Factors affecting the accuracy and safety of computed tomography-guided biopsy of intrapulmonary solitary nodules ≤30 mm in a retrospective study of 155 patients

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Abstract. Computed tomography (CT)-guided percutaneous fine needle biopsy is a common method for lung biopsy. The objective of this study was to investigate factors affecting the accuracy and safety of CT-guided percutaneous lung biopsy of nodules ≤30 mm in diameter. Between January 2013 and March 2014, 155 patients underwent a CT-guided percutaneous biopsy procedure on an intrapulmonary solitary nodule measuring ≤30 mm in diameter. Prospectively collected data were retrospectively reviewed and examined for the influence of clinical and pathological characteristics (age, gender, smoking status, adhesion of nodule to the pleura, puncture depth, nodule size and time of biopsy) on the accuracy of biopsy and incidence of pneumothorax and hemorrhage. The accuracy of CT-guided biopsy was 90.3% (140/155). Biopsies predominantly contained lung adenocarcinoma (114/140; 81.4%) or squamous cell carcinoma of the lung (10/140; 7.1%). Accuracy was significantly dependent on nodule size, ranging in accuracy from 85 to 97% for patients with nodule diameters of ≤20 or 21-30 mm, respectively (P<0.05). Pleural adherence of the nodule significantly increased the accuracy of the biopsy (P<0.05). Patients with a nodule of 11-20 mm in diameter had a significantly higher incidence of pneumothorax compared with patients with a smaller nodule (P=0.013). In conclusion, the nodule size and adhesion to the pleura influenced the accuracy of CT-guided biopsy of intrapulmonary nodules that were ≤30 mm in diameter. Nodule size may also affect the incidence of severe complications. CT-guided percutaneous lung biopsy has a high accuracy and is easy and safe to conduct for intrapulmonary solitary nodules of ≤30 mm in diameter.

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Introduction

The frequency of diagnosing small nodules in the lungs by biopsy is increasing due to a high incidence of lung cancer and the requirement for early diagnosis. Computed tomography (CT)-guided percutaneous fine needle biopsy is a common method for harvesting the lesion with adjacent lung tissue (1-3), thereby facilitating histological analysis of the pathology of the nodule (4,5). Solitary pulmonary nodules >30 mm in diameter are predominantly malignant (6,7). Malignant diagnoses of solitary pulmonary lesions <20 mm in diameter range from 60 (8) to 67% (9) and have a lower detection rate due to the absence of typical features, such as Spicule sign or Pleural indentation, in imaging examinations and limitations in bronchoscopy and sputum cell screening. Factors that markedly improve the accuracy of diagnosis are larger lesions (>10 mm) and a shorter needle path (≤40 mm) (10). In addition, dynamic observation of small nodules may result in a psychological burden on patients, and clinical resection of these small nodules may be radical. Resection of these nodules may not only cause physical injury to the patients, but also increase medical costs; therefore, qualitative diagnosis is important for nodules ≤30 mm in diameter.

CT-guided percutaneous fine needle biopsy is an economic method that rarely causes metastasis (11,12). The most common complications of CT-guided percutaneous fine needle biopsy include pneumothorax and hemorrhage. The rate of pneumothorax ranges from 4 to 17% (7) in patients who receive CT-guided biopsy for large pulmonary lesions (mean diameter, 36 mm; range, 5-136 mm) (4,13). The rate of pneumothorax following CT-guided percutaneous core needle biopsy of small lesions (<20 mm in diameter) varies widely, ranging from 10 to 35% (8-10,14,15). A high rate of pneumothorax (52.7%) has been reported following CT-guided fine needle aspirate biopsies of lesions ≤10 mm in diameter (16). Secondly, the rate of hemorrhage or hemoptysis ranges from 4 (17) to 27% (13,15) and can be influenced by the proximity of the nodule to the pulmonary hilum. Air embolisms and/or infarctions are rare complications in patients with CT-guided biopsies.

