DIAGNOSTIC PERFORMANCE OF LUNG ULTRASOUND IN DETECTING PNEUMOTHORAX AFTER CT- GUIDED TRANSTHORACIC BIOPSY

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This study aimed to describe the diagnostic performance of lung ultrasound (LUS) in detecting and semi-quantifying pneumothorax (PTX), using computed tomography (CT) as the reference standard. The study included 150 patients who underwent CT-guided transthoracic biopsy (TTB) for lung lesions. Within 30 minutes, two radiologists blinded to the participant's prior information performed LUS in asymptomatic patients. The results showed that PTX was present on CT in 49/150 (32.3%) cases. LUS was positive in 40/150 (26.7%) patients, with a substantial agreement between the two radiologists (Cohen κ statistics = 0.8). The sensitivity and specificity of LUS were 100% (95%CI 97.6% to 100%) and 91.8% (95%CI 87.4% to 96.2%), respectively. Moreover, the positive and negative predictive values were 87.5% (95%CI 82.2% to 92.8%) and 96.4% (95%CI 92.4% to 98.9%), respectively. In the semi-quantification of PTX by LUS, the location of lung point was described in 36/49 (73.5%) patients. The sensitivity and specificity of this sign were 87.5% (95%CI 82.2% to 92.8%) and 96.4% (95%CI 92.4% to 98.9%), respectively. The positive and negative predictive values were 87.5% (95%CI 82.2% to 92.8%) and 96.4% (95%CI 92.4% to 98.9%), respectively. In conclusion, LUS is a susceptible and specific diagnostic method for diagnosing and semi-quantifying PTX.

Keywords: Lung ultrasound, pneumothorax, CT-guided transthoracic biopsy, diagnostic performance, semi-quantification.

I. INTRODUCTION

Computed tomography (CT)-guided transthoracic biopsy (TTB) has become the procedure of choice to diagnose pulmonary lesions. The most complication post-biopsy is pneumothorax (PTX) which can occur during or immediately after the process.[1–3] The incidence of PTX in patients undergoing TTB has been reported to be from 9–54%, with an average of around 20%.[4] PTX is also a critical cause of respiratory failure in the emergency department, and the rate of PTX each year is estimated at 22.7 cases for 100,000 populations.[5] Therefore, timely and accurately confirmation or exclusion of PTX is of significant importance, especially in emergency and critical care situations.

In the past decade, the air was still believed to be the "enemy" of ultrasound, and lung ultrasound (LUS) could not bring any benefits. Instead, the posterior-anterior chest X-ray (CXR) is routine as a traditional method for diagnosing PTX. However, CXR has a disadvantage in showing low sensitivity in detecting PTX in trauma patients, especially in the supine position.[6,7] Although CT is the gold standard diagnostic test for PTX, it causes

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radiation exposure and is unsafe to transport these unstable patients.

A study by Lichenstein showed that the LUS signs assessed in adults could be used in the critically ill neonate.[8] In Vietnam, LUS is still a new issue, not yet widely used in clinical practice and research. Few studies on LUS compared the diagnostic power of LUS to CXR, which has low sensitivity for PTX. Therefore, it is reasonable to conduct a study with enough evidence of using LUS to confirm or exclude PTX, compared with CT as the gold standard. In addition, following confirmation of the existence of PTX, the next critical step is to quantify the amount of PTX. The study could evaluate in semi-quantification of PTX by LUS with the reference standard of CT.

For these reasons, we aim to conduct this research to evaluate the diagnostic performance of LUS in detecting and semi-quantifying PTX after CT- guided TTB, using CT as the reference standard.

II. MATERIALS AND METHODS

1. Subjective

In this study, participants had to meet all of these inclusion criteria, including being examined at Bach Mai hospital and diagnosed with a pulmonary lesion that required CT-guided TTB to histopathological diagnosis, being conscious with stable vital signs (in particular, according to The American College of Chest Physicians (ACCP) Guideline 2009, [9] patients could speak an entire sentence. They have stable vital signs, including the respiratory rate < 24/min, oxygen saturation ≥ 90% on room air, pulse rate between 60-120 beats/min, and normal blood pressure) and having undergone LUS after TTB. The exclusion criteria were any contraindications to CT- scans as pregnancy or refusal to participate in the study.

