

Complications with Endobronchial Ultrasound with a Guide Sheath for the Diagnosis of Peripheral Pulmonary Lesions

Manabu Hayama Takehiro Izumo Yuji Matsumoto Christine Chavez
Takaaki Tsuchida Shinji Sasada

Respiratory Endoscopy Division, Department of Endoscopy, National Cancer Center Hospital, Tokyo, Japan

Key Words

Bronchoscopy · Complications · Endobronchial ultrasound with a guide sheath · Radial endobronchial ultrasound · Transbronchial biopsy

Abstract

Background: Diagnostic bronchoscopy has been considered as a safe and effective procedure. Endobronchial ultrasound with a guide sheath (EBUS-GS) for the diagnosis of peripheral pulmonary lesions (PPLs) is becoming a common procedure, but reports about its safety are missing. **Objectives:** The aim of this study was to evaluate the safety profile of EBUS-GS for the diagnosis of PPLs. **Methods:** All patients with PPLs who underwent EBUS-GS between September 2012 and August 2014 at the National Cancer Center Hospital were included. Postprocedural complications and the durability of devices were retrospectively reviewed. **Results:** During the study period, EBUS-GS procedures were performed for 965 PPLs. The overall complication rate was 1.3% (13/965): 0.8% (8/965) for pneumothorax and 0.5% (5/965) for pulmonary infection. There was no significant hemorrhage, air embolism, tumor seeding or procedure-related death, and there was no breakage of the guide sheath. Only four radial probes were broken during the study period without any adverse reactions. **Conclusions:** EBUS-GS is a tolerable procedure, and the devices are durable.

© 2015 S. Karger AG, Basel

Introduction

Bronchoscopy is a widely performed procedure that is generally safe. In the past, its use for the diagnosis of peripheral pulmonary lesions (PPLs) has been limited by a low diagnostic yield [1]. As the years went by, improvements have been made [2]. In fact, a recent meta-analysis reported a 70% diagnostic yield of bronchoscopy for PPLs with the use of new guided techniques, including electromagnetic navigation bronchoscopy, radial endobronchial ultrasound (R-EBUS), EBUS with a guide sheath (EBUS-GS), virtual bronchoscopic navigation and ultrathin fiber; among these, the highest pooled diagnostic yield of 73.2% was attributed to EBUS-GS, which enables confirmation of the location of a lesion and repeated procurement of tissue samples from the same position [3]. Moreover, we have recently reported the diagnostic utility of EBUS-GS for ground-glass opacity (GGO) lesions [4, 5]. This evidence shows that, indeed, EBUS-GS is now becoming a common procedure for the diagnosis of PPLs which was difficult to attain by conventional bronchoscopy.

Along with the widespread application of EBUS-GS, an increase in problems associated with the procedure may be expected, especially at the learning curve phase. Until now, there have been few reports that cited procedural complications [6–8], but the majority of the avail-

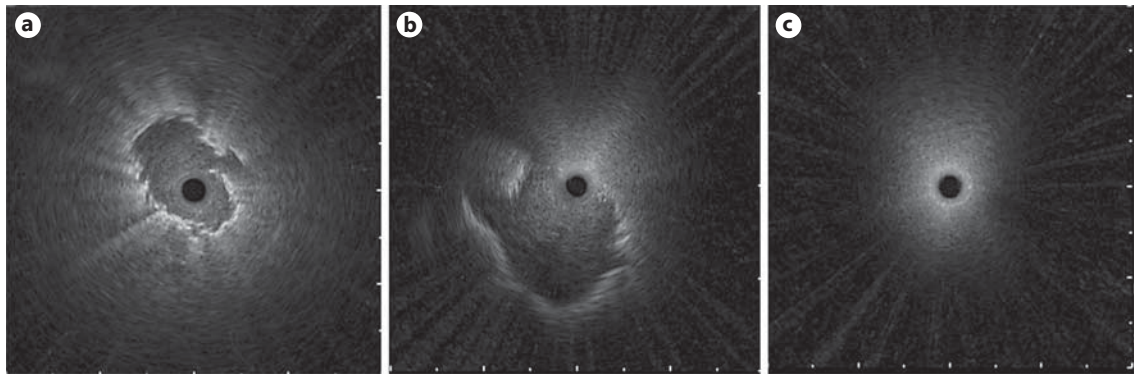


Fig. 1. EBUS images after PPL localization. **a** ‘Within’: the R-EBUS probe is located in a bronchus that is inside the lesion. **b** ‘Adjacent to’: the R-EBUS probe is located in a bronchus that ran alongside the lesion. **c** ‘Invisible’: the R-EBUS probe is not able to reach the lesion.

