Original Article

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Impact of Respiratory Phase during Pleural Puncture on Complications in CT-Guided Percutaneous Lung Biopsy

CT 유도 경피 폐생검에서 흉막 천자 시 호흡 시기가 합병증에 미치는 영향

Ji Young Park, MD[1], Ji-Yeon Han, PhD[1]*, Seok Jin Choi, PhD[1], Jin Wook Baek, PhD[1], Su Young Yun, MD[1], Sung Kwang Lee, MD[2], Ho Young Lee, MD[3], SungMin Hong, MD[3]

Departments of [1]Radiology and [2]Thoracic and Cardiovascular Surgery, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea
[3]Division of Pulmonary, Allergy and Critical Care Medicine, Department of Internal Medicine, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea

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***Corresponding author**
Ji-Yeon Han, PhD
Department of Radiology,
Busan Paik Hospital,
Inje University College of Medicine,
Bokji-ro 75 Bokji-ro, Busanjin-gu,
Busan 47392, Korea.

Tel 82-51-890-6549
Fax 82-51-896-1085
E-mail radjyhan@gmail.com

Purpose This study investigated whether the respiratory phase during pleural puncture in CT-guided percutaneous transthoracic needle biopsy (PTNB) affects complications.

Materials and Methods We conducted a retrospective review of 477 lung biopsy CT scans performed during free breathing. The respiratory phases during pleural puncture were determined based on the table position of the targeted nodule using CT scans obtained during free breathing. We compared the rates of complications among the inspiratory, mid-, and expiratory respiratory phases. Logistic regression analysis was performed to control confounding factors associated with pneumothorax.

Results Among the 477 procedures, pleural puncture was performed during the expiratory phase in 227 (47.6%), during the mid-phase in 108 (22.6%), and during the inspiratory phase in 142 (29.8%). The incidence of pneumothorax was significantly lower in the expiratory puncture group (40/227, 17.6%; $p = 0.035$) and significantly higher in the mid-phase puncture group (31/108, 28.7%; $p = 0.048$). After controlling for confounding factors, expiratory-phase puncture was found to be an independent protective factor against pneumothorax (odds ratio = 0.571; 95% confidence interval = 0.360–0.906; $p = 0.017$).

Conclusion Our findings suggest that pleural puncture during the expiratory phase may reduce the risk of pneumothorax during image guided PTNB.

Index terms Image-Guided Biopsy; Needle Biopsy; Lung Neoplasm; Respiration

INTRODUCTION

Image-guided percutaneous transthoracic needle biopsy (PTNB) plays a crucial role in diagnosing and treating lung lesions. CT-based guidance is commonly used for PTNB due to its superior contrast resolution and accessibility (1, 2). However, unlike real-time procedures, such as CT fluoroscopy or cone beam CT, conventional CT-guided biopsy is susceptible to the patient's respiratory motion, which can impact both the diagnostic accuracy and complication rates, particularly for small lesions or those located in the lower lungs (3).

Breath-holding during the procedure is commonly recommended to mitigate respiratory motion effects, although exceptions exist for larger masses, allowing calm breathing or sedation (4-7). However, guidelines for the specific respiratory phases of pleural puncture vary, ranging from a single breath-hold (6, 7) to no specific instructions (1, 8). Operators often make decisions based on individual cases and patient comfort, such as puncture during submaximal inspiration, gentle expiration of lung base lesions, or apnea (4-7).

At our institution, all PTNB procedures are performed during calm breathing to prioritize patient comfort. A previous study reported that free-breathing biopsy has accuracy and complication rates comparable to those of conventional respiratory-hold biopsy (9). As our procedure was consistently performed during free breathing, the patients were categorized into groups based on whether pleural puncture was performed during inspiration or expiration. In this study, we retrospectively classified patients who underwent PTNB according to the respiratory phase during pleural puncture and analyzed the differences in complications between these groups.

