

## CT-Guided Thoracic Biopsy: Evaluating Diagnostic Yield and Complications

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### Abstract

**Introduction:** This study retrospectively evaluated CT-guided thoracic biopsies for diagnostic yield, accuracy and complications. **Materials and Methods:** A retrospective analysis of 384 patients (mean age 62.7 years; male/female = 251/133) who underwent 399 CT-guided thoracic biopsies were performed for evaluating diagnostic yield, accuracy and complications. Correlations between patients age, procedure factors (biopsy-needle size, number of passes, lesion-size, lesion-depth and traversed lung-length) and complications such as pneumothorax, haemothorax and haemoptysis were evaluated. A comparison between fine needle aspiration (FNA) group and core ± FNA group for diagnostic yield and complications was also performed. **Results:** FNA was performed in 349 patients and core ± FNA in 50 patients. The biopsy samples were adequate in 91.9% and the diagnostic accuracy for malignant lesions was 96.8% with 95.7% sensitivity and 100% specificity. Pneumothorax (detected on CT) occurred in 139 cases (34.8%) and only 12 (3.0%) required insertion of an intercostal drain. Mild haemoptysis occurred in 13 patients (3.2%) and small haemothoraces in 2 patients. Pneumothorax occurrence was significantly associated with the traversed lung-length (>3mm), lesion-size (≤33 mm) and lesion-depth (≥60mm) ( $P < 0.05$ ). Haemoptysis occurrence was also significantly associated with traversed lung-length (>3mm) and lesion-size (≤33 mm) ( $P < 0.05$ ). There was no significant difference between diagnostic yield and complication rate between FNA and core ± FNA groups. **Conclusion:** CT-guided thoracic biopsy is a safe procedure with high diagnostic yield and low risk of significant complications. Traversed lung-length and smaller lesion size are associated with occurrence of pneumothorax and haemoptysis.

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**Key words:** Accuracy, Complications, Diagnostic yield, Haemoptysis, Pneumothorax

### Introduction

Percutaneous transthoracic needle biopsies which have been performed for more than a century have since gained wide acceptance for diagnosing malignant and benign lung lesions.<sup>1</sup> Technological advances in computed tomography (CT) have resulted in increased detection of pulmonary and mediastinal masses which are not only detected at an increased rate but also at smaller sizes.<sup>2</sup> Similarly, we have also seen CT-guided transthoracic biopsies gain widespread acceptance with other modalities such as fluoroscopy being used less frequently as compared to CT.<sup>1</sup>

Percutaneous transthoracic biopsies can be performed as a technique for obtaining pathological confirmation either by fine-needle aspiration (FNA), which provides a specimen for cytological examination or using an automated

core biopsy needle providing a specimen for histologic examination. FNA, which was introduced by Nordenstrom<sup>3</sup> in 1965, is a simple and safe technique with an accuracy of 95% for malignant lesions.<sup>4</sup> However, in comparison to automated cutting needle biopsies, several reports have cited cytology to be less reliable in determining the cell type in malignant lesions.<sup>5</sup> This drawback can be obviated through immediate on-site evaluation by a cytopathologist, which has been reported to increase diagnostic accuracy of FNA.<sup>6</sup> Some centers may also have limited access to onsite cytopathologists for image guided biopsies, and therefore several groups have advocated the use of automated cutting needles to obtain core tissue for histologic evaluation.<sup>5,7</sup>

The most common complications after percutaneous

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transthoracic lung biopsy are pneumothorax and bleeding.<sup>1</sup> Pneumothorax has been reported to occur in 8% to 64% of patients undergoing lung biopsies.<sup>8</sup> Bleeding as a complication occurs less often, ranging from 2% to 10%, but is more frequently fatal.<sup>1</sup> Many reports have evaluated the relationship between specific variables and the complications of percutaneous lung biopsy. However, the results of risk analysis reported by some studies are variable and often contradictory.<sup>9-12</sup> Yeow et al,<sup>13</sup> in one of the larger retrospective reviews consisting of 660 patients, concluded that the most significant risk factors affecting pneumothorax are lesion size, depth and experience of the radiologist. Risk factors affecting bleeding complications were lesion size, lesion depth and absence of pleural effusions.<sup>13</sup>

While there is an abundance in literature concerning the complications and diagnostic effectiveness of CT-guided thoracic biopsy, reports detailing CT-guided thoracic biopsy in the local Singapore population remain limited. Our aim was to determine the diagnostic yield of CT-guided thoracic biopsies and identify procedure related risk factors for the complications by performing a retrospective review of 384 subjects at a single institution.

