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Lung density in the trajectory path — a strong indicator of patients sustaining a pneumothorax during CT-guided lung biopsy

Abstract

Introduction: The purpose is to evaluate the prognostic significance of lung parenchymal density during percutaneous coaxial cutting needle lung biopsy (PNLB).

Materials and methods: Retrospective analysis of 179 consecutive patients (106 males, 73 females; mean age 59.16 ± 16.34 years) undergoing PNLB was included. Mean lobar parenchymal lung density, mean densities anterior to the lesion and posterior to the chest wall in the needle trajectory path were measured in HU. Lesion location and needle trajectory were also measured. Fisher's exact test and Chi-square test were conducted to analyze the categorical variables. ANOVA test was done to examine continuous and normally distributed variables. Statistical significance was considered when $p < 0.05$.

Results: Mean lobar parenchymal lung density ($p < 0.05$) and mean parenchymal lung density relative to the needle trajectory path were below -800 HU in patients who sustained a pneumothorax. Increase in the number of pleural passes was significantly associated with the risk of patients having pneumothorax ($p < 0.05$). The mean distance from the skin to the lesion and needle trajectory angle were not statistically different among patients with and without pneumothorax ($p > 0.05$).

Conclusion: Lobar parenchymal density and lung parenchymal density anterior to the lesion and posterior to the chest wall in the needle trajectory path could be used as predicting parameters in patients undergoing PNLB who sustained a pneumothorax. These findings can help interventional radiologist further assess risk of pneumothorax when performing such procedure.

Key words: lung biopsy, iatrogenic pneumothorax, lung parenchymal density, parenchymal mass, needle trajectory

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Introduction

Percutaneous computed tomography (CT) guided needle pulmonary lesion biopsy is an effective and safe method for the diagnosis of lung nodules. In order to facilitate repeat sampling and decrease procedural duration, the coaxial technique for percutaneous lung lesion biopsy can be used. This method achieves all the aforementioned objectives without increasing the number of passes through the pleura [1]. Thus, percutaneous coaxial cutting needle lung biopsy (PNLB) has replaced open surgical biopsies as the gold standard for obtaining tissue samples from intraparenchymal lung masses to establish an

accurate pathological diagnosis. The American College of Radiology and Society of Interventional Radiology have reported that there are no absolute contraindications that are addressed prior to PNLB [1]. However, there are relative contraindications for PNLB, including, but not limited to significant coagulopathy, compromised cardiopulmonary function, lack of a safe pathway to the lesion, an inability of the patient to cooperate with positioning and instruction, and pregnancy. Nevertheless, success rates are affected by many variables. The success rates in many quality improvement task forces are reliant on a combination of factors such as interventionist skill set, years of experience and rate of complications post PNLB.

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One important complication of PNLB is pneumothorax. Pneumothorax is reported to occur in 17 to 26.6% of patients, with 1 to 14.2% requiring chest tube insertion [2]. Risk factors for pneumothorax during PNLB include as follows: patient's age [3], greater lesion depth [4], lower lobe lesion [5], needle trajectory angle less than 45 degrees [3, 5, 6], lesion size [7], increased number of pleural passes [8] and radiographic emphysema [9].

This study aims to evaluate the possibility that lobar lung parenchymal density and lung parenchymal density relative to the trajectory path are linked to an increased risk of pneumothorax during PNLB. The primary end point of the study is to evaluate the ability of interventional radiologists to assess parenchymal lung density accurately as a quantitative specific threshold in predicting pneumothorax in patients undergoing PNLB. A secondary end point is to evaluate which factors related to the patient, the lesion, or the techniques of PNLB act as a strong indicator for pneumothorax. Such findings may be relevant to formulating a model that aids in assessing risks quantitatively, prior to intervention.

Materials and methods

Inclusion and exclusion criteria

The retrospective study included 179 patients (106 males and 73 females) who underwent CT-guided percutaneous lung biopsies and were classified according to a lung biopsy technique. Exclusion criteria were the following: lesion < 5 mm diameter, uncorrectable coagulopathy, positive pressure ventilation, severe respiratory compromise, pulmonary arterial hypertension, and incapacity to follow instructions or refusal of the procedure. The study had full IRB approval.