The wide range of accuracy and complication rates suggests that different instruments, operators and patient populations may contribute to the heterogeneity. Therefore, comparison of the effects of lesion sizes on the accuracy of CT-guided biopsy capture in patients without emphysema, pulmonary bullae, pulmonary fibrosis or interstitial lung diseases by an experienced team from a single facility may minimize confounding factors. It was hypothesized that the lesion size, proximity to pleura and the length of the needle path may affect the accuracy of CT-guided biopsy and/or the frequency of various complications. Therefore, the present retrospective study was undertaken to analyze the clinical outcomes of 155 patients who received CT-guided percutaneous lung biopsies of intrapulmonary solitary nodules of ≤30 mm in diameter between June 2013 and March 2014 at the Department of Radiology, Shengjing Hospital of China Medical University (Shenyang, China). Patients were grouped by lesion size to explore the factors affecting the accuracy of biopsy of intrapulmonary solitary nodules of ≤30 mm in diameter and the safety of the procedure. The findings may provide insights for the clinical use of CT-guided percutaneous fine needle biopsy for nodules ≤30 mm in diameter.

Materials and methods

Ethics statement. The Ethics Committee Institutional Review Board of Shenyang Hospital of China Medical University approved the present retrospective study (IRB2016PS192K). The informed consent requirement was waived.

Patients. Prospectively collected data on the medical records of 450 patients admitted to the hospital between June 2013 and March 2014 for lung biopsy were retrospectively reviewed. Inclusion criteria were preoperatively evaluated by enhanced CT. In order for the patients to be included, CT results had to show that bronchoscopy was not possible; nodules were free of major vessels; CT-guided biopsy of a single, intra-pulmonary, solid tumor of ≤30 mm in diameter had been conducted; and absence of prior therapy of intra-pulmonary nodules. Additionally, patients were required to be >18 years of age, with normal clotting and platelet function pre-biopsy and have sufficient tissue for pathological examination. Exclusion criteria included: Patients without pre-operative enhanced CT records; blood-rich nodules; two or more nodules; ground-glass opacity in the intrapulmonary solitary nodule (18); and major vessel involvement in the nodule. Patients were separated into three age subgroups (≤41, 41-67 and ≥67 years) three puncture depth subgroups (≤25.6, 25.6-34.6 and ≥34.6 mm).

In order to ensure the final results were reliable and convincing, two radiologists evaluated the image findings and confirmed that the solitary nodules were ≤30 mm in diameter. Following biopsy, imaging re-examination was performed. In total, 155 patients were included in the final analysis. Patients with extensive lung disease (including emphysema, pulmonary bullae, pulmonary fibrosis and interstitial lung diseases), and patients with coagulation abnormalities and bleeding-associated diseases were not included in the present study.

A routine chest X-ray was performed 10 min after biopsy to confirm the absence of complications, such as pneumothorax or bleeding. Patients were monitored for 24 h after surgery and delayed complications were determined according to the vital signs.

Instruments and methods. A Philips MX8000 IDT 16-row multislice spiral CT scanner (Philips Medical Systems, Inc., Bothell, WA, USA) and a MAX-CORE biopsy instrument (20 G/16 cm) (C.R. Bard, Inc., Murray Hill, NJ, USA) were utilized for transverse scanning by spiral CT and biopsy, respectively. The depth and angle of the needle were recorded prospectively and were measured retrospectively from images exhibiting the needle. The preoperative enhanced CT scan recorded the position of the major blood vessels. The site of needle puncture, puncture route, puncture depth and direction were calculated according to the findings in the preoperative chest enhanced CT scan, and followed the principle of the shortest distance and an angle between the pleura and needle as close as possible to 90˚ (19,20). CT scan images were used to identify the presence of pneumothorax prior to marking the site of needle insertion. For patients with pleural adhesion caused by tuberculosis (TB), a real-time CT scan was utilized to ensure the chosen needle path avoided the TB-induced adhesion region. The site of puncture was marked with lead. Patients breathed freely in the optimized prone, supine or lateral position and a 19-G locating needle was inserted into the proximal end of the nodule. Subsequent to the confirmation of needle location, the needle was withdrawn and a BARD 20-G needle was used for biopsy 2-3 times until sufficient tissue for further experiments was obtained. Biopsy tissue was subjected to immediate cytological evaluation by a technician with 15 years of experience to ensure there was sufficient tissue for adequate analysis. Tissues were subsequently fixed in formaldehyde and processed for pathological examination.

Pathological examination and diagnostic accuracy of CT-guided biopsy capture. Two pathologists, each with 25 years of experience, examined every whole biopsy specimen obtained from the first puncture for pathological characteristics, such as atypical adenomatous hyperplasia, squamous cell carcinoma, adenosquamous carcinoma and infectious nodules. Both pathologists agreed with the findings. A biopsy specimen with a pathological characteristic was scored as a successful biopsy. When a first puncture biopsy showed findings of only necrotic tissues or normal lung tissues, it was scored as a biopsy failure.