2. Methods

This was a cross-sectional, single-blinded research conducted at Bach Mai Radiology Center from March 2021 to July 2022.

Imaging protocol

In our hospital, the Radiology Center made a weekly schedule of CT-guided TTB for lung lesions. Immediately after the procedure, each participant underwent an additional CT with complete expanded lung fields to check for complications, especially PTX. These entire procedures were performed by those who did not participate in this study.

Conscious and stable patients, according to ACCP Guideline 2009, after CT-guided TTB were transferred to the follow-up room. Within 30 minutes in that room, the radiologists involved in this study performed post-procedure LUS. They were blinded to the prior CT imaging information. Those two radiologists had five and four years of experience in general radiology and were well-trained in LUS. 6-point LUS ***(Figure 1)*** was performed in supine positions as described in the BLUE protocol (*B*edside *L*ung *U*ltrasonography in *E*mergency).[10]

In this study, the CT scanner machine was a 128-slice multidetector (SOMATOM Definition Edge, Siemens, Erlangen, Germany or SCENAIRA, Hitachi Medical Corporation, Tokyo, Japan). The ultrasound machine was GE LOGIQ E9 XDclear 2.0 (GE Healthcare, Milwaukee, WI, USA) with a linear array transducer (ML 6-15Hz). They were connected to the hospital picture archiving and communication system (PACS) through Digital Imaging and Communications in Medicine networking.

Using PACS, finally, the data on those CT machines were compiled independently by a senior residency radiology doctor following the British Thoracic Society pleural disease guideline 2010 (BTS Guideline 2010).[11] This step was conducted after performing LUS.

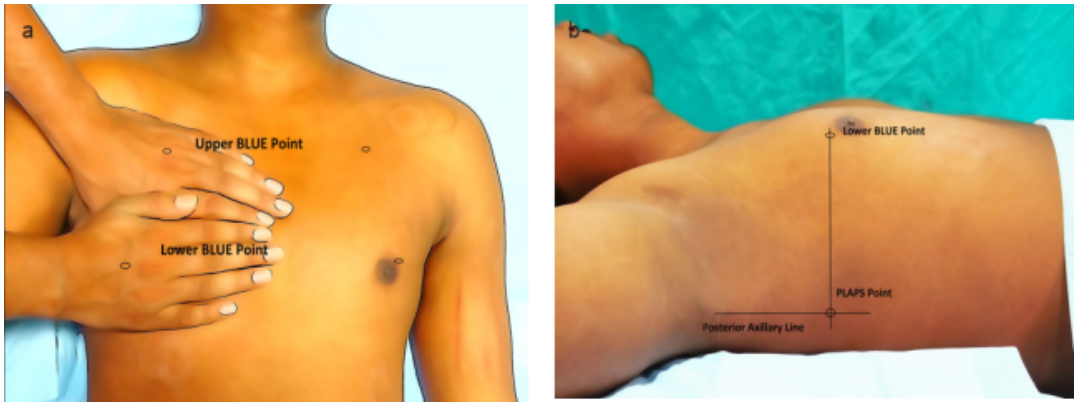

Figure 1. Areas of investigation and the BLUE-points in the BLUE protocol

Source: Diagnostic Performance of 6-Point Lung Ultrasound in ICU both sides. Patients: A Comparison with Chest X-Ray and CT Thorax. Turk J Anaesthesiol Reanim. 2019; 47(4):307-319.[12]

Study variables

The general statistics were: age, gender, body mass index (BMI), biopsy side and position. We used the BLUE protocol to perform LUS. The BTS Guideline 2010 was used to semi-quantify PTX by LUS and classify the size of PTX by CT. In particular, the following statistics were collected:

Normal lungs by LUS variables

The presence of lung sliding sign and B-lines on 2D imaging, seashore sign on M-mode.

