The PEARL Approach for CT-guided Lung Biopsy: Assessment of Complication Rate

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Background: Percutaneous CT-guided biopsy of lung nodules is an established method with high diagnostic accuracy but a high rate of pneumothorax and chest tube insertion compared with endobronchial methods.

Purpose: To investigate the effect of a protocol combining patient positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching (PEARL) on complication rate after percutaneous CT-guided lung biopsy, especially chest tube insertion.

Materials and Methods: In a secondary analysis of both prospectively and retrospectively acquired data from December 2019 to November 2020, consecutive participants underwent biopsy with use of the PEARL protocol (prospective data) and were compared with patients who underwent biopsy at the same tertiary cancer center according to the standard method without any additional techniques (controls, retrospective data). Patient demographics, lesion characteristics, intraprocedural data, complications, and histologic results were recorded and compared.

Results: One hundred patients in the control group (mean age ± standard deviation, 63 years ± 12; 61 men) and 100 participants in the PEARL group (mean age, 64 years ± 12; 48 men) were evaluated. No differences were found in patient and lesion characteristics. The emphysema rate was 47 of 100 patients (47%) in both groups. The rate of pneumothorax was 37 of 100 patients (37%) in the control group versus 16 of 100 (16%) in the PEARL group (P = .001). Of the pneumothoraxes that occurred, fewer were during the intervention in the PEARL group, with 21 of 37 onsets (57%) in the control group versus three of 16 onsets (19%) in the PEARL group ($P < .001$). A chest tube was inserted in 13 of 100 patients (13%) in the control group and only in one of 100 (1%) in the PEARL group (P = .002). Histologic findings were diagnostic in 94 of 100 patients (94%) in the control group and 95 of 100 (95%) in the PEARL group ($P > .99$).

Conclusion: During CT-guided percutaneous lung biopsy, a protocol of positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching, or PEARL, reduced rates of pneumothorax and chest tube insertion.

Percutaneous biopsy of primary and metastatic lung nodules is increasing due to the worldwide rise of cancer incidence and the growing need for molecular and immunohistologic analyses. Percutaneous CT-guided lung biopsy is an established method for histologic and molecular investigation of pulmonary nodules, with a technical success rate of nearly 100% and high overall diagnostic accuracy ranging from 83% to 98% (1–4), mostly influenced by size of the lesion, biopsy needle size, and technique (fine needle aspiration vs core biopsy). In comparison with transbronchial or surgical biopsy, it is performed under local anesthesia instead of conscious sedation and general anesthesia. However, due to the inherent risk of pneumothorax in 15%–38% patients and subsequent need for chest tube insertion in 5%–10% of patients (2–7), percutaneous biopsy is often a second option to transbronchial tissue sampling, which has reported pneumothorax rates of 1%–8% and chest tube insertion rates of 1%–4% (8–11).

To reduce risks of pneumothorax and chest tube insertion, several techniques have been reported. These include deep expiration and breath hold during needle extraction, shown to reduce both pneumothorax and chest tube insertion rate by 50% (12), presumably due to positive intrapleural pressure during deep expiration. In regard to patient positioning, the biopsy-down position (ipsilateral decubitus position) has been shown to reduce pneumothorax rate (from 15%–27% to 6%–10%) and hemoptysis rate (from 2%–10% to 0.5%–5%), although reduction of chest tube insertion rate in two large studies did not reach statistical significance (13,14). Interestingly, there was a significant reduction of the asymptomatic and symptomatic air embolism rate from 3.3% to 0.5%–0.16% to 0.0% (13), presumably because of increased hydrostatic pressure due to placement of the lesion below the left atrium.

Other authors have suggested performing a rapid needle-out patient-rollover technique, whereby the biopsy is performed with the patient in the prone or supine position and the patient is afterward rapidly rolled over to the biopsy-side down position within 10–15 seconds after needle removal. This reduced the chest tube insertion rate

Abbreviation

PEARL = positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching

Summary

For CT-guided percutaneous lung biopsy, positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching, or PEARL, reduced pneumothorax and chest tube insertion rates while maintaining diagnostic accuracy.

