Original Article

A retrospective study comparing the ultrathin versus conventional bronchoscope for performing radial endobronchial ultrasound in the evaluation of peripheral pulmonary lesions

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ABSTRACT

Background: Few studies have reported on the utility of ultrathin bronchoscopes (UTBs) for performing radial probe endobronchial ultrasound (EBUS). Herein, we describe our experience with UTB and conventional bronchoscope (CB) for performing radial EBUS. **Materials and Methods:** This was a retrospective study comparing the diagnostic yield of a prototype UTB (external diameter 3 mm, working channel diameter 1.7 mm) versus CBs (external diameter ≥ 4.9 mm) in performing radial EBUS for the evaluation of peripheral pulmonary lesions (PPLs). Fluoroscopic guidance was not available. **Results:** A total of 121 subjects (34, UTB; 87, CB; 69.4% males) with a mean (standard deviation [SD]) age of 55.2 (14.8) years underwent radial EBUS. The mean (SD) size of PPLs on computed tomography of the thorax was 22.2 (13.7) mm. The lesions were significantly smaller in the UTB group (16.4 vs 24.7 mm, P = 0.006). Eight lesions could be visualized within the lumen of the peripheral smaller bronchi with the UTB. The overall yield of radial EBUS was 52.9% and was similar in the two groups (UTB vs. CB, 55.9% vs. 51.7%; P = 0.7). The procedure time was significantly shorter in the UTB group. On multivariate logistic regression, the yield was similar in the two groups after adjusting for the size and location of the lesion and position of the radial probe in relation to the lesion. **Conclusion:** Despite smaller lesions, radial EBUS performed with the UTB was found to have similar efficacy to that performed with the CB. More lesions could be visualized endobronchially using the UTB making it an attractive alternative for performing radial EBUS.

KEY WORDS: Bronchoalveolar lavage, brush cytology, endobronchial ultrasound, pneumothorax, transbronchial lung biopsy, transbronchial needle aspiration

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INTRODUCTION

Peripheral pulmonary lesions (PPLs) are defined as those that cannot be visualized during routine flexible bronchoscopy. The diagnosis of PPLs can be made using computed tomography (CT)-guided percutaneous procedures (needle aspiration or trucut biopsy), using surgical lung biopsy (either video-assisted thoracoscopic surgery or open), or more recently using

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either electromagnetic navigation or with the radial probe endobronchial ultrasound (EBUS), with or without virtual bronchoscopic navigation.[1-5] CT-guided procedures provide a higher diagnostic yield compared to the radial EBUS but are associated with a greater risk of pneumothorax,[6,7] especially in those with emphysema or if the lesion is not abutting the chest wall.[8] On the other hand, radial EBUS is safer; however, its diagnostic yield is variable, being affected by several factors. These include the etiology of the lesion (benign vs. malignant), the size of the lesion (≤2 cm vs. >2 cm), the location (upper vs. lower lobes), the use of fluoroscopy, the presence of CT bronchus sign, the location of the radial probe in relation to the lesion (within or adjacent to the lesion), and the use of ancillary guidance procedures such as virtual navigation bronchoscopy and electromagnetic navigation bronchoscopy.[9,10] Whether the yield of radial EBUS is affected by the external diameter of the flexible bronchoscope remains unclear.

The conventional bronchoscope (CB), with an external diameter of 4–6 mm, can only be inserted up to the segmental or the subsegmental bronchus. This can cause difficulty in advancing the radial probe and other instruments beyond the angled subsegmental bronchi, especially when fluoroscopy is not available. The currently available CB with an external diameter of 2.8 mm can be navigated up to the fourth- or the fifth-generation segmental bronchi. However, its small working channel (diameter 1.2 mm) precludes the use of a radial probe to localize the target lesion.[11] Recently, a novel ultrathin bronchoscope (UTB; external diameter 3 mm; working channel diameter 1.7 mm; 240° insertion tube rotating function) has been used for performing radial EBUS.[12] The UTB has a theoretical advantage of better maneuverability in technically unapproachable areas of the airways, thereby improving the probability of locating the lesion. In one study, the prototype UTB offered a higher diagnostic yield compared to the CB (outer diameter 4 mm) in the diagnosis of PPLs.[12] This study, however, employed other localization techniques including fluoroscopy and virtual bronchoscopic navigation, which are not routinely available.