PTX by LUS variables

Absence of lung sliding sign, lack of B-lines on 2D imaging, barcode sign and lung point on M-mode.

Semi- quantification of PTX by LUS

Large and small PTX: using the location of the lung point with the cut-off is the mid-auxiliary line (MAL) ***(Figure 2).*** The more anterior to the MAL the lung point, the smaller the PTX.

Size of PTX by CT as the reference standard

Large and small PTX: A visible rim between the lung margin and the chest wall with the cut-off is 20mm at the level of the hilum in the lung window for both prone or supine biopsy position. This would be measured using reconstruction in the PACS system.

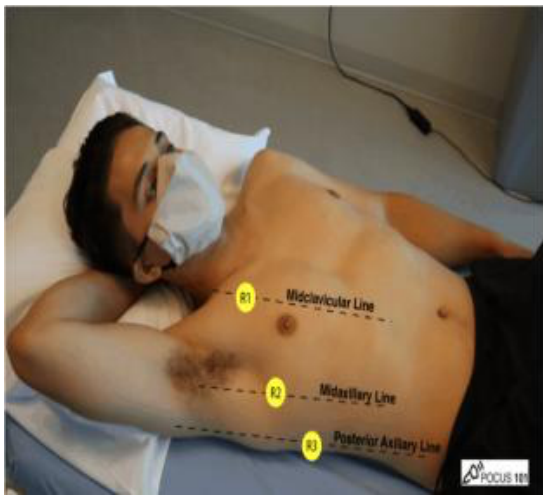

Figure 2. Mid- auxillary and posterior auxiliary lines

Source: Lung Ultrasound Made Easy: Step- By-Step Guide. POCUS 101. Accessed October 4, 2022.[13]

Statistical analysis

Consequently, the IBM Statistical Package for the Social Sciences, version 25 (IBM SPSS Statistics Corp; Armonk, NY, USA) was used for

data analysis. The study sample was described with descriptive statistics. Continuous variables are expressed as medians and standard deviations, while categorical variables are expressed as frequency and percentage.

The inter-reader, Cohen κ statistics, was used to calculate the degree of agreement between the two radiologists. We randomly selected 15 cases in the study sample and calculated the inter-reader Cohen κ statistics.

The sensitivity, specificity, positive and negative predictive value, and disease prevalence are expressed as percentages. The confidence intervals were Clopper-Pearson (Exact methods) or normal approximation for the qualitative variable. The significance level was $p < 0.05$.

3. Research ethics

All patients selected for the study were thoroughly explained about the research and the whole process of the imaging protocol. Participants in this study could withdraw from the study at any time if they so desired, especially when they have any inconvenience after the biopsy.

All patients participating in the study were not financially supported but were consulted, monitored, and received care entirely . All personal information of the patients participating in the study was kept confidential.

III. RESULTS

A total of 150 patients (mean age, 60.5 years; range, 26-83 years; male/female, 4.2/1) were included in this study. ***Table 1*** summarizes the general features of the participants.

The inter-reader *κ values were 0.8, indicating a s*ubstantial to almost perfect agreement between the two radiologists.

Table 1. Summary of patient's characteristics

Characteristic		Frequency (n)	Percent (%)
Gender (n, %)	Male	121	80.7
	Female	29	19.3
Biopsy side (n, %)	Left lung	78	52
	Right lung	72	48
Biopsy position (n, %)	Supine	64	42.7
	Prone	86	57.3
Age (years): mean, range		60.5, 26-83	

Of 150 patients, 110 (73.3%) showed lung sliding signs, normal B-lines and A-lines on 2D LUS. Besides, 73,3% (n=110) of patients had seashore signs on M-mode ***(Figures 1 and 2).*** This demonstrated that there was an absence of PTX detected on LUS. 40 of 150 patients (26.7%) had PTX on LUS due to a barcode sign on M mode, absence of lung sliding sign and B-lines on 2D imaging LUS ***(Figures 3 to 5).*** However, lung point was only detected in 36/40 cases (24%).