## Materials and Methods

Between January 2006 and March 2011, 386 consecutive patients underwent a total of 401 percutaneous thoracic biopsies. We retrospectively reviewed the patient's medical records and imaging studies to determine the demographics, procedural techniques, complications and pathological and final clinical diagnosis. The inclusion criteria were patients with a focal lung or pleural lesion that underwent a CT-guided biopsy. Two patients were excluded as complete information was not available. Fifteen patients underwent a second biopsy on a different session. The final study population consisted of 384 patients (mean age 62.7 years; range, 8 to 92 years) comprising 251 males and 133 females who underwent 399 CT-guided thoracic biopsies.

### *Biopsy Procedure*

Patients gave written informed consent for the CT-guided thoracic biopsy procedure. Patients were trained for regular breathing and breath holding before the biopsy.

The biopsies were performed by one of the 7 experienced consultant radiologists at our institution. Before the biopsy, a preliminary CT scan was obtained through the lesion. After reviewing the preliminary images, patient's position, site of needle entry and direction of approach for biopsy were planned to provide the most direct route for biopsy and to traverse the least through aerated lung with avoidance of bullae and fissures. Patients were placed either prone, supine or in a lateral decubitus position to facilitate sampling of

the lesion from a position closest to the body surface.

Each radiologist had a choice of different needle size ranging from 18 gauge (G) to 23 G. The type of needles employed included coaxial needles, single shaft needles and cutting needles. A 1% lidocaine solution was used for local anaesthesia. All patients underwent either a FNA biopsy or tissue core biopsy or a combination of both. Whenever a FNA biopsy was performed, an on-site cytotechnologist was available to confirm adequacy of the sample. After each biopsy, the sample was handed to the on-site cytotechnologist for evaluation of sample yield. Repeat passes were performed as needed to obtain suitable samples. The aspirated FNA samples were expressed onto glass slides, half of which were stained with Dif-Quick for on-site evaluation and half of which were fixed in 95% ethyl alcohol for staining in the labs. The tissue-core biopsy samples were placed in buffered formalin and submitted for paraffin embedding and tissue sections. When the lesion was suspected of being infective, the smears were also stained for identification of micro-organisms e.g. acid-fast bacilli or fungi. Aspirates were also diluted with small amounts of normal saline and sent for culture examination.

### *Post Biopsy Care*

After the removal of the biopsy needle, a post-biopsy CT scan was obtained to detect any complications. Patients were observed in the radiology department's observation bay for at least 1 hour after the procedure. The patients were then requested to lie supine for at least 4 hours in the day-care ward.

A pneumothorax was considered to be present when there was any visible retraction of the pleural surface away from the parietal pleura on post biopsy scan. Asymptomatic individuals with pneumothorax who showed no progression of pneumothorax on a follow-up CXR or were clinically asymptomatic were discharged after being observed overnight. Patients who developed symptomatic moderate or severe pneumothorax were treated with chest tube insertion. For the study purposes, only symptomatic pneumothoraces were considered significant.

Haemoptysis was considered as a complication when it occurred after biopsy and there was no history of haemoptysis before biopsy. Post-biopsy haemoptysis was graded into non-life threatening haemoptysis (without causing any abnormal gas-exchange/airway obstruction or haemodynamic instability) and life-threatening haemoptysis (causing abnormal gas exchange/airway obstruction and or haemodynamic instability). A haemothorax was diagnosed when there was a new fluid collection in pleural space following biopsy and attenuation of fluid 30 to 40 HU.

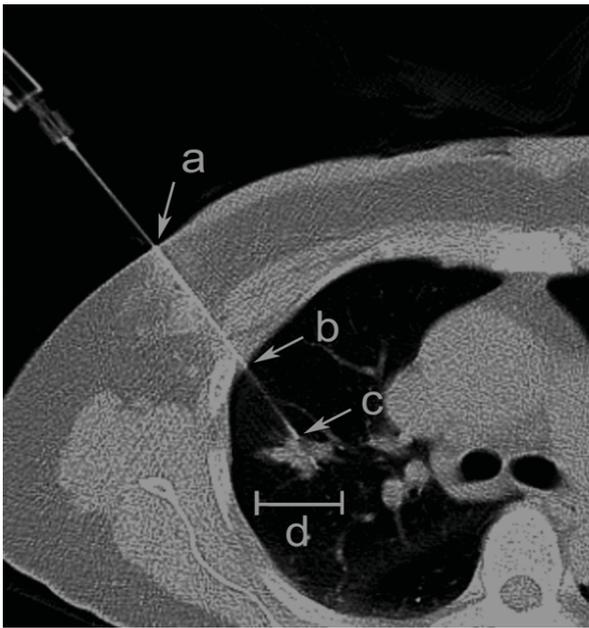


Fig 1. A 68-year-old male patient with adenocarcinoma in the right upper lobe diagnosed at CT-guided thoracic biopsy. The lesion depth was measured from the surface of the skin to the nearest edge of the lung lesion along the needle path (distance a to c). The traversed lung length was measured from the point of pleural puncture to the nearest edge of the lung lesion along the needle path (distance b to c). The lesion size was measured along the maximum long-axis diameter (d).