MATERIALS AND METHODS

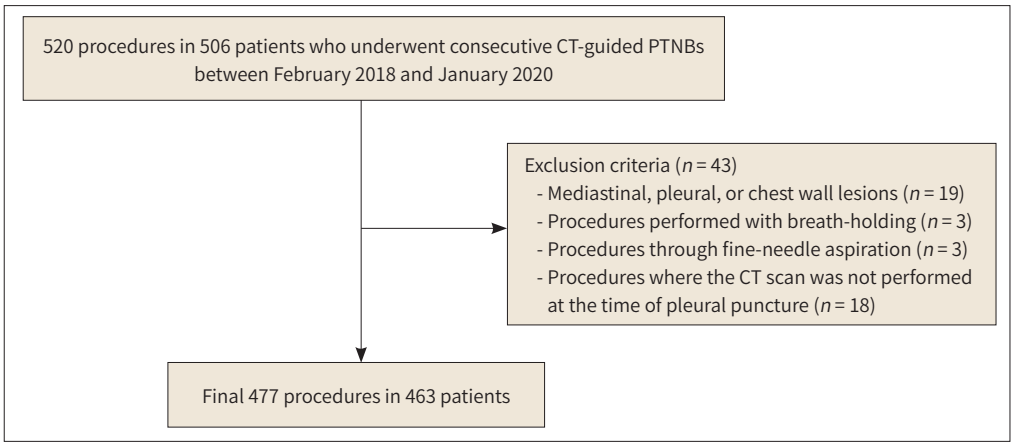
PATIENTS

This retrospective, single-center study was approved by the Institutional Review Board (IRB No. 2023-05-012). We included 520 procedures performed on 506 patients who underwent consecutive CT-guided PTNBs for chest lesions between February 2018 and January 2020. The inclusion criterion was CT-guided lung parenchymal core biopsy performed under free-breathing conditions. As a result, we excluded 19 patients with mediastinal, pleural, or chest wall lesions; three procedures were performed with breath-holding, and three were conducted through fine-needle aspiration. Additionally, we excluded 18 procedures in which CT was not performed at the time of pleural puncture, making the evaluation of the respiratory phase impossible. Ultimately, the study included 477 procedures involving 463 patients (Fig. 1). Among them, 14 patients underwent two procedures, including five with biopsies of different lesions and nine with biopsies of the same lesion.

PROCEDURE

PTNBs were performed under CT guidance using a 64-section CT scanner (Somatom Perspective; Siemens Healthcare, Erlangen, Germany). Low-dose thin-collimation axial scans were obtained with settings of 80 kVp, 12–15 effective mA per scan, a 0.48-second rotation time, and 64 × 0.6 mm collimation. CT fluoroscopy was not performed. Two thoracic radiol-

Fig. 1. The Flowchart of the case enrollment process of the patients.



PTNB = percutaneous transthoracic needle biopsy

ogists with 20 and 5 years of experience in image guided PTNB performed all the procedures. Core needle biopsies were performed using a coaxial technique with a semi-automatic 21-gauge and 20-gauge introducer needles (Stericut, TSK, Tochigi, Japan). Biopsies were performed with the patient breathing calmly.

The respiratory motion of the nodule was carefully observed through two to three procedural scans before performing a pleural puncture during the intervention. If the motion was not significant, the intervention followed an approach similar to conventional CT-guided biopsy procedures. However, respiratory targeting was used in cases where the nodules were highly mobile. During this technique, the operator inserted the needle at the end of the inspiratory or expiratory phase during a short respiratory pause while the patient continued to breathe (9). To avoid the ribs and minimize parenchymal vascular damage, the operator selected an appropriate respiratory phase for pleural puncture. We used a rapid needle out/patient rollover maneuver on the side of the pleural puncture (biopsy side dependent) but did not use the blood patch.

At each procedural step, a minimum of five to six CT scans were performed, including initial planning, grid attachment, needle insertion into the chest wall, puncture of the pleura, needle placement in the lung, core biopsy needle insertion into the target, and a final post-procedural scan after needle removal. Additional scans were obtained when adjustments were made to the direction of the needle.

IMAGING ANALYSIS: EVALUATION OF RESPIRATORY PHASE AT PLEURAL PUNCTURE

All the images were reviewed by the same operator. Procedural CT scans consisted of axially reconstructed images with a thickness of 2 mm. All CT scans were carefully reviewed to assess the respiratory phase during the pleural puncture. Scans in which the patient's position changed, those taken after the development of pneumothorax, and the final scan after needle removal were excluded, assuming a corresponding change in the nodule location. Of the 3224 scans performed in 477 procedures, 2480 were analyzed for respiratory phase assessment.