able literature on EBUS-GS for PPLs focused on the diagnostic yield. In our clinical experience, we hypothesize that precise PPL localization and the use of a guide sheath may reduce the risk of puncturing the visceral pleura and the risk of bleeding through a tamponade effect of the guide sheath after transbronchial sampling. In this study, we evaluated the complications associated with EBUS-GS for PPLs and the durability of EBUS-GS devices.

Patients and Methods

Subjects and PPL Characters

The medical records of all patients who underwent EBUS-GS for the diagnosis of PPLs between September 2012 and August 2014 at the National Cancer Center Hospital, Tokyo, Japan, were reviewed. This study was a retrospective chart review and, therefore, the Institutional Review Board of the National Cancer Center approved the study without the need to obtain informed consent of each participant. Written informed consent for bronchoscopy was obtained from all patients.

PPL was defined as an abnormal growth surrounded by pulmonary parenchyma and as bronchoscopically invisible. The size of each PPL was determined by measuring the largest diameter on cross-sectional computed tomography (CT) images. The distance from the lateral edge of each PPL to the costal pleura was recorded. The lesion character was categorized as solid, part solid or pure GGO, based on CT scan attenuation. Virtual bronchoscopic navigation systems (Ziostation2[®], Ziosoft Ltd., Tokyo, Japan; LungPoint[®], Bronchus Ltd., Mountain View, Calif., USA, or Bf-NAVI[®], Olympus Ltd., Tokyo, Japan) were used when the target bronchi were small and difficult to trace [9].

EBUS-GS Procedures

EBUS-GS procedures were carried out using either one of the following bronchoscopes (Olympus Ltd.): BF-1T260, BF-260, BF-P260, BF-F260, BF-1TQ290, BF-Q290, BF-P290, LF-TP, or BF-

Y0053, which is a new middle-range bronchoscope with a 5.1-mm outer diameter and a 2.6-mm working channel [10]. A large (K-203) or small (K-201) guide sheath kit (Olympus Ltd.) was respectively used in combination with a large R-EBUS probe (UM-S20-20R; Olympus Ltd.) or a small R-EBUS probe (UM-S20-17S; Olympus Ltd.). A small guide sheath was chosen when the lesion was ≤ 30 mm and close to the visceral pleura or when the lesion was very small (solid ≤ 10 mm or pure GGO ≤ 15 mm) [10].

All bronchoscopies were performed via the oral route under local anesthesia with intravenous administration of midazolam for mild sedation. During the procedure, oxygen was delivered to the patient via a nasal cannula, and continuous pulse oximetry was routinely used to monitor oxygen saturation and pulse rate. Blood pressure was intermittently measured.

Upon insertion of the scope to reach the target bronchus, the guide sheath together with the R-EBUS probe was inserted through the working channel and advanced under X-ray fluoroscopic guidance. If the target lesion was not detected by EBUS, the probe was manipulated under fluoroscopic guidance until an acoustic signal was generated. EBUS images before transbronchial sampling were categorized into 3 patterns (fig. 1): ‘within’ (the probe was located in a bronchus that was inside the lesion), ‘adjacent to’ (the probe was located in a bronchus that ran alongside the lesion) or ‘invisible’ (the probe was not able to reach the lesion) [11]. After localizing the lesion by EBUS, the probe was removed while the guide sheath was kept in place for subsequent sampling by brush and forceps, also under X-ray fluoroscopic guidance.