Key Results

- In a series of 100 participants in whom positioning with biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching (PEARL) protocol was used for CT-guided lung biopsy, the rate of pneumothorax (16% vs 37%; P = .001) and chest tube insertion (1% vs 13%; P = .002) was lower than in 100 control patients.
- With use of PEARL, fewer pneumothoraxes occurred during the intervention (three of 16 onsets [19%] vs 21 of 37 [57%]; $P < .001$).
- Diagnostic accuracy of lung biopsy with use of PEARL was similar to that of the standard technique (95% vs 94%, respectively; $P > .99$).

from 4%–15% to 2%–4% (15,16). However, not all studies about positioning the patient biopsy-side down after biopsy have yielded similar results (17,18), with rapid performance of the maneuver being discussed as one the main differencing factors. Other studies have assessed the effect of sealant material instillation into the biopsy tract, including saline, blood, gelatin sponge slurry, or fibrin glue (19–25), with varying but generally comparable effects on pneumothorax and chest tube insertion rates. An interesting technique is the autologous blood clot seal, leading to a more than 50% reduction in chest tube insertion rate (21). Most studies using autologous blood clot seals had already implemented other complication-reducing techniques, such as puncture-side down position after biopsy (22), so the pure sealant effect is difficult to determine. Finally, immediate manual aspiration of up to 550 mL of pleural air may prevent further progression of pneumothorax and subsequent chest tube placement by reapposition of visceral and parietal pleura. This prevented chest tube placement in over 85% of patients in one study (26). However, another study only reached this number after combining aspiration with simultaneous injection of 15 mL peripheral autologous blood into the pleural space and positioning the patient in the ipsilateral decubitus position for 1 hour (27), while aspiration alone was successful in only 46.7% of cases.

To our knowledge, there is no recommendation on which technique to use or how to combine these techniques. Our goal was to create a practical and efficient protocol that takes into account the known techniques to maximally reduce complications in percutaneous lung biopsies and to apply this protocol to an everyday clinical setting. The protocol was based on two hypotheses: *(a)* combination might have an additive effect and *(b)* different patients might benefit from different techniques, and all techniques combined might yield better safety results. Both hypotheses led us to believe that combination should achieve a marked reduction in complication rate. The positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching (PEARL) protocol combines five different techniques and was purposefully designed for clinical usability (eg, when positioning the patient biopsy-side down was not feasible and would have led to a complicated route, it was dismissed).

Materials and Methods

Study Sample and Setup

Before June 2020, all percutaneous lung biopsies were performed with the patient in the supine, prone, or lateral decubitus position with no use of additional techniques to reduce complications. After extensive literature review, a protocol was developed and set as the new institutional standard to reduce complications. From June to November 2020, CT-guided percutaneous lung biopsies were performed with PEARL (Fig 1). Indication and biopsy trajectories were discussed with interventional radiology attending physicians with at least 5 years of experience in percutaneous lung biopsy. The biopsies themselves were performed by three interventional radiology fellows with up to 2 years of experience.

In a secondary analysis of both prospectively and retrospectively acquired data from December 2019 to November 2020, consecutive participants who underwent biopsy performed with use of the PEARL protocol (prospective data) were compared with patients who underwent biopsy at the same tertiary cancer center according to the standard method without any additional techniques (controls, retrospective data). Only biopsy tracts traversing aerated lung were included in the study.

Written informed consent for study participation was obtained from participants in accordance with the policy of our institution. Approval of the institution's internal review board and local ethics committee was obtained (no. GR131020).

Standard Biopsy Technique (Nonprotocol)

Procedures were performed on an Aquilion ONE scanner (Canon Medical Systems) with a 17-gauge coaxial needle and an 18-gauge semiautomatic core biopsy needle (Mission Disposable Biopsy Instrument Kit). Planning was performed with use of an initial noncontrast chest CT scan and the most direct pathway chosen, avoiding fissures and large vessels. A single pleural puncture was performed with the coaxial needle, and multiple core samples were obtained. Patients were asked to hold breath during needle exchange, and care was taken to block the inner lumen of the coaxial needle with a finger or with an inner stylet to minimize risk of air embolism. Target sample number was two to four. In case of a relevant pneumothorax (ie, size or patient symptoms), chest tube insertion was decided according to the interventional radiologist's discretion and patient's clinical condition. In postprocedural care, patients were allowed to keep the most comfortable position in their bed, and a chest radiograph was obtained after 4 hours.