Diagnostic criteria of pulmonary complications. For the present study, two clinicians were invited to review and evaluate the postoperative images to assure the reliability of complication identification. Immediately following surgery, CT imaging was performed by two physicians to examine the puncture site for complications. A third physician was consulted in the case of disagreement. Symptomatic pneumothorax (referred to as pneumothorax in the present study) was defined as: The presence of free gas in the pleural cavity with no intrapulmonary hemorrhage and no intrapleural hemorrhage; the presence of clinical symptoms (chest tightness, shortness of breath within 24 h and unilateral auscultation breath sounds); and X-ray confirmation after 24 h. Hemorrhage was defined as the presence of intrapulmonary bloody exudate or intrapleural bloody fluid, with no free gas in the pleural cavity. Hemorrhage concomitant with pneumothorax was defined as free gas within the pleural cavity and intrapulmonary hemorrhage and/or intrapleural bloody fluid. Hemoptysis was defined as the presence of >10 ml of blood in the sputum and/or spit.

Statistical analysis. The cut-off points that defined the three age subgroups (≤41, 41-67 and ≥67 years) and three puncture depth subgroups (≤25.6, 25.6-34.6 and ≥34.6 mm) were calculated as the mean ± one standard deviation. Puncture depth was an indicator of the nodule's proximity to the pulmonary hilum. Patients with a pathological characteristic in their biopsy tissue were presented as counts and percentages within associated factors. Chi-square or Fisher's exact tests were performed to investigate the correlation between the success (and non-success) of puncture and the associated factors, such as gender, age and tumor diameter. The pleural-lesion angle was presented as the mean ± one standard deviation and a two-tailed, independent *t*-test was performed to compare the differences between the successful and non-successful punctures. Univariate logistic regression analyses were performed to identify the factors associated with the success of puncture. P<0.05 was considered to indicate a statistically significant difference. SPSS 22.0 statistical software (IBM SPSS, Armonk, NY, USA) for Windows was used for statistical analysis.

Results

Patients. Medical records of 155 patients (128 smokers and 27 non-smokers) diagnosed with an intrapulmonary solitary nodule were retrospectively reviewed and the images and biopsy slides were re-examined. The 105 males and 50 females had a mean age of 54±13 years (range, 21-91 years). The mean diameter of the solitary nodules examined was 19.8±6 mm (range, 6-30 mm). The mean biopsy depth, which was determined as the distance between visceral pleura and outside border of nodules, was 25.6±9 mm (range, 6-78 mm). The mean number of biopsies per person was 2±1 (range, 1-6). A single puncture event (n=25) yielded an 86.2% [95% confidence interval (CI): 67.43-95.49%] accuracy of diagnostic CT-guided biopsy capture, and two to three punctures (n=111) demonstrated a 91.7% (95% CI: 84.96-95.75%) diagnostic accuracy of the CT-guided capture (P=0.331). Insertion of a chest tube was not required for any of the patients and no patients experienced an air embolism.

Pathological findings were detected in 140 (90.3%) of 155 biopsies, and these were defined as successful biopsy punctures. Regardless of their gender of age, 90.3% of patients exhibited pathology in their biopsies (Table I). The diameter of the tumor and pleural adhesiveness were significantly correlated with the success or non-success of the puncture. The percentage of successful punctures was significantly higher in patients with a tumor diameter of 21-30 mm [97.01% (95% CI: 88.68-99.48%)] compared with those with a tumor diameter of ≤10 [85.71% (95% CI: 42.00-99.25%)] and 11-20 mm [85.19% (95% CI: 75.16-91.79%)] (P=0.049). The percentage of successful punctures was significantly higher in patients with negative pathological findings in pleural adhesiveness [100% (95% CI: 86.27-100%)] compared with those subjects with positive pathological results [87.9% (95% CI: 80.53-92.84%); P=0.042]. The puncture success rate of the puncture depth of 25.6-34.6 mm was higher [96.6% (95% CI: 87.05-99.4%)] than the shallower or deeper punctures; however, the differences observed between the depths did not reach statistical significance. The puncture success rate was 91.74% (95% CI: 84.96-95.75%) with puncture repetition of 2-3 times, which was greater than those with punctures performed once or >3 times. The mean pleural lesion angle was 61.29˚ in subjects with successful puncture (Table I).

