Review Article

Endobronchial ultrasonography using a guide sheath technique for diagnosis of peripheral pulmonary lesions

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ABSTRACT

Endobronchial ultrasonography using a guide sheath (EBUS-GS) is a novel method used for collecting peripheral pulmonary lesion (PPL) samples. EBUS-GS is performed by introducing a guide sheath-covered miniprobe into the target bronchus and then withdrawing the miniprobe after lesion detection, leaving the guide sheath *in situ* as a working channel for obtaining lesion samples. EBUS-GS can improve PPL diagnosis rates and be used for obtaining specimens for molecular analysis. In this review, we discuss the clinical applications of EBUS-GS, the factors that affect its diagnostic sensitivity, and potential complications. We also compare EBUS-GS with other available diagnostic techniques and discuss the strengths and limitations of this method.

Key words: Bronchoscopy, diagnosis, endobronchial ultrasonography, guide sheath, peripheral pulmonary lesions

INTRODUCTION

Lung cancer is one of the most common cancers worldwide. Peripheral pulmonary lesions (PPLs) detected during screening for lung cancer require further evaluation, for which tissue samples need to be obtained through biopsy. Bronchoscopy is commonly performed to obtain tissue samples, with various guidance methods used to improve diagnostic yield.[1] Endobronchial ultrasound (EBUS) guidance was first used by Herth *et al.* in 2002 for performing transbronchial biopsy (TBB) of PPLs.[2] Radial EBUS has a diagnostic sensitivity of 73% for peripheral lung cancer (PLC). The American College of Chest Physicians guidelines for Diagnosis and Management of Lung Cancer (3rd edition) recommends radial EBUS as an adjunctive imaging modality in patients with suspected lung cancer in whom a tissue diagnosis is required.[3]

Endobronchial ultrasonography using a guide sheath (EBUS-GS) was first reported by Kurimoto *et al.*[4] as a method to increase the reliability of sample collection from PPLs. The guide sheath is a plastic tube with a radiopaque metal mark near its tip. In the EBUS-GS technique, the miniprobe covered by the

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guide sheath is introduced into the target bronchus through the working channel of a bronchoscope. The miniprobe with the guide sheath is gently moved back or forward along the target bronchus until the lesion is detected. After the ultrasound image of the lesion is obtained, the miniprobe is withdrawn, leaving the guide sheath *in situ* as a working channel. Lesion samples can then be obtained through the guide sheath with a brush, biopsy forceps, or other devices. Guide sheaths with diameters of 1.95 mm and 2.55 mm are available for miniprobes with diameters of 1.4 mm and 1.7 mm, respectively. A bronchoscope with a working channel diameter of 2.0 mm is suitable for a guide sheath with a diameter of 1.95 mm, whereas a bronchoscope with a working channel diameter of 2.8 mm is needed for a guide sheath with a diameter of 2.55 mm.

CLINICAL APPLICATION

In the past decade, the increased use of the EBUS-GS technique has significantly increased the PPL diagnosis rate. In Japan, EBUS-GS has replaced fluoroscopy-guided transbronchial lung biopsy as the main method for diagnosis of PPLs. However, EBUS-GS has not yet been universally adopted in other countries. For PPLs, the overall diagnostic sensitivity of bronchoscopy by the EBUS-GS method is reported to range between 58.3%[5] and 84.4%[6] [Table 1]. Even for small lesions (≤10 mm), the diagnostic yield of EBUS-GS is as high as 76%. Lesions that are invisible under fluoroscopy can also be detected and sampled using the EBUS-GS technique.[4]

