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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Effectiveness of autologous blood injection in reducing the rate of pneumothorax after percutaneous lung core needle biopsy

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PURPOSE
To assess the effectiveness and safety of autologous intraparenchymal blood patch (IBP) application in reducing the frequency of pneumothorax (PTX) after percutaneous transthoracic pulmonary core needle biopsy.

METHODS
The records of patients who underwent the transthoracic pulmonary core needle biopsy procedure under CT guidance between January 2015 and October 2018 were screened retrospectively. Patients whose traversed pulmonary parenchymal length was ≥20 mm during biopsy were included in the study irrespective of lesion size. The IBP procedure was made a department policy in November 2017; patients who underwent biopsy after this date comprised the IBP group, while those who underwent the procedure before this date comprised the control group. IBP recipients received 2–5 mL of autologous blood injection to the needle tract. Demographic data, procedural reports, tomography images, and the follow-up records of patients were assessed.

RESULTS
A total of 262 patients were included in the study. Of the 91 patients that received an IBP, PTX developed in 13 (14.1%), with 7 (7.7%) requiring a thoracic tube. Of the 171 patients who did not receive an IBP, PTX developed in 45 (26.3%), with 19 (11.1%) requiring a thoracic tube. Patients who received an autologous IBP showed a significantly lower rate of PTX development versus those who did not ($P = 0.01$). Similarly, a significantly lower number of patients who received the blood patch required chest tube placement ($P = 0.015$).

CONCLUSION
Autologous IBP is a safe, inexpensive and easy to use method that reduces the rate of PTX development and thoracic tube application after percutaneous core needle biopsies of the lung.

Percutaneous computed tomography (CT)-guided lung biopsy is an effective, highly accurate, and safe method for obtaining tissue for the diagnosis of indeterminate pulmonary lesions (1, 2). With coaxial biopsy systems, multiple core biopsy specimens can be obtained through an introducer needle, which remains within the lung parenchyma for some time (3).

CT-guided lung biopsy is associated with complications such as pneumothorax (PTX), hemoptysis, hemothorax, infection, and air embolism (4). Among these complications, PTX is the most frequently observed complication as reported by a recent meta-analysis which determined that 25.3% of the 8133 patients included in their analysis had suffered PTX after core biopsy (5).

Multiple studies have been published on the application of various materials and methods to reduce the rate of PTX after percutaneous lung biopsy. These interventions include regulation of patient positioning, breath-holding techniques, and injection of embolizing materials (6–8). A variety of methods aimed at sealing the biopsy tract during needle retraction have been proposed in an effort to decrease PTX rates. The application of products such as fibrin glue, gelfoam, hydrogel, gelatin powder, gelatin sponge, isobutyl-2-cyanoacrylate, collagen, and 0.9% NaCl into the coaxial needle channel have been evaluated in pre-

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vious studies (9–14). In addition, relatively new techniques such as hydrogel "plugs" have been utilized for the same purpose with interesting results in terms of other complications, but findings were only mildly promising in terms of PTX rates (14, 15). Intraparenchymal pulmonary blood patch (IBP) application to the coaxial needle tract has also been reported in a few studies that have shown around 20%–30% reduction in PTX frequency (16, 17). However, there are only a few studies which have evaluated the effectiveness and safety of this procedure, and the results of these studies have mostly focused on whether the patient required advanced intervention for the treatment of PTX and the success of these treatments.

The purpose of this study was to evaluate the effectiveness and safety of autologous IBP application in the prevention of PTX development, and to determine whether this method reduces requirement for thoracic tube placement in patients undergoing percutaneous core needle biopsy.

Methods

This work was approved by the local ethics committee (decision no.: 2019/2073). Treatment methods were performed according to approved guidelines. Permission was obtained from the ethical committee for the retrospective evaluation of patients' files and images. Written consent was obtained from all patients prior to biopsy procedures. All patients were informed that their data could be used in scientific research. In addition, approval by telephone was obtained from patients whose images were used during the preparation of the manuscript.

