare computed tomography (CT)-guided transthoracic lung biopsies (CTLB) with and without pre-procedure ^{18}F-fludeoxyglucose positron emission tomography (^{18}F-FDG PET)/CT images in the diagnosis of pulmonary nodules/masses.

METHODS

This is a case-control study in a single center. The data of patients with a transthoracic lung biopsy guided by CT and pre-procedure ^{18}F-FDG PET/CT (group 2, here called the "PETCTLB" group), including demographics, clinical characteristics, and biopsy-related parameters, were collected. The PET/CT scan was performed within 15 days before the biopsy. The data from patients with CTLB were used as controls (group 1). Biopsies for all patients were performed by the same physician between January 2019 and December 2021. The final diagnosis was based on surgical outcomes, or imaging findings, and the results of at least one 6-month follow-up. The demographics and clinical characteristics of patients, lesions and biopsy-related variables, diagnostic yields, and incidence of complications were compared between the two groups. Two-tailed t-tests were used to compare the mean values in the two independent groups, while categorical variables were compared using the Pearson chi-squared test, and *P* values < 0.05 were considered to be significant.

RESULTS

A total of 84 patients were included, and 84 biopsies of 84 lung nodules/masses were analyzed. The demographics and clinical characteristics of group 2 (n = 39; 21 men; mean age, 63.2 ± 9.29 years) and group 1 (n = 45; 30 men; mean age, 61.2 ± 12.3 years) had no significant difference (*P* = 0.230 and 0.397, respectively). The procedure duration (11.1 ± 3.0 vs. 12.9 ± 3.3 minutes, *P* = 0.008), the number of samples (2.6 ± 0.5 vs. 3.1 ± 0.4, *P* < 0.001), diagnostic accuracy (97.4% vs. 82.2%, *P* = 0.033), and bleeding complication (25.6% vs. 42.2%, *P* = 0.034) of group 2 and group 1 were statistically different.

CONCLUSION

A biopsy guided by CT plus pre-procedure ^{18}F-FDG PET/CT (PETCTLB) is a safe procedure that can provide a precise diagnosis in the majority of lung nodules/masses. It has better diagnostic performance than CTLB.

KEYWORDS

^{18}F-FDG PET/CT, CT-guided transthoracic biopsy, lung, nodule, mass

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Lung cancer is currently the leading cancer in incidence and cancer-related mortality worldwide,[1] and tumor screening is an important approach to its early diagnosis and management.[2] Lung nodules/masses are frequent findings on radiography and/or computed tomography (CT) scans. With the gradual promotion and popularization of low-dose CT as a device for lung cancer screening, a large number of suspicious lung nodules/masses are being discovered. The biggest challenge in the management of suspected lung nodules/masses is the need to distinguish malignant and benign occurrences, as malignant lesions are treated using a completely different strategy when compared with benign lesions.

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Common methods for clinical diagnosis of malignant lung nodules/mass include the detection of serum biomarkers (DSB), exfoliative sputum cytological analysis (ESC), chest imaging, fiberoptic bronchoscopy examination (FBE), and transthoracic lung biopsy.[3] Tumor cells can be found only in a small number of patients with lung cancer using ESC;[4] the application of FBE (including endobronchial ultrasound-guided transbronchial needle aspiration) is restricted by its limited scope;[5] DSB and imaging fail to obtain histological and cytological evidence in the diagnosis. A computed tomography-guided transthoracic lung biopsy (CTLB) is a minimally invasive procedure and widely implemented for the histologic analysis of suspected lung lesions, but may be inconclusive. Strategies that improve CTLB performance are required. Both CTLB and ^{18}F-fludeoxyglucose positron emission tomography (^{18}F-FDG PET)/CT are conducted routinely in patients with suspected pulmonary nodules/masses for diagnosis and staging. ^{18}F-FDG PET/CT metabolic information about lung lesions, and several studies have explored its use in lung biopsies.[6,7] In the present study, we aim to evaluate the performance of CTLB without and with pre-procedure ^{18}F-FDG-PET/CT images [i.e., a transthoracic lung biopsy by CT plus pre-procedure ^{18}F-FDG PET/CT (PETCTLB)].