Region of interest measurements

One expert in medical imaging (C.S.) measured the attenuation of lung parenchyma and lesion in all 179 patients. Lung parenchymal attenuation that was in the trajectory path of the needle (Figure 1) was determined by placing the routinely used region of interest (ROI) within the lung segments of greatest dimension in the transaxial plane and was calculated by using the average measurement over three ROI. Attenuation was measured at the level of each angle (I–V), then the average measurement was taken to calculate lung parenchymal attenuation anterior to the lesion and posterior to the chest wall as per Figure 1. Total lobular parenchymal density was

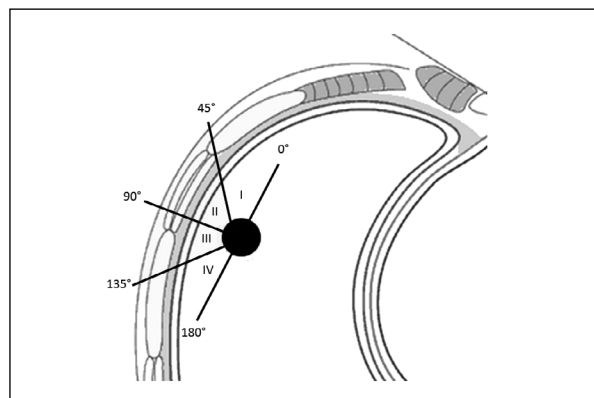


Figure 1. Lung parenchyma density within the trajectory angle from the chest wall

calculated employing an automated dedicated lung density software (Intellispace, 5.0, Philips Healthcare, Best, The Netherlands) to determine the mean attenuation of the lung parenchyma in each lobe of the lung.

Biopsy protocol

Informed consents were obtained from all patients prior to the lung biopsy. Coagulation parameters of all subjects were checked to ensure platelet counts > 50,000/mL and an international normalized ratio < 1.5 as recommended in consensus guidelines [10]. All patients had chest CT scans that were checked and cross-referenced with the referring physician and the patient history, prior to the procedure. The scan parameters prior to the biopsy were the following: detector width 256 × 0.625 mm; pitch 1.1; rotation time 0.4 sec; exposure factors 100 kVp, 200 mA, with z-axis modulation; and a scanning time of 2.1 sec. The patients were then positioned in the prone, supine, or lateral decubitus position on the basis of the location of the target lesion to minimize the number of pleural reflections, avoid major fissures, predetermine the needle trajectory, the shortest distance to the lesion, and the amount of crossed lung parenchyma. The study subjects were instructed to take a reproducible breath inspiration and abstain from talking during scans, needle positioning, and sampling. The localizing CT scan was used to determine the position of the target lesion.

By using sterile technique, local anesthesia was employed with 1% lidocaine. A small subcutaneous incision was made for needle entry, and a 16-gauge guiding needle was placed to the thoracic wall just proximal to the pleura. Subsequently, the pleura was passed with a single puncture (Quick Core, Cook, USA), and the needle was placed into the lesion. Then, the inner

part (stylet) of the biopsy needle was removed and the orifice of the needle was water sealed using normal saline while asking the patient to hold his breath. Then, the 18-gauge cutting needle was inserted into the lesion over the introducer. All PNLB was performed by 4 interventional radiologists with a mean of 17 years of experience.

Limited CT scan was obtained of each patient that underwent lung biopsy to identify complications such as pneumothorax and bleeding. If the pneumothorax was confined and not symptomatic, a repeat limited CT scan was taken 2 hours post biopsy. If on repeat scan, the pneumothorax was stable, the patients with normal vital signs were sent home with safety instructions. If the pneumothorax increased and/or the patients became unstable, an 8 French pleural drain was placed, and the patient was admitted to hospital for 24 hours.

