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Diagnostic Role of Bronchoscopic Brush Biopsy Guided by Thin-Section Computed Tomography in Peripheral Pulmonary Lesions

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Abstract

Objective: The diagnosis of peripheral pulmonary lesions (PPLs) is important as they may be malignant. It is difficult to diagnose PPLs in the absence of a diagnostic guiding tool. Computed tomography (CT) thin-section multiplanar reconstruction (MPR) images have been used as an alternative guide for bronchoscopic diagnosis of PPL. In this study, we aimed to investigate the diagnostic efficacy of MPR image guidance for PPL. *Methods:* Patients with PPL who underwent bronchoscopic brush biopsy guided by thoracic CT thin-section MPR images at our center were retrospectively reviewed. The distance of the lesion to the distal bronchus, the presence of the CT-Bronchus sign, the location of the PPL, and the size of the PPL were recorded from the hospital image record archive. The diagnosis rate was obtained from the procedure records. *Results:* The study included 92 cases. The mean PPL size was 40 ± 21 mm and the mean distal bronchial lesion distance was 27 ± 19 mm. A total of 49 (53.3%) patients had a positive CT-Bronchus sign. The diagnostic yield of the method was 48.9%. The diagnosis rate was significantly higher in patients with positive CT-Bronchus sign (67.3%) compared to those without (26.7%) ($P = 0.001$). Factors affecting the diagnosis in the logistic regression analysis were distal bronchial lesion distance, presence of CT-Bronchus sign, and localization of the lesion. *Conclusion:* CT thin-section MPR images can be used for bronchoscopy guidance in cases with PPL larger than 20 mm and positive CT-Bronchus sign in centers where an interventional radiology unit and other guidance tools are not available.

Keywords

Lung cancer
Computed tomography
Peripheral pulmonary lesion

1. Introduction

Peripheral pulmonary lesions (PPLs) are defined as lesions in the lung periphery that cannot be visualized by bronchoscopy. The frequency of PPL visualization has increased due to the widespread use of computed tomography (CT) [1]. The diagnosis of PPL is important because it may be cancerous. There is no definite diagnostic method to be applied in the diagnosis of PPL yet. While transthoracic biopsy and fluoroscopically guided bronchoscopic brushing were initially used for the diagnosis of PPL [2], advanced technological tools such as electromagnetic navigation bronchoscopy (ENB), radial probe endobronchial ultrasound (R-EBUS), virtual bronchoscopy navigation (VBN) have been developed in recent years [3,4]. However, the diagnostic efficiency of the new devices is unsatisfactory [5]. In addition, these devices are costly and require practitioners to undergo a training process for their usage. Developments in CT technology have led to the possibility of obtaining thin-section reconstruction images of the lung in sagittal, horizontal, and axial planes. This has provided a new guiding tool for physicians performing bronchoscopy in terms of determining and accessing the PPL site. Although this approach has started to be used by physicians, the ability of this application to diagnose PPL has not been evaluated by a sufficient number of studies. Our study aimed to evaluate the effect of CT thin-section multiplanar reconstruction (MPR) image guidance on the peripheral brush biopsy diagnosis in PPLs.

2. Materials and methods

This study was conducted prospectively with the approval of decision number 612 from Izmir Katip Çelebi University Faculty of Medicine Clinical Research Ethics Committee on the 13th of February, 2020. Patients who underwent procedures in the Bronchoscopy Unit of the Chest Diseases Clinic of our hospital between January 2018 and June 2020 were analyzed. Patients with PPL who underwent peripheral brush biopsy by flexible bronchoscopy under the guidance of CT thin-section MPR images were included in the study.