Main points

- Compared with a computed tomography (CT)-guided biopsy, a biopsy guided by CT plus pre-procedure ^{18}F-fludeoxyglucose positron emission tomography (^{18}F-FDG PET)/CT can offer better diagnostic performance.
- ^{18}F-FDG PET/CT can distinguish between viable tumors and necrosis or fibrosis in residual masses.
- The complementary morphological and metabolic data (using 40% of maximum standardized uptake value as the threshold) can be relevant for defining biopsy targets.
- Marking the target of a percutaneous biopsy in the ^{18}F-FDG PET/CT images before puncture biopsy can improve the success rate of a CT-guided puncture biopsy.

Methods

This is a retrospective case-control study in a single center concerning the period between January 2019 and December 2021. The Research Ethics Committee of the Institutional Ethics Committee of Jiangxi Provincial People's Hospital (the First Affiliated Hospital of Nanchang Medical College) has confirmed that no ethical approval is required. Individual consent for this retrospective study was exempted.

Inclusion and exclusion criteria

All patients were considered for a biopsy due to pulmonary nodules. All enrolled patients had signed written informed consent forms for the biopsy and had undergone a routine blood test, coagulation function test, renal and hepatic function test, and electrocardiogram before the biopsy. The inclusion criteria of the PETCTLB patients were as follows: PET/CT imaging was performed within 15 days before the biopsy; no suspicious distant metastases were found on the PET/CT images; the lesion had high metabolic activity (the FDG uptake in the lesion was higher than that in the liver); all biopsies were performed by the same physician and guided by the same PET/CT scanner. The exclusion criteria were as follows: patients with preoperative pneumothorax or hemothorax; patients with obstructive emphysema before the biopsy; patients with incomplete medical records, including follow-up data. The inclusion criteria of the patients undergoing CTLB were as follows: as the control group, the CTLB was performed on the same days on which PETCTLB was performed; the CTLB was performed by the same practitioner who performed the PETCTLB. The exclusion criteria were the same as the PETCTLB exclusion criteria. The patients with CTLB and PETCTLB each formed a consecutive series.

The histological specimens were reviewed, and the pathological diagnoses of the histologic grades and types were confirmed by a pathologist.

The patients who had undergone CTLB were assigned to group 1 (the control group), and the patients who had undergone PETCTLB were assigned to group 2 (the study group).

Computed tomography-guided transthoracic lung biopsy

A CTLB is a commonly performed and minimally invasive diagnostic procedure for pulmonary nodules and masses.

Group 1: all relevant laboratory examinations and imaging (not including ^{18}F-FDG PET/CT) were performed before the biopsy to exclude patients with contraindications to transthoracic biopsy; the CT technician trained the patients to breath-hold to ensure that they could cooperate with the biopsy; the principles of the biopsy pathway selection were the minimum vertical distance, no big blood vessel on the pathway, and easy for the patient to cooperate. The entry site, depth, and inclination angle to direct the needle into the lesion were determined by initial low-dose CT localization scans (tube voltage 120 kV, tube current 80–100 mA, reconstruction thickness 5.0 mm. PET/CT scanner; GE Healthcare, USA, Discovery STE) with a gradient grid metallic marker fixed on the patient's body surface (Figure 1). The biopsy was performed using an 18-gauge × 160 mm co-axial core needle.

Computed tomography-guided transthoracic lung biopsy with pre-procedure ^{18}F-FDG PET/CT

Group 2: all the patients underwent an ^{18}F-FDG PET/CT examination. PET/CT imaging: all patients were instructed to fast for at least 6 hours before the ^{18}F-FDG injection, and their blood glucose levels remained in a normal range. Each patient was injected via a venous line with an activity of mean 282 MBq (5.5 MBq/kg) ^{18}F-FDG. The patient was rested