Statistical analysis

Statistical analysis was performed using SPSS (statistical package for social sciences, version 21, SPSS Inc., Chicago, IL, USA). Fisher's exact test, and Chi-square test were conducted to analyze the categorical variables. Fisher's exact test was done when the sample size within the categories was very minimal (i.e. when comparing lesion lobes and needle angles). Using the central tendency theorem stating that when the sample size is greater than 30 patients, the non-normally distributed variables are considered normal, we were able to conduct ANOVA test. The tested variables were gender, age, smoking status, the number of pleural passes, the distance from the skin and the chest wall, lung density posterior to the chest wall and anterior to the lesion, lung density relative to the needle trajectory (Figure 1) and total lobar parenchymal lung density. Lung lesion density ratio was compared between each group and the ratio of lobar lung density to lesion density was calculated. Logistic regression approach was implemented to conduct bivariate and multivariate analysis to assess the crude and adjusted odds ratios of the risk of having a pneumothorax. Only variables that showed statistical significance of having pneumothorax on the bivariate level with a p-value less than 0.2 were included in the multivariate analysis. Results with a p-value less than 0.05 were considered statistically significant.

Study protocol

A single investigator, who was an expert in medical imaging and was not included in the proper study, reviewed clinical records of

each patient. All technical parameters were measured and the lung attenuation values employed an ROI of 2 mm. Lung density, lesion characteristics (location, size measured in greatest transverse diameter, and depth from the pleura along the biopsy track, if the lesion abutted the pleural surface), and the presence of a lung fissure or blood vessel intersecting the biopsy path were assessed and recorded (Figure 1).

Results

Patients' demographics

During the study period, 179 consecutive patients fulfilled the inclusion criteria and underwent image-guided lung biopsy at our institution. The mean age of males (61.58 ± 15.53 years) demonstrated a statistical difference compared to that of females (55.55 ± 16.97) ($p < 0.014$). Whereas, the mean age of smokers (60.77 ± 15.03) was not statistically different from that of non-smokers (57.89 ± 17.24 ; $p < 0.247$).

Of the 179 lung lesions, 48 (27%) were located in the right upper lobe, 17 (9%) in the right middle lobe, 27 (15%) in the right lower lobe, 47 (26%) in the left upper lobe, 29 (16%) in the left lower lobe, and 11 (7%) within the mediastinum. Malignant and benign lesions were diagnosed in 138 and 15 patients, respectively, with 26 non-diagnostic sample. The final diagnosis was adenocarcinoma ($n = 55$), small-cell carcinoma ($n = 16$), squamous cell carcinoma ($n = 23$), large-cell carcinoma ($n = 12$), lymphoma ($n = 7$) and metastatic tumors ($n = 45$).

Lung parenchymal characteristics and lung lesion density ratio

The lobar parenchymal lung density in all patients with pneumothorax demonstrated a threshold lower than -800 HU (increased aeration and reduced lung density), which included the segmental range (I – IV; $0-180^\circ$; Figure 1) of the needle trajectory (Table 1). Average lung density anterior to the mass and posterior to the chest wall showed an overall decrease in the subjects with pneumothorax compared to the patients without pneumothorax with varying significance. Significant decrease was noted at the right upper lobe ($p < 0.02$) and left upper lobe ($p < 0.02$).

Additionally, mean lesion density did not differ between both groups (Table 1). Finally, the lung (anterior to the lesion and posterior to the

Table 1. Mean lobar lung parenchymal density among the patients with and without pneumothorax

| Pneumothorax | Yes N = 79 | No N = 100 | P-value |
|-------------------|-----------------|------------------|---------|
| Right lung | | | |
| Right upper lobe | -831.95 ± 52.03 | -791.41 ± 51.88 | < 0.001 |
| Right middle lobe | -830.15 ± 54.05 | -792.94 ± 59.69 | < 0.001 |
| Right lower lobe | -823.52 ± 67.48 | -757.08 ± 58.97 | < 0.011 |
| Left lung | | | |
| Left upper lobe | -830.21 ± 53.36 | -786.82 ± 58.97 | < 0.001 |
| Left lower lobe | -817.31 ± 75.88 | -756.45 ± 172.10 | < 0.030 |