The value of the EBUG-GS technique has also been investigated in other types of lesions. In the diagnosis of benign peripheral pulmonary diseases, EBUS-GS performed significantly better than bronchoscopy without EBUS-GS did and was able to correctly diagnose 58% (99/171) of lesions.[19] In peripheral cavitary lung lesions, it is difficult to obtain adequate biopsy samples because of the limited target area of the cavity wall and the surrounding reactive normal tissue. Despite this, research has shown that adequate tissue samples can be obtained by employing EBUS-GS, which has high diagnostic sensitivity (80%).[20] Ikezawa *et al.*[21] reported that EBUS-GS is useful for the diagnosis of ground-glass opacity (GGO) lesions: 57% of GGO predominant-type lesions located at the lung periphery were successfully diagnosed by EBUS-GS. Furthermore, 6 out of 11 pure GGO lesions that were invisible under fluoroscopy were also correctly diagnosed using the EBUS-GS technique. Another study[22] on EBUS-GS reported a diagnostic sensitivity of 65% for GGO lesions. This is comparable to its diagnostic sensitivity for solid nodules[22] and is consistent with the findings of a meta-analysis of studies on guided bronchoscopy.[23] This diagnosis sensitivity is also similar to that of transthoracic needle aspiration (TTNA) for GGO.[22] The EBUS-GS technique can also be used for obtaining specimens for molecular analysis. Izumo *et al.*[24] demonstrated the value of the EBUS-GS procedure for re-biopsy and mutation analysis of epidermal growth factor receptor tyrosine kinase inhibitor-resistant nonsmall cell lung cancer. In 44 patients who underwent EBUS-GS TBB,

Table 1. Diagnostic rates of endobronchial ultrasonography using a guide sheath

Author (year)	Lesion number	Lesion diameter	Bronchoscope type	Miniprobe type	Navigation system	Fluoroscopy	Sampling method	Diagnostic rate (%)
Minezawa *et al.* (2015)[7]	149	≤30 mm	BF-P260F, 1T260	UM-S20-17S	No	Yes	F, B	72.5
Minami *et al.* (2015)[8]	60	All sizes	BF-260 or P260F	UM-S20-17S	UN	UN	F, B, W	83.3
Sánchez-Font *et al.* (2014)[9]	50	All sizes	BT180-Q	UM-S20-17S	No	Yes	F, B	78
Tamiya *et al.* (2013)[10]	68	≤30 mm	P260F	XUM-S20-17R	Yes	Yes	F, B, T	77.9
Ishida *et al.* (2012)[11]	65	All sizes	BF T200	UM-S20-17S	No	Yes	F, B, W	64.6
Oki *et al.* (2012)[12]	102	All sizes	P260F	UM-S20-17S	No	Yes	F, B, W	62
Ishida *et al.* (2011)[13]	102	≤30 mm	P260F	UM-S20-17S	Yes	Yes	F, B, L	80.4
Oshige *et al.* (2011)[14]	57	All sizes	BF1T-260R and BF-P260F	UM-S20-20R and UM-S20-17S	Yes	Yes	F, B	84.2
Asano *et al.* (2008)[5]	32	All sizes	P260F	XUM-S20-17R	Yes	Yes	F, B, W	84.4
Yamada *et al.* (2007)[15]	158	≤30 mm	BF-P-260F, BF-1T-30, and BF-1T260	XUM-S20-17R, UM-S20-20R	No	Yes	F, B	67
Yoshikawa *et al.* (2007)[16]	123	All sizes	BF-260 and BF-P240	XUM-S20-17R	No	No	F, B	61.8
Asahina *et al.* (2005)[17]	30	≤30 mm	BF-P-260F, BF-P-240	XUM-S20-17R	Yes	Yes	F, B	63.3
Kikuchi *et al.* (2004)[18]	24	≤30 mm	BF-P-260F, BF-P-240, BF-P-200	XUM-S20-17R	No	Yes	F, B	58.3
Kurimoto *et al.* (2004)[4]	150	All sizes	BF 1T-30, 40, or 240R	UM-S20-20R	No	Yes	F, B	77