Table I. Baseline distribution of successful biopsies.

Variable	Unsuccessful	Successful	P-value
Total	15	140	
Gender			0.285
Male	12 (11.43)	93 (88.57)	
Female	3 (6.00)	47 (94.00)	
Age (years)			0.055
≤41	4 (17.39)	19 (82.61)	
41-67	11 (10.78)	91 (89.22)	
≥67	0 (0.00)	30 (100.00)	
Diameter of tumor (mm)			0.049[a]
≤10	1 (14.29)	6 (85.71)	
11-20	12 (14.81)	69 (85.19)	
21-30	2 (2.99)	65 (97.01)	
Pleural adhesiveness			0.042[a]
+	15 (12.1)	109 (87.9)	
-	0 (0.00)	31 (100.00)	
Puncture depth (mm)			0.088
≤25.6	9 (12.00)	66 (88.00)	
25.6-34.6	2 (3.45)	56 (96.55)	
≥34.6	4 (18.18)	18 (81.82)	
Puncture times			0.331
1	4 (13.79)	25 (86.21)	
2-3	10 (8.26)	111 (91.74)	
>3	1 (20.00)	4 (80.00)	
Pleural-lesion angle[b]	59.67±9.32	61.29±12.19	0.617

Data are presented as N or N (%), as appropriate. [a]P<0.05, significant difference according to puncture success. [b]Pleural-lesion angle was presented as the mean ± standard deviation and analyzed with independent *t*-test to compare success of puncture rate with unsuccessful puncture rate.

Factors associated with successful biopsy. The factors associated with successful biopsy that were examined in the present study did not reach statistical significance in the univariate and multivariate logistic analysis (P>0.05; Table II).

Diagnoses and complication rates. The predominant diagnosis of the successful biopsies was cancer [94.3% (95% CI: 88.69-97.32%)], particularly adenocarcinoma of

Table II. Factors associated with successful puncture.

	Univariate		Multivariate	
Variable	OR (95% CI)	P-value	OR (95% CI)	P-value
Gender				
Male	0.49 (0.13-1.84)	0.293	0.51 (0.13-2.08)	0.352
Female	Ref		Ref	
Age	1.04 (1.00-1.08)	0.076	1.04 (0.99-1.09)	0.093
Diameter of tumor	1.09 (0.99-1.2)	0.071	1.08 (0.97-1.21)	0.157
Pleural-lesion angle	1.01 (0.97-1.06)	0.615	1.02 (0.97-1.09)	0.419
Pleural adhesiveness				
+	NA		NA	
-	Ref		Ref	
Puncture depth (mm)	1.01 (0.95-1.07)	0.760	1.01 (0.95-1.08)	0.733
Puncture times				
1	Ref		Ref	
2-3	1.78 (0.51-6.13)	0.363	1.44 (0.36-5.72)	0.609
>3	0.64 (0.06-7.29)	0.719	0.73 (0.05-10.42)	0.813

OR, odds ratio; CI, confidence interval; NA, non-available estimate; Ref, reference.

the lung [81.4% (95% CI: 73.79-87.9%)] (Table III). Four successful CT-guided percutaneous lung biopsies of solitary pulmonary lesions with diameters of 6, and 6 mm are shown in Figs. 1 and 2, respectively.

The incidences of pneumothorax, bleeding and pneumothorax plus bleeding in the successful puncture subjects were 20 (95% CI: 13.91-27.78%), 10 (95% CI: 5.78-16.51%) and 7.14% (95% CI: 3.67-13.08%), respectively. The incidences of pneumothorax, bleeding and pneumothorax plus bleeding in the patients with the non-successful biopsies were 20 (95% CI: 5.31-48.63%), 13.3 (95% CI: 2.34-41.61%) and 0% (95% CI: 0.00-25.35%), respectively (Table IV). No patients experienced hemoptysis and no patients received a chest tube (i.e. chest tube rate is 0). The following factors were examined for their potential effect on the development of pneumothorax, bleeding and pneumothorax plus bleeding: Lesion size; pleural adhesion; puncture depth; and number of punctures (Table IV). The lesion size was significantly associated with the development of pneumothorax, bleeding, and pneumothorax plus bleeding (P=0.013). The highest incidence of pneumothorax occurred in the 11-20 mm lesion size group [23.19% (95% CI: 14.22-35.18%)]. The highest incidence of bleeding occurred in the ≤21-30 mm lesion size group [16.92% (95% CI: 9.14-28.68%)]. The highest incidence of pneumothorax plus bleeding was observed in patients with lesions <10 mm in diameter [33.33% (95% CI: 6.00-75.89%); P=0.013; Table IV). The incidences of pneumothorax, bleeding and pneumothorax plus bleeding were not significantly associated with pleural adherence, puncture depth or number of punctures (P>0.05; Table IV).