PEARL Protocol

Beginning in June 2020, all percutaneous lung biopsies were performed using the PEARL protocol (Fig 1) by three interventional radiology fellows with up to 2 years of experience.

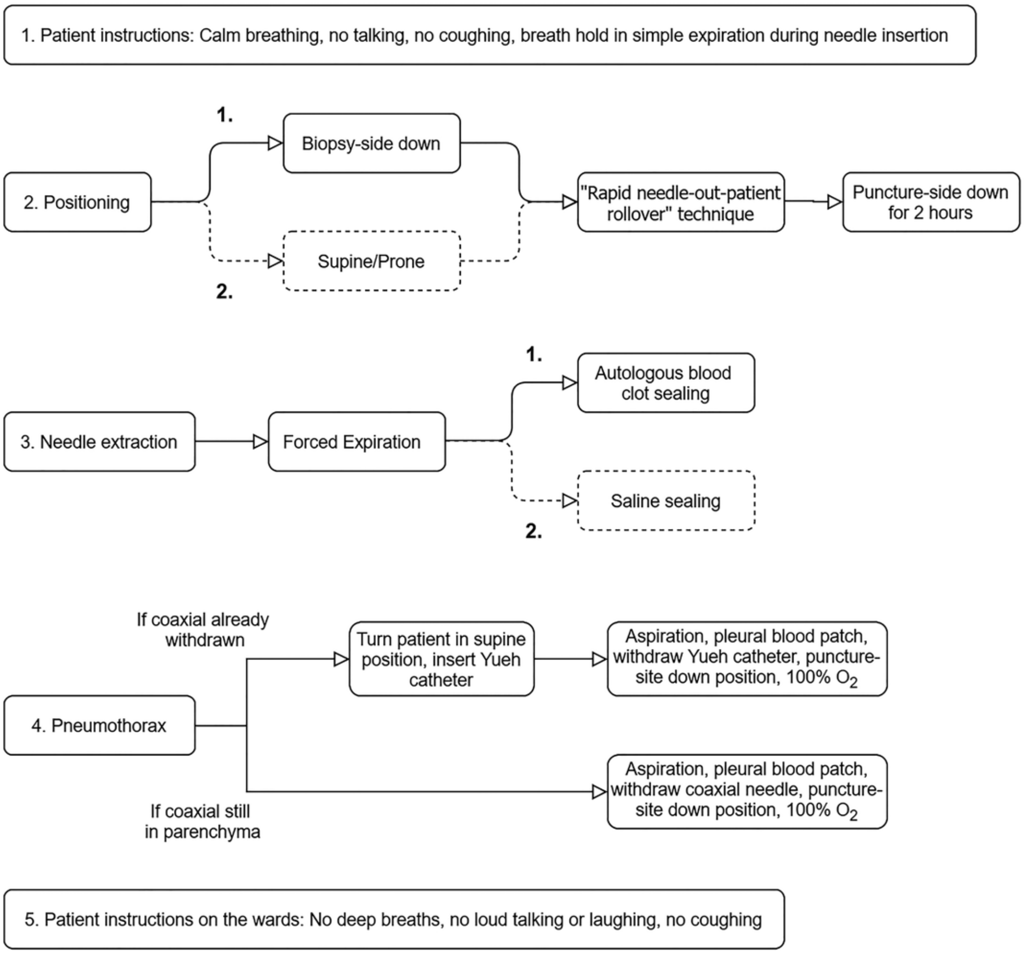

Figure 1: Diagram shows the positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching, or PEARL, protocol.

Positioning.—The primary position was declared as biopsy-side down, defined as any position where the lesion as well as the needle tract were situated below the left atrium as much as technically feasible. Supine or prone positions were only used if they simplified the biopsy tract, such as to avoid large vessels and fissures or in cases where a biopsy-down position would cause the lesion to become situated in a direct subpleural location, thus increasing the risk of pleural transgression during biopsy.

Tract sealing.—Needle extraction was performed under forced expiration. During needle removal, the tract was sealed with an autologous blood clot seal technique using 10 mL of blood. The blood was withdrawn beforehand by technicians during insertion of the intravenous line and stored vertically after all air in the syringe was emptied. If it was not possible to withdraw blood, then saline was used.