On the lung window of CT scans, 49/150 patients had pneumothorax (32.7%). The others (n=101, 67.3%) were absent from PTX. PTX presence or absence on LUS and CT are summarised in ***Table 2.***

Table 2. Diagnostic performance of LUS compared with CT as the reference standard

		Pneumothorax by CT as the reference standard (n)		Total (n)
		No	Yes	
Pneumothorax by LUS (n)	no	101	9	110
	yes	0	40	40
Total (n)		101	49	150

The sensitivity and specificity of LUS in the detection of PTX, compared with CT as the gold standard, were 100% (95%CI 97.6% to 100%) and 91.8% (95%CI 87.4% to 96.2%), respectively. Moreover, the positive and negative predictive values were 87.5% (95%CI 82.2% to 92.8%) and 96.4% (95%CI 92.4% to 98.9%), respectively.

Table 3. Performance of LUS (Lung-point projections) to predict the size of PTX

		Classification of the size of PTX on CT as the reference standard (n)		Total (n)
		small PTX	large PTX	
Classification of the size of PTX on LUS (n)	no detected	13	0	13
	small PTX	27	1	28
	large PTX	1	7	8
Total (n)		41	8	49

Of 49 PTX cases confirmed by CT, there were 40/49 found on LUS (81.6%). Lung point was detected in 36/49 (73.6%) cases. In comparison, the location of lung points with the MAL, 28/49 patients had lung points located anteriorly (57.1%) and 8/49 posteriorly (16.3%). The others (n=13, 26,4%) failed to detect lung points. Consequently, according to BTS Guideline 2010, 57.1% of cases (n=28/49) were small PTX, and 16.3% (n=8/49) were large PTX on LUS.

The sensitivity and specificity of lung point sign in the semi-quantification of PTX were 87.5% (95%CI 82.2% to 92.8%) and 96.4%, respectively. The positive and negative predictive values were 87.5% (95%CI 82.2% to 92.8%) and 96.4% (95%CI 92.4% to 98.9%), respectively.

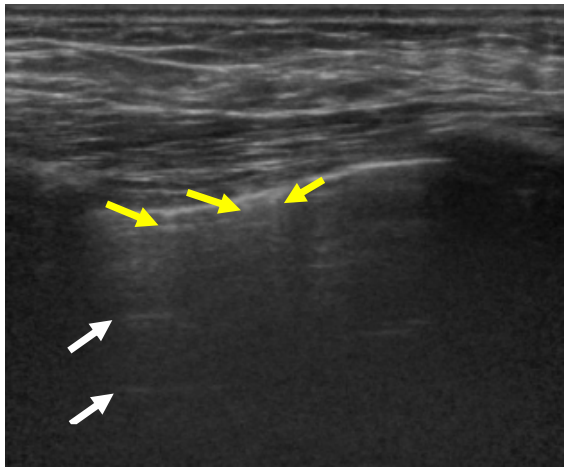

Figure 3. A-lines and B-lines in typically normal lungs. The A-line artefact is horizontal artifactual repetitions of the pleura line (white arrows). B-lines (yellow arrows) are the vertical lines perpendicular to the pleural line

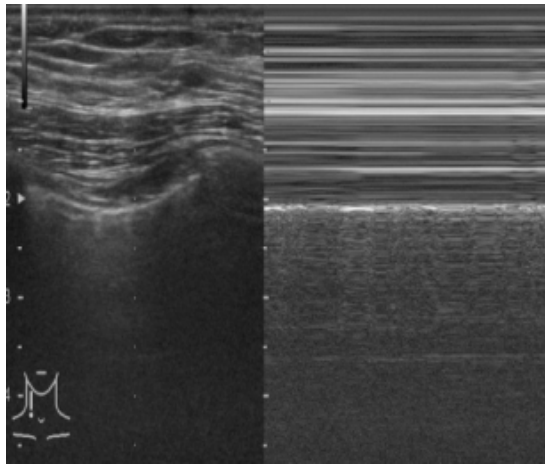

Figure 4. Seashore sign in M-mode in a patient with normal lung. Since the structure above the pleural line is static during respiration, it produces parallel lines that look like waves in M-mode. Beneath the pleural line, the cyclic movement of the lung with respiration creates a sand-like appearance

