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INTERVENTIONAL RADIOLOGY

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# Diagnostic accuracy and safety of CT-guided fine needle aspiration biopsy of pulmonary lesions with non-coaxial technique: a single center experience with 442 biopsies

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**PURPOSE**
We aimed to evaluate the diagnostic accuracy and safety of computed tomography (CT)-guided biopsy of pulmonary lesions with fine needle aspiration (FNA) using non-coaxial technique.

**METHODS**
We analyzed 442 patients who underwent CT-guided lung biopsy with FNA and non-coaxial technique to determine the diagnostic outcomes, complication rates, and independent risk factors for diagnostic failure and pneumothorax.

**RESULTS**
Diagnostic accuracy, sensitivity, and specificity were 97.6%, 97.3%, and 100%, respectively. Age and >35 mm lesion size were significant risk factors for diagnostic failure. The rates of pneumothorax and chest tube placement were 19% and 2.9%, respectively. Middle and lower lobe location, lesion to pleura distance >7.5 mm, and >45° needle trajectory angle were significant risk factors for pneumothorax.

**CONCLUSION**
CT-guided FNA of pulmonary lesions with non-coaxial technique is a safe and reliable method with a relatively low pneumothorax rate and an acceptably high diagnostic accuracy.

CT-guided percutaneous transthoracic biopsy of the lung is a well-established method for diagnosis of pulmonary lesions yielding a diagnostic accuracy of 71%–95% (1–5), with pneumothorax being the most common complication varying between 17% and 26% (5–7). Currently coaxial technique is more commonly employed than the non-coaxial technique. The risk of pneumothorax may play a decisive role on this preference. Theoretically, fewer pleural passes means less risk of pneumothorax with the coaxial technique. However, introduction of relatively large bore needles are needed in the coaxial technique, which is a known risk factor for the development pneumothorax (8, 9). To the best of our knowledge, there are only a few studies on CT-guided transthoracic fine needle aspiration (FNA) biopsies with non-coaxial technique on large patient populations (10, 11).

The purpose of this retrospective study was to evaluate the diagnostic accuracy and safety of CT-guided transthoracic biopsy of pulmonary lesions with FNA using the non-coaxial technique.

## Methods

### Patients

The institutional review board approved this retrospective study protocol and waived informed consent.

CT images and biopsy records were retrospectively evaluated in 442 patients (346 males [78.3%] and 96 females [21.7%]; mean age, 64±10.8 years; range, 22–89 years) who underwent CT-guided transthoracic FNA of pulmonary lesions between July 2011 and June 2015. Bronchoscopy or transbronchial biopsies were nondiagnostic or not feasible in these patients.

Exclusion criteria for the procedure were lesions <5 mm in maximum diameter, lesions suspected to be of vascular origin, uncorrectable coagulopathy (international normalized ratio ≥1.5, platelet count <50,000 K/UL), patients who were unable to maintain the appro-

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priate position during the procedure, and patients' refusal. Any anticoagulants or antithrombotic medications were discontinued 3–7 days prior to the procedure.

### Biopsy procedure

All biopsies were performed under CT guidance (GE Healthcare Medical Systems, Lightspeed) by radiologists who were experienced in thoracic radiology and CT-guided biopsies with at least six years of experience. Patients were positioned in supine, prone, or lateral decubitus position, according to the location of the lesion, to provide the shortest and safest route from the chest wall to the lesion. Before the biopsy, lesions were scanned using the following technical parameters without breath holding: 20 mAs, 120 kV, collimation 8×1.25 mm, slice thickness 2.5 mm. Biopsy route was chosen as the most vertical to the pleural surface as possible avoiding the fissures, bullae, large vessels, visible bronchi, ribs, and scapulae. The angle of the planned needle trajectory route, the depth of the lesion from the skin according to the trajectory route, and the distance from the skin surface to the pleura were measured on CT scans. After skin disinfection, 5 mL of 2% prilocaine hydrochloride (Citanest, injection flacon 2%, AstraZeneca) was injected subcutaneously as local anesthetic. Routinely, the procedure was performed without any premedication, sedation, or neuroleptic anesthesia.