F: Forceps biopsy, B: Cytological brushing, L: Bronchial lavage, W: Bronchial washing, T: Transbronchial needle aspiration cytology, UN: Unknown

the technical success rate was 100%; furthermore, 75.0% of specimens (33/44) obtained with EBUS-GS were found to be adequate for gene profiling. Iwabu *et al*.[25] reported the case of a patient who presented with Stage 4 colon cancer followed by a left upper lobe primary pulmonary adenocarcinoma; subsequently, a new nodule appeared in the contralateral lung field. Liquid samples obtained by EBUS-GS from this lesion revealed a *KRAS* mutation, which was not detected in the metachronous left upper lobe cancer but was detected in the resected sigmoid colon. Thus, although the results of EBUS-GS-based histopathologic examinations were inconclusive, the method did assist in preoperative diagnosis. The diagnosis was confirmed after wedge resection.

FACTORS AFFECTING DIAGNOSTIC SENSITIVITY OF ENDOBRONCHIAL ULTRASONOGRAPHY USING A GUIDE SHEATH FOR PERIPHERAL PULMONARY LESIONS

Many factors are associated with successful diagnosis using EBUS-GS [Table 2]. Probe position is the most significant factor affecting the diagnostic sensitivity of EBUS-GS for PPLs.[4,10,15,26-28] On the EBUS image, the position of the probe can be classified as within, adjacent to, or outside the PPL. The "within" position provides the highest diagnostic yield (68%–92.1%), followed by the "adjacent" position (42%–61%) and the "outside" position (4%). Several studies have found that the bronchus sign is associated with the diagnostic sensitivity of EBUS-GS for PPLs.[16,27,28] On the basis of the relationship between the target lesion and the nearest bronchus, Minezawa *et al*.[7] defined three types of computed tomography (CT) bronchus signs: A, B, and C. When CT images show the bronchus clearly extending inside the target lesion, it is categorized as Type A; when no bronchus can be detected within the lesion, it is categorized as Type C; and when the CT findings cannot be categorized as either Type A or C, it is classified as Type B. They found that a Type A CT bronchus sign was significantly related to a "within" EBUS finding and that the diagnostic success rate was the highest for Type A lesions.

It remains unclear whether lesion diameter, PPL consistency, and lesion location influence the diagnostic sensitivity of EBUS-GS. Some studies have shown that the diagnostic sensitivity of EBUS-GS is similar for lesions of different diameters[10,26,28] and that the efficacy of the technique did not decrease even for lesions <10 mm in diameter.[4] Other studies have indicated that the diagnostic sensitivity of EBUS-GS for bigger PPLs (≥15 mm in mean diameter or >20 mm in diameter) was significantly higher than that for smaller PPLs (<15 mm in mean diameter or ≤20 mm in diameter).[7,15,16] The consistency of PPLs also affects the diagnostic sensitivity of EBUS-GS, with the diagnostic sensitivity for solid nodules being higher than that for part-solid or pure GGO lesions.[10,16,27] Difficulty in obtaining an EBUS image of GGOs and the lack of bronchus penetration by a GGO lesion are two explanations that have been proposed for the lower sensitivity of EBUS-GS for nonsolid lesions.[16] However, other studies[7,26,28] have revealed that the consistency of PPLs does not significantly affect EBUS-GS sensitivity.

Lobe location, the relationship between the lesion and pleura, visibility during fluoroscopy, and fluorine-18 fluorodeoxyglucose (^{18}F-FDG) uptake are other factors that can contribute to successful diagnosis of PLC.[7,26,27,29] A study showed that the diagnostic yields for lesions in the right middle lobe and left lingular segment were higher than those for lesions in other locations,[16] whereas another study found that the diagnostic yield for lesions in the left upper apical posterior segment was significantly lower than that for lesions in other locations.[4] The diagnostic rate of lesions that were not touching or adjacent to the visceral pleura (distance ≥10 mm) was significantly higher than that of lesions on the pleura.[26,29] Minezawa *et al*. reported that visibility under fluoroscopy was a factor significantly associated with a definitive diagnosis.[7] Multivariate analysis has shown that high ^{18}F-FDG uptake (maximum standardized uptake value [SUV_{max}] ≥2.8) is a significant predictor of PLC. The diagnostic yield of PLC was 84.6% when the ^{18}F-FDG uptake was high (SUV_{max} ≥2.8), and the bronchus sign was positive, as opposed to only 33.3% when ^{18}F-FDG uptake was low (SUV_{max} <2.8) and the bronchus sign was negative.[27]