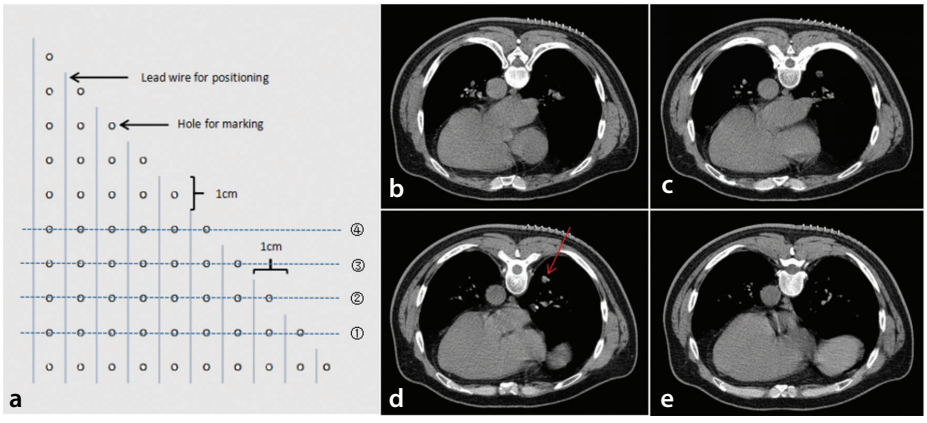

Figure 1. Schematic diagram of body surface gradient grid locating technique. The dashed lines ①–④ on the locator correspond to the slices **(b-e)**, respectively, on the computed tomography (CT) scan. **(a)** Homemade body surface gradient grid locator; **(b-e)** CT localization slices; red arrow, indicating the biopsy path.

for a scheduled 45–60-minute uptake period, followed by image acquisition on a PET/CT scanner (Discovery STE; GE Healthcare, USA). No oral or intravenous contrast was administered. A CT scan from the vertex of the skull to the upper thigh, with the patient supine, was performed for PET attenuation correction and anatomical location. The CT parameters were as follows: 120 kV, automatic tube current, and CT reconstruction thickness of 3.75 mm. The PET data were acquired covering the same area in three-dimensional mode, the acquisition time per bed position was 2.5 or 3.0 minutes, with a total of 6–8 bed positions acquired. Two-dimensional PET images were reconstructed with a slice thickness of 3.75 mm using the ordered subset expectation maximization iterative image reconstruction method. Forty percent of the maximum standardized uptake value of the lesion was used as a threshold to delineate the target on axial, coronal, and sagittal fusion images (Figure 2); the optimal entry sites and pathway were then determined according to the metabolic distribution and the shortest distance from the surface puncture site. The remaining procedures were the same as in group 1.

The depth of the needle was measured from the pleura to the edge of the intrapulmonary lesion along the needle path (Figure 3a).

After the biopsy was completed, a low-dose chest CT scan was performed to observe whether there were complications, such as pneumothorax or lung bleeding (Figure 3b), and corresponding treatment was carried out.

Biopsy results

(1) Definition of "diagnosis": tumor cells (primary or metastatic), mycobacterium tuberculosis, and fungi were found; (2) definition of "possible diagnosis": the pathological diagnosis of the specimen was non-specific inflammation or granuloma; (3) definition of "biopsy failure": no pathological tissues were observed, or only normal lung, diaphragm, and liver tissues were observed.

The final diagnosis was based on surgical outcomes or imaging findings and the results of a 6-month follow-up.

Follow-up

All patients were routinely followed up. The patients in this study were followed up for 6–28 months (mean: 12.8 ± 9.3 months). The follow-up methods included telephone or web chat (n = 47), outpatient examination (n = 19), and assessment of inpatient medical records (n = 4). Patients who did not have surgery (n = 35) were followed up for at least 6 months, during which at least one CT was performed. The follow-up time was calculated from the biopsy date to the last CT follow-up date of patients; the mean CT follow-up time was 6.2 months (range: 3–11 months). When the suspected lung nodules/masses were confirmed to be stable in size and features, or subsided on CT, it was considered to be truly benign.

Statistical analyis

The measurement data was described as mean ± standard deviation (SD) and categorical variables were reported as n (%). Statistical analysis was performed using SPSS v19 statistical software. The t-test was used to compare continuous variables in the groups. Pearson's chi-squared test or Fisher's exact test was used to compare categorical variables in the groups. The significance level was established as $\alpha = 0.05$.