Study plan and patients

This study was planned as a collaborative study between the Interventional Radiology and Thoracic Surgery Clinics at a tertiary care medical center. The records of patients who underwent core needle biopsy under CT guidance at a tertiary care medical center between January 2015 and October 2018 were screened retrospectively. Demographic data, procedural reports, pathology reports, tomography images, and follow-up examinations were assessed and recorded. Current CT images were obtained and the location and size of the lung lesion in patients were recorded. The presence of emphysema was evaluated in the CT images performed before the biopsy in the patients. Emphysema was scored as mild, moderate, or severe using the Goddard classification: a visual scale in which the area of vascular disruption and low attenuation value are scored for each lung region. The depth of the pulmonary parenchyma to be traversed to reach the nodule and the distance between the lesion and pleura were measured on axial tomography images. Lesions were classified according to their depth: <1 mm, 1–20 mm, and 20 mm and deeper. Only patients in whom ≥20 mm of pulmonary parenchyma was traversed (irrespective of lesion size) were included in this study. Thus, the study included a total of 262 patients who had or had not received IBP application into the needle tract.

The grouping of patients was time-bound, as autologous blood patch application was not performed at this center until the use of a non-clotted blood patch during biopsy was made a departmental policy in November 2017. The amount of autologous blood applied to the needle tract was determined as 2–5 mL, according to published literature (16–17). The development of PTX and associated thoracic tube placement (if required) were recorded.

All biopsy procedures were performed by one interventional radiologist who had at least 2 years of experience. All core needle biopsy procedures were performed under multidetector CT guidance (Somatom Emotion 6, Siemens). The technical parameters for CT were as follows: 120 mAs; 100kV; collimation, 6×2 mm; slice thickness, 2.5 mm; and reconstruction interval, 1 mm. An Estacore fully automatic coaxial system, 20 G with a 15–20 cm core biopsy needle (Geotek Healthcare Products), was used in all biopsies. The coaxial needle's thickness was 19 G. 20 G needles have been used for the last five years at our center and no problems have been experienced in obtaining sufficient tissue.

Procedure and follow-up

First, 10 cm axial CT images were taken and used to determine the most appropriate coaxial needle, as well as the length and size of the lesion. Skin antisepsis and local anesthesia were performed. The coaxial system was cautiously advanced and CT images were constantly evaluated to confirm entrance into the lesion. Approximately 3–4 pieces were taken with the 20 G core biopsy needle until sufficient tissue was obtained. Autologous IBP injection was performed along the needle tract from the coaxial needle. To prepare the blood patch, 6 mL of blood from the patient was drawn into a 10 mL syringe before the procedure. This syringe was attached to another syringe with a 3-way tap. Blood was injected from one syringe to the other several times, a technique that is effective in breaking down clotted blood. Injection of 2–5 mL of autologous blood was performed during needle withdrawal and injection was continued until the edge of the pleura was passed (the exact withdrawal distance was calculated beforehand) (Fig. 1).

In the follow-up assessments after the procedure, CT images of the same area were obtained immediately after the proce-

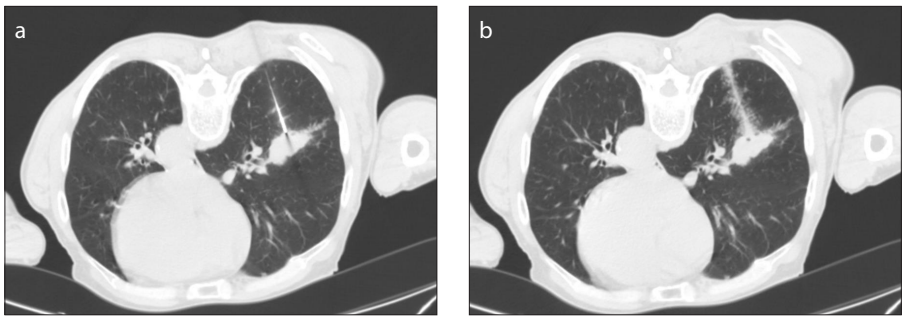

Figure 1. a, b. Image **(a)** shows a 33×22 mm solid lesion in the lower lobe of the right lung. Image **(b)** shows approximately 3.5 cc of autologous blood injected into the needle traction from the coaxial system. PTX did not develop.