Whether the diagnostic yield of radial EBUS without fluoroscopic guidance would be higher with the use of the UTB (without guide sheath) compared to a CB (with guide sheath) in the evaluation of PPLs remains unclear. Herein, we describe our experience with a prototype UTB for performing radial EBUS in the diagnostic evaluation of PPLs.

MATERIALS AND METHODS

This was a retrospective study performed between October 1, 2014, and March 31, 2017, in the Interventional Pulmonology suite of this Institute. Radial EBUS was performed using CBs before June 2016, and in the later period, a hybrid prototype UTB was used. The study protocol was approved by the Ethics Review Committee, and consent waiver was allowed as this was a retrospective analysis of anonymized patient data. However, a procedural consent was obtained from all study participants.

Data collection
Consecutive participants who underwent radial EBUS for the diagnosis of PPLs were included in the current study. We defined PPL as a lesion in the lung parenchyma that could not be visualized during routine flexible bronchoscopy. The following information was retrieved from the bronchoscopy database: (a) clinical history and demographic profile; (b) size of the lesion on the CT chest; (c) location of the lesion on CT thorax; (d) size of the lesion on radial EBUS; (e) type of bronchoscope used (CB or UTB); (f) location of the radial probe in relation to the lesion (within the lesion or adjacent to lesion); (g) type of sampling technique used (brush, bronchial washing [BW], transbronchial lung biopsy [TBLB]); (h) duration of procedure; (i) diagnostic yield of procedures such as brush cytology, BW, and TBLB; (j) overall yield of radial EBUS; and (k) complications including bleeding, pneumothorax, and hypoxia during the procedure. Bleeding was classified as mild if it necessitated instillation of cold saline, epinephrine, or tamponade for control of bleeding and severe if it necessitated blood transfusion and endotracheal intubation or resulted in hospitalization or death.

Study procedure
All bronchoscopic procedures were performed on an outpatient basis using conscious sedation (intravenous midazolam and pentazocine). Topical anesthesia was administered with nebulized 4% lignocaine (2.5 mL) followed by two puffs of 10% lignocaine spray over the oropharynx.[13] Aliquots of 1% lignocaine (2 mL) were instilled over the vocal cords and the airways using the spray-as-you-go method.

Conventional bronchoscope method
Before June 2016, radial EBUS was performed using the CBs (BF-TE2 [outer diameter 5.9 mm], BF-1T 150 [outer diameter 6 mm], or BF-1T 180 [outer diameter 6 mm], Olympus, Japan; FB-19 TV [outer diameter 6.2 mm], Pentax, Japan). If an endobronchial lesion was identified proximal to or at the level of the subsegmental bronchus, it was labeled as central lesion. In this situation, the patient underwent routine endobronchial biopsy and was excluded from the study.

Ultrathin bronchoscope method
The prototype UTB (Y-0028; Olympus Medical Systems, Tokyo, Japan) has an outer diameter of 3.0 mm with a working channel of 1.7 mm. It moves 210° anterior and 130° posterior and has an insertion tube rotating function (total angle of rotation of 240°). The bronchial subsegments up to the sixth generation can be examined only using the UTB to identify any endobronchial abnormality. If any endobronchial abnormality was observed beyond the subsegmental bronchi, an endobronchial biopsy was

obtained and this was considered a positive yield in the UTB arm as such peripheral locations are beyond the reach of CB visualization.

Radial endobronchial ultrasound

It was performed with an endoscopic ultrasound scanner (EU-ME1; Olympus Medical Systems, Japan) and a radial probe transducer (20 MHz, mechanical-radial type [UM-S20-20R; Olympus, Tokyo, Japan]), with an outer diameter of 1.7 mm and a length of 115 cm. The radial probe was housed in a guide sheath (SG-200C [inner diameter 2.0 mm; length 105 cm]) with the CB method. On the other hand, the radial probe was introduced without the guide sheath, through the working channel of the UTB. The radial probe was then navigated through the bronchial segments to localize the target lesion. Once the target lesion was visualized, the bronchoscope was kept fixed at that position, and the length of the radial probe at the external end of the working channel was marked with a guide. The probe was removed, bronchial brush and biopsy forceps (length marked using radial probe as guide) were then introduced through the working channel of the bronchoscope advanced into the segment with target lesion (or the guide sheath), and the samples were then taken. The samples were obtained using brush cytology, BW, and TBLB in that order. A maximum of 10 attempts were used for obtaining TBLB. Fluoroscopy guidance was not used. Transbronchial needle aspiration was not performed.