### Data Collection

The patient information and technical data relating to the biopsy procedure, post procedure complications and their treatment were recorded. Variables analysed with regard to the occurrence of post biopsy complications included patient's age, lesion-size, lesion-depth, needle size, traversed lung-length and the number of passes. The lesion-size was measured along the maximum long-axis diameter and the lesion-depth was measured from the surface of the skin to the nearest edge of the lung lesion along the needle path using the lung window display (Fig. 1). The traversed lung-length was measured from the point of pleural puncture to the nearest edge of the lesion along the needle path using the lung window display (Fig. 1).

The needle size was defined by the size of the cutting needle. The coaxial outer needle guide was one gauge larger in size. The adequacy of the FNA samples was evaluated by the cytotechnologist. Samples labelled as non-diagnostic or limited cellularity were considered inadequate.

The diagnosis from the biopsies was compared with the final diagnosis (combination from the clinical and pathologic information). As most of the biopsies were performed to rule out malignancy, we evaluated the accuracy of CT-guided thoracic biopsy based on the presence or absence of

a malignant diagnosis. The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy were also calculated for all biopsies with subsequent follow-up data on the basis of clinical and imaging follow-up and review of medical records for at least 12 months after the biopsy was performed. The accuracy of the histocytological findings were evaluated by reviewing the patient's follow-up data for at least 12 months after biopsy to confirm or revise the initial diagnosis. A total of 367 patients with sufficient follow-up data were grouped into: true-positive, true-negative, false-positive and false-negative diagnosis. The patients were categorised by the accuracy of their diagnosis into 4 groups (true-positive, true-negative, false-positive and false-negative). The patients in the true-positive group included those who received (i) a definitive malignant diagnosis at biopsy and/or (ii) a diagnosis of suspicious for malignancy at biopsy and either underwent a second procedure (subsequent biopsy or surgery) that confirmed the malignant diagnosis or had a malignant course during follow-up of at least one year. The patients in the true-negative group included those with (i) no malignant cells at biopsy, and/or (ii) a specific benign diagnosis or (iii) a biopsy result that showed atypical cells/suspicious for malignancy/negative for malignancy and showed a benign clinical course during a follow-up of more than 1 year and/or stable or decreased lesion size on a follow-up chest radiograph or CT scan. Patients in the false-negative group included those with a benign or non-specific diagnosis at biopsy and later proved to be a malignancy either by another procedure or in whom a malignant clinical course was documented either as increased lesion size or other signs of malignancy such as metastatic disease. Patients in the false-positive group were those who received a malignant diagnosis at CT-guided biopsy but had a subsequent histopathological evaluation of resected tissue and/or clinical follow-up of more than one year confirming a benign disease.

### Statistical Analysis

Data analysis was performed using a statistical software package (MedCalc® MedCalc Software, Mariakerke, Belgium). The sensitivity, specificity and accuracy for diagnosis of malignancy with biopsy was computed. The procedure factors: lesion-size, lesion-depth, traversed lung-length, needle size, number of passes and patients' age were analysed with regard to the occurrence of pneumothorax and haemoptysis using a multiple logistic regression model, which was built in a stepwise approach. Independent variables that were significant in univariate analysis at  $P \leq 0.10$  were retained for stepwise inclusion in the model. Variables with the strongest association in univariate analysis were fit first into the model. Only predictor variables that were independently associated with pneumothorax and

haemoptysis at  $P \leq 0.05$  were retained for inclusion in the final model.

The variables associated with pneumothorax and haemoptysis was also independently analysed with a receiver operator characteristic (ROC) graphs. The optimal cut-offs were determined automatically by the software with the best sensitivity and specificity.

A subgroup analysis comparing diagnostic accuracy and post biopsy complications between FNA group and core  $\pm$  FNA group was performed with chi square tests.