Immediately following needle removal, participants were quickly turned to a puncture-dependent position (puncture-site down) using the rapid needle-out patient-rollover technique before the final scan.

In case of pneumothorax.—If there was relevant acute (discovered at immediate postinterventional CT) or delayed (discovered at chest radiography after 4 hours) pneumothorax, then a 5-F Yueh centesis catheter (Cook Medical) was inserted with the participant in supine position, and the pleural air was aspirated using a tube extension, three-way stopcock, and 60-mL syringe. After complete air evacuation, 20 mL of freshly drawn blood was injected and the needle withdrawn under forced expiration.

If the pneumothorax was peracute (ie, occurring during the intervention with the coaxial biopsy needle still inside the parenchyma), then the tract was sealed with an autologous blood clot or saline and the coaxial needle withdrawn into the pleural space. All air was evacuated, and 20 mL of freshly drawn blood was injected into the pleural space. The needle was then withdrawn under forced expiration.

One hundred percent oxygen was administered through a nasal canula with flow of 4–6 L/min. The participant was turned to the puncture-site down position with use of the rapid needle-out patient-rollover technique as fast as possible.

All participants were monitored for 4 hours after the procedure. Routine vital signs were recorded, and participants remained in the puncture-side down position for 2 hours. In case of peri-interventional pneumothorax, the nasal canula was kept until a chest radiograph was obtained. An erect posteroanterior chest radiograph was obtained at 4 hours following the procedure. If the chest radiograph showed no pneumothorax or asymptomatic small pneumothorax (defined as <3 cm pleural

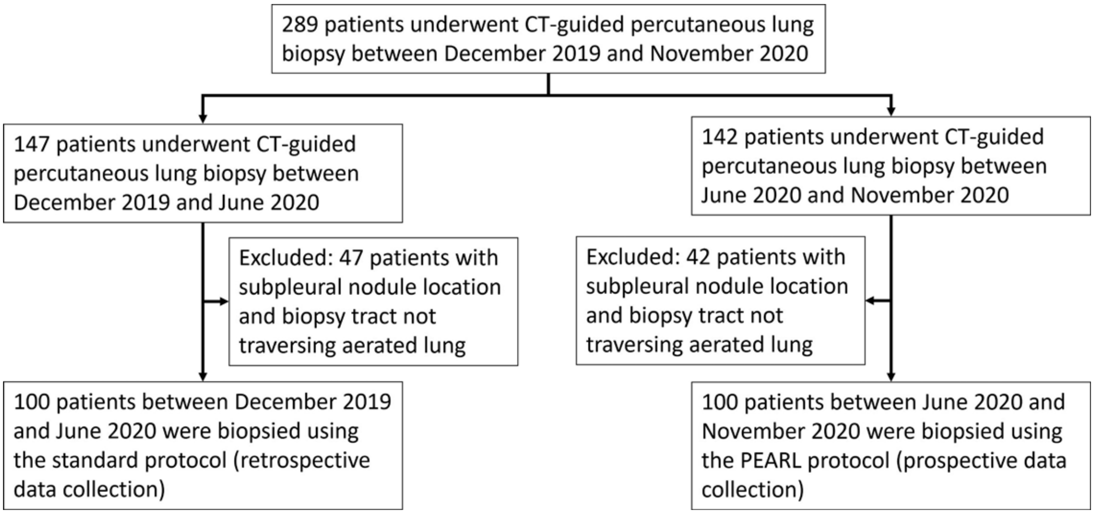

Figure 2: Flowchart shows inclusion and exclusion criteria for 200 patients who underwent percutaneous CT-guided lung biopsy. PEARL = positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching.

distance apically or <2 cm distance at the level of the hilum), then the participant was discharged. In case of symptomatic or relevant delayed pneumothorax, the aforementioned aspiration procedure was performed. If this had already been performed unsuccessfully, then a chest drain of at least 10 F was inserted.

Data Collection

The following parameters were recorded prospectively for the protocol group and retrospectively for the nonprotocol group: patient age and sex, prior lung surgery or irradiation, tobacco use and presence of emphysema, lesion diameter and location (lobe), cavitation, intrapulmonary biopsy tract length (distance from lesion periphery to pleura), patient positioning, presence and acuity of pneumothorax, hemoptysis, air embolism, and usability and type of histologic findings. Additionally, the number of pleural punctures, number of core biopsies, and intraprocedural coughing were recorded for the protocol group. Pneumothorax at CT was defined as air within the pleural space of more than 1-cm width because a few air bubbles or focal unopposed pleura can be seen in a large number of patients after percutaneous biopsy, especially when tract sealant is injected.