Main points

- Percutaneous transthoracic core needle biopsy is a safe method.
- Intraparenchymal pulmonary blood patch application reduces the pneumothorax complication rate.
- Intraparenchymal pulmonary blood patch is an easy and cheap method.
- The potential for side effects is low compared with other synthetic materials.

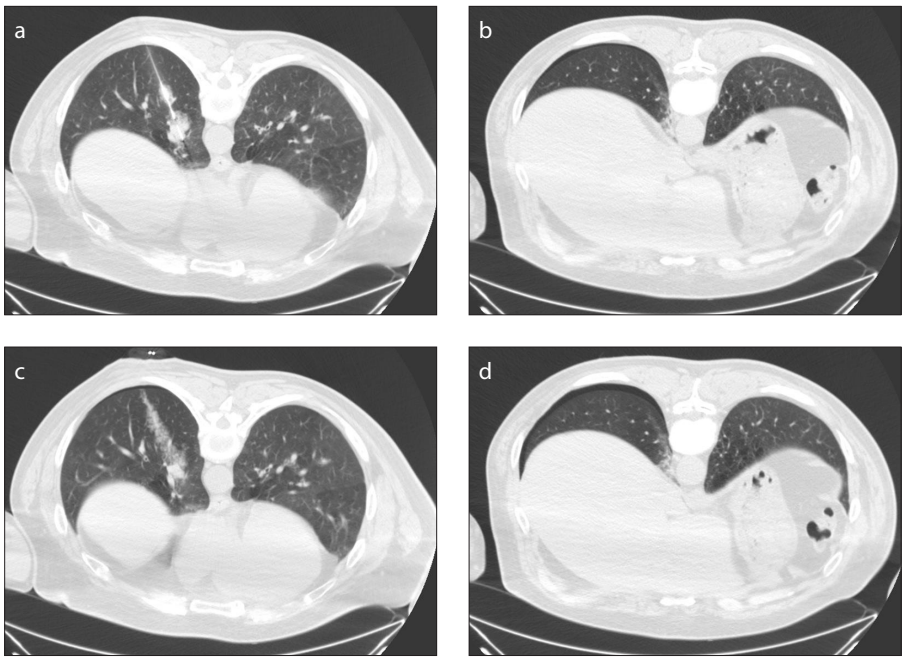

Figure 2. a–d. Image **(a)** shows a core needle biopsy performed on a 27×16 mm lesion in the medial region of the lower lobe of the left lung. Image **(b)** shows a 6 mm thick PTX during the needle insertion in the same procedure. Image **(c)** shows approximately 5 cc autologous blood patch applied to the coaxial tract. Immediately after the blood patch **(d)**, the level of PTX was measured as 6.6 mm at the table and no significant increase was observed.

dure while the patient was still on the table, and the images were checked. After 6 hours of follow-up in the thoracic surgery ward, standing pulmonary radiographs were taken and evaluated. During this process, patients who did not develop complications and those who had been successfully treated for minor complications were discharged. After the biopsy procedure, patients who developed PTX that did not require intervention were closely monitored with administration of nasal oxygen (Fig. 2). For patients who were symptomatic and/or showed PTX progression (>3 cm), a chest tube was inserted and regular treatment was continued.