Note: (±) is standard deviation

Table 2. Mean lung density anterior to the lesion and posterior to the chest wall, mean lesion density, and lung to lesion tissue ratio among the patients with and without pneumothorax

| Pneumothorax | Lung density anterior to the lesion | | | Lesion density | | | Ratio | |
|-------------------|-------------------------------------|------------------|---------|----------------|---------------|---------|-------|-------|
| | Yes | No | P-value | Yes | No | P-value | Yes | No |
| Right lung | | | | | | | | |
| Right upper lobe | -819.4 ± 45.90 | -768.9 ± 80.13 | 0.02 | 37.41 ± 15.93 | 36.26 ± 14.15 | 0.80 | 1.31 | 1.29 |
| Right middle lobe | -841.0 ± 42.90 | -800.93 ± 47.90 | 0.10 | 38.59 ± 14.76 | 31.27 ± 23.17 | 0.44 | 1.13 | 4.17 |
| Right lower lobe | 747.87 ± 156.12 | -782.10 ± 65.90 | 0.47 | 31.26 ± 12.40 | 30.16 ± 15.94 | 0.84 | 1.22 | 1.59 |
| Left lung | | | | | | | | |
| Left upper lobe | -830.05 ± 61.70 | -777.18 ± 48.67 | 0.02 | 32.28 ± 18.71 | 32.45 ± 20.29 | 0.98 | 1.14 | 1.24 |
| Left lower lobe | -799.26 ± 97.84 | -755.55 ± 110.22 | 0.27 | 37.08 ± 14.02 | 35.73 ± 16.99 | 0.82 | 1.16 | 1.41 |
| Mediastinal | -811.05 ± 75.65 | -725.15 ± 147.55 | 0.15 | 39.85 ± 12.33 | 42.71 ± 7.42 | 0.58 | 1.10 | 1.048 |

Note: (±) is standard deviation

chest wall) to lesion density ratio in the patients with pneumothorax ranged from 1.24 to 4.14, compared to a narrower range from 1.1 to 1.3 in individuals who sustained a pneumothorax (Table 2). This study suggests a possible risk of pneumothorax in patients with a lung to lesion ratio less than 1.3.

Lung parenchymal density relative to the needle trajectory

The mean lung density relative to needle trajectory in the patients with pneumothorax was lower than -800 in all five angles (0–180°; Table 3). Mean lung densities of 135° and 180° relative to trajectories showed statistically significant difference between the subjects with and without pneumothorax ($p < 0.001$ and $p < 0.012$, respectively). Although there was no statistically significant difference for the other angles ($p > 0.05$), all had a mean lung parenchymal threshold below -800 HU, which is compatible with the results shown in Table 1. This finding was irrespective of the trajectory needle angle.

Needle entry, trajectory, depth and distance characteristics

The mean of the number of pleural passes in the patients with and without pneumothorax was 2.61 ± 1.85 and 1.95 ± 1.234 , respectively, which was not statistically significant ($p < 0.061$). Needle trajectory angle showed no statistical significance ($p = 0.79$). The majority of needle angles fell within 0 to 45 degrees (Table 3).

The total mean distance from the chest was statistically significant comparing the patients with versus those without pneumothorax ($p < 0.032$). This was not the case when we were looking at the total mean distance from the skin ($p < 0.823$; Table 3). There was no statistical significance between lesion lobes and lesion depth for both populations nor between depth and having pneumothorax in each lesion lobe ($p > 0.05$).

Bivariate and multivariate analyses of risk of having pneumothorax

At the bivariate logistic regression level, smoking status, the mean distance from the chest

Table 3. Needle trajectory angle, lesion lobes and distance characteristics among the patients with and without pneumothorax