ENDOBRONCHIAL ULTRASONOGRAPHY USING A GUIDE SHEATH-RELATED COMPLICATIONS

EBUS-GS is a safe method for PPL diagnosis, with reported complication rates between 0%[6,14,17] and

Table 2. Factors affecting the diagnostic sensitivity of endobronchial ultrasonography using a guide sheath for peripheral pulmonary lesions

Factors	Chavez *et al.*, 2015[26]		Tamiya *et al.*, 2013[10]		Yamada *et al.*, 2007[15]		Umeda *et al.*, 2014[27]		Okachi *et al.*, 2016[28]		Minezawa *et al.*, 2015[7]		Yoshikawa *et al.*, 2007[16]		Kurimoto *et al.*, 2004[4]		Fielding *et al.*, 2008[29]	
	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*	Diagnostic rate (%)	*P*
Probe position																		
Within	68	0.001	92.1	0.004	83	<0.001	80.9[c]	<0.0001	77.1	<0.001	-	-	-	-	87	<0.0001	-	-
Adjacent/invisible	54		60.0		61/4		7.7[d]		68.9/19.4		-		-		42		-	
Bronchus sign																		
Positive	-	-	-	-	71	0.211	74.2	0.0002	68.8	0.005	-	-	67.3	<0.01	-	-	-	-
Negative	-		-		45		44.0		41.9		-		0		-		-	
Lesion size by diameter (mm)																		
≥20, ≤30	71	0.179	74.1	0.534	91[a]	<0.001	-	-	71.3[e]	0.031	82.6	0.01	75.6[e]	<0.01	77	0.99/0.41 /0.96	-	-
<20	62		80.5		68[b]		-		55.6[f]		63.8		29.7[f]		76/76/69[g]		-	
Consistency																		
Solid	68	1.000	91.7	0.007	-	-	71.6	0.017	68.6	0.061	73.2	0.24	67	<0.05	-	-	-	-
GGO (pure/ part-solid)	67		62.5		-		52.8		48.4/42.9		66.7		35		-		-	
Lobe location																		
Upper (right/left)	66	0.803	82.4	0.382	60/76	0.66	65.3	0.23	65.6	0.662	71.4[i]	0.82	48.6/68.2	<0.05	40[k]	0.003	-	-
Middle/lingula	73		80.0		67		84.2		70.6		73.1[j]		90/80		54-100[l]		-	
Lower	67		70.8		67/65		64.4		60.0				54.8/72.2					
Relationship with pleura																		
Not touching	77	0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	74	<0.01
Touching/ within 10 mm[h]	55		-		-		-		-		-		-		-		35	
Visibility under fluoroscopy																		
Clearly visible	-	-	-	-	-	-	-	-	-	-	81.9	0.01	-	-	67	0.96	-	-
Vague/invisible	-		-		-		-		-		63.6		-		74		-	
Relationship between lesion and bronchus																		
A	-	-	-	-	-	-	-	-	-	-	83.7	0.001	-	-	-	-	-	-
B	-		-		-		-		-		65.3		-		-		-	
C	-		-		-		-		-		28.6		-		-		-	
SUV_{max}																		
<2.8	-	-	-	-	-	-	46.8	<0.0001	-	-	-	-	-	-	-	-	-	-
≥2.8	-		-		-		75.5		-		-		-		-		-	