Transbronchial needle aspiration through a guide sheath (GS-TBNA) was additionally performed when the operator deemed that the sample amount was insufficient. GS-TBNA procedures were performed using a 13-mm-long 21-gauge needle with a metallic sheath (NA-1C-1; Olympus) through a large guide sheath. The length of the large guide sheath was adjusted by cutting the proximal end by about 30 mm to adapt the length of the needle sheath and facilitate the insertion of the needle apparatus for TBNA [12].

Rapid on-site evaluation of the specimen was routinely performed. After collecting adequate samples, the guide sheath was left in place for 2 min for hemostasis before it was eventually removed. The procedure time was recorded from the point when the

scope has passed the vocal cords to its withdrawal out of the trachea. Final diagnoses were established by pathologic evidence from EBUS-GS, EBUS-TBNA, CT-guided transthoracic needle biopsy or surgery, by microbiological analysis, or by clinical follow-up of >3 months.

When the collected specimen showed malignancy or specific benign findings with compatible subsequent clinical outcomes, EBUS-GS was considered as diagnostic. When a sample was not adequate (e.g., peripheral lung tissue, peribronchial tissue), EBUS-GS was designated as nondiagnostic.

All EBUS-GS procedures were performed by expert bronchoscopists or trainees with enough experience on conventional bronchoscopy and EBUS-GS assistance. During all the procedures, the trainees were supervised by the experts [13, 14].

Postprocedure Course

All bronchoscopy procedures were performed on an outpatient basis, except if there were other reasons for admission. After every procedure, the patient was observed at a recovery room for 2 h until discharged. Chest X-ray was performed only when the patient reported any symptoms suggestive of pneumothorax [15], because previous studies reported that routine chest X-ray to detect pneumothorax was not necessary for all patients after bronchoscopy [16, 17]. A major complication was defined as an event which necessitated premature termination of the procedure or symptomatic postprocedural sequela, including pneumothorax, hemorrhage, infection, air embolism or another untoward life-threatening outcome [18]. Breakage of the guide sheath and/or the radial probe was also recorded.

Statistical Analysis

Descriptive statistics are presented as frequency, percentage and median (range). Correlations of study variables were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Overall, EBUS-GS procedures were performed for 965 PPLs. A summary of patient characteristics and EBUS-GS findings is shown in table 1. The study population had a median age of 69 years and mostly consisted of male patients. The median lesion size and the median distance from the costal pleura was 25 and 6 mm, respectively. A large guide sheath kit was used for 590 lesions (61.1%). The EBUS image before sampling was 'within' in 544 lesions (56.4%), 'adjacent to' in 283 lesions (29.3%) and 'invisible' in 138 lesions (14.3%). In addition to brushing or forceps biopsy, GS-TBNA was performed for 165 lesions (17.1%). The median procedure time was 22 min. Malignancy was the final diagnosis in 744 lesions (77.1%). The overall diagnostic yield was 64.4% (623 of 965 PPLs).

Overall, major complications after EBUS-GS occurred in 13 patients (1.3%; table 2). There were 8 patients (0.8%)

Table 1. Baseline characteristics of patients who underwent EBUS-GS for the diagnosis of PPLs (n = 965)

Age, years	69 (29–94)
Gender	
Male	575 (59.6)
Female	390 (40.4)
Size, mm	25 (6–107)
Distance from costal pleura, mm	6 (0–65)
Character	
Solid	726 (75.2)
Part solid	202 (20.9)
Pure GGO	37 (3.8)
Guide sheath kit type	
K-203, large	590 (61.1)
K-201, small	375 (38.9)
EBUS image	
Within	544 (56.4)
Adjacent to	283 (29.3)
Invisible	138 (14.3)
Procedure time, min	22 (5–60)
Final diagnosis	
Malignant lesion	744 (77.1)
Benign lesion	194 (20.1)
Not determined	27 (2.8)

Data are presented as the median (range) or number (%).

Table 2. Complications and equipment broken during EBUS-GS for PPLs (n = 965)

Complication	
Total	13 (1.3)
Pneumothorax	8 (0.8)
Pulmonary infection	5 (0.5)
Significant hemorrhage	0 (0)
Air embolism	0 (0)
Tumor seeding	0 (0)
Equipment broken	
Radial probe broken	4 (0.4)
Guide sheath broken	0 (0)

Data are presented as number (%).

with pneumothorax, and 3 (0.3%) of them required chest tube drainage. Five patients (0.5%) developed pulmonary infection. There was no case of significant hemorrhage which necessitated premature termination of the procedure, air embolism, tumor seeding, or procedure-related death.