The biopsies were performed using the 20-gauge (G) or 22 G Chiba aspiration needles (Matek). Pleural crossing was avoided in the initial insertion. Needle position was checked using consecutive CT images of the biopsy area. At this point, if the position was appropriate, the needle was pushed forward to the lesion according to the planned trajectory route. Otherwise insertion angle or site was changed. The patients were told to hold their breath when the needle was penetrating the pleura. The position of the needle tip and the lesion was again checked on CT. After CT confirmation of adequate needle-tip position, the biopsy material was aspirated with a 20 mL syringe. During aspiration the needle was moved with slight to and fro movements. When the aspirated material was seen filling the needle hub, aspiration was discontinued and the needle was totally retracted. These steps were repeated for every sampling throughout the procedure. The procedure lasted approximately 15 min for a single sample starting from planning of optimal needle route to placement of the sample on slides. If multiple samples were taken, the procedure lasted 10–20 min more depending on the number of additional samples.

Specimens were immediately placed on slides. If present, tissue fragments were collected from the slide or the syringe, immersed in 10% formalin solution for the cell blocks, and sent to the cytologist. Since an on-site cytopathologist was not routinely available, decisions for additional sampling were based on visual inspection of the adequacy of the specimen by the operator. Care was taken to ensure that samples do not simply consist of blood and clots. Sampling was continued despite presence of asymptomatic and nonprogressive pneumothorax in some cases as long as precise sampling was achieved. A maximum of five samples were obtained in each biopsy. Biopsy had to be terminated in some patients due to symptomatic and progressive pneumothorax, regardless of the adequacy of the specimens.

Postprocedure CT was routinely performed to detect pneumothorax and pulmonary hemorrhage immediately after the procedure; chest radiography was obtained whenever indicated. Small and stable pneumothoraces, and asymptomatic patients were treated conservatively. Patient stability was confirmed with chest radiographs obtained in the first six hours after the procedure and the next morning. Pneumothoraces that were symptomatic or large (≥30% of the hemithorax) were drained by chest tube.

### Data collection and statistical analysis

Maximum lesion diameter was measured at lung window settings. Lesion depth from the pleural surface was measured according to the needle trajectory. Each needle trajectory angle was determined by the angle between the needle route and the line perpendicular to the pleura at the insertion point of the needle (Fig.). In patients with multiple passes, the average of the angles for each pass before the appearance of pneumothorax was accepted as the needle trajectory angle.

Diagnostic accuracy and failure were calculated excluding patients who did not

**Main points**

- Fine needle aspiration (FNA) biopsy of lung lesions using the non-coaxial technique has a high accuracy comparable to cutting needle biopsy and coaxial technique.
- Non-coaxial technique may actually increase diagnostic accuracy because multiple different segments of the lesion can be biopsied, as opposed to the coaxial technique.
- Rate of pneumothorax and active intervention was lower with the non-coaxial technique compared to the coaxial technique and cutting needle biopsy despite many passes. Lower complication rate was likely due to thinner needle use.

**Table 1.** Characteristics of patients, lesions, and procedures

| | |
|---|---|
| Patient characteristics | |
| Age (years) | 64.0±10.8 (22–89) |
| Sex (female/male) | 96 (21.8)/346 (78.2) |
| Emphysema (yes/no) | 307 (69.5)/135 (30.5) |
| Lesion characteristics | |
| Size (mm) | 54.9±29.2 (7–180) |
| Location (upper lobe/middle lobe or lingula/lower lobe) | 263 (59.5)/20 (4.5)/159 (35.9) |
| Procedure characteristics | |
| Distance to pleura (mm) | 8.40±12.3 (0–64) |
| Positioning (supine/prone/lateral) | 167 (37.7)/246 (55.6)/29 (6.5) |
| Number of pleural passes | 2.00±0.80 (1–5) |
| Number of single pleural pass/≥2 passes | 137 (30.9)/305 (69.0) |
| Number of obtained specimens | 1.90±0.90 (0–5) |
| Needle thickness (20 G/22 G) | 364 (82.4)/78 (17.6) |
| Needle trajectory angle (°) | 15.7±15.2 (0–85) |

Data are presented as mean±SD (range) or n (%).
SD, standard deviation; n, number of patients; G, gauge.

have postprocedural pathologic, radiologic, or clinical follow-up in our institute. The remaining patients were classified according to their biopsy results as malignant, benign, and nondiagnostic.