Table III. Pathological findings in subjects with a successful biopsy.

Variable	N	Incidence rate (%)
Pathology		
Adenocarcinoma	114	81.4
Squamous cell carcinoma	10	7.1
Alveolar cell carcinoma *in situ*	1	0.7
Malignant mesothelioma	1	0.7
Small cell lung cancer	1	0.7
Lung metastasis	4	2.9
Adenosquamous carcinoma	1	0.7
Chronic inflammation	4	2.9
Pulmonary tuberculosis	3	2.1
Coccidioidomycosis	1	0.7

Discussion

The present retrospective study of 155 patients demonstrated that CT-guided percutaneous lung biopsy of intrapulmonary solitary nodules of ≤30 mm in diameter had a high accuracy rate (90.3%), which is consistent with the findings reported by Lee *et al* (4), Hwang *et al* (9), Choi *et al* (15), Li *et al* (21) and Capalbo *et al* (22). Preoperative evaluation of puncture routes, preoperative guidance to properly control respiratory amplitude and frequency, avoidance of injury to major vessels and precise recognition of the tip position of the needle may help to maintain an acceptable risk/benefit ratio of the CT-guided biopsy, particularly for the examination of nodules close to major vessels. Additionally, CT-guided biopsy can be used to determine the nature of small nodules without the requirement of additional surgery, which is beneficial for both patients and clinicians (7,23).

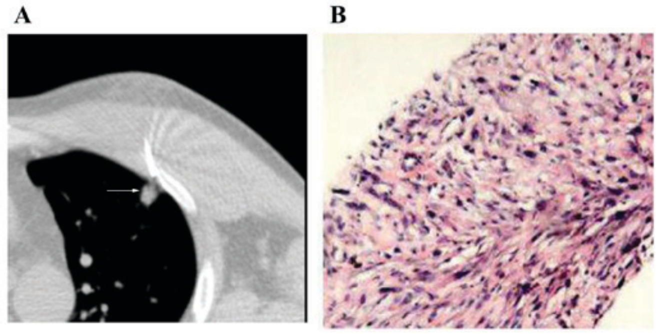

Figure 1. Representative images of a 45-year-old female with a solitary pulmonary lesion of 6 mm in diameter. (A) This female patient underwent computed tomography-guided percutaneous lung biopsy for a 6-mm nodule (arrow) in the left upper lobe at a depth of 6 mm. (B) Post-operative pathological analysis using hematoxylin and eosin staining exhibited a poorly differentiated squamous cell carcinoma (magnification, x100).

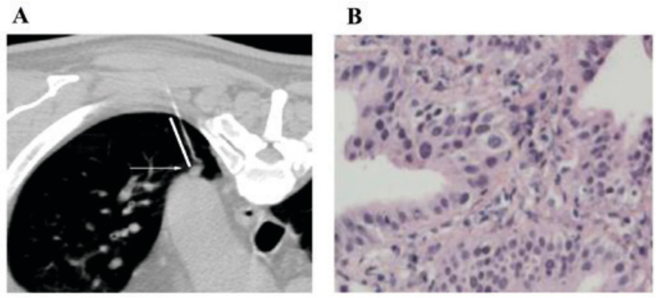

Figure 2. Representative images of a 69-year-old male with a solitary pulmonary lesion of 6 mm in diameter. (A) This male patient underwent computed tomography-guided percutaneous lung biopsy for a 6-mm nodule (arrow) in the left upper lobe at a depth of 29 mm. (B) Post-operative pathological analysis using hematoxylin and eosin staining exhibited a lung adenocarcinoma (magnification, x200).