A clinical course summary of the 13 cases with complications is shown in table 3. The patients were 59–81 years of age and were predominantly male. Six cases had

Table 3. Clinical course of the 13 cases with complications

Patient No.	Age, years	Gender	Comorbidity	Size, mm	Character	Location	EBUS image	Complication
1	70	Female	None	25	Part solid	Left S6	Invisible	Pneumothorax without chest tube drainage
2	81	Female	None	63	Solid	Left S1+2	Adjacent to	Pneumothorax without chest tube drainage
3	76	Male	Emphysema	41	Solid	Right S3	Within	Pneumothorax without chest tube drainage
4	61	Male	Emphysema	21	Solid	Right S4	Invisible	Pneumothorax without chest tube drainage
5	77	Female	Diabetes mellitus	38	Part solid	Right S1	Within	Pneumothorax without chest tube drainage
6	59	Female	None	31	Part solid	Right S1	Within	Pneumothorax with chest tube drainage
7	80	Male	Emphysema	17	Part solid	Right S4	Invisible	Pneumothorax with chest tube drainage
8	80	Male	Rheumatoid arthritis	23	Solid	Right S8	Within	Pneumothorax with chest tube drainage
9	69	Male	Emphysema	33	Part solid	Left S4	Within	Pneumonia requiring admission
10	64	Female	Lung adenocarcinoma	32	Solid (with cavity)	Right S1	Within	Lung abscess requiring admission and surgery
11	76	Male	Emphysema	30	Solid (adjacent to a bulla)	Right S9	Within	Lung abscess requiring admission and surgery
12	63	Male	None	38	Solid (with cavity)	Right S2	Within	Lung abscess requiring admission
13	79	Female	None	54	Solid	Right S2	Within	Empyema requiring admission

underlying lung diseases, including emphysema and rheumatoid lung disease. The lesion size ranged from 17 to 63 mm. All 8 cases with pneumothorax (cases 1–8) had PPLs that were adjacent to the visceral pleura or major fissure; among these, only 4 (50%) could be localized by EBUS ‘within’. All the 8 patients who developed pneumothorax had suggestive symptoms right after EBUS-GS procedures. Moreover, there was no patient who did not undergo chest X-ray on the day of EBUS-GS and developed pneumothorax after discharge. Among the 5 cases with pulmonary infections (cases 9–13), 2 had cavitory lesions and 1 was adjacent to a bulla. Particularly, these pulmonary infections were pneumonia (n = 1), lung abscess (n = 3) and empyema (n = 1). In these 5 patients, infectious symptoms (e.g., fever, cough, dyspnea or chest pain) appeared within 2 weeks after EBUS-GS, and no other etiology was found on the review of the medical records. All 13 cases with complications recovered after specific treatment.

In the 2-year study period, 4 R-EBUS probes (0.4%) were broken during the procedure: 3 of 375 (0.8%) small R-EBUS probes and 1 of 590 (0.2%) large R-EBUS probes. There were no adverse events during the time the probe was broken, and no breakage of the guide sheath was observed.

Representative Cases

An 80-year-old male (case No. 7; table 3) was referred for pathologic diagnosis of a right middle lobe part-solid nodule measuring 17 mm (fig. 2). The nodule was adjacent to the visceral pleura and major fissure, and there were underlying emphysematous changes. EBUS-GS was performed but the nodule could not be visualized by EBUS (invisible). Under X-ray fluoroscopic guidance, brushing was performed once and forceps biopsy 7 times. After the procedure, the patient complained of chest pain, and pneumothorax was revealed on chest X-ray. He required 1 week of admission with chest tube drainage.