The results were considered nondiagnostic when the biopsy had been terminated before specimen acquisition due to complications or insufficient patient cooperation, or when the obtained specimens were inadequate for diagnosis. Biopsy diagnoses of malignant and benign lesions were determined as positive and negative results. Biopsy diagnoses were considered as true positive or true negative according to the final diagnoses, which were determined by surgical confirmation and postprocedural course of the disease. A positive biopsy result was considered true positive if it was confirmed surgically, if there was a malignant biopsy result of an another organ with the same histologic characteristics, or if there was a postprocedural malignant clinical course like increased lesion size, lesion regression by anticancer therapy, or new metastases. A negative biopsy result was considered true negative if the surgical resection confirmed a benign diagnosis, if the lesion regressed spontaneously or without anticancer therapy, or if the lesion remained stable for at least 24 months.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the diagnosis of malignancy and the diagnostic accuracy were calculated. For diagnostic accuracy, nondiagnostic biopsies were excluded from the total number of cases.

Patient-, lesion-, and procedure-related variables were evaluated by univariate analyses. Categorical variables were evaluated by chi-square test, Fisher's exact test, or Fisher-Freeman-Halton test, where applicable. Mann-Whitney U test was used to test the difference between two groups in terms of non-normally distributed continuous variables or ordinal variables. Receiver operating characteristic (ROC) curve was used to describe the diagnostic performance of tests. The area under the corresponding curves gives an estimate of the overall accuracy of each test. An area of 0.50 implies that the variable adds no information. The areas under the ROC curves and 95% confidence intervals (CI) for all variables were calculated in the manner described by Hanley and McNeil (12). The Youden's Index was used to determine cutoff values. In order to define risk factors of outcome variable (diagnostic failure and pneumothorax), multiple Poisson regression analysis was used and incidence rate ratio (RR) were calculated. The Poisson distribution overestimates the variation in binary data, a robust variance estimator (also known as the sandwich estimator) is used to obtain correct standard errors for model coefficient estimates (13). *P* values less than 0.05 were considered significant.

**Table 2.** Univariate analysis to determine the potential risk factors for diagnostic failure

| Variables | Diagnostic success[a] n=410 (95%) | Diagnostic failure[b] n=22 (5%) | *P* |
|---|---|---|---|
| Patient factors | | | |
| Age (years), mean±SD | 58.4±12.1 | 64.3±10.7 | 0.018 |
| Sex, n (%) | | | |
| Female | 88 (21.5) | 7 (31.9) | 0.289 |
| Male | 322 (78.5) | 15 (68.1) | |
| Emphysema, n (%) | | | |
| Yes | 287 (66.4) | 12 (2.77) | 0.126 |
| No | 123 (28.4) | 10 (2.31) | |
| Lesion factors | | | |
| Size (mm), mean±SD | 55.0±28.1 | 57.7±44.3 | 0.352 |
| Size cutoff, n (%) | | | |
| ≤35 mm | 313 (72.4) | 10 (2.31) | 0.001 |
| >35 mm | 97 (22.4) | 12 (2.77) | |
| Location | | | |
| Upper lobe | 248 (57.4) | 11 (2.54) | 0.321 |
| Middle lobe or lingual | 18 (4.16) | 2 (0.46) | |
| Lower lobe | 144 (33.3) | 9 (2.08) | |
| Procedure factors | | | |
| Length from pleura (mm), mean±SD | 8.40±12.0 | 9.30±17.3 | 0.491 |
| Length from pleura cutoff, n (%) | | | |
| ≤3.5 mm | 227 (52.5) | 15 (3.47) | 0.234 |
| >3.5 mm | 183 (42.3) | 7 (1.62) | |
| Positioning, n (%) | | | |
| Supine | 153 (35.4) | 12 (2.77) | 0.187 |
| Prone | 230 (53.2) | 10 (2.31) | |
| Lateral | 27 (6.25) | 0 (0) | |
| Number of specimen obtained, mean±SD | 1.92±0.80 | 1.72±1.20 | 0.208 |
| Needle thickness, n (%) | | | |
| 20 G | 334 (77.3) | 20 (4.62) | 0.394 |
| 22 G | 76 (17.5) | 2 (0.46) | |
| Needle trajectory angle (°), mean±SD | 15.7±15.3 | 15.0±0.14 | 0.928 |
| Needle trajectory angle cutoff, n (%) | | | |
| ≤45° | 390 (90.2) | 22 (5.09) | 0.614 |
| >45° | 20 (4.62) | 0 (0) | |