Inclusion criteria included:

(1) Having peripheral pulmonary lesions detected by imaging methods
(2) Multiplanar 1.5 mm cross-sectional computed tomography of the thorax
(3) Having performed brush biopsy guided by thin-section reconstruction images
(4) No endobronchial lesion was detected during the use of bronchoscopy

Patients' names, ages, gender, bronchoscopy procedure information, and biopsy pathology results were recorded from the hospital record system application. CT images were obtained from the hospital image archive system PAACS, and bronchoscopy procedure records were obtained from the bronchoscopy procedure archive system ENDOCAM. The largest size of the PPL, presence of CT-Bronchus sign, localization, and distance of the distal segment bronchus to the lesion were recorded **(Figure 1)**. Flexible bronchoscopy was performed with a standard therapeutic video bronchoscope device (Fujinon Fujifilm EB-530T). The device had a diameter of 6.0 mm and a working channel of 2.8 mm. The procedures were performed under sedation with midazolam, fentanyl, propofonol, as well as topical 2% lidocaine. A brush biopsy was performed from all segment entries in the targeted area (Lookmed cytology brush 1.8 mm 120 cm, Changzhou, China). The CT-Bronchus sign was recorded as positive if there is the presence of an airway leading into the target lesion. Pathways that were compressed by the lesion and did not pass through the lesion were considered negative. The distance from the bronchial inlet to the lesion was measured from the CT reconstruction sections where the bronchoscopy device could be transmitted and recorded at the distance, and the brush biopsy was advanced in the measured amount to avoid the risk of pneumothorax. The path to be followed to reach the PPL was determined from multiplanar CT sections. Peripheral brush biopsy was performed on all subsegment entrances associated with PPL at the target endpoint. When the brush biopsy result came back, the procedure was recorded as a success.

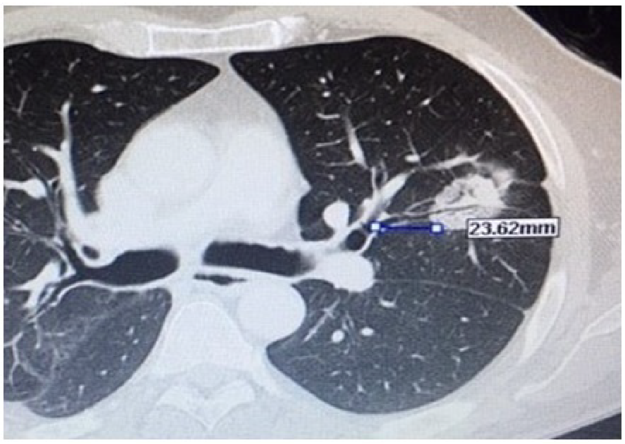

Figure 1. Presence of CT-Bronchus sign and distal bronchial lesion distance measurement

IBM SPSS Statistics 21.0 was used, categorical variables were calculated as frequency and percentage, and continuous variables were calculated as mean and standard deviation. Categorical variables were analyzed by the Chi-square test and continuous variables by the *t*-test. Binary logistic regression analysis was performed to evaluate potential factors affecting bronchoscopy success. The optimal distance for the lesion distance, which was found to be effective on the diagnosis, was determined by receiver operating characteristic (ROC) curve analysis. P value < 0.05 was considered significant in all analyses.

3. Results

A total of 118 patients with PPL were identified, and a total of 92 patients fulfilled the inclusion criteria. Seventy-two (78.3%) were male, 20 (21.7%) were female and the mean age was 61 ± 9 (30–83) years. The mean size of the PPL was 40 ± 20 (10–100) mm and the mean distance from the distal bronchus was 27 ± 19 (5–80) mm. The characteristics of the successful and unsuccessful cases and their lesions are given in **Table 1**.