A 64-year-old female (case No. 10; table 3) was referred to our department for gene analysis of a primary lung adenocarcinoma that increased in size despite chemotherapy (fig. 3). The tumor was a 32-mm solid mass with cavity in the right S1. After the EBUS probe was located within the mass, brushing was performed 2 times followed by forceps biopsy 6 times. Eleven days after the procedure, she was admitted to our hospital because of fever and elevated inflammatory markers. Chest CT showed a progressive increase in the size of the mass and appearance of air-fluid level and consolidation. After intravenous antibiotics had failed, the mass was resected surgically. She recovered thereafter and was discharged

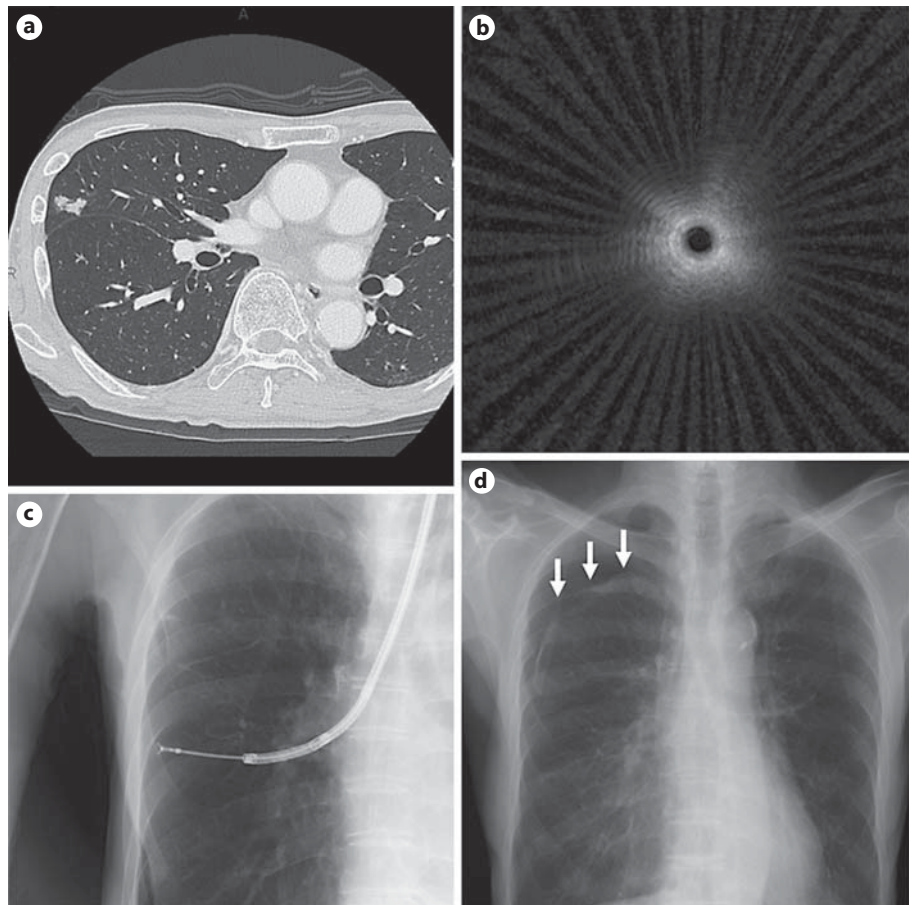


Fig. 2. An 80-year-old male who developed pneumothorax after EBUS-GS. **a** A 17-mm solid nodule in the right S4 was adjacent to the costal pleura and major fissure. **b** The radial probe could not reach the nodule. **c** X-ray fluoroscopic image of EBUS-GS TBB. **d** Chest X-ray after the procedure revealed right pneumothorax (arrows).

on day 18 of hospitalization. Chemotherapy was restarted after confirming a diagnosis of lung adenocarcinoma without any driver mutation.

Discussion

EBUS-GS for PPL diagnosis is now becoming a widespread procedure. A considerable amount of the literature that mainly focused on diagnostic yield has been published. To the best of our knowledge, this is the first report about complications and device durability of the procedure. Based on our results, EBUS-GS was a tolerable procedure and the devices were durable. The overall complication rate was 1.3% and included pneumothorax and pulmonary infection. The rate of breakage of R-EBUS probes was also low (0.4%), and no breakage of the guide sheath was shown.