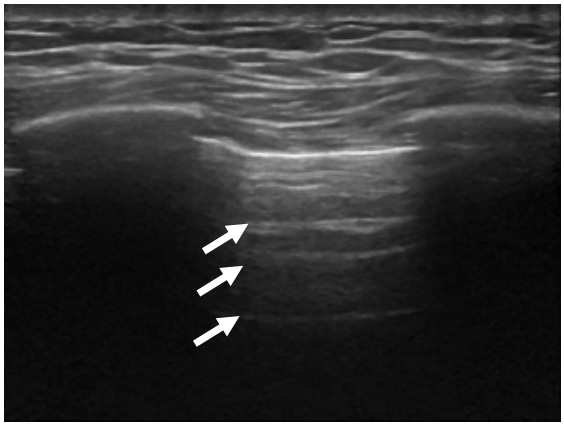

Figure 5. The absence of B-lines and the replacement by multiple A-lines (arrows)

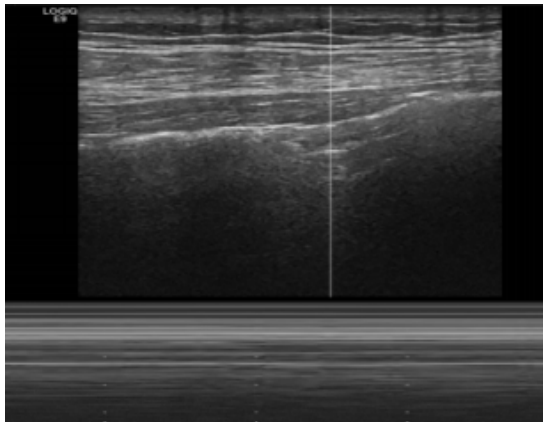

Figure 6. Barcode signs in pneumothorax in M- mode. The lung sliding is abolished in the pleural line, and parallel lines, called barcode signs, replace the sand-like appearance beneath the pleural line

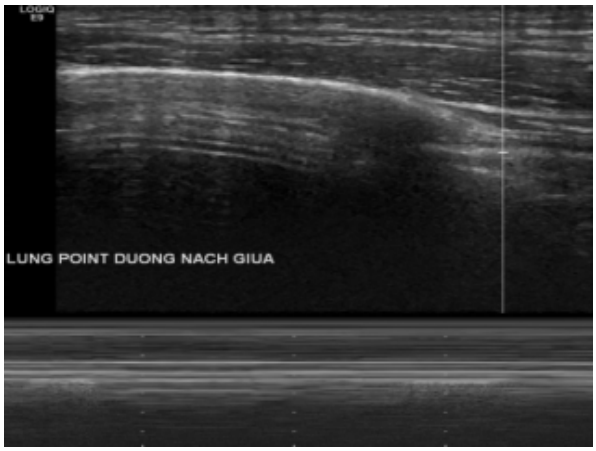

Figure 7. Lung point identified at the junction where visceral and parietal pleura contact each other. In this case, the lung point located in the MAL indicated a large PTX on LUS.