If the lesion could not be identified using the radial EBUS after 20 min of examination, the procedure was abandoned, and the tissue sampling was performed blindly from the segment with the target lesion on CT thorax. The procedure in such a case was classified as failure.

Specimen preparation

The lung biopsies were immersed in 40% formaldehyde solution and submitted for histopathological examination. Biopsy slides were additionally stained with Ziehl–Neelsen (for mycobacteria) and fungal stains. Brush samples were smeared on glass slides and were air-dried or alcohol-fixed.

Diagnosis

The histological and cytological samples were separately interpreted by a dedicated histopathologist (AB) and a cytopathologist (NG) blinded to the bronchoscopy details. "Suspicious" findings were regarded as negative in the current analysis. A finding of nonspecific fibrosis and inflammation was labeled as a negative specimen. The final diagnosis was established by histocytopathological findings, microbiological analysis of the brush, BW, and TBLB specimens, or clinical follow-up. The yield of radial EBUS was considered successful if it resulted in a specific diagnosis such as malignancy, tuberculosis, and others.

Study objectives

The main objective of the study was to compare the diagnostic yield (successful yield) of radial EBUS using either the UTB or the CB method. We also evaluated whether the UTB could identify endobronchial abnormality in the fourth- or fifth-generation bronchi.

Statistical analysis

Statistical analysis was performed using the commercial statistical software SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). Data are presented as mean with standard deviation (SD) or number with percentage. Chi-square test or Fisher's exact test was used to analyze differences between categorical variables, while the Mann–Whitney U-test was used for continuous variables. A logistic regression analysis was performed to identify factors associated with a successful yield with radial EBUS. A P value < 0.05 was considered statistically significant.

RESULTS

We performed 4760 bronchoscopies during the study period. Assessment of PPLs formed an indication for bronchoscopy in 124 (2.6%) individuals. In three subjects, endobronchial abnormality was identified in the central airways, and hence, they were excluded from further analysis. Finally, radial EBUS was performed in 121 subjects (34 using UTB and 87 using CB).

The baseline characteristics were similar between the two groups [Table 1]. The mean (SD) age of the study population (69.4% males) was 55.2 (14.8) years. The mean (SD) size of PPLs on CT thorax was 22.2 (13.7) mm. The

Table 1: Demographic profile and other parameters of the study population

Parameter	Ultrathin scope (*n*=34)	Conventional scope (*n*=87)	*P*
Age (years)	55.3±14.6	55.1±14.9	0.991
Male gender, *n* (%)	25 (73.5)	59 (67.8)	0.662
Size of lesion on CT (mm)	16.4±9.1	24.7±14.6	0.006
Location of lesion on CT, *n* (%)			
Right upper lobe	13 (38.2)	28 (32.2)	0.449
Right middle lobe	7 (20.6)	11 (12.6)	
Right lower lobe	3 (8.8)	19 (21.8)	
Left upper lobe	6 (17.6)	17 (19.5)	
Lingula	2 (5.9)	2 (2.3)	
Left lower lobe	3 (8.8)	10 (11.5)	
CT findings			
Consolidation	16 (47.1%)	27 (31.0%)	0.10
Solitary pulmonary nodule	6 (17.6%)	0	0.0001
Multiple nodules	11 (32.4%)	29 (33.3%)	0.92
Location of probe in relation to the lesion, *n* (%)			
Adjacent to the lesion	3 (15.8)	16 (32.7)	0.164
Within the lesion	16 (84.2)	33 (67.3)	
Bronchoscopy procedures, *n* (%)			
Bronchial washings	24 (70.6)	82 (94.3)	<0.001
Brush cytology	26 (76.5)	86 (98.9)	<0.001
TBLB	19 (55.9)	63 (72.4)	0.080

Chi-square test or Fisher's exact test was used to analyze differences between categorical variables while the Mann–Whitney U-test was used for continuous variables. CT: Computed tomography, TBLB: Transbronchial lung biopsy, USG: Ultrasonography

size of the lesion was significantly smaller in participants who underwent radial EBUS using the UTB (UTB vs. CTB, 16.4 vs. 24.7, $P = 0.006$). The most common site of lesion was the right upper lobe (41/121, 33.9%) followed by the left upper lobe (23/121, 19%); the lobar distribution of lesions was similar between the two groups [Table 1]. The right upper lobe posterior segment (26/121, 21.5%) followed by left upper lobe apicoposterior segment (16/121, 13.2%) was the most common segment with the target lesion. The segmental distribution was also similar between the two groups. Radial EBUS-guided BW, brush sampling, and TBLB were performed in majority of the participants; the distribution of procedures was different between the two groups [Table 1].