Pneumothorax is one of the major complications after transbronchial biopsy (TBB) [19–21]. A nationwide survey in Japan showed that the rate of pneumothorax after

TBB for PPLs was 0.63% [22]. Our result on pneumothorax risk (0.8%) was just about similar and may be accounted for by the close location of the PPL to the visceral pleura or major fissure. Moreover, localization of the EBUS within a lesion was possible in only 4 of 8 patients who developed pneumothorax. A recent study reported that the probe position adjacent to the lesion was an independent risk factor for pneumothorax after R-EBUS-guided TBB [23]. This suggests that even with the use of EBUS-GS, we should still be aware of the risk of pneumothorax for lesions close to the visceral pleura or fissure, especially when the lesion cannot be precisely detected by EBUS.

Hemorrhage is another major complication after TBB. Although the majority of hemorrhages spontaneously resolved or required local vasoconstrictor therapy only [15, 24], severe hemorrhage after TBB has been reported to occur on rare occasions (0.73–2.8%) [18, 19, 21]. In the present study, there was no case of significant hemorrhage which required us to terminate the procedure prematurely. Wedging the guide sheath in the target bronchus may

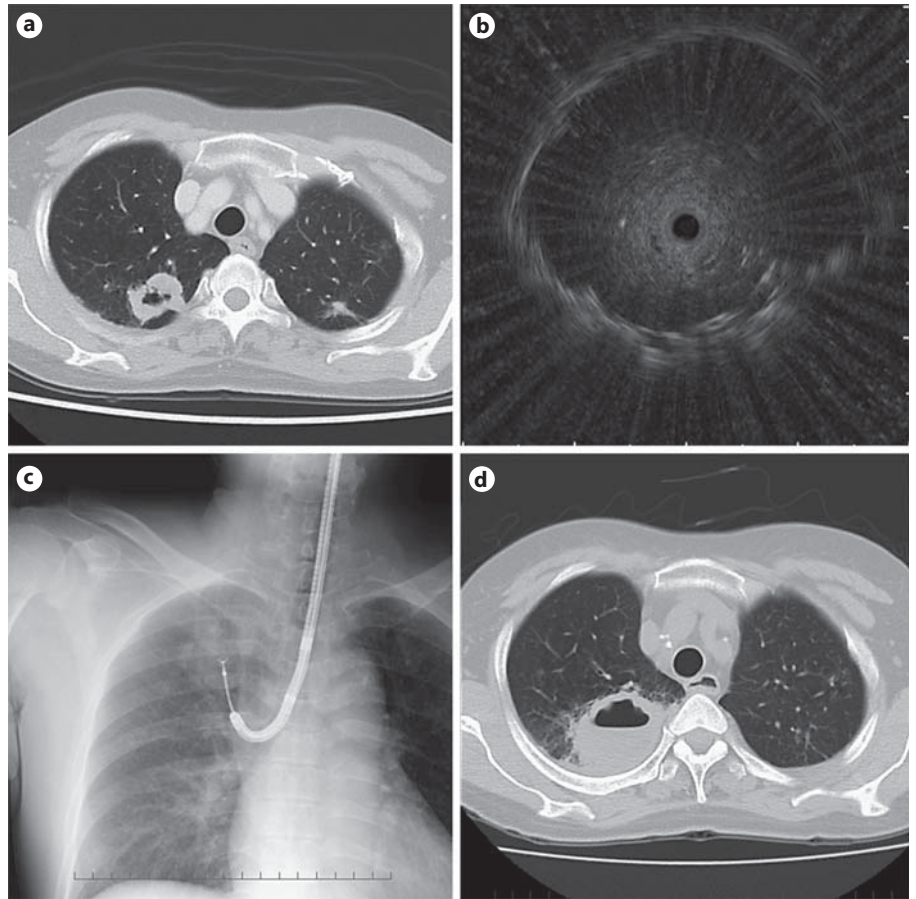


Fig. 3. A 64-year-old female who developed lung abscess after EBUS-GS. **a** A 32-mm mass with cavity in the right S1. **b** The radial probe could be located within the mass. **c** X-ray fluoroscopic image of EBUS-GS TBB. **d** Chest CT on day 9 after admission showed an increase in size and appearance of air-fluid level and consolidation.

have helped stop the bleeding during TBB, in addition to the advantage of sufficient specimen procurement.