Statistical Analysis

Statistical analysis was performed by using SPSS Statistics (version 26, IBM). Continuous variables are expressed as means ± standard deviations and as ranges. Categorical variables are expressed as frequencies with percentages. The independent *t* test was performed for differences in continuous variables with normal distribution. The χ^2 test was performed to test for proportional differences. $P < .05$ was considered indicative of statistically significant difference.

Table 1: Patient and Tumor Characteristics

Characteristic	Control Group (*n* = 100)	PEARL Group (*n* = 100)	*P* Value
Age (y)*	63 ± 12 (34–89)	64 ± 12 (28–87)	.65
Sex			.09
Male	61	48	
Female	39	52	
Location (lobe)			
Right upper lobe and middle lobe	35	40	.56
Right lower lobe	26	25	>.99
Left upper lobe	18	14	.56
Left lower lobe	21	21	>.99
Tobacco use	61	62	>.99
Visible emphysema at CT	47	47	>.99
Prior lung surgery	9	5	.41
Prior radiation therapy	7	4	.54
Lesion diameter (mm)*	21 ± 11	21 ± 13	.97
Biopsy tract length (mm)*	23 ± 14	27 ± 16	.13
Lesion cavitation	4	4	>.99

Note.—Unless otherwise specified, data are numbers of patients. PEARL = positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching.

* Data are means ± standard deviations. Data in parentheses are ranges.

Results

Patient Characteristics

Among 142 consecutive patients who underwent CT-guided lung biopsy using the PEARL protocol, 42 were excluded because the biopsy tract did not traverse lung tissue. The control group consisted of the last 147 patients at our institution who underwent CT-guided lung biopsy with use of the standard protocol, of whom 47 were excluded because the biopsy tract did not traverse lung tissue (Fig 2). This resulted in 100 patients in the control group (mean age ± standard deviation, 63 years ± 12; 61 men) and 100 patients in the PEARL group (mean age, 64 years ± 12; 48 men) who were evaluated. We found no signifi-