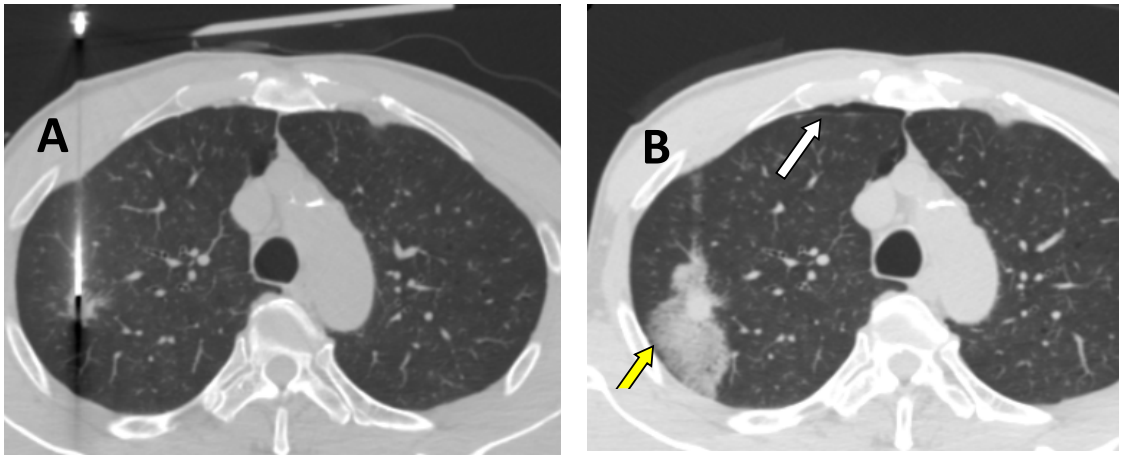

Figure 8. Pneumothorax after biopsy on lung window of chest CT. The patient was in the supine position. (A): The needle inside the right lung nodule. (B): Rim of gas after removing the biopsy needle (white arrow). Besides, the hemothorax surrounding the lesion was present (yellow arrow)

IV. DISCUSSION

Our study demonstrated that LUS is feasible and accurate in detecting PTX with high sensitivity and specificity after CT-guided TTB. However, nine false-negative normal lungs on LUS had PTXs on CT. These might be due to small focal PTXs localised to the site of needle entry outside the monitored zone (for example: in the back in the prone biopsy position). The focal PTX at the needle entry site can be seen on CT images during or at the end of the procedure; in our study, patients remained stable. Performing the LUS over the needle entry location may require patients to reposition and remove the dressing, which did not benefit post-procedure patients in our experience. In our study, we chose the BLUE protocol with 6 BLUE points on both sides of the chest wall to perform LUS. The BLUE protocol is widely used in the onsite exploration of acute respiratory failure, including PTX, because it is simple,

time-saving, and allows quicker treatment decisions.[10]

LUS's widespread availability in emergency and critical care settings has been studied extensively for its diagnostic accuracy in determining PTX.[8] Our study's results were similar to publications.In a study by Chung et al.[14] Using CT as the gold standard, LUS showed significantly higher sensitivity than supine or semierect CXR when both sides of the entire anterior chest wall were examined. Particularly, this study was designed to compare the detectability of LUS and CXR for PTX in 97 patients. Both LUS and CXR were performed immediately after the transthoracic needle biopsy procedure. They showed that the sensitivities in detecting PTX were 80 and 47% in LUS and CXR, respectively. The specificities were 94 and 94%. The diagnostic accuracies were 89 and 77%. The inter-observer agreement was excellent (kappa=0.85) in the LUS images and moderate (kappa=0.49) in the CXR. The results of this study suggest that LUS is a more sensitive and confident method for diagnosing a pneumothorax compared to bedside CXR.

In another study, Luca Viglietta et al.[15] Studied 43 patients to evaluate the accuracy of LUS in detecting PTX after transbronchial lung cryobiopsy. They aimed to assess post-procedure PTX prevalence and concordance between operators for CXR and LUS in detecting PTX. They showed that PTX was diagnosed in 10 (23%) patients by CXR. Radiologists had complete agreement interpreting CXR (*k* = 1, 95% CI). LUS was positive for PTX in 11 (25%) patients. There was complete agreement between pulmonologists interpreting LUS (*k* = 1, 95% CI). The prevalence of PTX diagnosed by the concordance of CXR and LUS was 23% (10/43, 95% CI 11.8–38.7). The sensitivity and specificity of LUS were 90% (95% CI 55.5–99.7) and 94% (95% CI 79.8–99.3), respectively. Moreover, the positive and negative predictive values were 82% (95% CI 48–98) and 97% (95% CI 84–100), respectively. They concluded that LUS is a compassionate and specific diagnostic tool for diagnosing PTX after transbronchial lung cryobiopsy.