Statistical analysis

Research data was evaluated with SPSS version 22 software for Windows (IBM Corp.). Descriptive statistics were presented as mean ± standard deviation (minimum–maximum), frequency distribution and percentage. Pearson's chi-squared test and Fisher's exact test were used to compare categorical variables. The normality of distribution of continuous variables was analyzed by using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The Mann-Whitney U test was used for the comparison of continuous variables with non-normal distribution. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated via the Pearson chi-square and Fisher's exact tests. Statistical significance level was accepted as $P < 0.05$.

Results

A total of 262 operations were included and examined in this study. IBP application was performed in 34.7% of the cases. Overall, PTX developed in 22.1%, and thoracic tube placement was performed in 9.9% of the cases. The diagnostic yield of the core biopsies was determined as 98.5%. Of the 91 patients who received IBP, PTX developed in 13 (14.1%), and 7 (7.7%) required thoracic tube placement. Of the 171 patients who did not receive an IBP, PTX developed in 45 (26.3%), and 19 (11.1%) required thoracic tube placement (Table 1). There were no complications or side effects associated with IBP.

The frequency of PTX development and thoracic tube requirement were significantly lower in IBP recipients ($P = 0.010$ and $P = 0.015$, respectively).

The mean (min–max) lesion size was 32 mm (20–44 mm) in those who underwent IBP, while lesion size was 30 mm (20–39 mm) in those without IBP application. There was no relationship between lesion size and PTX development ($P = 0.574$). None of the patients in this study had findings consistent with cavitation.

PTX developed in 20.3% (49/241) of the patients without emphysema and 42.9% (9/21) of the patients who had emphysema. The frequency of PTX development was significantly higher among those with emphysema ($P = 0.026$), while tube placement frequency was not significantly influenced by the presence/absence of emphysema ($P = 0.14$). The results of univariate analyses were as follows: there was no difference between groups with and without emphysema regarding IBP application (OR, 1.17; 95% CI, 0.47–2.94; $P = 0.92$). In the comparison of PTX and tube placement frequencies, we found that while the presence of emphysema (grade 1–4) was significantly associated with PTX development (OR, 2.94, 95% CI, 1.17–7.37; $P = 0.026$), tube placement frequency was not effected by emphysema (OR, 2.34; 95% CI, 0.72–7.58; $P = 0.14$) (Table 2).

In the group of patients with emphysema (n=21), PTX developed in 37.5% (3/8) of those who underwent IBP and 46.2% (6/13) of those biopsied without IBP, with no statistically significant difference between the two groups ($P = 0.70$).

Discussion

The results of this study show that IBP application after lung core needle biopsy reduces the frequency of PTX development and the subsequent requirement for chest tube placement. The fact that PTX frequency dropped by almost half with IBP application shows that this method is a safe, inexpensive, and effective method of PTX prevention, while also being an easy-to-apply procedure compared with the use of other synthetic products.

Previous studies reported that the development of hemorrhage during percutaneous lung biopsies reduced the frequency of PTX development. It was suggested that the mechanism underlying this effect could be associated with a reduction in ventilation caused by the presence of free blood in the alveolar cavity. These findings may be considered as the first steps which sparked the use of autologous blood applications in PTX prevention. Initial attempts involved the injection of large amounts of blood into the pleural cavity to treat PTX. For these procedures, around 50–150 mL of

Table 1. Descriptive and clinical characteristics of the biopsy procedures

n=262	IBP applied n=91	IBP not applied n=171	*P*
Age (years), mean±SD	62.6±10.4	59.3±11.7	0.63[a]
Sex (male/female)	80/11	153/18	0.55[b]
Presence of emphysema, n	8	13	0.13[b]
Localization, n			0.078[b]
Right lung upper lobe	31	59	
Left lung upper lobe	25	48	
Right lung lower lobe	19	40	
Left lung lower lobe	11	19	
Right lung mid lobe	5	5	
Size (mm), median (25%–75%)	32 (20–44)	30 (20–39)	0.092
Biopsy approach, n			0.080[b]
Posterior	52	90	
Anterior	23	51	
Lateral	16	30	
Length of lung parenchyma traversed (mm), median (25%–75%)	25(21–44)	26 (20–46)	0.90
PTX on the PA radiograph at 6 hours, n (%)	13 (14.1)	45 (26.3)	0.010[b]
Placement of thoracic tube, n (%)	7 (7.7)	19 (11.1)	0.015[b]
Pathology results, n			0.87[c]
Malignant	62	115	
Benign	28	53	
Insufficient material	1	3	
Diagnostic capability value, %	98.9	98.2	