MAXIMAL RESPIRATORY MOTION ANALYSIS

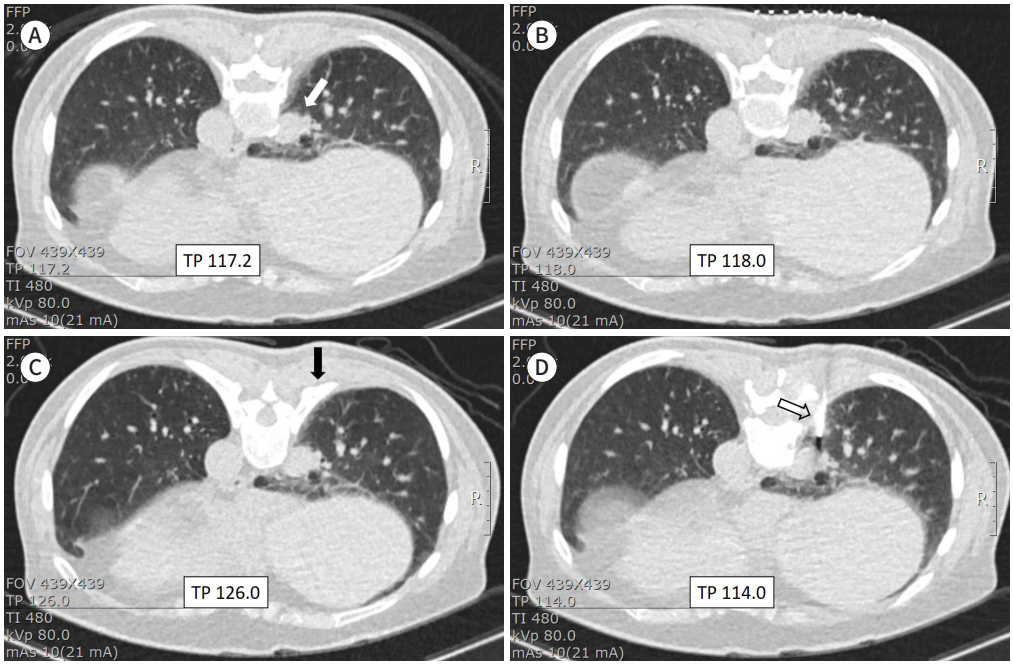
During the first procedural CT scan, the ideal target point of the nodule was arbitrarily set. The target point could either be at the same location or different from the actual biopsy site. In the subsequent scans, the table position of the constant target point was determined. Adjacent anatomical landmarks, such as pulmonary vessels or bronchi, were considered to establish the same constant location of the nodule. Second, maximal respiratory motion was measured by calculating the difference between the highest and lowest table positions of the target point on multiple CT scans.

RESPIRATORY PHASE ANALYSIS AT PLEURAL PUNCTURE

Given that CT scanning is not real-time imaging, it was hypothesized that once the needle punctures the pleura and nodule, the motion of the nodule might become less significant as it is fixed to the chest wall.

For each procedure, the CT series in which the first pleural puncture was performed was selected to assess the respiratory phase of the pleural puncture. The difference between the

Fig. 2. CT scan based respiratory phase assessment during pleural puncture (expiratory phase).
A-D. The target point was determined to be the most appropriate site for biopsy of the nodule in the right lower lobe (white arrow, A). The TP (figure) of the target point was 117.2 in the first scan (A), 118.0 in the second scan (B), 126.0 in the third scan (C), 114.0 in the fourth scan (D), and 118.0 in the fifth scan (not shown). The TP at the same target point was significantly different in each scan because of respiratory motion. The maximal respiratory motion was measured at 12.0 mm (subtraction between the highest TP in (C) and the lowest TP of the target in (D): 126.0–114.0 = 12.0). The scan obtained at the first pleural puncture (open arrow) was identified as the one shown in (D); since the difference between the TP at the time of pleural puncture (D, 114.0) and the lowest TP among all scans (D, 114.0) was 0, it was considered an expiratory puncture corresponding to the lower 1/3 of maximal respiratory motion. Respiratory targeting was performed during the expiratory phase, because the access path was obstructed by the rib, as shown in (C) (black arrow), which was obtained during the inspiratory phase.
TP = table position



JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

table position of the target point at the time of pleural puncture and the lowest table position of the target point was obtained and classified into one of three respiratory phases. If the difference in the table position was lower than the lower 1/3 of the maximal respiratory motion, it was classified as an expiratory phase puncture (Fig. 2). Similarly, if the difference in table position fell within the mid 1/3 of the maximal respiratory motion, it was classified as a mid-phase puncture (Fig. 3). Differences in the upper 1/3 of the maximal respiratory motion were classified as inspiratory phase puncture (Fig. 4). Additionally, steady-state puncture was defined when the table position of the target point remained the same among multiple CT scans, indicating that respiratory motion was barely detectable in the chest CT image. The respiratory phase of steady-state puncture, while not visibly detectable, was still presumed to be present and thus was classified as the mid-phase puncture.