[a]15-30 mm, [b]≤15 mm, [c]Within and adjacent, [d]Invisible, [e]>20; ≤30 mm, [f]≤20 mm, [g]≤10 mm/>10; ≤15/>15 mm; ≤20 mm, [h]From the costal visceral pleura, [i]Upper lobe or superior segment of lower lobe, [j]Middle or lower lobe except for superior segment, [k]Left upper apical posterior segment, [l]Other location. GGO: Ground-glass opacity, SUV_{max}: Maximum standardized uptake value of ^{18}F-FDG uptake, ^{18}F-FDG: Fluorine-18 fluorodeoxyglucose

6.7%[7] [Table 3]. Only one previous study, in which a small number of patients crossed over to TTNA, has reported a slightly higher complication rate.[32] The main EBUS-GS-related complications include bleeding, pneumothorax, and infection. The incidence rates of bleeding and pneumothorax are reported to be 0%–5.6% and 0%–4.2%, respectively. In a study by Minezawa *et al.*, 4 of 149 patients developed pneumonia after EBUS-GS, which is highest reported incidence of infection after EBUS-GS.[7] In the largest study to date on the complications of EBUS-GS, 13 (1.3%) of the 965 included patients developed EBUS-GS-related complications. Among these patients, 0.8% (8/965) developed pneumothorax and 0.5% (5/965) developed pulmonary infection. In four patients (0.4%), the radial probes broke during the procedure; however, the breakage did not cause any adverse event. There were no cases of significant hemorrhage.[31] Rare complications, such as transient delirium, have also been occasionally reported.[7] In another case report, a patient with a left S6 segment pulmonary nodule and left pleural effusion required thoracic drainage through the respiratory tract during a EBUS-GS procedure because of the appearance of yellow turbid fluid in the sheath. After 200 mL fluid was drained, chest CT showed decreased pleural effusion. The authors suspected that the sheath tip had ruptured the pleural cavity.[33]

IMPROVEMENT OF THE DIAGNOSTIC YIELD OF ENDOBRONCHIAL ULTRASONOGRAPHY USING A GUIDE SHEATH

Some studies have demonstrated that the diagnostic sensitivity of EBUS-GS significantly increases when it is combined with a guidance system. For example, when EBUS-GS was used in combination with virtual bronchoscopic navigation, the overall diagnostic yield increased to 63.3%–84.4%, and for lesions ≤2 cm in diameter, the diagnostic yield increased to 44.4%–75.9%.[34] However, a few studies have shown that although virtual bronchoscopic navigation does not improve diagnostic sensitivity, it can shorten the operation time.[35]

Table 3. Complications of endobronchial ultrasonography using a guide sheath

Complications	Rate/*n*
Main complications (%)	0-6.7[7]
Bleeding (%)	0-5.6[30]
Pneumothorax (%)	0-4.2[18]
Infection	0-2.7[7]
Radial probes broken (%)	0-0.4[31]
Rare complications	2 cases
Transient delirium	1
Pleural rupture	1

In addition, fluoroscopic guidance can also improve the diagnostic sensitivity of EBUS-GS by (1) allowing confirmation of the PPL location, (2) enabling selection of the most appropriate bronchus by manipulating the angulated curette, (3) keeping the operator aware of movement of the guide sheath during deep respiration, (4) recognizing pleural position and thus avoiding pneumothorax, and (5) confirming whether the forceps are open.[36] EBUS-GS without fluoroscopic guidance has a diagnostic sensitivity of 61.8% for PPLs, whereas EBUS-GS with fluoroscopic guidance has a reported sensitivity of 58.3%–84.4%. No controlled studies have been performed to examine this difference.[16] Radiation exposure to the operator during fluoroscopy is reported to be low, with nurses and other assistants receiving negligible doses.[37]