n, number of procedures; IBP, intraparenchymal pulmonary blood patch; SD, standard deviation; PTX, pneumothorax; PA, posteroanterior.
[a]Mann-Whitney U test; [b]Pearson's chi-square test; [c]Fisher's exact test.

Table 2. Distribution of PTX complications with regard to emphysema in the lung lobe which underwent biopsy

	Emphysema Grade 0, n (%)	Emphysema Grade 1–4, n (%)	*P*
IBP application			
Yes (n=91)	83 (34.4)	8 (38.1)	0.92[a]
No (n=171)	158 (65.6)	13 (61.9)	
Pneumothorax			
Yes (n=58)	49 (20.3)	9 (42.9)	0.026[b]
No (n=204)	192 (79.7)	12 (57.1)	
Tube placement			
Yes (n=26)	22 (9.1)	4 (19)	0.14[b]
No (n=236)	219 (90.9)	17 (81)	
Total (n=262)	241	21	

PTX, pneumothorax; n, number of procedures; IBP, intraparenchymal pulmonary blood patch.
[a]Pearson's chi-squared test with continuity correction; [b]Fisher's exact test.

blood was generally used (18). However, in percutaneous core needle biopsy, blood is directly injected to the coaxial needle tract, reducing the amount required for successful patching. This patch functions as a plug or barrier by filling the entry region to the pleura and the needle tract, which reduces air flow into the pleural cavity (19). In a study by Malone et al. (20), the frequency of PTX requiring chest tube placement in IBP recipients was significantly lower than that of those without IBP ($P = 0.048$). In another study, the frequency of PTX was reduced but not to a statistically significant level ($P = 0.12$). However, the latter study included patients in whom the aerated pulmonary parenchyma was traversed, which may have affected their results. In the current study, it was thought that a more accurate result could be obtained by categorizing patients in terms of the distance between the lesion and the pleura; because as this distance increases, so does the risk of PTX. Some authors have even defined that a needle tract traversing ≥4 cm of the pulmonary parenchyma constitutes a major risk factor for PTX development (21, 22), while others have suggested that the risk for PTX increases when the lesion is more than 2 cm from the pleura (23). Clayton et al. (24) placed great importance on the lesion-pleura distance, leading to a preference of autologous IBP application in biopsy procedures where >2 cm of the pulmonary parenchyma is traversed. Similarly, the current study included only cases with ≥20 mm distance. Our findings showed that the IBP procedure significantly reduced the rate of PTX and subsequent tube requirements compared with characteristically similar controls.

In regard to other materials and techniques, various options have been used to close the needle tract in patients undergoing percutaneous pulmonary biopsy. The injection of 0.9% NaCl (physiologic serum) causes very little side effects and has been used in a limited number of studies, but this technique is proved to be inconsistent (25). In a study by Baath et al. (26), which utilized gelatin powder hemostat to prevent tract leakage, there was no statistically significant decrease in the incidence of chest tube placement. Another disadvantage of the hemostat gelatin powder is that it requires additional time to prepare the mixture; therefore, increasing total procedure time. Additionally, there is a risk for embolization in the event that the absorbable gelatin powder leaks into intravascular compartments. Furthermore, due to risks for infection and abscess formation, the application of gelatin powder must be performed meticulously (27). Teodora et al. (9) found no statistically significant difference in the inci-

dence of PTX between two patient groups with and without fibrin glue injections. In addition, fibrin glue presents with the disadvantage of being rather expensive. In regard to the widely known tissue repair agent, isobutyl-2-cyanoacrylate, studies have shown that this agent may lead to granulomatous inflammatory reaction (13). Methods involving plugs such as the hydrogel plug are also expensive, similar to fibrin glue, and their effectiveness has not been proven to be superior to IBP in terms of reducing PTX frequency (28).