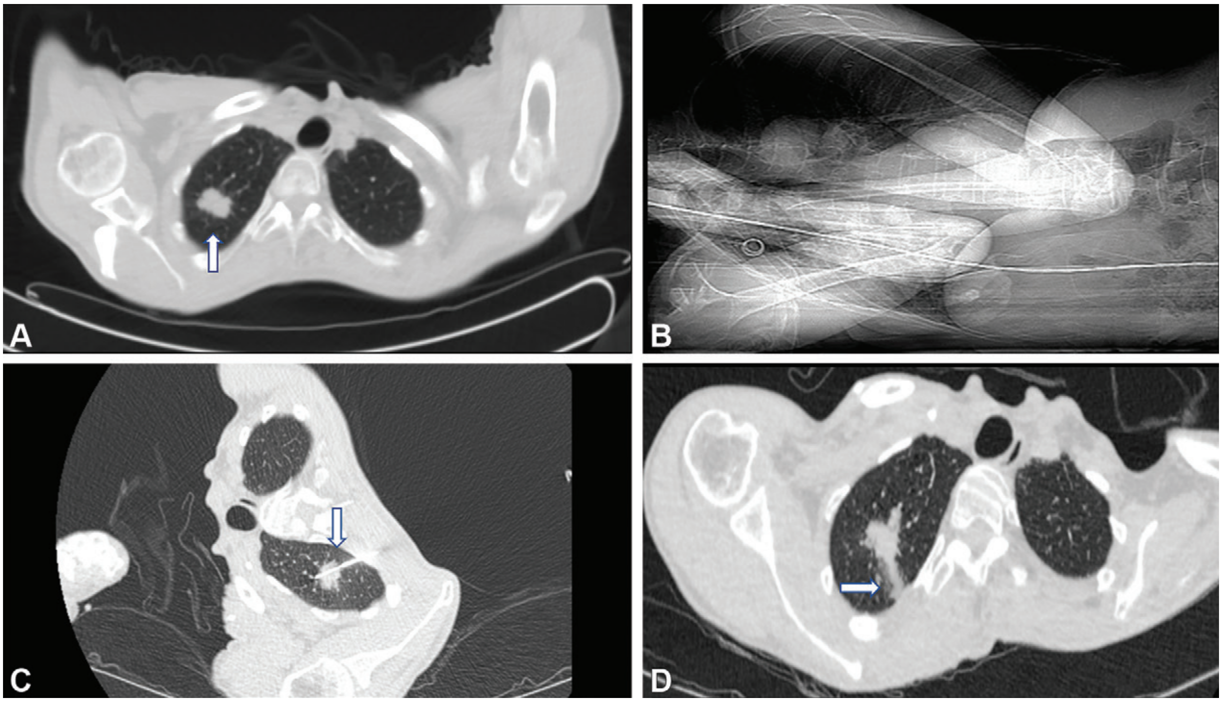

Figure 3: Biopsy in ipsilateral decubitus position. **(A)** Unenhanced axial CT scan 3 weeks before biopsy in a 67-year-old man shows the solid lesion in the apical right upper lobe (arrow). **(B)** Scout on day of biopsy with the patient in ipsilateral decubitus position. Note how the left lung has expanded while the right lung is clearly less aerated. **(C)** Unenhanced axial CT scan depicts biopsy of the apical lesion in decubitus position with the 18-gauge biopsy needle stylet inside the lesion (arrow). **(D)** Unenhanced axial CT scan obtained with patient in biopsy tract–down position shows the autologous blood patch delineated as a consolidative stripe (arrow) from the lesion periphery to the pleura.

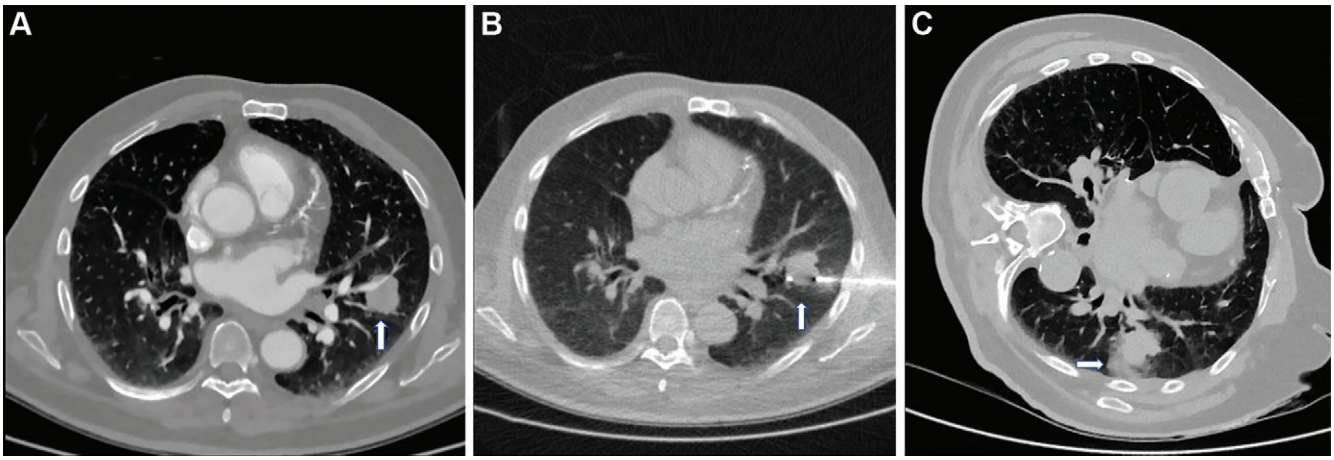

Figure 4: Biopsy in supine position. **(A)** Contrast-enhanced CT image in arterial phase in a 75-year-old man before the intervention to identify pulmonary vasculature for planning. Biopsy target was the solid mass in the left upper lung abutting the oblique fissure (arrow). The mass was at the same height as the left atrium. **(B)** CT/fluoroscopy image shows the 18-gauge biopsy needle with its stylet in the lesion (arrow), avoiding the fissure and vessels. **(C)** Unenhanced CT image shows the patient in a biopsy tract–down position with some postbiopsy alveolar hemorrhage and after tract sealing with autologous blood (arrow).

cant differences in patient and lesion characteristics between the groups (Table 1). Tobacco use (control group, 61 of 100 patients [61%] vs PEARL group, 62 of 100 patients [62%]; $P > .99$) and emphysema rate (47 of 100 [47%] in both groups; $P > .99$) were not significantly different. Notably, the ipsilateral decubitus position did not result in increased intrapulmonary biopsy tract length (control group, 23 mm ± 14 vs PEARL group, 27 mm ± 16; $P = .13$), which is a known risk factor for pneumothorax.