The risk for pulmonary infection was 0.5% in the present study. Fever after bronchoscopy is common, but a chest X-ray was rarely indicated [15, 25]. Although the presence of cavitation or bulla may have influenced post-procedural infections, an additional explanation could be contamination from repeated insertion of sampling devices through the guide sheath. Further studies are necessary to evaluate the possibility of increased risk for infection by using a guide sheath.

The Japanese nationwide survey [22] reported that 47.2% of all facilities experienced breakage of the bronchoscope and/or devices during the study period; therefore, all devices should be carefully handled especially when performing new methods like EBUS-GS. In the present study, we found that the R-EBUS probe could be broken on rare occasions and that small R-EBUS probes were more fragile than large R-EBUS probes. To minimize the cost, proper handling and gentle insertion of the

R-EBUS probe and guide sheath during EBUS, localization and sampling of the PPLs are recommended. Further, it is important to keep the long axis of the bronchoscope and the long axis of the guide sheath always aligned to prevent kinks and breakage. Nevertheless, in the instances that the R-EBUS probes were broken, there was no adverse reaction to the patient.

The diagnostic yield in the present study was similar to those reported in previous studies [6, 7, 26]. The target lesions were close to the costal pleura (median distance: 6 mm), and 138 'invisible' lesions (14.3%) were also included in the present study. These situations may have contributed to the diagnostic success; therefore, careful case selection is warranted.

This study has several limitations. First, it was a retrospective analysis in a single institute. Second, the procedures were not performed by the same bronchoscopist. Further multicenter prospective studies would be ideal.

In conclusion, EBUS-GS is a tolerable procedure for PPL sampling and the devices are durable.

Acknowledgment

This work was supported by The National Cancer Center Research and Development Fund (25-A-12).

Financial Disclosure and Conflicts of Interest

The authors have no conflicts of interest to disclose.