n, number of patients; SD, standard deviation; G, gauge.
[a]Diagnostic success includes true positive and true negative results.
[b]Diagnostic failure includes nondiagnostic results, false positive results, and false negative results.

## Results

Patient demographics, lesions, and procedure characteristics are summarized in Table 1. The number of biopsies was equal to the number of patients. Ten patients who did not have postprocedural pathologic, radiologic and clinical follow-up at our in-

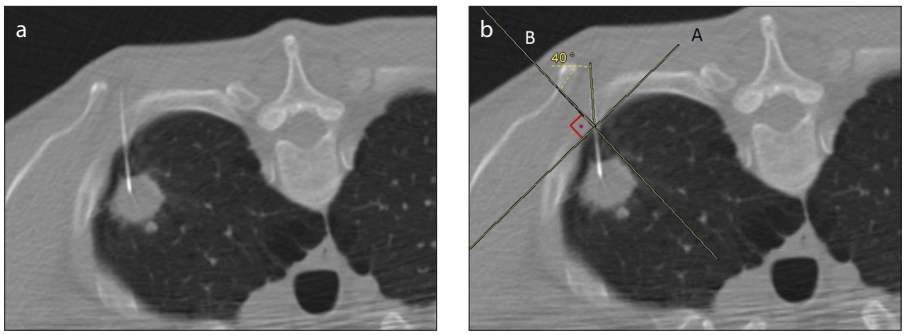


**Figure. a, b.** Axial CT image **(a)** shows the needle penetrating pulmonary lesion. Axial CT image **(b)** shows the measurement of needle trajectory angle. Line A was drawn tangential to the pleura at the point of needle puncture. Line B was drawn perpendicular to line A. Needle trajectory angle was determined by the angle between the needle route and the line B.

**Table 3.** Multivariate analysis to determine the potential risk factors for diagnostic failure and pneumothorax

| | Reference value | *P* | Adjusted incidence rate ratio* | 95% CI |
|---|---|---|---|---|
| Risk factors for diagnostic failure | | | | |
| Size cutoff >35 mm | Size cutoff ≤35 mm | 0.006 | 3.22 | 1.40–7.40 |
| Age | | 0.022 | 0.96 | 0.91–0.99 |
| Risk factors for pneumothorax | | | | |
| Lower lobe location of the lesion | Upper lobe location | 0.002 | 2.29 | 1.36–3.86 |
| Middle lobe location of the lesion | Upper lobe location | 0.007 | 1.65 | 1.15–2.36 |
| Distance to pleura >7.5 mm | ≤7.5 mm | <0.001 | 5.35 | 3.42–8.37 |
| Needle trajectory angle (°) >45° | ≤45° | <0.001 | 2.26 | 1.59–3.21 |

CI, confidence interval.
*Adjusted for sex.

stitute were excluded from diagnostic accuracy and diagnostic failure calculations. Of the remaining 432 patients, 12 (2.7%) had nondiagnostic biopsies. Among the nondiagnostic biopsies, two biopsies were terminated before specimen acquisition because of progressive pneumothorax, one biopsy was terminated because of insufficient patient cooperation during the procedure and nine biopsy specimens were inadequate for diagnosis. The biopsy specimens that were considered inadequate contained extensive necrosis (n=6, 66.6%), peripheral blood (n=2, 22.2%), and bronchial epithelium (n=1, 11.1%). Among 12 cases with nondiagnostic biopsy results, seven (58.3%) proved to be malignant and five (41.7%) proved to be benign.