As a result of the procedure, 45 (48.9%) cases were diagnosed. 43 of the cases were diagnosed with cancer and 2 were diagnosed with infection (tuberculosis and aspergillosis). Subtyping of non-small cell lung cancer could not be made in 17 malignant cases. The age, lesion distance, and lesion size of the patients with and without tissue diagnosis were compared; no significant difference was found in age and lesion size, but lesion distance was significantly different between the two groups. As the lesion distance increased, the rate of diagnosis decreased (**Figure 2**). ROC curve analysis was performed for the lesion distance to reach the diagnosis (AUC: 0.719; 0.613–0.825; P = 0.001) (**Figure 3**). The most optimal distance with

Table 1. Evaluation of the rate of return of results with patient and PPL-related data

	With results		No results		P value
	n	**Mean ± SD**	***n***	**Mean ± SD**	
Age	45	61 ± 10	47	62 ± 8	0.618
Gender (Male *n*, %)	45	36, 80.0	47	36, 76.6	0.800
Size	45	42 ± 21	47	39 ± 20	0.272
Distance	45	20 ± 16	47	34 ± 19	0.001
CT-Bronchus sign (n,%)	45	33, 67.3	47	12, 27.9	0.001
Placement					
Right upper lobe	19, 51.4		18, 48,6		0.146
Right lower lobe	5, 29.4		12, 70.6		0.186
Left upper lobe	13, 48.1		14, 51.9		0.110
Left lower lobe	6, 85.7		1, 14.3		0.037

sensitivity and specificity was 24 mm. The diagnosis rate was higher in cases with a positive CT-Bronchus sign. Of the 49 patients with positive CT-Bronchus sign, 33 (67.3%) were diagnosed, while 12 (26.7%) of the 43 patients with negative CT-Bronchus sign were diagnosed (*P* = 0.020). When the localization of the lesions was examined, it was seen that the most common lesion was in the right upper lobe. 40.2% of the lesions were located in the right upper lobe, 29.3% in the left upper lobe, 18.5% in the right lower lobe, and 7.6% in the left lower lobe. When the relationship between the result and localization was examined, it was diagnostically significant to be localized in the left lower lobe (*P* = 0.037), while it was not significant in other anatomical locations. Binary logistic regression analysis was applied for the effect of age, lesion distance, CT-Bronchus sign, and localization data to determine the factors affecting the success of the procedure; lesion distance, presence of CT-Bronchus sign, and localization were found to be significant for the success of the procedure (**Table 2**). It was found that lesion distance increased the probability of diagnosis 1.08 times, CT-Bronchus sign 3.62 times and left lower lobe localization 20 times (**Table 3**).