Results

Demographics and clinical characteristics of the eligible patients

A total of 84 patients were finally included in this study, including 51 men and 33 women, with a mean age of 61.2 ± 12.3 years. Of 84 biopsy lesions, 17 were benign and 67 were malignant. The longest diameter of the lesion measured in the axial CT ranged from 10 mm to 68 mm, with a mean of 33.1 ± 13.9 mm. A CTLB was performed in 45 (53.6%) patients (group 1) and PETCTLB in 39 (46.4%) patients (group 2). All biopsies were completed between January 2019 and December 2021. The demographic and clinical data of the two groups are summarized in Table 1 and show that there was no significant difference between the two groups ($P > 0.05$).

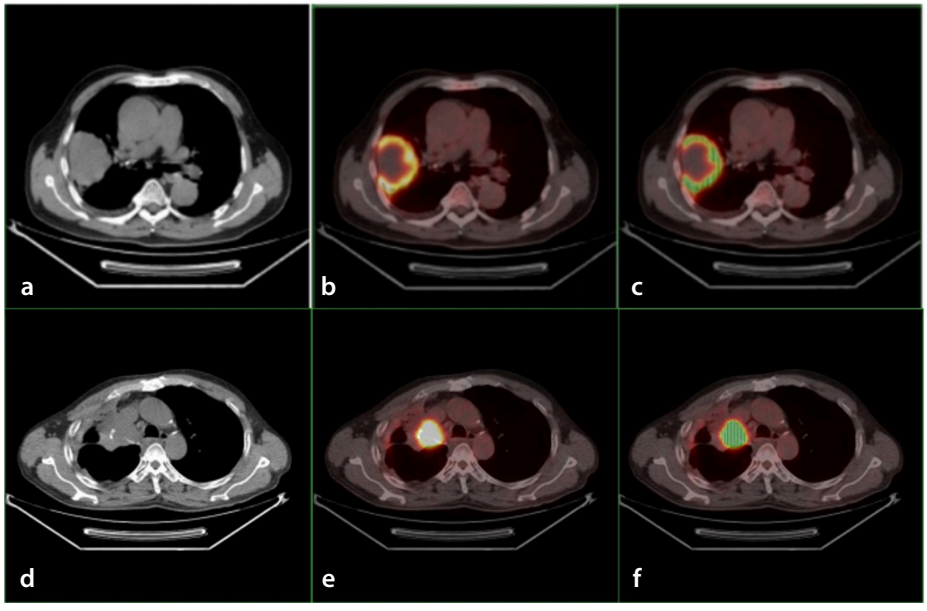

Figure 2. Metabolic distribution of lung lesions on positron emission tomography/computed tomography image. **(a-c)** An adenocarcinoma of the right upper lung; **(d-f)** postoperative recurrence of the right upper lung squamous cell carcinoma. Left: axial CT; middle: fused image; right: the biopsy area represented by green on the fused image.

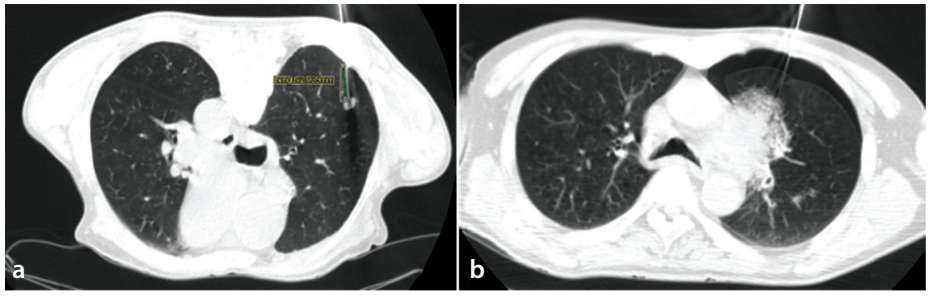

Figure 3. Needle path length and complication. **(a)** Needle path length through the ventilated lung, measured from the pleura to the edge of the lesion; **(b)** pneumothorax and pulmonary hemorrhage.

The number of needle adjustments, the number of samples, and the procedure time

The needle placement efficiency for obtaining specimens was evaluated by the number of needle adjustments and the procedure time.