Ten patients required rebiopsy to confirm a certain diagnosis of malignancy or specify the subtype of malignancy (n=6, 60%) and to definitely rule out malignancy in cases clinically highly suspicious for malignancy despite benign biopsy results (n=4, 40%). As the repeat biopsies were concordant with the initial biopsies, only the initial biopsies were included in the study. In patients with nondiagnostic biopsies, diagnosis was achieved by means of surgery, mediastinoscopy or biopsy of other lesions in other organs.

The specimens were adequate for diagnosis in 420 patients (97.2%): biopsy results were positive for malignancy in 367 patients (87.4%) and negative in 53 patients (12.6%). Final diagnosis of malignant disease in 383 patients was confirmed by surgical resection (n=57, 14.8%), a malignant biopsy result of another organ with the same histologic characteristics (n=27, 7.1%), and clinically evident malignant progression of disease in the follow-up of the patient (n=299, 78.1%). Benign diagnosis was confirmed in 49 patients by surgery (n=5, 10.2%), spontaneous lesion regression or regression without anticancer therapy (n=37, 75.5%), and stable lesion for at least 24 months (n=7, 14.3%).

Among 420 diagnostic biopsies, 367 results (87.4%) were true positive, 43 results (10.2%) were true negative, and ten results (2.4%) were false negative. There were no false positive results. The final diagnoses in the ten patients with false-negative results were adenocarcinoma (n=6, 60.0%), pulmonary squamous cell carcinoma (n=1, 10.0%), lymphoma (n=2, 20.0%), and esophageal squamous cell carcinoma (n=1, 10.0%).

Diagnostic accuracy was 97.6% (410/420 patients). For the diagnosis of malignancy, sensitivity was 97.3% (367/377), specificity 100% (43/43), PPV 100% (367/367), and NPV 81.1% (43/53). Diagnostic accuracy was 98.0%, 98.2%, 97.4%, and 90.9% in biopsies performed with one, two, three, and four samplings, respectively. There was no significant relationship between the number of samplings and diagnostic accuracy ($P = 0.200$).

Diagnostic success group (n=410, 95.0%) comprised 367 true positive results and 43 true negative results. Diagnostic failure group (n=22, 5.0%) comprised 10 false negative results and 12 nondiagnostic results. No false positive diagnosis occurred.

Results of univariate analyses for potential risk factors of diagnostic failure are shown in Table 2. Patient's age was significantly associated with diagnostic failure ($P = 0.018$). Lesion size >35 mm was also significantly associated with diagnostic failure ($P < 0.001$); however, mean lesion size was not significantly different between successful and failed diagnoses ($P = 0.352$).

Results of the multivariate analyses for independent risk factors of diagnostic failure are shown in Table 3. The significant independent risk factors were age (RR, 3.22; 95% CI 1.40–7.40; $P = 0.006$) and >35 mm lesion size (RR, 0.96; 95% CI 0.91–0.99; $P = 0.022$).

In this study, 87 of 442 patients (19.6%) developed postprocedural pneumothorax. In two patients, biopsies were terminated before specimen acquisition due to progressive pneumothorax during the procedure. Pneumothorax appeared after the first needle entry in 58 patients (66.6%), after the second entry in 26 patients (30.0%), and after the third entry in three patients (3.4%). Only 13 patients (2.9%) required chest tube insertion. Tension pneumothorax did not occur in any patient. There were 92 patients (20.8%) with pulmonary hemorrhage, 35 patients (7.9%) with hemoptysis and two patients (0.4%) with mild hemothorax that were treated conservatively. No mortality was observed.