In the present study, it was demonstrated that nodule size and adhesion of the nodule to the pleura significantly affected the accuracy of biopsy. The accuracy of the biopsy was significantly higher for nodules of 21-30 mm in diameter compared with the accuracy for smaller nodules, particularly for those that were <10 mm in diameter. It is possible to speculate that the small nodules are more likely to move during respiration, which may result in the CT failing to accurately indicate the needle path throughout the respiration cycle. A slight change in needle angle or respiration phase during insertion may cause the needle to miss the nodule, resulting in failure of the biopsy. In addition, the small nodules may not possess sufficient tissue to render a conclusive pathological diagnosis, reducing the likelihood of a successful diagnosis. Secondly, adhesion of a nodule to the pleura may fix the position of the nodule, resulting in less movement during respiration. This may explain why increased biopsy accuracy is obtained with pleural-adhered nodules during CT-guided biopsy.

Ohno *et al* (10) found that biopsy depth affected the accuracy of biopsy; for example, biopsies with needle path lengths of ≤40 mm exhibited an accuracy rate of ≥88%, while those with lengths of 41-80 mm decreased to an accuracy rate of 50-62% and those with needle path lengths of >81 mm exhibited a 12.5% accuracy rate. In comparison, the majority of biopsies in the present study utilized shorter needle path lengths; 87.1% of successful biopsies utilized needle paths <34.5 mm and the needle path lengths of the 15 unsuccessful biopsies exhibited a median length of 24 mm (range, 12-37 mm). In addition, Choi *et al* (15) found no correlation between accuracy and needle path lengths (biopsy depth) up to 120 mm, suggesting that increased accuracy rates may decrease the ability to detect potential factors that are important at other facilities. An additional contributing factor to biopsy accuracy may be the use of larger needles (20- or 18-G), which may obtain larger and more complete samples compared with smaller needles.

Hemorrhage and pneumothorax are the two most common complications of CT-guided percutaneous needle biopsy (24). Rates of hemorrhage or hemoptysis have varied in previous studies; with values reported to be 4 (17), 9 (22), 14.5 (15), 20-22 (2) and 27% (13,23). Similar to Capalbo *et al* (22) and Choi *et al* (15), bleeding occurred in 10% of patients in the present study; patients with nodules of 21-30 mm had a significantly higher risk of hemorrhage compared with those with smaller nodules. Elevated bleeding risk may be associated with a rich blood supply in larger nodules. Both needle path length and a needle path that traversed a pulmonary vessel were observed as risk factors for hemorrhage in a study by Nour-Eldin *et al* (2). Additionally, lesions measuring <20 mm have been identified as a significant risk factor for hemorrhage (2), but there are conflicting reports (22). However, the present study demonstrates that smaller nodules are associated with a higher risk for postoperative pneumothorax and hemorrhage. A smaller nodule size may increase the risk of the needle damaging the surrounding small vessels or lung tissue. The results of the present study indicated that a shallower biopsy depth was associated with a higher risk for pneumothorax and hemorrhage. It may be speculated that the needle was not effectively fixed in the lung when the biopsy depth was shallow, meaning the needle was more likely to move with respiration, resulting in injury to the pleura and an increased risk of hemorrhage and pneumothorax.

Successful CT-guided biopsy of a solitary pulmonary nodule involves: Fixing the positions of the needle and the nodule by preoperative training of the respiration of each patient; intraoperative precise localization of both the nodule and the needle; a larger needle bore size to reduce the number of biopsies; and a longer depth of the intramuscular part of the needle, which allows the position of the needle to be fixed, thus reducing displacement and increasing the accuracy rate. One biopsy of a nodule may result in the nodule becoming covered by surrounding lung tissue or gas cavity, resulting in the movement of this nodule and a decrease in the accuracy of subsequent biopsies of the same nodule. Decreasing the number of biopsies is also a key factor in reducing postoperative complications, such as hemorrhage and pneumothorax. Biopsy depth should be accurately controlled to prevent needle-induced injury to the local lung tissues and subsequent hemorrhage. A thorough discussion with patients before the procedure reduces intraoperative stress. In addition, administration of local anesthesia close to the parietal pleura may reduce any potential pleural twitching or reflex (25) and may improve the patient cooperation during surgery.

As medium and large nodules (>20 mm) may have central necrosis, the selection of an appropriate site for biopsy is

Table IV. Effect of lesion size on the incidence of pneumothorax, bleeding, and pneumothorax plus bleeding in patients with successful biopsies.