The mean number of needle adjustments for each patient was (3.3 ± 1.0 SD, range: 2–6) for PETCTLB procedures and (3.6 ± 1.1 SD, range: 2–8) for CTLB procedures. A comparison of the two groups showed no significant statistical difference between them ($P > 0.05$). The mean number of samples was (2.6 ± 0.5 SD, range: 2–3) in group 2 and (3.1 ± 0.4 SD, range: 2–5) in group 1, respectively; the difference between the two groups was significant ($P < 0.05$). The procedure time was calculated from the start of the localization scan to the acquisition of the specimen. The mean procedure time was (11.1 ± 3.0 SD, range: 7–17) minutes in group 2 and (12.9 ± 3.3 SD, range: 7–19) minutes in group 1; a significant statistical difference was observed in the comparison of the procedure time in the two groups ($P < 0.05$, Table 2), with the procedure time in group 2 being less than that in group 1.

Initial pathological results and complications

In group 1, the initial pathological results in 37 (82.2%) patients were consistent with the final diagnosis, biopsies failed in 1 patient, and no malignant cells were observed in the samples of 6 patients with malignancies. In group 2, the initial pathological results in 38 (97.4%) patients were consistent with the final diagnosis, and only one case of pulmonary tuberculosis was misdiagnosed as non-specific inflammation. The difference between the two groups was statistically significant for them ($P < 0.05$), and the diagnostic coincidence rate was higher in group 2 than in group 1. Developed pneumothorax and/or subcutaneous emphysema were observed in 10 (22.2%) patients of group 1 and in 9 (23.1%) patients of group 2, during or after the procedure; no statistically significant differences were observed between the two groups ($P > 0.05$). However, the incidence of hemorrhage (intrapulmonary hemorrhage and/or hemothorax) during or after the biopsy was observed in 13 (42.2%) patients of group 1 and 4 (25.6%) patients of group 2, and a significant statistical difference was observed between the two groups ($P < 0.05$); bleeding complications occurred less in group 2 than in group 1. One patient in group 1 developed massive hemoptysis (single hemoptysis >100 cc), there were four cases of massive pneumothorax (pneumothorax volume >30% of volume thoracic cavity) in each group, and no procedures-related deaths were reported in either group.

Table 1. Demographic data and clinical characteristics of the two groups

	CTLB (group 1) n = 45	PETCTLB (group 2) n = 39	*P* value
Age (years)	61.2 ± 12.3	63.2 ± 9.3	0.397
Sex, male, n (%)	66.7% (30/45)	53.8% (21/39)	0.230
Lesion sites			
U/M lobes	26	24	0.726
Lower lobe	19	15	
LD of lesion (mm)	32.8 ± 14.0	33.4 ±13.9	0.837
Lesion nature			
Benign	10	7	0.627
Malignant	35	32	

CTLB, computed tomography guided transthoracic lung biopsy; PETCTLB, computed tomography guided transthoracic lung biopsy with pre-procedure ^{18}F-FDG PET/CT images; UM lobes, upper and middle lobe of the lung; LD, the longest transverse diameter in the axial computed tomography plane; ^{18}F-FDG PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography.

Table 2. Comparison of the procedure and results of biopsies between the two groups

	CTLB (group 1) n = 45	PETCTLB (group 2) n = 39	*P* value
Number of needle position checks	3.6 ± 1.1	3.3 ± 1.0	0.329
Procedure time (minutes)	12.9 ± 3.3	11.1 ± 3.0	0.008
Needle path length (mm)			
≤20	18	17	0.739
>20	27	22	
Number of samples	3.1 ± 0.4	2.6 ± 0.5	<0.001
Diagnostic accuracy of the biopsy (cases)	82.2% (37/45)	97.4% (38/39)	0.033
Complications, % (cases)			
Subcutaneous emphysema and/or pneumothorax	22.2% (10/45)	23.1% (9/39)	0.926
Intrapulmonary hemorrhage and/or hemothorax	42.2% (13/45)	25.6% (4/39)	0.034
Biopsy failure, % (cases)	4.4% (2/45)	0% (0/39)	0.497

CTLB, computed tomography guided transthoracic lung biopsy; PETCTLB, computed tomography guided transthoracic lung biopsy with pre-procedure ^{18}F-FDG PET/CT images; needle path length, needle path length through the ventilated lung, measured from the pleura to the edge of the lesion; ^{18}F-FDG PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography.