Radial EBUS provided a successful yield in 52.9% (64/121) participants, with no difference in yield between the two methods (UTB vs. CTB, 55.9 vs. 51.7; $P = 0.68$). The diagnostic yield of TBLB was the highest (35/82, 42.7%) followed by BW (29/106, 27.4%) and brush cytology (26/112, 23.2%); the yield of individual specimens (brush, BW, and TBLB) was similar between the two groups [Table 2]. There was no difference in the diagnostic yield based on the location of the lesion (upper lobes vs. nonupper lobes, 46.9% vs. 56.1; $P = 0.31$), the size of the lesion on CT ($\leq$2 cm vs. >2 cm, 47.4% vs. 58.8%; $P = 0.29$) or on the ultrasound ($\leq$1 cm vs. >1 cm, 50% vs. 72.2%; $P = 0.17$), and the location of the radial probe in relation to the lesion (within the lesion vs. adjacent to the lesion, 59.2% vs. 36.8%; $P = 0.09$).

We were unable to visualize the lesion on radial EBUS in 28.9% (35/121) of the participants. With the UTB, we identified eight endobronchial lesions in the fourth–fifth-generation subsegmental bronchi that could not have been visualized using the CB [Table 3]. The procedure time was significantly lesser with the UTB [Table 3]. Complications were encountered in six participants [Table 3] and were not different between the two groups. There were two pneumothoraces (one in each group) that resolved with supplemental oxygen.

On multivariate logistic regression analysis, the yield was similar between the two types of bronchoscopes after adjusting for several covariates [Table 4].

DISCUSSION

The current study found no difference in the diagnostic yield when radial EBUS was performed using either the UTB (without guide sheath) or CB (with guide sheath). The use of the UTB, however, led to a direct endoscopic visualization of PPLs on several occasions with reduction in the procedure time.

Only one study has investigated the utility of the prototype UTB for performing radial EBUS using virtual

Table 2: Diagnostic yield of procedures performed using radial endobronchial ultrasound

Parameter	Ultrathin scope (*n*=34)	Conventional scope (*n*=87)	*P*
Bronchial washing			
Nondiagnostic	16 (66.7)	61 (74.4)	0.461
Malignancy	6 (25)	13 (15.7)	
Tuberculosis	2 (8.3)	4 (4.8)	
Fungal pneumonia	0 (0)	4 (4.9)	
Brush cytology			
Nondiagnostic	21 (80.8)	65 (75.6)	0.639
Malignancy	4 (15.4)	11 (12.8)	
Tuberculosis	1 (3.8)	6 (7)	
Fungal pneumonia	0 (0)	4 (4.7)	
TBLB			
Nondiagnostic	12 (63.2)	35 (55.6)	0.971
Malignancy	3 (15.8)	12 (19)	
Tuberculosis	2 (10.5)	9 (14.3)	
Fungal pneumonia	1 (5.3)	4 (6.5)	
Lymphoma	0 (0)	1 (1.6)	
Sarcoidosis	1 (5.3)	2 (3.1)	
Final diagnosis			
Malignancy	14 (41.2)	24 (27.6)	0.369
Lymphoma	0 (0)	1 (1.1)	
Tuberculosis	2 (5.9)	12 (13.8)	
Fungal pneumonia	1 (2.9)	6 (6.9)	
Sarcoidosis	1 (2.9)	2 (2.3)	
Foreign body	1 (2.9)	0 (0)	

All values are represented as *n* (%). Chi-square test or Fisher's exact test was used to analyze differences between categorical variables while the Mann–Whitney U-test was used for continuous variables. TBLB: Transbronchial lung biopsy