Furthermore, in another research, Sartori et al.[16] Showed that LUS is as accurate as the upright posterior-anterior view of CXR in detecting PTX after ultrasound-guided biopsy of peripheral lung lesions extending to the pleura. They examined the entire chest in both supine and prone positions and used CT as the gold standard only when there was a discrepancy between the LUS and CXR. The LUS protocol by Sartori et al. costs a significant amount of time to perform, which may explain why it is not widely used.

Following confirmation of the existence of PTX, the next critical step is to quantify the amount of PTX. The latter is significant since it may indicate whether a conservative or surgical technique is required. By LUS, we used the lung point location to the MAL according to the BTS Guideline 2010. The data showed that the location of lung point had significantly high sensitivity and specificity in the semi-quantification of PTX. Compared to CXR, Volpicelli et al. discovered that the position of the lung point might correctly categorize PTX size.[17] Overland et al. showed in PTX animal models that LUS may effectively monitor the course of PTX during mechanical breathing.[18] Hooman Hosseini-Nik et al. showed that the LUS had the sensitivity and specificity of 69.23% (95%CI 38.6% to 90.1%) and 96.0% (95%CI 79.6% to 99.9%) respectively in detecting PTX of any size, and the sensitivity and specificity of 100% (95%CI 39.8% to 100%) and 100% (95%CI 89.7% to 100%) respectively in the

detecting large PTX.[19] In our study, thanks to the gold standard of CT in the lung window, we could measure precisely the size and classify PTX.

This study had several limitations. Firstly, the sample size was relatively small. Although the LUS in our study showed high diagnostic performance in detecting PTX, future studies with a more significant number of patients should be conducted. Secondly, our study did not perform CXR within 30 minutes post-procedure. After 1 hour in the follow-up room at the radiology department, conscious and stable patients were transferred to their clinical departments for continuous follow up. The study process ended at that time. The study mainly focused on the imaging features of LUS and its accuracy in detecting PTX, using CT as the reference standard. The availability and low cost of LUS, which can be done at the bedside and repeatedly performed without radiation exposure are beneficial. We believe this study's results could be extrapolated to other conditions of PTX with or without trauma in emergency and critical care settings, especially in pregnant women, pediatric or neonatal.[8] However, further studies using CXR should be performed to determine the possibility of replacement of CXR by LUS in detecting PTX.

V. CONCLUSION

In summary, by using CT as the reference standard, our study had an advantage in evaluating the power of LUS in detecting PTX. LUS showed high sensitivity and specificity in diagnosing the presence and the semi-quantification of the PTX.

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REFERENCES

1. Liao WY, Chen MZ, Chang YL, et al. US-guided transthoracic cutting biopsy for peripheral thoracic lesions less than 3 cm in diameter. *Radiology*. 2000; 217(3): 685-691. doi:10.1148/radiology.217.3.r00dc21685.

2. Vorwerk D. Percutaneous nonvascular thoracic interventions. *Syllabus*. 2000; 11: 235-6. Hally Project 1998–2000.

3. Morello FA, Wright KC, Lembo TM. New suction guide needle designed to reduce the incidence of biopsy-related pneumothorax: experimental evaluation in canine model. *Radiology*. 2005; 235(3): 1045-1049. doi:10.1148/radiol.2353040433.

4. Kazerooni EA, Lim FT, Mikhail A, et al. Risk of pneumothorax in CT-guided transthoracic needle aspiration biopsy of the lung. *Radiology*. 1996; 198(2): 371-375. doi:10.1148/radiology.198.2.8596834.