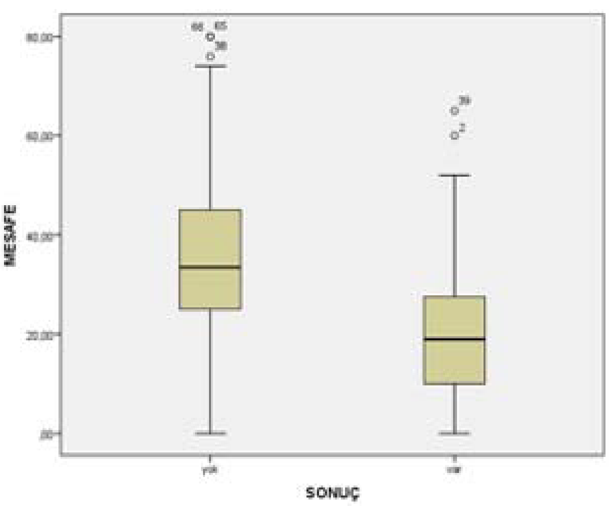

Figure 2. Distal bronchial lesion distance and outcome relationship

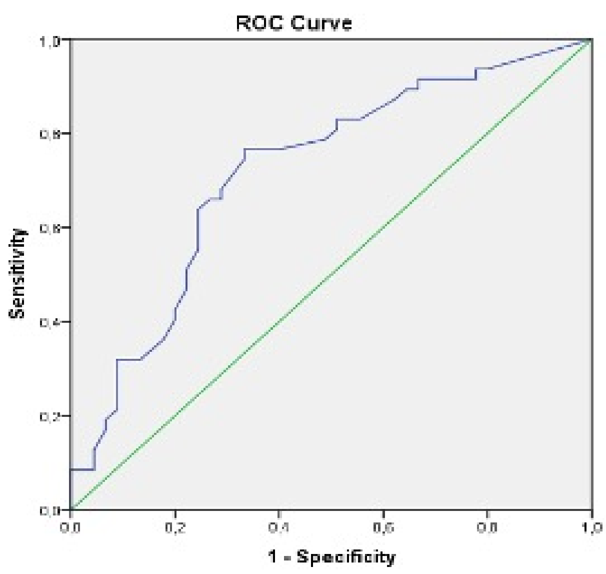

Figure 3. ROC curve calculated for the most effective distance to reach the diagnosis. Sensitivity for 24 mm, 74.5 specificity, 66.6 AUC 0.719 (0.613–0.825)

Table 2. Diagnoses and rates resulting from the procedure. Among malignancies, adenocarcinomas were the most common.

Diagnosis	*n*	%
Non-Small Cell Lung Cancer	17	37.8
Adenocancer	13	28.9
Neuroendocrine Tumor	1	2.2
Squamous Cell Cancer	6	13.3
Small Cell Lung Cancer	6	13.3
Aspergillus fumigatus	1	2.2
Mycobacterium tuberculosis	1	2.2
Total	45	100.0

Table 3. Factors significantly associated with diagnosis in the logistic regression analysis.

Variable	B	S.E.	Odds ratio (OR)	95% C.I. for OR		
				Lower	Upper	*P*
Distance	-0.046	0.018	0.955	0.923	0.989	0.009
CT-Bronchus sign	-1.287	0.551	0.276	0.094	0.814	0.020
PPL placement	-2.980	1.429	0.051	0.003	0.837	0.037