The results of univariate analysis for potential risk factors of pneumothorax are shown in Table 4. Lesion size ≤45 mm ($P < 0.001$), middle and lower lobe location ($P = 0.008$), lesion to pleura distance >7.5 mm ($P < 0.001$),

**Table 4.** Univariate analysis to determine the potential risk factors for pneumothorax

| Variables | Patients without pneumothorax n=355 (80.4%) | Patients with pneumothorax n=87 (19.6%) | *P* |
|---|---|---|---|
| Patient factors | | | |
| Age (years), mean±SD | 64.0±11.0 | 64.1±10.1 | 0.839 |
| Sex, n (%) | | | |
| Female | 77 (21.7) | 19 (21.9) | 0.976 |
| Male | 278 (78.3) | 68 (78.1) | |
| Emphysema, n (%) | | | |
| Yes | 248 (62.8) | 59 (13.3) | 0.711 |
| No | 107 (24.2) | 28 (6.33) | |
| Lesion factors | | | |
| Size (mm), mean±SD | 58.3±30.1 | 41.0±19.7 | <0.001 |
| Size cutoff, n (%) | | | |
| ≤45 mm | 140 (31.6) | 54 (12.2) | <0.001 |
| >45 mm | 215 (48.6) | 33 (7.46) | |
| Location | | | |
| Upper lobe | 222 (50.2) | 41 (9.27) | 0.008 |
| Middle lobe | 12 (2.71) | 8 (1.80) | |
| Lower lobe | 121 (27.3) | 38 (8.59) | |
| Procedure factors | | | |
| Distance to pleura (mm), mean±SD | 6.20±10.8 | 17.5±14.0 | <0.001 |
| Distance to pleura cutoff, n (%) | | | |
| ≤7.5 mm | 259 (58.5) | 21 (4.75) | <0.001 |
| >7.5 mm | 97 (21.9) | 65 (14.7) | |
| Positioning, n (%) | | | |
| Supine | 137 (30.9) | 30 (6.78) | 0.257 |
| Prone | 198 (44.7) | 48 (10.8) | |
| Lateral | 20 (4.52) | 9 (2.03) | |
| Number of needle insertion, mean±SD | 2.00±0.90 | 1.90±0.70 | 0.646 |
| Needle thickness, n (%) | | | |
| 20 G | 293 (66.2) | 71 (16.0) | 0.839 |
| 22 G | 62 (14.0) | 16 (3.61) | |
| Needle trajectory angle (°), mean±SD | 15.8±14.9 | 15.4±16.3 | 0.631 |
| Needle trajectory angle cutoff, n (%) | | | |
| ≤45° | 342 (77.3) | 79 (17.8) | 0.045 |
| >45° | 13 (2.94) | 8 (1.80) | |

n, number of patients; SD, standard deviation; G, gauge.

and needle trajectory angle >45° ($P = 0.045$) were statistically significant.

The results of multivariate analysis for potential risk factors of pneumothorax are shown in Table 3. The significant independent risk factors were middle lobe (RR, 1.65; 95% CI, 1.15–2.36; $P = 0.002$) and lower lobe location of the lesion (RR, 2.29; 95% CI, 1.36–3.86; $P = 0.007$), lesion to pleura distance >7.5 mm (RR, 5.35; 95% CI, 3.42–8.37; $P < 0.001$), and needle trajectory angle >45° (RR, 2.26; 95% CI, 1.59–3.21; $P < 0.001$), compared with upper lobe location, lesion to pleura distance ≤7.5 mm, and needle trajectory angle less than ≤45°.

## Discussion

In this retrospective study we evaluated the diagnostic accuracy, sensitivity, specificity, complication rates of CT-guided transthoracic FNA of pulmonary lesions with non-coaxial technique and assessed the independent risk factors for diagnostic failure and rate of pneumothorax.

The current trend favors coaxial technique either with FNA or cutting needle. In this study, non-coaxial FNA technique was comparable to coaxial technique. Overall, the diagnostic accuracy of coaxial technique in the literature ranges between 93% and 97%. To our knowledge, there are only few studies on transthoracic biopsy using FNA and non-coaxial technique in recent literature (11, 12). Table 5 summarizes some of the previous studies performed by other investigators (2, 4, 5, 9, 10, 14, 15). In the present study, the diagnostic accuracy was 97.6%, with 97.3% sensitivity and 100% specificity for malignant disease. With non-coaxial technique different parts of the lesions can be sampled, which is more advantageous than coaxial technique in terms of diagnostic accuracy, but it is more time consuming because proper needle adjustment is needed in each entry.