| Pneumothorax | Yes N = 79 | No N = 100 | P-value |
|--|------------------|------------------|---------|
| Needle angle | | | |
| 0–45 ° | 72 | 80 | 0.791 |
| 46–90 ° | 6 | 17 | |
| 91–135° | 1 | 3 | |
| Mean lung density relative to needle trajectory | | | |
| 0° left | -806.89 ± 194.71 | -780.46 ± 78.87 | 0.211 |
| 45° middle left | -801.86 ± 200.35 | -771.17 ± 94.22 | 0.172 |
| 90° perpendicular to pleura | -804.38 ± 112.19 | -791.96 ± 81.22 | 0.232 |
| 135° middle right | -810.48 ± 79.58 | -764.75 ± 111.47 | 0.001 |
| 180° right | -811.39 ± 117.70 | -763.76 ± 119.44 | 0.012 |
| Mean distance from skin | | | |
| Right lung | 60.07 ± 17.902 | 55.34 ± 20.683 | 0.281 |
| Right upper lobe | | | |
| Right middle lobe | 56.32 ± 17.521 | 51.98 ± 21.161 | |
| Right lower lobe | 56.25 ± 20.634 | 55.57 ± 18.892 | |
| Left lung | 48.93 ± 13.134 | 59.64 ± 20.131 | |
| Left upper lobe | | | |
| Left lower lobe | 55.42 ± 23.472 | 60.28 ± 17.397 | |
| Mediastinal | 57.26 ± 36.421 | 41.11 ± 20.702 | |
| Total | 55.3 ± 20.842 | 55.97 ± 20.023 | 0.823 |
| Mean distance from chest wall | | | |
| Right lung | | | 0.836 |
| Right upper lobe | 20.36 ± 13.382 | 11.63 ± 12.784 | |
| Right middle lobe | 15.47 ± 13.025 | 10.07 ± 14.418 | |
| Right lower lobe | 17.14 ± 18.866 | 10.85 ± 13.816 | |
| Left lung | 13.04 ± 11.53 | 13.72 ± 17.409 | |
| Left upper lobe | | | |
| Left lower lobe | 18.83 ± 19.02 | 16.31 ± 19.174 | |
| Mediastinal | 18.33 ± 24.521 | 4.19 ± 9.921 | |
| Total | 17.02 ± 16.199 | 12.06 ± 15.202 | 0.032 |
| Number of passes | 2.61 ± 1.85 | 1.95 ± 1.234 | 0.061 |

Note: (±) is standard deviation

wall, and the number of pleural passes were significantly associated with the risk of having pneumothorax ($p < 0.05$). For instance, smokers were 2.75 times more liable to have pneumothorax compared to non-smokers (OR = 2.75; 95%CI: 1.51–5.03). Whereas, age, gender, lesion depth and lesion lobes were not statistically significant with the risk of having pneumothorax ($p > 0.05$; Table 4).

Whereas at the multivariate logistic regression level, adjusting for age and gender, smoking

status and the number of pleural passes remained in statistically significant association with the risk of having pneumothorax: smokers were 2.67 times more prone to having pneumothorax compared to non-smokers (OR = 2.67; 95%CI: 1.139–5.15). With every unit growth in the number of pleural passes, the odds of having pneumothorax increased multiplicatively by 1.33 folds (OR = 1.33; 95%CI: 1.69). However, the mean distance from the chest wall was not associated with the risk of having a pneumothorax ($p = 0.39$). Moreover,

Table 4. Bivariate and multivariate analyses of risk of having pneumothorax and other covariates showing adjusted ORs

| Variables | Bivariate analysis | | | Multivariate analysis | | |
|--------------------------------------|--------------------|------------|---------|-----------------------|-----------|---------|
| | OR | 95%CI OR | P-value | OR | 95%CI OR | P-value |
| Age | 1.01 | 0.99–1.02 | 0.62 | 1 | 0.98–1.02 | 0.92 |
| Gender | | | | | | |
| Male | Reference | | 0.45 | Reference | | 0.78 |
| Female | 0.79 | 0.44–1.44 | | 0.91 | 0.46–1.79 | |
| Smoking status | | | | | | |
| No | Reference | | 0.001 | Reference | | 0.003 |
| Yes | 2.75 | 1.51–5.03 | | 2.67 | 1.39–5.15 | |
| Mean distance from chest wall | 1.05 | 1.00–1.1 | 0.04 | 1.01 | 0.99–1.04 | 0.39 |
| Mean number of passes | 1.34 | 1.08–1.66 | 0.007 | 1.33 | 1.05–1.69 | 0.02 |
| Mean lesion depth | | | | | | |
| Peripheral | Reference | | 0.12 | Reference | | 0.23 |
| Central | 2.33 | 1.04–5.21 | 0.04 | 2.16 | 0.83–5.65 | 0.12 |
| Deep | 1.14 | 0.55–2.36 | 0.71 | 0.98 | 0.38–2.54 | 0.96 |
| Lesion lobes | | | | | | |
| Left lung | | | | | | |
| Left upper lobe | Reference | | 0.33 | | | |
| Left lower lobe | 2.05 | 0.80–5.233 | 0.13 | | | |
| Right Lung | | | | | | |
| Right upper lobe | 1.09 | 0.48–2.49 | 0.83 | | | |
| Right middle lobe | 3.06 | 0.96–9.69 | 0.06 | | | |
| Right lower lobe | 1.44 | 0.56–3.72 | 0.45 | | | |
| Mediastinal | 1.88 | 0.61–5.73 | 0.27 | | | |
| Types of lung lesions | | | | | | |
| Benign | Reference | | 0.23 | | | |
| Malignant | 0.56 | 0.19–1.66 | | | | |