Discussion

In the present study, we compared the outcomes of PETCTLB and CTLB. We found that (1) the mean procedure time was less (11.1 ± 3.0 vs. 12.9 ± 3.3), (2) the mean number of samples was less (2.6 ± 0.5 vs. 3.1 ± 0.4), (3) the diagnostic accuracy was higher (97.4% vs. 82.2%), and (4) bleeding complications occurred less (25.6% vs. 42.2%) in the PETCTLB group than in the CTLB group, respectively. These results suggest that PETCTLB is a feasible approach that improves the diagnostic performance of a transthoracic lung biopsy, thus providing greater potential benefits for patients than CTLB.

As a reliable and safe procedure for the diagnosis of indefinite pulmonary lesions, CTLB, which allows both histological and biomolecular study, is a standard sampling technique and is widely used.[8] Although it has a higher accuracy,[1,9] the inhomogeneity (such as necrotic and cystic area) of lung nodules/masses, atelectasis or consolidation, obstructive pneumonia, and peripheral region of reactive inflammatory tissue inevitably leads to an increase in false negatives. Since histological cuts of biopsies can only obtain a small part of the lesion for analysis, CTLB of lung nodules/masses may be subject

to sampling errors.[10] There are more advantages to PETCTLB than CTLB, since PET/CT can show the distribution of metabolic activity in the lesion, providing a well-defined biopsy target and effectively avoiding areas of necrosis, cystic degeneration, atelectasis, and some inflammation, leading to higher accuracy.

There is currently no consensus or guidelines for the number of samples to be taken, but the number of samples taken is usually 3–4,[11] and to obtain reliable samples during CTLB, the sampling sites are often scattered in the lesion. However, in the metabolic distribution provided by PET/CT images, the biopsy target is specific, the biopsy sites selected are relatively concentrated, and with the accumulation of technique experience, a smaller number of samples may be required, thus reducing the adjustment range of inclination of the needle and shortening the procedure time. In the present study, comparing the number of samples taken by the two groups, the difference was statistically significant, and the mean number of samples taken in group 2 was less than that in group 1; the procedure time and the bleeding complication incidence were also reduced correspondingly.

Biopsies guided by PET/CT can be broadly divided into real-time PET/CT-guided biopsies and PETCTLB.[6,11,12] One study[13] showed that the accuracy of real-time PET/CT-guided lung biopsies was higher than that of CTLB, reducing re-biopsies. However, there are currently no guidelines on real-time PET/CT-guided biopsies, and they also carry some radiation risks for the operators and patients. ^{18}F-FDG PET/CT has been widely used in the evaluation of tumors, and despite patients being inevitably also exposed to a certain amount of radiation, it has been proven to be safe. A study of PET/CT examinations in children showed that a proper scanning regimen can minimize the radiation dose received during the examination.[14] Lin et al.[11] compared the results of intraprocedural CT-guided biopsies with prior PET/CT fusion images and CT-guided biopsies alone, showing no significant difference in procedure time, but there was a higher diagnostic yield for malignancy in the fusion images group than that in the routine group. Our study is a more comprehensive comparison of CTLB and PETCTLB. Although PETCTLB requires less time and fewer samples, it has higher diagnostic accuracy and fewer bleeding complications.

In group 2, the low incidence of bleeding may be because the sample was taken in the middle of the tumor tissue rather than the edge.

In addition, we also highlight herein the importance of body surface determination during a transthoracic biopsy. In the present study, we used a self-made gradient grid locator. Verified through clinical application and evaluation, it is simple, practical, and effective in ensuring the stability and reliability of body surface positioning.

There are several limitations in our study. First, this is a single-center retrospective study. Second, PET/CT is not a routine item covered by health insurance in China, and a potential selection bias is inevitable for the patients in PETCTLB. Third, in both group 1 and group 2, the range of sizes of the pulmonary lesions was large.

In conclusion, compared with CTLB, PETCTLB can reduce the number of samples taken, shorten procedure time, improve diagnostic yield, and reduce bleeding complications; it is a safe procedure that can provide a precise diagnosis in the majority of lung nodules/masses, and it has a better diagnostic performance.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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