Some studies focused on comparing the diagnostic values of FNA and cutting needle biopsies. Klein et al. (16) determined that the diagnostic accuracy for detecting malignant lesions with cutting needle biopsy was not superior to FNA biopsy (92% vs. 86%); however, the diagnostic accuracy of detecting benign lesions was significantly higher with the cutting needle biopsy (44% vs. 100%). Boiselle et al. (17) found the diagnostic accuracy for FNA to be significantly higher compared with the cutting needle (94% vs. 59%) for malignant lesions. But for benign pathologies other than acute infections, they found a significantly higher diagnostic accuracy rate with cutting needle biopsy. Considering that the main focus of transthoracic biopsies is to rule out malignancy, the diagnostic superiority of cutting needle in detection of benign lesions may not be of primary concern. On the other hand, Arakawa et al. (3) reported a significant diagnostic superiority with the cutting needle (FNA 71.7% vs. cutting needle 75.4%) and Laurent et al. (14) reported a significantly higher sensitivity with the cutting needle (FNA 82.7% vs. cutting needle 97.4%). We were unable to compare FNA with cutting needle due to the design of the study as all biopsies were performed using FNA. Even so, the diagnostic accura-

**Table 5.** Comparison of diagnostic outcomes of this study with previous studies

| First author, year (ref. no) | Technique | Needle type | Number of cases | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | DA (%) |
|---|---|---|---|---|---|---|---|---|
| Laurent et al. 2000 (14) | Coaxial | FNA or CN | 125 (FNA)<br>98 (CN) | 83 (FNA)<br>97 (CN) | 100 (FNA)<br>95 (CN) | 100 (FNA)<br>97 (CN) | 61 (FNA)<br>90 (CN) | – (FNA)<br>95 (CN) |
| Geraghty et al. 2003 (9) | Coaxial | FNA and CN | 846 | 91 | 99 | 99 | 81 | 94 |
| Yeow et al. 2003 (5) | Coaxial | CN | 631 | 93 | 98 | 99 | 86 | 95 |
| Montaudon et al. 2004 (15) | Coaxial | CN | 605 | 89 | 100 | 100 | 67 | – |
| Hiraki et al. 2009 (2) | Coaxial | CN | 1000 | 94 | 99 | 99 | 83 | 95 |
| Priola et al. 2010 (10) | Non-coaxial | FNA and CN | 321 | 87 | 98 | 99 | 45 | 80 |
| Takeshita et al. 2015 (4) | Coaxial | FNA and CN | 750 | 91 | 99 | 100 | 74 | 93 |
| Present study | Non-coaxial | FNA | 420 | 97 | 100 | 100 | 81 | 97 |

Dash (–) indicates value not reported.
PPV, positive predictive value; NPV, negative predictive value; DA, diagnostic accuracy; FNA, fine needle aspiration; CN, cutting needle.

cy, sensitivity, and specificity results were as good as the other studies employing cutting needles.

In this study, the diagnostic success group (n=410, 95.0%) consisted of 367 true positive results and 43 true negative results. In the diagnostic failure group (n=22, 5.0%) there were 10 false negative results and 12 nondiagnostic results. No false positives for malignancy were encountered. Independent factors for diagnostic failure were patient age and >35 mm lesion size.

The frequency of nondiagnostic biopsy results (12/432, 2.7%) was higher in this study compared with studies done by Hiraki et al. (0.6%) (2), Yeow et al. (0.8%) (5), and Montaudon et al. (0.2%) (15), but similar to Geraghty et al. (3.3%) (9). Nine of the nondiagnostic biopsy results have been reported as inadequate specimens, six of which could not be differentiated as malignant or benign by the cytopathologist due to extensive tissue necrosis. The mean diameter of the lesions reported as inadequate specimens was 96 mm, slightly higher than the average size of the lesions, and contained widespread necrosis. Unavailability of an on-site cytopathologist in each and every biopsy and large lesion size and necrosis may have contributed to the higher number of nondiagnostic results.