CI — confidence interval; OR — is odds ratio

lesion depth remained unassociated with the risk of having pneumothorax ($p > 0.05$; Table 4).

Discussion

The decision to perform PLNB depends on the site of the abnormality, the performance status, the co-morbidities, and how much of an impact the procedure will carry in terms of management. In the literature, there is insufficient data on the ability of radiologists and other clinicians to predict the occurrence of iatrogenic pneumothorax [9]. Previous studies have reported an increased risk of pneumothorax with lesion depth, angle of trajectory, and visually assessed emphysema on chest CT [9, 11–14]. Our findings suggest that although radiologists can predict

the proportion of pneumothorax occurring in a cohort of patients, they are unable to do this in an individual case. To the best of our knowledge, this is the first study aiming to evaluate the quantitative lung parenchymal density and the risk of pneumothorax when performing PLNB.

Previously reported studies demonstrated a significant increase in pneumothorax rates from 13% for lesions abutting the pleural surface to 29% for lesions where the needle traverses the aerated lung, which is likely due to the decreased stability of the needle in a short intrapulmonary course leading to pleural tears [15]. Another study demonstrated that higher rates of pneumothorax were associated with needle paths greater than 4 cm [16]. Additionally, the interventional radiologist experience is the third major risk

factor for pneumothorax. The incidence rate of pneumothorax among experienced radiologists was 17% compared to 30% among unexperienced ones [15]. Our study demonstrated that overall lobar parenchymal density below -800 HU was associated with having pneumothorax. Also, we showed that lower lung densities (less than -800 HU) relative to needle trajectory (0° to 180° anterior to the lesion and posterior to the chest wall) are associated with having pneumothorax. Adding to the current literature and data, quantification of the lung parenchyma in the trajectory path of the biopsy could further reduce the rate of pneumothorax during PNLB.

Other suggested risk factors for pneumothorax during PNLB include smoking, older age, needle thickness, biopsy needle angle, lesion position, lesion volume and distance from the pleura to the tumor [17]. In our study, initial bivariate analysis showed that pneumothorax was associated with a positive smoking history, increased mean distance from the chest wall, and the higher number of pleural passes. However, when we adjusted for age and gender, the mean distance from the chest wall was not associated with having a pneumothorax. Moreover, age was not linked to an increased risk of pneumothorax, which is not compatible with the current literature [17]. Finally, gender, lesion depth (peripheral, central or deep) and lesion lobes were not associated with having pneumothorax.

There were shortcomings in our study. First, the retrospective design of the research made it difficult to determine the clinical indication for ordering a lung biopsy in each patient accurately. Also, for reasons such as lack of follow-up, final results from surgical pathology or autopsy were not available to confirm a benign or malignant etiology for all of the non-diagnostic core biopsies. Second, the relationship between the distance of a target from the diaphragm and the likelihood of a diagnostic success on the basis of the etiology of the lesion was not addressed. Third, our study did not measure the associated post-biopsy complication rates such as bleeding, infection and clinical outcome. Finally, there was no comparison between operators.

Conclusions

Pneumothorax is still a major issue in PNLB with a myriad of risk factors. This is the first study to investigate and prove that the density of lobar lung parenchyma and parenchyma anterior to the lesion and relative to the needle trajectory

path could be used as parameters in predicting pneumothorax in patients undergoing percutaneous coaxial cutting needle biopsy. This finding can help interventional radiologist further assess risk of pneumothorax when performing such procedure.

Conflict of interest

Authors declare no grants, financial support or conflict of interest.

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