## Results

The mean lesion size was 37.6 mm (range, 6 to 123 mm). The mean lesion depth from the skin surface was 64.1 mm (range, 3 to 117 mm) and the mean traversed lung length during the biopsy was 11.9 mm (range, 0 to 70 mm). The mean number of needle passes was 2.5 times (range, 1 to 8 passes). There was no significant difference between FNA and core  $\pm$  FNA group with regards to procedure factors (Table 1).

### Diagnostic Yield

The pathological diagnoses determined by CT-guided thoracic biopsy are detailed in Table 2. A pathological diagnosis of malignancy with biopsy was made in 269 (67.4%) cases and in 3 (0.8%) lesions as suspicious for malignancy. This included metastases from primary malignant tumors arising from breast, kidney, prostate and colon. An attempt at histological typing was made in every case where a malignant diagnosis was made (Table 2). Eighty-five (21.3%) lesions were diagnosed as benign (inflammation, and infection such as tuberculosis and aspergillosis). Inflammatory lesions formed the majority of the benign lesions (Table 2). Twenty-nine (7.25%) biopsies were non-diagnostic as they contained inadequate cellular material. Thirteen biopsies (3.25%) showed non-specific findings and were considered non-diagnostic. The overall diagnostic yield of CT-guided lung biopsy in our study was 89.5%. There was no significant difference between diagnostic yield between FNA and core  $\pm$  FNA groups (88.8% vs 92%,  $P = 0.80$ ).

The overall sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of CT-guided thoracic biopsies for a malignant lesion was 96%, 100%, 97%, 100% and 88% respectively (Table 3).

Twelve malignant lesions had false-negative biopsy results. The diagnostic procedure was repeated with fiberoptic transbronchial biopsy in 4 that revealed non-small cell cancer (NSCLC). Two patients had metastatic NSCLC confirmed via cervical lymph node biopsy. One

Table 1. Comparison of Procedure Factors and Diagnostic Yield Between FNA and Core  $\pm$  FNA Groups

Characteristics	FNA	Core $\pm$ FNA	P value
Number of passes	2.53 $\pm$ 1.382	2.5 $\pm$ 1.055	0.88
Lesion size	(36.5 $\pm$ 21.6) mm	(39.3 $\pm$ 22.5) mm	0.39
Lesion depth	(64.1 $\pm$ 21) mm	(65.4 $\pm$ 21.9) mm	0.69
Traversed lung length	(11.9 $\pm$ 14.5) mm	(14 $\pm$ 16.1) mm	0.33
Diagnostic yield	88.2%	92.4%	0.80

Table 2. Pathological Diagnosis of Samples from 399 CT-guided Thoracic Biopsies

Pathologic diagnosis	Number (%)
Malignant	269 (67.4%)
Adenocarcinoma	113
Non-small cell carcinoma	64
Squamous cell carcinoma	31
Metastases	21
Small cell carcinoma	15
Lymphoma	3
Miscellaneous	25
Benign	85 (21.3%)
Inflammatory	32
Tuberculosis	7
Fungal infection	6
Pyogenic abscess	1
Neoplasm	3
Miscellaneous	36
Suspicious for malignancy	3 (0.8%)
Non-diagnostic biopsy	42 (10.5%)
Non-specific findings	13
Inadequate sampling	29
Total	399

Table 3. Diagnostic Accuracy of Tissue Samples for Malignancy

Description	Number/accuracy
True-positive	270
True-negative	85
False positive	0
False negative	12
Sensitivity	95.7% (270/282)
Specificity	100% (85/85)
Diagnostic accuracy	96.8% (355/367)
Positive predictive value	100% (270/270)
Negative predictive value	87.6% (85/97)

Table 4. Risk of Complications Correlated with Various Procedural Factors

Complication	P value
<b>Pneumothorax</b>	
Patient age	0.45
Lesion depth	0.044 (>60 mm)
Lesion size	0.007 ( $\leq$ 33 mm)
Needle size	0.75
Number of passes	0.76
Traversed lung-length	<0.0001 (>3 mm)
<b>Haemoptysis</b>	
Patient age	0.60
Lesion depth	0.256
Lesion size	0.048
Needle size	0.55
Number of passes	0.97
Traversed lung-length	0.001 (>3mm)

patient had metastatic NSCLC confirmed via liver biopsy. Two patients underwent wedge-resection of lung which confirmed a diagnosis of NSCLC. One patient underwent mediastinal mass excision, which confirmed a mediastinal sarcoma. One patient underwent surgical resection with a subsequent histological diagnosis of lymphoma. There were no false-positive malignant results.