Table 3: Outcome parameters between two bronchoscopes type

Parameter	Ultrathin scope (*n*=34)	Conventional scope (*n*=87)	*P*
Radial USG outcomes			
Lesion visible on USG	23 (67.6)	55 (63.2)	<0.001
Lesion not visible on USG	3 (8.8)	32 (36.8)	
Endobronchial lesion	8 (23.5)	0 (0)	
Duration of procedure in minutes, mean±SD	20.1±8.7	22.6±9.2	0.018
Overall yield	19 (55.9)	45 (51.7)	0.680
Complications			
Hypoxia	0 (0)	2 (2.3)	0.629
Mild bleeding	1 (2.9)	1 (1.1)	
Pneumothorax	1 (2.9)	1 (1.1)	

All values are represented as *n* (%) unless otherwise stated. Chi-square test or Fisher's exact test was used to analyze differences between categorical variables, while the Mann–Whitney U-test was used for continuous variables. SD: Standard deviation, USG: Ultrasonography

Table 4: Multivariate regression analysis of variables predicting successful yield of radial endobronchial ultrasound

	Adjusted OR (95% CI)	*P*
Type of scope (ultrathin vs. conventional)	0.6 (0.2-2.2)	0.45
Size of lesion on CT thorax (mm)	1.0 (0.9-1.1)	0.86
Upper lobe lesion on CT thorax	2.2 (0.7-7.3)	0.19
Position of radial probe within the lesion (within vs. adjacent)	2.6 (0.7-10.2)	0.17

CI: Confidence interval, CT: Computed tomography, OR: Odds ratio

navigation bronchoscopy in the diagnostic evaluation of PPLs.[12] In that study, 305 subjects were randomized to undergo radial EBUS with the UTB or the CB. The diagnostic yield was significantly higher in the UTB group (74% vs. 59%).[12] In the current study, the diagnostic yield in the UTB group was only 55.9%. There could be several reasons for a lower yield in the UTB arm. Unlike the previous study, we did not use other localization techniques such as virtual navigational bronchoscopy and fluoroscopy. The use of virtual navigational bronchoscopy has been shown to enhance the procedural yield of radial EBUS.[9,14] Another reason for a lower yield with the UTB in the present study could be the significantly smaller size of lesions in the UTB arm (16.4 mm vs. 24.7 mm). In fact, the procedural yield of lesions smaller than 2 cm has been demonstrated to be lower in comparison to larger lesions.[9] This might have lowered the diagnostic yield in the UTB arm. However, the use of the UTB resulted in better direct visualization of PPLs compared to the CB as the UTB could be advanced closer to the target lesion. The better maneuverability and direct visualization reduced the procedure time similar to a previous study using the UTB.[15]

The overall yield of radial EBUS in our study was lower than the previous studies.[12,15] In a pooled analysis of 57 studies, the diagnostic yield of radial EBUS was found to be 70.6% (95% confidence interval, 68–73).[9] One major reason is that most of the studies have been conducted at centers with significant experience in performing radial EBUS. The other reason is that the current study had large number of benign causes of PPLs, unlike the previous studies. The yield of radial EBUS has been demonstrated to be lower in benign as compared to malignant causes.[9,10] Furthermore, due to a high prevalence of tuberculosis and other infections in our region, PPLs due to healed infection are commonly encountered. Finally, the upper lobes were the most common site of PPLs in the current study. The yield of radial EBUS in the upper lobes is lower than other lobes.[9] Interestingly, however, our results are similar to the AQuIRE Registry (57%) and reflect the yield of radial EBUS in real-life scenario where patients are randomly included.[16]

There are a few limitations of our study. The retrospective design of the study with its inherent flaws including selection bias is the major limitation. The small number of patients in the UTB arm does not allow us to draw a firm conclusion regarding the yield of the UTB and needs further evaluation in a larger trial. We also did not use fluoroscopic guidance. It is likely that the results could have been different had we used fluoroscopic guidance although the yield has not been shown to be affected by fluoroscopic guidance.[10] Finally, the procedures were performed by several different operators. However, all the operators were faculty with at least 5 years' experience in performing flexible bronchoscopy.

CONCLUSION

The use of radial EBUS is safe and results in the diagnosis of over 50% of PPLs. The prototype UTB provided similar yield as the CB despite smaller lesions and with reduction in procedure time (due to better maneuverability), is an attractive alternative to the CB in performing radial EBUS. More studies are required to study the utility of the novel UTB in the diagnosis of PPLs.

Conflicts of interest
There are no conflicts of interest.

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