Variable	N	PTx	Bleeding	PTx + Bleeding	P-value
Total successful punctures	140	28	14	10	
Size of lesion (mm)					0.013
≤10	6	0 (0.0)	1 (16.7)	2 (33.3)	
11-20	69	16 (23.2)	2 (2.9)	3 (4.4)	
21-30	65	11 (16.9)	11 (16.9)	5 (7.7)	
Pleural adhesion					0.400
Yes	31	9 (29.0)	2 (6.45)	1 (3.2)	
No	109	18 (16.5)	12 (11.0)	9 (8.3)	
Puncture depth (mm)					0.062
<25.6	66	15 (22.7)	5 (7.6)	4 (6.1)	
25.6-34.6	56	9 (16.1)	5 (8.9)	2 (3.6)	
>34.6	18	3 (16.7)	4 (22.2)	4 (22.2)	
Number of punctures					0.704
1	25	6 (24.0)	2 (8.0)	1 (4.0)	
2	111	20 (18.0)	12 (10.8)	8 (7.2)	
≥3	4	1 (25.0)	0 (0.0)	1 (25.0)	

Data are presented as N or N (%), as appropriate. PTx, pneumothrorax.

pivotal to increase the accuracy of biopsy (26). It has been demonstrated that a biopsy of larger nodules with central necrosis may require inclusion of the border of the nodule for adequate live cells for pathological analyses (26). Furthermore, preoperative enhanced CT or positron emission tomography (PET)-CT is can be used to identify the solid components and display the internal structure of the nodule, when compared with general CT. Enhanced CT or PET-CT are able to identify the tissues rich in blood supply and display the necrotic tissues and nonviable tissues in the nodule, which increases the accuracy of the biopsy.

The present study has several limitations. Firstly, it is a retrospective study at a single institution. While the accuracy and complication rates may be more applicable to this particular facility, the additional insights gained on these essential details may encourage additional facilities to test and/or adopt them and subsequently improve their CT-guided percutaneous biopsy procedures. The success rate of a biopsy and the complication rate may vary due to inter-performer variability. However, the success rate of the biopsies in the present study was determined by the pathology, and thus the success rate variation should be limited. The incidence of complications was determined by two physicians independently, and another physician was consulted if necessary. The same technique criteria were was used in all patients and all biopsies were by the same investigator. Secondly, the number of lesions <10 mm in diameter was low in our patient population (7/155; 4.5%) in comparison to the studies by Li *et al* (32/169; 18.9%) (8), Ohno *et al* (21/162; 13%) (10) and Choi *et al* (23/173; 13.3%) (15). A possible reason may be that patients with emphysema, who were excluded from the present study, may be more likely to be examined and found to possess small nodules compared with patients without emphysema. However, the accuracy rate demonstrated in the present study was consistent with rates reported by Ng *et al* (16). Although the number of nodules <10 mm in diameter was low, the puncture accuracy of these nodules was significant lower (P=0.049) than observed in the other two subgroups. Nodules sized 10-20 mm in diameter were analyzed separately to the nodules measuring <10 mm in diameter. The accuracy of the CT-guided biopsy capture procedure on patients who did not have extensive lung disease (no emphysema, pulmonary bullae, pulmonary fibrosis or interstitial lung diseases) was analyzed. Spirometry was not utilized to assess lung function. In previous studies, emphysema, interstitial lung disease and pulmonary fibrosis were confounding factors affecting biopsy accuracy; therefore, such patients were excluded from the present study (8,10,15). Thirdly, only biopsies containing sufficient tissue for pathological examination were included in the analysis, which created a bias. Furthermore, the patients' smoking history, which may have influenced the pathology of the nodules, was not included in the analysis. Finally, unintentionally, the study group was young (mean age, 54 years). Further studies are required to determine whether the results of the present study are applicable to patients with emphysema or other lung diseases.

In conclusion, CT-guided percutaneous lung biopsy is an accurate and safe method for micro-invasive examinations. It has an important role in harvesting a portion of an intrapulmonary lesion (particularly a nodule of ≤30 mm in diameter). Nodule size and the adhesion of the nodule to the pleura are major factors affecting the accuracy of biopsy. Mastering the techniques for biopsy of small nodules and rationally utilizing the natural advantage of nodule adherence to the pleura may increase biopsy accuracy. The rate of complications in the present study was only associated with the lesion size.

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