The diagnostic sensitivity of EBUS-GS for PPLs can also be increased if it is combined with other technologies such as transbronchial needle aspiration (TBNA).[38,39] Hayama *et al.*[38] reported that performing additional GS-TBNA could significantly increase the diagnostic yield of EBUS-GS for lesions not detected by EBUS after usual transbronchial sampling by brush and forceps. In addition, a Japanese study has shown that bronchoscopy training is an important factor for improving the diagnostic yield of EBUS-GS in PLC.[40]

COMPARISON WITH OTHER TECHNIQUES

There are several studies which have compared the EBUS-GS with other techniques [TABLE 4]. A retrospective analysis showed that EBUS-GS under fluoroscopy has a diagnostic sensitivity of 64.6% for PPLs as opposed to a diagnostic sensitivity of 46.7% with fluoroscopy-guided TBB. Moreover, the yield with EBUS-GS guidance was found to be 1.46 times higher than that without EBUS guidance.[11] A prospective controlled study revealed that for pulmonary lesions <30 mm in diameter, the diagnostic performance of EBUS-GS under fluoroscopy was significantly better than that of fluoroscopy alone (90% vs. 52%, respectively).[9]

The diagnostic performance of EBUS-guided TBB using a thin bronchoscope (outer diameter 3.4 mm) for PPLs

Table 4. Comparison of endobronchial ultrasonography using a guide sheath with other techniques

Comparing method	Diagnostic sensitivity (%)	Procedure time (min)	Complications
Ishida *et al*. (2012)[11]			
EBUS-GS	64.6	-	1 pneumothorax
Fluoroscopy-guided TBB	46.7	-	1 pneumothorax
P	0.08	-	-
Sánchez-Font *et al*. (2014)[9]			
EBUS-GS	92	5±2 longer	6% (2 groups together)
Fluoroscopy-guided TBB	52	-	
P	0.05	NS	-
Oki *et al*. (2012)[12]			
EBUS-GS	62	33±13.8	2%
EBUS plus TB	65	27.4±11.3	5%
P	NS	0.002	0.28
Oki *et al*. (2015)[41]			
UTB	74	27.5	3%
TB-GS	59	28.5	5%
P	0.044	0.101	0.595
Fielding *et al*. (2008)[29]			
EBUS-GS	66	24.5±6	1%*
TTNA	64	-	28%*
P	-	-	<0.001
Fielding *et al*. (2012)[32]			
EBUS-GS	50#	-	3 pneumothorax
TTNA	80#	-	10 pneumothorax
P	0.05	-	0.02

#For lesions ≤2 cm, *Pneumothorax. NS: Not significant, UTB: EBUS plus 3.0 mm ultrathin bronchoscope, TB-GS: EBUS plus 4.0 mm thin bronchoscope with a guide sheath, EBUS-GS: Endobronchial ultrasonography using a guide sheath, TBB: Transbronchial biopsy, TTNA: Transthoracic needle aspiration

has been shown to be noninferior to that of the guide sheath method, with no significant difference between the complication rates for the two methods. However, the mean procedure time was significantly shorter with the EBUS plus thin bronchoscopy method.[12] A prospective randomized study compared the diagnostic performance of the 3.0 mm ultrathin bronchoscope with that of EBUS-GS plus a thin (4.0 mm) bronchoscope. The results revealed that the ultrathin bronchoscope could reach bronchi that were more distal than the thin bronchoscope could (median fifth-generation vs. fourth-generation) and had a greater diagnostic yield than the usage of the thin bronchoscope did.[41]

TTNA is a well-established technology with high sensitivity for PPL diagnosis. Fielding *et al.* compared EBUS-GS with TTNA for the diagnosis of PPLs. The overall diagnostic sensitivities of the two methods were similar, but the rate of pneumothorax and intercostal catheter placement was higher with TTNA. The diagnostic yield of EBUS-GS was found to diminish significantly for lesions in contact with the visceral pleura. The authors proposed that this fact should be considered when choosing between TTNA and EBUS-GS.[29] Another study by the same group showed that TTNA had higher diagnostic yields in lesions <2 cm; however, EBUS-GS was better tolerated by patients and had fewer complications.[31]