To summarize, it is evident that many studies investigated various plugging methods for the tract of the coaxial needles used in lung biopsy. Although there are significant differences in the type and preparation of each material used, the technical applications are very similar. It is very difficult and also may be ethically questionable (as there is no consensus on which material to choose for each patient) to use all of these methods in a single study to determine differences in success rates. Therefore, the majority of studies on this topic only provide data about the specific material used by the authors. Similarly, we have only reported results from the use of IBP in this study; however, we have also evaluated these findings with a thorough review of the literature which enabled us to perform comparisons between the success of various materials used in the prevention of PTX after coaxial core needle biopsies. These comparisons are lacking in the majority of studies on this topic.

In the previously described techniques, synthetic materials such as fibrin glue, gelfoam, hydrogel, gelatin powder, gelatin sponge, isobutyl-2-cyanoacrylate or collagen, are injected into the coaxial needle tract. The common disadvantage of these methods is that little is known about the complications of each material. Whereas, in the IBP technique, the patient's own blood is taken before the biopsy and this autologous material is used to seal the needle tract. This method causes minimal additional cost and does not increase procedure time. Furthermore, it does not pose a threat to the patient in terms of the potential side effects observed with the use of synthetic materials. There were no complications or side effects in any of the IBP recipients in our study. These results indicate that the IBP procedure is a safe and effective method of preventing PTX development in patients undergoing percutaneous core needle biopsy.

It has been reported that the presence of moderate or severe emphysema are among the risk factors that increase the frequency of PTX (17). There are also studies which have not reported any association between PTX and emphysema. For instance, in a study by Li et al. (23), no relationship between emphysema and PTX development was found in 169 patients (of which 23 had emphysema). However, the grade of emphysema was not determined and thus may have caused the lack of significant relationships. In the current study, although we determined the emphysema grade of all patients, statistical analyses could not be reliably performed with regard to these groups. However, univariate analyses showed that patients with emphysema had significantly higher likelihood of PTX, while requirement for tube placement was similar among those with and without emphysema.

Percutaneous lung core needle biopsy is a safe technique; however, PTX is a common complication. Although PTX is usually clinically insignificant in the majority of patients, it may require additional imaging and observation until the patient stabilizes. In relatively fewer cases, patients may need placement of a chest tube. In addition to this being a significant problem for the patient, it also increases the cost of treatment. In today's medicine, limiting unnecessary procedures and decreasing monitoring and observation time are considered to be almost as crucial as providing quality healthcare to the patients. Therefore, it is apparent that methods which can reduce the frequency of PTX after percutaneous transthoracic core needle biopsy are important for patient care as a whole. As such, materials that are inexpensive, have virtually no side effects and can be easily applied should be preferred. In this study, IBP application was utilized with significant success, and the procedure causes no additional cost and is simple.

There are various limitations to be mentioned. First, the retrospective single-center design may have caused bias in evaluation and patient selection; however, as the use of IBP was made a department policy after November 2017, selection bias was nonexistent and evaluation bias can be considered to be minimal. Second, although a large group of patients was included in the current study, the percentage of patients who underwent IBP was lower than those who did not, which may have affected our comparisons. Third, patients' smoking status which is a risk factor for PTX development, was not evaluated. This may have resulted in differences between baseline characteristics; however, other characteristics of patients were similar.

In conclusion, in light of our findings and the literature on this topic, autologous IBP has been demonstrated to be a safe, inexpensive and simple method that reduces the frequency of PTX and subsequent chest tube requirement in patients undergoing percutaneous core needle biopsy.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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