5. Bobbio A, Dechartres A, Bouam S, et al. Epidemiology of spontaneous pneumothorax: gender-related differences. *Thorax*. 2015; 70(7):

653-658. doi:10.1136/thoraxjnl-2014-206577.

6. Abdulrahman Y, Musthafa S, Hakim SY, et al. Utility of extended FAST in blunt chest trauma: is it the time to be used in the ATLS algorithm? *World J Surg*. 2015; 39(1): 172-178. doi:10.1007/s00268-014-2781-y.

7. Soult MC, Weireter LJ, Britt RC, et al. Can routine trauma bay chest x-ray be bypassed with an extended focused assessment with sonography for trauma examination? *Am Surg*. 2015; 81(4): 336-340.

8. Lichtenstein DA. Ultrasound examination of the lungs in the intensive care unit: *Pediatric Critical Care Medicine*. 2009; 10(6): 693-698. doi:10.1097/PCC.0b013e3181b7f637.

9. Mayo PH, Beaulieu Y, Doelken P, et al. American College of Chest Physicians/La Société de Réanimation de Langue Française statement on competence in critical care ultrasonography. *Chest*. 2009; 135(4): 1050-1060. doi:10.1378/chest.08-2305.

10. Lichtenstein DA. BLUE-Protocol and FALLS-Protocol. *Chest*. 2015; 147(6): 1659-1670. doi:10.1378/chest.14-1313.

11. MacDuff A, Arnold A, Harvey J, et al. Management of spontaneous pneumothorax: British Thoracic Society pleural disease guideline 2010. *Thorax*. 2010; 65(Suppl 2):ii18-ii31. doi:10.1136/thx.2010.136986.

12. Department of Anaesthesiology and Intensive Care, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, UP, India, Danish M, Agarwal A, et al. Diagnostic Performance of 6-Point Lung Ultrasound in ICU Patients: A Comparison with Chest X-Ray and CT Thorax. *Turk J Anaesthesiol Reanim*. 2019; 47(4):307-319. doi:10.5152/TJAR.2019.73603

13. Lung Ultrasound Made Easy: Step-By-Step Guide. POCUS 101. Accessed October 4, 2022. https://www.pocus101.com/lung-ultrasound-made-easy-step-by-step-guide/

14. Chung MJ, Goo JM, Im JG, et al. Value of high-resolution ultrasound in detecting a pneumothorax. *Eur Radiol*. 2005; 15(5): 930-935. doi:10.1007/s00330-004-2518-7.

15. Viglietta L, Inchingolo R, Pavano C, et al. Ultrasonography for the Diagnosis of Pneumothorax after Transbronchial Lung Cryobiopsy in Diffuse Parenchymal Lung Diseases. *Respiration*. 2017; 94(2): 232-236. doi:10.1159/000477818.

16. Sartori S, Tombesi P, Trevisani L, et al. Accuracy of transthoracic sonography in detection of pneumothorax after sonographically guided lung biopsy: prospective comparison with chest radiography. *AJR Am J Roentgenol*. 2007; 188(1): 37-41. doi:10.2214/AJR.05.1716.

17. Volpicelli G, Boero E, Sverzellati N, et al. Semi-quantification of pneumothorax volume by lung ultrasound. *Intensive Care Med*. 2014; 40(10): 1460-1467. doi:10.1007/s00134-014-3402-9.

18. Oveland NP, Lossius HM, Wemmelund K, et al. Using Thoracic Ultrasonography to Accurately Assess Pneumothorax Progression During Positive Pressure Ventilation. *Chest*. 2013; 143(2): 415-422. doi:10.1378/chest.12-1445.

19. Hosseini-Nik H, Bayanati H, Souza CA, et al. Limited Chest Ultrasound to Replace CXR in Diagnosis of Pneumothorax Post Image-Guided Transthoracic Interventions. Can Assoc Radiol J. 2022; 73(2): 403-409. doi:10.1177/08465371211034016.