For the PEARL group, specific intraprocedural data were collected. Eighty-three participants were positioned in an ipsilateral decubitus position (Fig 3). Nine participants were positioned supine because in this position, the lesion was already situated below the left atrium, and these were mostly lesions that abutted the oblique fissures and were biopsied tangentially (Fig 4). Overall, the biopsy-side down position could be attained in 92 of 100 participants (92%). In eight participants (8%), the supine or prone position was assumed because an ipsilateral decubitus position would have complicated the biopsy path, and all such lesions were located apically or basolaterally near the pleural reflection.

Table 2: Outcomes for the Control Group versus PEARL Group

Outcome	Control Group (*n* = 100)	PEARL Group (*n* = 100)	*P* Value
Pneumothorax	37	16	.001
Pneumothorax timing			
Peracute*	21 (57)	3 (19)	<.001
Acute	11 (30)	7 (44)	.08
Delayed	5 (14)	6 (38)	<.001
Chest tube insertion	13	1	.002
Air embolism	1	0	>.99
Hemoptysis	7	3	.33
Diagnostic histologic finding	94	95	>.99
Primary lung cancer	25	33	.28
Metastasis	55	43	.12
Noncancer	14	19	.45

Note.—Unless otherwise specified, data are number of patients. Data in parentheses are percentages. PEARL = positioning biopsy-side down, needle removal during expiration, autologous blood patch sealing, rapid rollover, and pleural patching.

* Peracute indicates an event that occurred during the intervention with the coaxial biopsy needle still inside the lung parenchyma.

In 93 of 100 participants (93%) in the PEARL group, there was one pleural puncture. In seven participants (7%), there were two or three pleural punctures because the nodule was located subpleurally or abutting a fissure, causing the biopsy stylet to repeatedly traverse the adjacent pleura. Mean and median number of samples were 3.1 ± 1.1 and three samples (range, one to six samples), respectively. An autologous blood clot seal was used in 95 of 100 participants (95%), whereas saline was used as sealant in five participants (5%). Positioning the participant biopsy-tract side down immediately after needle withdrawal was not possible in 13 of 100 (13%) participants due to musculoskeletal-related problems.

Outcomes: PEARL Group versus Control Group

Outcomes are summarized in Table 2 for both groups. The rate of pneumothorax was 16 of 100 participants (16%) in PEARL group versus 37 of 100 patients (37%) in the control group (P = .001). Of the pneumothoraxes, fewer occurred during the intervention (per-acute pneumothoraxes): 21 of 37 onsets (57%) in the control group versus three of 16 onsets (19%) in the PEARL group ($P < .001$).

In four participants in the PEARL group (4%), the pneumothorax required aspiration and pleural blood patching. There was one participant (1%) who needed a chest tube in the PEARL group versus 13 patients (13%) in the control group (P = .002). This is an absolute reduction in chest tube insertion rate of 12%.

No air embolism was detected in the PEARL group, while there was one asymptomatic air embolism in the left ventricle in the control group. Three participants experienced hemoptysis in the PEARL group (3%) versus seven patients in the control group (7%) (P = .33). Histologic findings were diagnostic in 95 of 100 participants (95%) in the PEARL group and 94 of 100 patients (94%) in the control group ($P > .99$).

Discussion

In this study, we demonstrated that the combination of five different techniques in CT-guided percutaneous lung biopsy can reduce rates of pneumothorax to 16% and chest tube insertion rate to 1% in everyday practice. Importantly, this can be achieved without decreasing diagnostic accuracy, which in our study reached 95%. Additionally, there were fewer pneumothoraxes during the intervention in the protocol group (three of 16 onsets [19%] vs 21 of 37 onsets [57%]; $P < .001$).