ANALYSIS OF COMPLICATIONS

Complications, including pneumothorax, significant pneumothorax requiring chest tube placement or immediate aspiration, CT parenchymal hemorrhage, and hemoptysis, were assessed by reviewing postprocedural scans and medical charts. The severity of CT parenchymal hemorrhage was graded according to a previously used grading scheme for CT-guided

Fig. 3. Respiratory phase assessment during pleural puncture (mid-phase).
A-D. The TP in the figure of the target point in the right lower lobe (arrow) is determined in the first scan, as shown in (A). The maximum respiratory motion was calculated as 16.2 mm, obtained by subtracting the lowest TP of the target in (B) from the highest TP in (A): 172.2–156.0 = 16.2. (D) illustrates the scan taken during the first pleural puncture (arrow), which was categorized as a mid-phase puncture, with an 8.0 mm difference from the lowest TP.
TP = table position

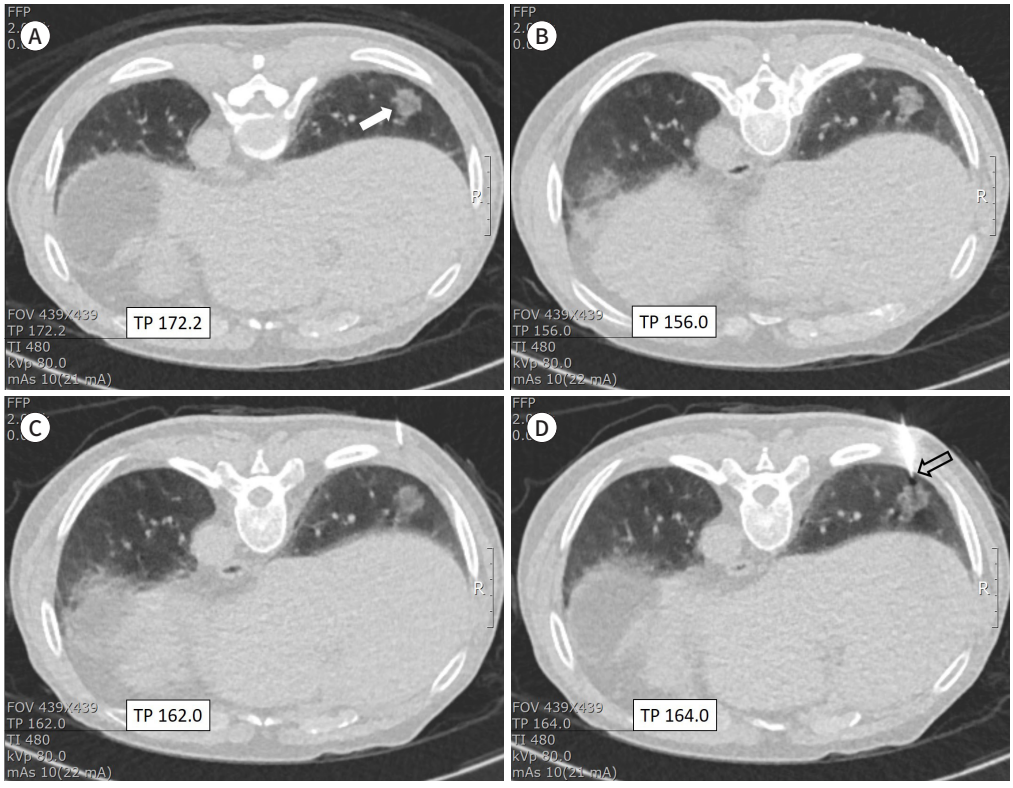
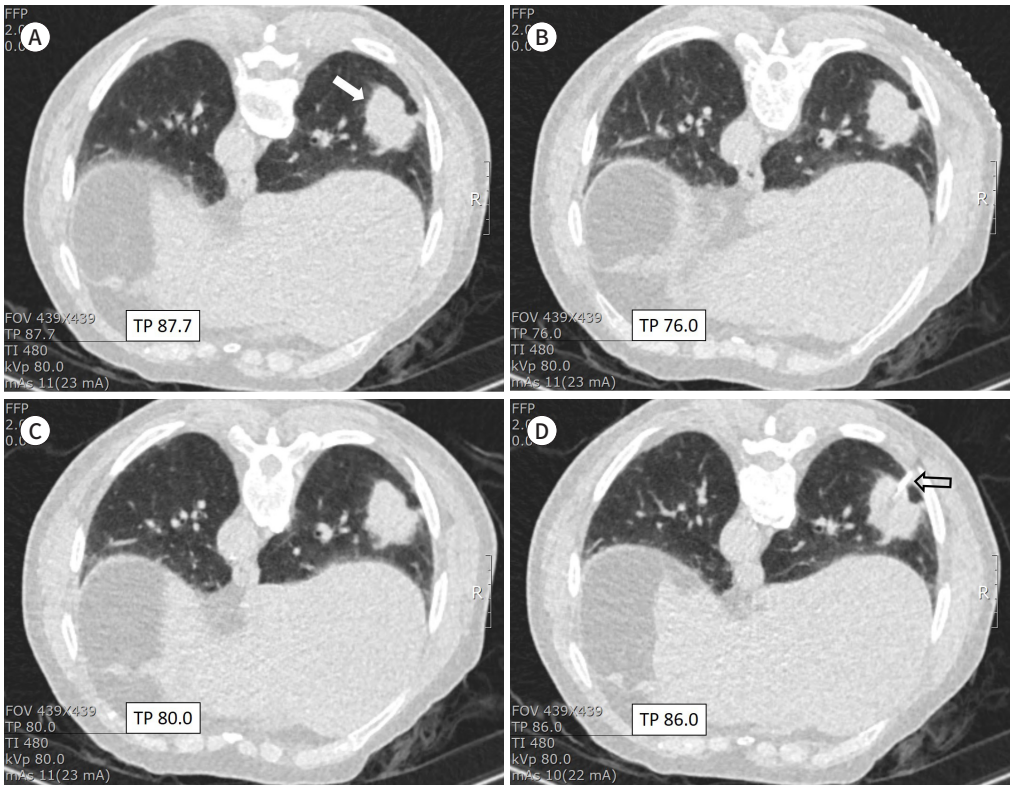