### Complications

Complications occurred in 149 of the 399 (34.8%) biopsy procedures, including 139 (34.8%) pneumothoraces (12 of which required chest drain insertion), haemoptysis in 13 (12 of which was not life-threatening and one which was life-threatening and associated with mortality), haemothorax not requiring chest drain insertion in 2, subcutaneous emphysema in 1 and mortality in 1.

Multiple independent risk factors for pneumothorax were examined (Table 4). Of these, the traversed lung length (>3mm;  $P < 0.0001$ ) and lesion-size ( $\leq 33$  mm;  $P = 0.0072$ ) were significant. The depth of the lesion was also borderline significant (>60 mm;  $P = 0.0442$ ). No significant relationship was found between the pneumothorax rate and patients' age, needle size or the number of passes.

The occurrence of haemoptysis also correlated significantly with the traversed lung length (>3 mm;  $P = 0.016$ ) and lesion size ( $P = 0.0478$ ). No significant relationship was found between the haemoptysis and lesion-size, needle-size, patients' age or the number of passes. None of the patients had haemoptysis prior to the procedure. There was no significant differences in the incidence of complications between the FNA and core  $\pm$  FNA groups.

The single case of mortality was a 60-year-old man with acute myelocytic leukemia and multiple pulmonary masses suspected to be invasive pulmonary aspergillosis but failed to respond to treatment. He developed haemoptysis and chest pain post biopsy after transferring to recovery room. He was transferred back to the CT room for assessment but unfortunately went into cardiopulmonary arrest on the table and died.

### Discussion

Since CT-guided lung biopsy was first described in 1976,<sup>14</sup> it has become widely accepted as a safe and accurate diagnostic method for the evaluation of pulmonary lesions.<sup>15,16</sup> The most common complications after percutaneous biopsy of the chest are pneumothorax and pulmonary haemorrhage.<sup>1,17</sup> The frequency of pneumothorax (34.8%) and chest tube placement (3.0%) in our study is within the range reported in previous studies.<sup>11,16,18</sup>

Previous studies have reported that many factors influence the complications of CT-guided thoracic biopsies. Our study showed that there was significant association between the traversed lung-length, lesion-size and lesion-depth with the rate of pneumothorax. These findings parallel the results obtained by previous studies.<sup>13,19</sup> Our study did not find a correlation between the patient's age, needle size and number of needle passes with the risk of pneumothorax.

We found that an increased traversed lung length is a risk factor for haemoptysis. These findings are similar to previous studies by Khan et al,<sup>19</sup> and Yeow et al,<sup>13</sup> who also found that the traversed lung-length is a risk factor for bleeding. Other factors such as lesion-size, age, number of passes, needle size and lesion depth did not appear to affect the rate of haemoptysis.

The overall sensitivity, specificity and diagnostic accuracy of CT-guided biopsy in our study (Table 3) is similar to those obtained in previous studies.<sup>18,20,21</sup> Previous studies have also shown that on site evaluation of FNA specimens can improve the diagnostic ability of CT-guided lung biopsies.<sup>22,23</sup> Yamagami et al<sup>24</sup> also showed that the combined use of fine-needle aspiration and core biopsy also improves the diagnostic ability of CT-guided lung biopsy. We believe that our high diagnostic accuracy of 96.8% was partly due to by the on-site of evaluation FNA specimens as well the use of a combined FNA and core biopsies in some of our patients. There was no significant difference in the diagnostic accuracies between FNA group and the core biopsy group. While a higher rate of complications was reported to occur with the combined use of 2 types of biopsies compared to with their single use by Klein et al,<sup>25</sup> our data showed complication rates similar to other studies that employed a single type biopsy technique,<sup>11,16,18</sup>

and there were no significant differences in complication rates between the FNA group and Core group.

There are some limitations to our study. First, this is a retrospective study and is therefore limited by the patients who have already been selected to undergo biopsies. Second, the experiences varied among the different radiologists and this could affect the yield, accuracy and complication rate. We also did not perform the analysis of experience with complications as the numbers were not uniformly distributed. Third, the needle sizes varied and this was unavoidable as the study was retrospective. Fourth, the technique of biopsy and choice of FNA and core were performed based on the radiologists' discretion and this may have affected the diagnostic yield. Despite these limitations, our results represent a tertiary care centre's experience with the state of art equipment and multiple operators which is the routine clinical practice.

## Conclusion

In conclusion, post CT-guided thoracic biopsy pneumothorax rate are associated with traversed lung-length, lesion-size, and lesion-depth while the risk factors affecting the haemoptysis rate are traversed lung-length and lesion-size. CT-guided thoracic biopsy is a safe technique with low complication rates and has a high diagnostic yield and accuracy for diagnosing malignant thoracic lesions.

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