The diagnostic accuracy rates of transthoracic biopsies decline as the lesion size gets smaller, particularly for lesions <2 cm (1, 2, 4, 5, 18). In previous studies, different thresholds were suggested for diagnostic failure risk. Some authors suggest that lesions <20 mm consitute a risk for diagnostic failure, while others found that lesions >5 cm are likely to have diagnostic failure (1, 4, 5, 18). Hiraki et al. (2) suggested that lesions <10 mm and >31 mm could be a risk factor for diagnostic failure. In this study, we found a diameter of 35 mm or larger as a risk factor for diagnostic failure. The number of lesions ≤2 cm was very limited (≤1 cm, 4 lesions; 1.1–2 cm, 31 lesions), therefore statistical analysis could not be performed. However, we had no lesions ≤2 cm among the false negative or nondiagnostic results.

Advanced age was determined to be a risk factor for diagnostic failure in this study. The inability of old patients to sustain the required body position for the duration of the biopsy procedure and comply with the breath-holding instructions may cause difficulty in targeting the lesion. To our knowledge, no such observation was reported in the previous studies.

In accordance with the literature, the most common complication was pneumothorax. The rate of pneumothorax in this study was 19% including the most minute cases, and the rate of chest tube insertion was only 2.9%. The technique appears to be relatively safe, because these figures are lower than most of the previous studies, where the rate of pneumothorax ranges from 17% to 26.6%, and that of chest tube insertion from 1% to 14.2% (5–7). Although the number of pleural passes is less with the coaxial technique, this was not shown to correlate with decreased risk of pneumothorax in various studies (9, 19, 20). However, this topic is controversial because studies by Kuban et al. (8) and Nour-Eldin et al. (21) stated the contrary. No significant relationship between the number of samplings and diagnostic accuracy was noted in our study, but in the study by Hiraki et al. (2), the number of samplings appears to be a significant factor for diagnostic failure.

A significant correlation was noted between the size of the needle and the risk of pneumothorax in the studies by Kuban et al. (8) and Geraghty et al. (9), where 18 G needles carried a higher risk compared to 19 G needles. In this study, there was no significant relationship between 20 G and 22 G needles regarding pneumothorax. Cox et al. (19) also found no correlation between needle size and pneumothorax with 19 G compared with 22 G (pneumothorax rates 39.1% and 39.6%, respectively).

Pneumothorax following biopsies of middle and lower lung lesions were more prevalent compared with upper lobe lesions in this study and in the literature (21, 22). This may be related to the effect of diaphragmatic movements on middle and lower lung lobes and excessive movement of the biopsy needle during the procedure by respiration, widening the puncture hole in the pleura resulting in a higher pneumothorax risk.

The lesion to pleura distance was also a significant factor for pneumothorax in this study and in some other studies in the literature (4, 8, 21–24). In the literature, the needle entry angle is either defined as the angle between the pleura and needle axis or the line perpendicular to the pleura at the entry point and needle axis. We defined the needle entry angle as the latter. Our results were in compliance with the previous studies (20, 22, 23). More than 45° of entry angle was a risk factor for pneumothorax causing a wider hole in the pleura if the needle crosses the pleura in an oblique fashion.

Pulmonary hemorrhage is the second most common complication of pulmonary biopsies, with reported frequencies ranging from 4% to 27% (6, 25). In this study pulmonary hemorrhage complications related to

the procedure were not different than the studies employing coaxial technique in the literature despite multiple needle passes in the current study.

Our study had several limitations. The study was retrospective with possible bias. Multiple testing is associated with an inflated type I error rate. As some of our patients could not be operated, the final diagnoses were made on the basis of clinical and radiologic follow-up. Seeding was not assessed due to study design. As other means of diagnosis were employed in the cases with initial nondiagnostic biopsy results, the value of rebiopsy could not be evaluated.

We conclude that CT-guided FNA of pulmonary lesions with non-coaxial technique is a safe and reliable method with relatively low complication rates and an acceptably high diagnostic accuracy.

## Conflict of interest disclosure

The authors declared no conflicts of interest.

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