Fig. 4. Respiratory phase assessment during pleural puncture (inspiratory phase).
A-D. In the first scan (A), the TP (in the figure) of the target point in the right lower lobe (arrow) is 87.7. The maximum respiratory motion was measured at 11.7 mm, which was ascertained by subtracting the lowest TP of the target in (B) from the highest TP in (A): 87.7–76.0 = 11.7. The scan taken during the first pleural puncture (open arrow), which is indicative of inspiratory phase puncture, is presented in (D).
TP = table position



PTNB (10). Grade 0 was defined as no pulmonary hemorrhage, grade 1 as needle tract hemorrhage ≤ 2 cm in width, grade 2 as hemorrhage > 2 cm in width but sublobar, grade 3 as lobar hemorrhage or greater, and grade 4 as hemothorax. Technical failure (i.e., non-diagnostic result) was designated when the pathologic reports of the biopsy were graded "insufficient for diagnosis" or "lung parenchyma tissue only."

STATISTICAL ANALYSIS

Complications among the three respiratory phases were differentiated using Pearson's chi-squared test. Differences in demographic, nodule, and technical features that might contribute to pneumothorax, including small size, subpleural or lower lobe location, emphysema, and multiple pleural punctures, were compared among the different respiratory phase groups (3, 4, 6, 7). Logistic regression analysis was conducted to control for confounding factors influencing pneumothorax and determine whether the respiratory phase was an independent influencing factor during pleural puncture. Independent variables included small nodule size, lower lobe location, nodule depth, use of respiratory targeting, presence of emphysema, multiple pleural punctures, and expiratory phase puncture. Statistical analysis was performed using SPSS software (version 27.0, IBM Corp., Armonk, NY, USA), with statistical

JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

significance set at $p < 0.05$.

RESULTS

Table 1 summarizes the characteristics of the nodules, respiratory phases during pleural puncture, and associated complications of the 477 PTNB procedures performed. The maximal respiratory motion of nodules was 5.5 ± 4.4 mm, with a range of 0–40 mm. The pleural puncture was performed in the expiratory phase in 47.6% (227/477) of the cases, mid-phase in

Table 1. Characteristics of Pulmonary Nodule in Percutaneous Transthoracic Needle Biopsy (*n* = 477)