Although pneumothorax rate after percutaneous biopsy is relatively high when compared with endobronchial biopsies (8–11), this should actually be regarded as a feature of the intervention rather than a real complication because the majority is self-limiting, and most patients remain asymptomatic. However, chest tube insertion is associated with patient discomfort, additional procedure time, referring physician dissatisfaction, and higher costs due to hospitalization. In a meta-analysis by Heerink et al (5) of 8133 core biopsies, chest tube insertion rates among different study populations varied between 0.5% and 16.7%, with a pooled incidence of 5.6%. Studies with very low rates of chest tube insertion of 0.5%–3% usually reported a varying combination of a low rate of emphysema, use of complication-reducing techniques, and smaller-gauge needles (5). Some also include subpleural lesions, where no aerated lung parenchyma is traversed (28).

Our relatively high chest tube insertion rate in the control group of 13% can be explained by several factors. First, the proportion of patients with emphysema (47%) is among the highest reported in the literature for lung biopsies. This is presumably due to selection bias in a tertiary highly specialized cancer center with many patients with primary pulmonary and head or neck cancer. Second, biopsies were performed by using a 17-gauge coaxial needle with an 18-gauge biopsy needle, which is associated with higher pneumothorax and chest tube insertion rates compared with 20–22-gauge biopsy needles (29). Third, no complication-reducing techniques were deployed. Fourth, at our institute, lung biopsies are mainly performed by interventional radiology fellows with up to 2 years of experience in percutaneous biopsies, which is in contrast to most published articles, in which the interventionalists are typically more experienced (19,24,30).

From this perspective, the absolute chest tube insertion rate of 1% after implementation of the protocol is even more impressive because, to our knowledge, this is the lowest reported rate among a study sample with roughly half of the sample having emphysema. Additionally, by having the patient in a dependent position, complications such as hemoptysis and air embolisms might be reduced as well, although this was not statistically demonstrated in our study. Furthermore, our data show that if there is a pneumothorax, then its onset can be delayed in the biopsy-side down position. In our experience, this allowed the interventionalist to calmly finish the procedure without the patient complaining of pain or the nodule changing its position due to expanding pneumothorax.

With an absolute chest tube insertion rate of 1% in a high-risk population, percutaneous biopsy with use of PEARL now demonstrates a similar complication rate to transbronchial biopsy (8–11). Technologic advancement in transbronchial biopsy has led to diagnostic accuracy up to 88% (9–11), and sophisticated robotic-assisted bronchoscopy techniques promise diagnostic yields of up to 97% with a complication rate less than 1% (31). Because diagnostic accuracy of transbronchial biopsy might be approaching the accuracy of percutaneous biopsy, the next important factors are complication rate, costs, and patient comfort. Few studies have tried to compare costs of the two methods. Although highly dependent on local reimbursement policies, one study from Australia reported similar cost efficiency for both procedures (32). Interestingly, CT-guided percutaneous biopsy had an advantage at base-case values by having higher diagnostic sensitivity, which was offset by higher costs of complications. To the best of our knowledge, no study has compared these techniques for patient comfort. For these reasons, every measure should be taken to reduce complication rate after percutaneous imaging-guided biopsies, and this study shows that PEARL can significantly lower pneumothorax and chest tube insertion rate.

Our study had limitations. First, it was a combination of both retrospectively and prospectively collected data from a single center. Because of this, there was a lack of patient randomization. Finally, there was a change of some physicians in the department during the study period, although physician experience in performing lung biopsies remained the same.

In conclusion, percutaneous lung biopsy remains a technique with high diagnostic accuracy. By combining several known complication reducing-techniques, a very low rate of complications, especially chest tube insertion, can be achieved even in high-risk populations without compromising diagnostic accuracy. Further validation in studies, including in low- and high-risk patients, is necessary to better evaluate this technique.

Author contributions: Guarantors of integrity of entire study, A.N., M.A.A., T.d.B., L.T.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, A.N., M.A.A., B.B., A.D., C.R., T.d.B., L.T.; clinical studies, A.N., M.A.A., B.B., A.D., A.K., C.R., F.D., T.d.B., L.T.; statistical analysis, A.N., B.B.; and manuscript editing, A.N., M.A.A., A.D., A.K., T.d.B., L.T.

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