4. Discussion

This study showed that CT thin-section MPR images significantly increased the diagnostic yield by guiding bronchoscopic diagnosis of PPL. CT-guided transthoracic biopsy (TTB) is one of the oldest methods in the diagnosis of PPL. Although the diagnostic sensitivity of the procedure has been reported as 74%–90% in various series, the diagnostic sensitivity decreases in lesions < 3 cm [6,7]. Bleeding may occur as a complication and pneumothorax may be seen in 10%–20.5% of cases [8,9]. Kavita M. Bhat and colleagues found a diagnosis rate of 86% in PPL cases with CT guidance [10]. Because of the mentioned complications, CT scanning is mostly performed in large centers with an interventional radiology unit. In the diagnosis of PPLs, brush biopsy with bronchoscopy under fluoroscopy was frequently used in the past, but it has started to be used less frequently today due to radiation exposure. Kovnat DM and colleagues made a diagnosis in 12 of 23 cases with PPL [11]. Chechanitanı reported a diagnosis rate of 52% [12]. In this method, while the patient and physician are exposed to radiation during the procedure, radiation exposure may be prevented by thin-section reconstructive CT image guidance. The diagnosis rate of both procedures is similar. Eberhardt *et al.* reported a diagnostic rate of 67% regardless of lesion size and pneumothorax without intervention in two cases in their study in which ENB was performed in 89 cases [13]. Kavita M. Bhat *et al.* reported a diagnostic sensitivity of 86% for TTB and 66% for ENB, and a similar frequency of complications in their study evaluating the effectiveness of CT-guided TTB and ENB for PPL [10]. Pneumothorax continued to be a complication encountered in this method as well. In a retrospective review of 467 patients in which R-EBUS was used in the diagnosis of PPL, the diagnosis rate was found to be 69% (58% for 1–2 cm, 72% for 2.1–3 cm, 77% for 3.1–4 cm, 87% for 4.1–5 cm and 88% for > 5 cm) [14]. Eberhart *et al.* evaluated the efficacy of ENB, R-EBUS, and ENB/R-EBUS combination in their study; the diagnosis rate was 88% for ENB/R-EBUS combination, 59% for ENB alone, and 69% for REBUS alone. It was reported that the use of R-EBUS and ENB together significantly increased the diagnosis rate and the pneumothorax rate was 6% [13]. In the study by Ozgul *et al*., the diagnostic rate was 71.4% when ENB was used alone and 73% when combined with R-EBUS [15]. In another randomized controlled study, the diagnostic rate was found to be 63.7% when R-EBUS and ENB were used together, 38.5% with R-EBUS alone and 38.5% with ENB alone, and the diagnostic yields of ENB and REBUS were lower than expected [16]. These methods, which are difficult to access due to cost, learning time, and opportunity, are now recommended to be used together, yet it is a fact that this cannot be met by many centers. Winantea *et al*. reported a diagnostic sensitivity of 66.7% for VBN guided by thin-section CT images with computer software [17]. Asano *et al*. compared VBN and fluoroscopy and found 76.9% and 85.9% diagnostic sensitivity for VBN and fluoroscopy in the study in which samples were sampled with R-EBUS [18]. Bo *et al*. compared fiberoptic bronchoscopy (FOB), R-EBUS, and R-EBUS + VBN combinations and found 41.2%, 72.3%, and 74.3% respectively. The difference between R-EBUS and R-EBUS + VBN groups was not found to be significant [19]. In a cadaveric robotic bronchoscopy study by Yarmuss L. *et al*., when ENB, R-EBUS, ultrathin bronchoscopy, and robotic bronchoscopy were compared, robotic bronchoscopy was found to be better in localizing and reaching PPLs. In the same study, the rates of reaching the lesion and performing a biopsy were 45% with ENB and 25% with ultrathin bronchoscopy and R-EBUS [20]. In the study by Miyoshi S. *et al.*, 69 patients who underwent bronchoscopy without VBN and 56 patients who underwent bronchoscopy with VBN were included in the study. Diagnostic success was found to be higher in patients who underwent bronchoscopy with VBN compared to the other group (57.1% versus 33.3%) [21]. In our study, the diagnostic rate was found to be significantly higher than the group without VBN and close to the rate in bronchoscopy with VBN. This indicates that it may be an alternative method. Thinner bronchoscopes have been developed to reach peripheral lesions more easily. Abhishek Biswas *et al*. found the success rate of ultrathin bronchoscopy under ENB guidance to be 67.3% [22]. Mashide *et al*. compared the thin (4 mm) and ultrathin (3 mm) bronchoscopy and found the ultrathin bronchoscopy was more effective than the thin bronchoscopy (70.1% vs 58.7%, respectively, P = 0.027). In this study, EUS, VBN, and fluoroscopy were used for bronchoscopy guidance [23]. In our study, the target was reached using CT thin-section MPR images without the need for any other device and the success rate was comparable. Similar to our study, the diagnosis rate of PPL by bronchoscopic biopsy was 80.1% in a study guided by CT sections [24]. The high success rate was thought to be related to patient selection. The diagnosis rate was found to be the best in patients with a lesion larger than 20 mm, positive CT-Bronchus sign, at least 6 biopsies, and multiple sampling modalities (BAL, TBB) [24]. Considering the presence of the CT-Bronchus sign, which was significant in our study, the diagnostic yield increased in the group with the positive CT-Bronchus sign in a similar study by Marienne *et al.* [24]. In a meta-analysis evaluating the CT-Bronchus sign to predict the diagnostic success of PPL, the positive CT-Bronchus sign was found to be associated with a high diagnostic yield (74.1%) [25].The high prevalence of malignancy in the group examined in our study, variability between bronchoscopists, and the fact that our study was retrospective are limiting factors.

5. Conclusion

CT thin-section MPR images can be used for bronchoscopy guidance in patients with PPL and with a positive CT-Bronchus sign in centers where there is no interventional radiology unit and other guidance tools.

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Disclosure statement

The authors declared no conflict of interest.

Author contributions

All authors contributed to the conception, design, data collection, and/or processing of the study. BS performed the analysis and/or interpretation of the study.

Ethical approval

Ethics committee approval was obtained from Izmir Katip Çelebi University Faculty of Medicine, Clinical Research Ethics Committee on 13.02.2020 with decision number 612.

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