Characteristic	
Patient	
Sex, male	302 (63.3)
Age (year)	67.6 ± 11.6 (21–95)
Location	
Lower lobes	195 (40.9)
Middle lobe or lingular segment	53 (11.1)
Upper lobes	229 (48.0)
Nodule depth	
Subpleural (distance from pleura ≤ 20 mm)	399 (83.6)
Central (distance from pleura > 20 mm)	78 (16.4)
Size of target nodule (cm)	
≤ 1.0	22 (4.6)
1.1–2.0	136 (28.5)
2.1–3.0	121 (25.4)
3.1–4.0	68 (14.3)
> 4.1	130 (27.3)
Dose length product (mGy*cm)	24.1 ± 10.7 (11–137)
No. of performed CT scans	6.8 ± 2.0 (0–15)
Respiratory targeting performed	119 (24.9)
Maximal respiratory motion (mm)	5.5 ± 4.4 (0–40)
Multiple pleural puncture (≥ 2)	74 (15.5)
Complication	
Pneumothorax, total	104 (21.8)
*Significant pneumothorax	16 (3.4)
Hemoptysis	40 (8.4)
CT parenchymal hemorrhage	231 (48.4)
Grade 1	132 (27.7)
Grade 2	96 (20.1)
Grade 3	3 (0.6)
Grade 4	0 (0)
Nondiagnostic result (failure)	9 (1.9)

Data are presented as mean ± standard deviation (range) or *n* (%).
*Significant pneumothorax: chest tube placement or immediate aspiration required.

22.6% (108/477), and inspiratory phase in 29.8% (142/477). Notably, in 10 patients, no detectable respiratory movements were observed, indicating a steady-state puncture on chest CT. These cases were classified as mid-phase puncture. The rates of complications observed in free-breathing biopsy were as follows: pneumothorax, 21.8%; significant pneumothorax requiring chest tube placement or aspiration of air, 3.4%; hemoptysis, 8.4%; and CT parenchymal hemorrhage, 48.4%. Nondiagnosable results or biopsy failure were obtained in 1.9% of the cases.

Table 2 presents a comparison of complication rates among the three respiratory phases. A significantly lower rate of pneumothorax was observed in the expiratory phase (17.6%, 40/227; $p = 0.035$), whereas a significantly higher rate was observed in the mid-phase (28.7%, 31/108; $p = 0.048$) than in other phases. The grade 2 or higher CT parenchymal hemorrhage rate was lowest in the expiratory phase, although no statistically significant differences were detected (18.1%, 41/227; $p = 0.167$). In addition, no significant differences in the rates of hemoptysis, chest tube placement, immediate air aspiration, or technical failure were observed in the respiratory phase. There were no significant differences among the different respiratory phase groups that might have contributed to the pneumothorax rates, except for multiple pleural punctures (Table 3).

Furthermore, expiratory-phase puncture was identified as an independent protective factor

Table 2. Differences in Complications according to Respiratory Phase

	Total (*n* = 477)		Expiratory (*n* = 227)		Mid* (*n* = 108)		Inspiratory (*n* = 142)	
	n (%)	*p*-Value†	*n* (%)	*p*-Value‡	*n* (%)	*p*-Value‡	*n* (%)	*p*-Value‡
Pneumothorax (total)	104 (21.8)	0.063	40 (17.6)	0.035	31 (28.7)	0.048	33 (23.2)	0.621
Significant pneumothorax	16 (3.7)	0.949	7 (3.1)	0.754	4 (3.7)	0.819	5 (3.5)	0.895
Hemoptysis	40 (8.4)	0.418	23 (10.1)	0.190	7 (6.5)	0.491	10 (7.0)	0.417
CT hemorrhage (≥ grade 2)	99 (20.8)	0.385	41 (18.1)	0.167	25 (23.1)	0.486	33 (23.2)	0.384
Failure	9 (1.9)	0.861	5 (2.2)	0.629	2 (1.9)	0.976	2 (1.4)	0.617

*Includes mid-phase puncture (*n* = 98) and steady state puncture (*n* = 10).
†Differences of complications among the three respiratory phases.
‡Comparison with different respiratory phase groups.

Table 3. Differences of Variables among the Different Respiratory Phase Groups

	Expiratory (%) (*n* = 227)	Mid (%) (*n* = 108)	Inspiratory (%) (*n* = 142)	*p*-Value*
Sex, male	143 (63.0)	70 (64.8)	89 (62.7)	0.933
Age ≥ 65 years	27 (11.9)	11 (10.2)	21 (14.8)	0.525
Nodule size ≤ 10 mm	10 (4.4)	4 (3.7)	8 (5.6)	0.755
Subpleural location	190 (83.7)	92 (85.2)	117 (82.4)	0.839
Lower lobe location	96 (42.3)	48 (44.4)	51 (35.9)	0.332
Emphysema	30 (13.2)	10 (9.3)	19 (13.4)	0.536
Respiratory targeting	58 (25.6)	33 (30.6)	28 (19.7)	0.140
Pleural puncture ≥ 2	38 (16.7)	23 (21.3)	13 (9.2)	0.025

*Differences among three respiratory phase groups.