References

- 1 Rivera MP, Mehta AC, Wahidi MM: Establishing the diagnosis of lung cancer: diagnosis and management of lung cancer, 3rd ed. American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143:e142S–e165S.
- 2 Gompelmann D, Herth FJ: Role of endobronchial and endoscopic ultrasound in pulmonary medicine. *Respiration* 2014;87:3–8.
- 3 Wang Memoli JS, Nietert PJ, Silvestri GA: Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. *Chest* 2012;142:385–393.
- 4 Izumo T, Sasada S, Chavez C, Tsuchida T: The diagnostic utility of endobronchial ultrasonography with a guide sheath and tomosynthesis images for ground glass opacity pulmonary lesions. *J Thorac Dis* 2013;5:745–750.
- 5 Izumo T, Sasada S, Chavez C, Matsumoto Y, Tsuchida T: Radial endobronchial ultrasound images for ground glass opacity pulmonary lesions. *Eur Respir J* 2015;45:1661–1668.
- 6 Fielding DI, Chia C, Nguyen P, Bashirzadeh F, Hundloe J, Brown IG, Steinke K: Prospective randomised trial of endobronchial ultrasound-guide sheath versus computed tomography-guided percutaneous core biopsies for peripheral lung lesions. *Intern Med J* 2012;42:894–900.
- 7 Fielding DI, Robinson PJ, Kurimoto N: Biopsy site selection for endobronchial ultrasound guide-sheath transbronchial biopsy of peripheral lung lesions. *Intern Med J* 2008;38:77–84.
- 8 Ishida T, Asano F, Yamazaki K, Shinagawa N, Oizumi S, Moriya H, Munakata M, Nishimura M: Virtual bronchoscopic navigation combined with endobronchial ultrasound to diagnose small peripheral pulmonary lesions: a randomised trial. *Thorax* 2011;66:1072–1077.
- 9 Tamiya M, Okamoto N, Sasada S, Shiroyama T, Morishita N, Suzuki H, Yoshida E, Hirashima T, Kawahara K, Kawase I: Diagnostic yield of combined bronchoscopy and endobronchial ultrasonography, under LungPoint guidance for small peripheral pulmonary lesions. *Respirology* 2013;18:834–839.
- 10 Sasada S, Izumo T, Chavez C, Matsumoto Y, Tsuchida T: A new middle-range diameter bronchoscope with large channel for transbronchial sampling of peripheral pulmonary lesions. *Jpn J Clin Oncol* 2014;44:826–834.
- 11 Shirakawa T, Imamura F, Hamamoto J, Honda I, Fukushima K, Sugimoto M, Shirkakusa T: Usefulness of endobronchial ultrasonography for transbronchial lung biopsies of peripheral lung lesions. *Respiration* 2004;71:260–268.
- 12 Takai M, Izumo T, Chavez C, Tsuchida T, Sasada S: Transbronchial needle aspiration through a guide sheath with endobronchial ultrasonography (GS-TBNA) for peripheral pulmonary lesions. *Ann Thorac Cardiovasc Surg* 2014;20:19–25.
- 13 Bellinger CR, Chatterjee AB, Adair N, Houle T, Khan I, Haponik E: Training in and experience with endobronchial ultrasound. *Respiration* 2014;88:478–483.
- 14 Stather DR, MacEachern P, Chee A, Dumoulin E, Tremblay A: Trainee impact on procedural complications: an analysis of 967 consecutive flexible bronchoscopy procedures in an interventional pulmonology practice. *Respiration* 2013;85:422–428.
- 15 Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, Mandal S, Martin J, Mills J, Navani N, Rahman NM, Wrightson JM, Munavvar M: British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. *Thorax* 2013;68(suppl 1):i1–i14.
- 16 Izbicki G, Shitrit D, Yarmolovsky A, Bendayan D, Miller G, Fink G, Mazar A, Kramer MR: Is routine chest radiography after transbronchial biopsy necessary? A prospective study of 350 cases. *Chest* 2006;129:1561–1564.
- 17 Milam MG, Evins AE, Sahn SA: Immediate chest roentgenography following fiberoptic bronchoscopy. *Chest* 1989;96:477–479.
- 18 Hsu LH, Liu CC, Ko JS, Chen CC, Feng AC: Safety of interventional bronchoscopy through complication review at a cancer center. *Clin Respir J* 2014, Epub ahead of print.
- 19 de Fenoyl O, Capron F, Lebeau B, Roche-maure J: Transbronchial biopsy without fluoroscopy: a five year experience in outpatients. *Thorax* 1989;44:956–959.
- 20 Jin F, Mu D, Chu D, Fu E, Xie Y, Liu T: Severe complications of bronchoscopy. *Respiration* 2008;76:429–433.
- 21 Pue CA, Pacht ER: Complications of fiberoptic bronchoscopy at a university hospital. *Chest* 1995;107:430–432.
- 22 Asano F, Aoe M, Ohsaki Y, Okada Y, Sasada S, Sato S, Suzuki E, Senba H, Fujino S, Ohmori K: Deaths and complications associated with respiratory endoscopy: a survey by the Japan Society for Respiratory Endoscopy in 2010. *Respirology* 2012;17:478–485.
- 23 Huang CT, Ruan SY, Liao WY, Kuo YW, Lin CY, Tsai YJ, Ho CC, Yu CJ: Risk factors of pneumothorax after endobronchial ultrasound-guided transbronchial biopsy for peripheral lung lesions. *PLoS One* 2012;7:e49125.
- 24 Kozak EA, Brath LK: Do ‘screening’ coagulation tests predict bleeding in patients undergoing fiberoptic bronchoscopy with biopsy? *Chest* 1994;106:703–705.
- 25 Um SW, Choi CM, Lee CT, Kim YW, Han SK, Shim YS, Yoo CG: Prospective analysis of clinical characteristics and risk factors of postbronchoscopy fever. *Chest* 2004;125:945–952.
- 26 Yamada N, Yamazaki K, Kurimoto N, Asahina H, Kikuchi E, Shinagawa N, Oizumi S, Nishimura M: Factors related to diagnostic yield of transbronchial biopsy using endobronchial ultrasonography with a guide sheath in small peripheral pulmonary lesions. *Chest* 2007;132:603–608.