ADVANTAGES OF ENDOBRONCHIAL ULTRASONOGRAPHY USING A GUIDE SHEATH

One of the advantages of EBUS-GS is that it can help reduce fluoroscopy time.[36] Average fluoroscopy time (±standard deviation) is 4.08 ± 3.27 min with EBUS-GS as opposed to 7.06 ± 3.99 min with non-EBUS-GS techniques. Two possible reasons could explain this marked reduction in fluoroscopy time with EBUS-GS. The first is that, because of the use of EBUS, determination of the lesion location is no longer completely dependent on fluoroscopy. The second possibility is that the guide sheath simplifies the process of repeated sampling from the lesion, thus saving time; in addition, the guide sheath guarantees that the sample is taken from the lesion and, in the process, reduces exposure to radiation.

EBUS-GS has some advantages over EBUS alone.[4,5] First, because EBUS-guided sampling of PPLs is not

performed in real time, the brush or biopsy forceps could move into another bronchus after the miniprobe is withdrawn. The guide sheath can guarantee that the sample is taken from the lesion site detected by EBUS and thus increase the reliability of the specimen. Second, the guide sheath allows repeated sampling from the target bronchus. In the absence of the guide sheath, the friction due to repeated insertion of the miniprobe or collecting device can cause edema and obstruct further insertion attempts. Third, in some patients, the lesion bronchus can only be reached by repeated curette manipulation, and in these cases, the guide sheath can be left in the target bronchus as a working channel to make sample collection possible. Fourth, the guide sheath can lower bleeding risk and prevent the flushing of blood into the proximal bronchus. As the outer surface of the plastic sheath is in close contact with the bronchus wall, blood drains into the sheath when bleeding occurs.

LIMITATIONS

The guide sheath, however, has some limitations. The use of the guide sheath changes EBUS-guided PPL sample collection into a semi-real-time modality instead of a completely real-time technique. During EBUS, the guide sheath is left *in situ* when the miniprobe is withdrawn, but its position may shift because of the patient's breathing or during withdrawal of the brush or biopsy forceps. To overcome this problem, two studies tried to perform real-time EBUS. Shinagawa *et al*.[42] attempted to diagnose PPLs using a flexible bronchoscope with two working channels to perform real-time EBUS under fluoroscopic guidance in six patients. During the procedure, the ultrasound image of the biopsy forceps or brush could be identified in four patients. However, the forceps tip could not be distinguished from the forceps body. Chen and Misselhorn[43] used real-time EBUS-guided sampling by TBNA and forceps biopsy in three patients with lung masses. They fixed an external catheter to the bronchoscope, parallel to its inner working channel, and thus created a simulated double-barrel bronchoscope. Using this technique, they were able to perform successful diagnosis in two patients with relatively large lesions. They were unable to perform diagnosis in another patient who had a more challenging lesion location and a smaller-sized lesion although the lesion was clearly visualized by radial EBUS.

Another limitation with the use of the guide sheath is that the specimen size is a little smaller than that of specimens collected by routine transbronchial lung biopsy because the instruments are necessarily smaller when a thin guide sheath is used. Moreover, the guide sheath may sometimes crease when the scope is bent at a sharp angle,[44,45] and this can make insertion of the brush or forceps more difficult.

CONCLUSIONS

EBUS-GS makes PPL sample collection easier and more reliable, thus yielding a high diagnosis rate. The diagnostic sensitivity of EBUS-GS is affected by the position of the probe relative to the PPLs as well as the consistency of the PPLs. In addition, EBUS-GS results in fewer complications and reduced fluoroscopy time, which makes the procedure safer.

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Conflicts of interest
There are no conflicts of interest.

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