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Table 4. Univariable and Multivariable Logistic Regression Analysis for Pneumothorax

	Univariable Analysis				Multivariable Analysis			
	B	OR	95% CI	*p*-Value	B	OR	95% CI	*p*-Value
Size ≤ 10 mm	0.759	2.137	0.871–5.242	0.097				
Lower lobe location	0.376	1.456	0.940–2.255	0.092				
Subpleural location	0.187	0.829	0.450–1.527	0.548				
Emphysema	1.064	2.897	1.632–5.142	< 0.001	1.150	3.159	1.741–5.730	< 0.001
Respiratory targeting	0.615	1.850	1.154–2.965	0.011	0.541	1.717	1.049–2.811	0.031
Pleural puncture ≥ 2	0.889	2.432	1.425–4.151	0.001	0.907	2.477	1.418–4.330	0.001
Expiratory phase puncture	-0.475	0.622	0.399–0.969	0.036	-0.560	0.571	0.360–0.906	0.017

CI = confidence interval, OR = odds ratio

against the development of pneumothorax, as revealed by multivariable logistic regression analysis after controlling for other risk factors (odds ratio [OR], 0.571; 95% confidence interval [CI] = 0.360–0.906; $p = 0.017$) (Table 4). Other independent risk factors for pneumothorax were respiratory targeting (OR, 1.717; 95% CI = 1.049–2.811; $p = 0.031$), emphysema (OR, 3.159; 95% CI = 1.741–5.730; $p < 0.001$) and multiple pleural punctures (OR, 2.477; 95% CI = 1.418–4.330; $p = 0.001$).

DISCUSSION

In this study, we compared the complication rates based on the respiratory phase during pleural puncture in CT-guided lung biopsies performed under free-breathing conditions and without specific breathing instructions. Among the three respiratory phases, the expiratory phase was the most punctured. Notably, the pneumothorax rate was significantly lower in the expiratory puncture group than in the mid-phase puncture group. Furthermore, our analysis revealed that expiratory-phase puncture independently acted as a protective factor against pneumothorax, even after controlling for well-known risk factors.

Previous reviews on the PTNB technique have presented varying information regarding the preferred respiratory phases, including inspiratory or expiratory apnea, normal end-expiration, small inspiration, and quiet breathing, with some lacking specific data (3-6, 11-17). The rationale behind inspiratory puncture is to maintain a comfortable breath-hold and reduce the risk of air embolism in cases where patients fail to hold their breath and inhale during expiration (16). In contrast, end-expiratory puncture is suggested because of its advantages, such as puncturing within the respiratory plateau, longer patient respiration time, greater patient comfort, and reliability in needle positioning (11, 12, 17). However, there is a lack of scientific evidence supporting the selection of an appropriate respiratory phase for PTNB.

In our study, we observed that expiratory phase puncture resulted in a reduced pneumothorax rate (17.6%), whereas mid-phase puncture showed a higher rate of pneumothorax (28.7%). When comparing our findings with previous meta-analyses of CT-guided core biopsy (18, 19), we found a 30.0% pneumothorax rate in one study where pleural puncture was performed during expiratory hold (20) and a range of 12.9%–41.6% pneumothorax rate in another study with puncture during mid-inspiration (21). It is worth noting that most studies did not men-

tion the respiratory phase of the procedure unless breath-holding was employed.

The physiological basis for the decrease in pneumothorax during expiratory puncture may be increased intrapleural pressure during expiration. Min et al. (22) described this phenomenon by demonstrating a decrease in pneumothorax when the biopsy needle was removed during the expiratory hold. Another potential contributing factor is the minimization of chest wall motion during expiration. In a study by Furukawa et al. (23), the location of the pulmonary nodule during expiration was found to be closer to its actual location than during inspiration on the virtual airway map of chest CT, which was obtained for bronchoscopy. Considering that chest movements are expected to be substantial during mid-inhalation without a respiratory plateau, this could increase the risk of pneumothorax during mid-inspiration punctures.

Our study did not identify any significant difference in hemoptysis based on the respiratory phase of pleural puncture. It is well-known that deeper inspiration during the procedure may lead to the tearing of the pleural surface (5, 16). The rate of CT parenchymal hemorrhage was lower in the expiratory phase than in the other respiratory phases, although the difference was not statistically significant. This observation could be attributed to the procedure being performed during shallow rather than deep breathing during the expiratory phase.

The overall rates of parenchymal hemorrhage (48.4 vs. 41.1%) and hemoptysis (8.4 vs. 0.7%–14%) in our study were slightly higher than those reported in previously published studies (2, 10, 24, 25). This may be because, according to our medical records, minimal blood-tinged sputum was considered hemoptysis. Another possibility is lung parenchymal injury resulting from free-breathing biopsy. Although our study did not show a significant difference in hemoptysis between the respiratory phases, it is essential to acknowledge that hemorrhage and potential complications cannot be entirely excluded when performing CT-guided lung biopsies under free-breathing conditions.

This study had some limitations. First, given the lack of real-time visualization, the assignment of respiratory phases, may not be entirely precise because it relies on retrospective CT analysis. Particularly in patients with minimal respiratory movement, the classification of the respiratory phase can be prone to inaccuracies. Further investigations through a comparative study with proper segregation of maximal inspiration and expiration are required to validate these hypotheses. Another limitation is that the results obtained under free-breathing conditions may not directly correlate with those of conventional breath-holding biopsies. However, as there are currently no other comparative studies exploring complications based on various respiratory phases, it should be acknowledged that the selection of the respiratory phase in the breath-holding procedure does not entail any additional efforts or drawbacks. Comparative prospective studies of breath-holding biopsies are necessary to further support this hypothesis.

In conclusion, the respiratory phase of pleural puncture can influence the complications during CT-guided PTNB. Based on the findings of this study, it is recommended to avoid pleural puncture during mid-breathing and instead perform puncture during the expiratory pause during image-guided lung biopsy. Further research and validation using prospective studies are required to confirm these findings.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Author Contributions

Conceptualization, H.J., B.J.W.; data curation, P.J.Y., H.J., C.S.J., B.J.W.; formal analysis, P.J.Y., H.J., C.S.J.; investigation, P.J.Y., H.J.; methodology, P.J.Y., H.J., C.S.J.; project administration, H.J., B.J.W.; resources, C.S.J., L.S.K., L.H.Y., H.S.; supervision, H.J.; validation, H.J.; visualization, L.S.K., L.H.Y., H.S.; writing—original draft, P.J.Y., H.J.; and writing—review & editing, H.J., B.J.W., Y.S.Y.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

ORCID iDs

Ji Young Park https://orcid.org/0000-0001-6003-1018
Ji-Yeon Han https://orcid.org/0000-0003-3780-358X
Seok Jin Choi https://orcid.org/0000-0002-2688-4006
Jin Wook Baek https://orcid.org/0000-0003-4632-4951
Su Young Yun https://orcid.org/0000-0001-5064-1082
Sung Kwang Lee https://orcid.org/0000-0002-5015-9277
Ho Young Lee https://orcid.org/0000-0001-7976-3753
SungMin Hong https://orcid.org/0009-0005-0307-3410

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CT 유도 경피 폐생검에서 흉막 천자 시 호흡 시기가 합병증에 미치는 영향

박지영[1] · 한지연[1*] · 최석진[1] · 백진욱[1] · 윤수영[1] · 이성광[2] · 이호영[3] · 홍성민[3]

목적 전산화단층촬영(이하 CT) 유도 경피 폐 생검에서 흉막 천자 시에 호흡 시기가 합병증 발생에 영향을 미치는지 조사하는 것이다.

대상과 방법 자유 호흡 중 시행된 폐 생검의 CT 스캔 477개를 후향적으로 검토하였다. 흉막 천자 시 호흡 시기는 자유 호흡 중 얻은 CT 영상에서 목표 결절의 table position의 차이로 분석 평가하였다. 세 가지 호흡 시기(흡기, 중간, 호기)에서의 합병증 발생률을 비교하였다. 기흉에 대한 교란변수를 통제하기 위해 로지스틱 회귀 분석을 하였다.

결과 477건의 시술 중에서 흉막 천자는 227건(47.6%)에서 호기, 108건(22.6%)에서 중기, 142건(29.8%)에서 흡기에서 시행되었다. 기흉 발생률은 호기에서 유의하게 낮았고(40/227, 17.6%; $p = 0.035$) 중기에서 유의하게 높았다(31/108, 28.7%; $p = 0.048$). 교란변수를 통제한 후, 호기 시 흉막 천자는 기흉에 대해 독립적인 보호 요인으로 작용하였다(오즈비 = 0.571; 95% 신뢰구간 = 0.360–0.906; $p = 0.017$).

결론 본 연구 결과는 이미지 유도하 경피적 폐 생검시 호기에서 흉막 천자를 시행하는 것이 기흉 발생률을 감소시킬 수 있음을 보여주었다.

인제대학교 부산백병원 [1]영상의학과, [2]심장혈관흉부외과, [3]호흡기알레르기내과