Computed tomography–guided bronchoscopy in the diagnosis of small peripheral pulmonary lesions: A retrospective study of 240 examinations in a single academic center

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Abbreviations: CT, computed tomography; PPLs, peripheral pulmonary lesions; CT-BS, CT bronchus sign; TTNA, transthoracic needle aspiration; EBUS, endobronchial ultrasonography; GS, guide sheath; TBNA, transbronchial needle aspiration; VBN, virtual bronchoscopic navigation; GGO, ground glass opacity

Abstract

Background: Factors that affect the diagnostic yield in computed tomography (CT)-guided bronchoscopy have not yet been fully evaluated. To improve the diagnostic yield of peripheral pulmonary lesions (PPLs) by CT-guided bronchoscopy, we quantitatively analyzed factors affecting the diagnostic yield.

Methods: The data were collected for 240 PPLs in 237 patients examined by using CT-guided bronchoscopy between October 2003 and November 2011 in our respiratory center. The association of diagnostic yield with the CT bronchus sign (CT-BS), lesion size, location, number of tissue specimens, and type of bronchoscope was retrospectively assessed.

Results: The diagnostic yield of PPLs with negative CT-BS was significantly lower (2.9%) than that for PPLs with positive CT-BS (52.2%; $p < 0.01$). Among the PPLs with positive CT-BS, the yield was significantly higher in those in the left S^3 than for lesions in other bronchial segments (83.3% vs. 50.3%; $p < 0.05$). Lesion size was not significantly associated with diagnostic yield. The yield was significantly lower in PPLs without lung tissue specimens than in lesions with biopsy specimens ($p < 0.01$). Moreover, a thin bronchoscope produced a higher yield in comparison with other bronchoscope types (66.0% vs. 47.6%; $p < 0.05$). Multivariate analysis revealed that the number of biopsy

specimens was an independent factor affecting diagnostic yield.

Conclusions: CT-guided bronchoscopy is valuable in the diagnosis of PPLs with positive CT-BS regardless of lesion size; however, PPLs with negative CT-BS are not good candidates for CT-guided bronchoscopy. Obtaining tissue specimens by biopsy is a critical factor in diagnosing PPLs.

Keywords

Diagnostic sensitivity; Bronchoscopy; CT-guided bronchoscopy; CT-guided transbronchial biopsy; Small peripheral pulmonary lesion

1. Introduction

Developments in computed tomography (CT) and CT-related health screening have enabled the detection of smaller peripheral pulmonary lesions (PPLs) [1-3], including lesions that are invisible under X-ray fluoroscopy. While flexible bronchoscopy with X-ray fluoroscopy can be used to diagnose small PPLs, the diagnostic yield varies with lesion size and location and with the proportion of benign and malignant lesions. Thus, although the diagnostic yield for PPLs is reported to range widely from 18% to 76% with X-ray fluoroscopy [4-14], the range is markedly lower (14% to 54%) in PPLs less than 20 mm [11, 12, 14]. Transthoracic needle aspiration (TTNA) or surgical biopsy may also be performed to diagnose small PPLs. However, although TTNA has a high diagnostic yield [15-18], a higher rate of pneumothorax is observed compared with bronchoscopic procedures [14, 17-21]. Moreover, TTNA carries the risk of rare but fatal adverse effects including arterial air embolisms [22]. Another common procedure used for both diagnostic and curable purposes is surgical resection. However, surgical resection is highly invasive and it cannot be performed on older patients, patients in poor general condition, or patients with poor lung function.

Although flexible bronchoscopy is a less invasive procedure with fewer complications, the comparatively low diagnostic yield remains an issue. To overcome this

problem, adjunct modalities for bronchoscopy, such as endobronchial ultrasonography (EBUS) with a guide sheath (GS), electromagnetic navigation bronchoscopy, and CT-guided bronchoscopy have been developed. In CT-guided bronchoscopy, real-time CT imaging during examination enables visualization of the positional relationship between the PPLs and biopsy forceps. According to Tsushima et al. [23], CT-guided bronchoscopy significantly increases diagnostic yield for small PPLs. However, there are several drawbacks associated with this technique. CT-guided bronchoscopy is labor-intensive, requires a dedicated CT room, and involves high radiation exposure for both bronchoscopists and patients.

With the development of EBUS-GS and other new diagnostic modalities, CT-guided bronchoscopy is no longer the only reliable diagnostic procedure for small PPLs. Several studies [24,25] have reported that the diagnostic yield using CT-guided bronchoscopy is particularly high for PPLs with a positive CT bronchus sign (CT-BS) associated with the target lesion [5]. However, additional factors that affect the diagnostic yield in CT-guided bronchoscopy, such as the size and location of lesions and the number of tissue specimens, have not yet been fully evaluated.

In the present study, we retrospectively reviewed 240 CT-guided bronchoscopy examinations involving the diagnoses of small PPLs to analyze quantitatively the

usefulness and application of CT-guided bronchoscopy in PPL diagnosis. In addition, various factors were analyzed to provide a better understanding of their contributions to the diagnostic yield.

2. Patients and methods

2.1. Subjects

The data for 240 consecutive PPLs in 237 patients examined by CT-guided bronchoscopy from October 2003 to November 2011 at Shinshu University were collated. All of the PPLs were detected by chest X-ray, by CT scan screening, or through a follow-up CT scan of other underlying diseases. PPLs that were not visible on X-ray fluoroscopy, were undiagnosed by previous conventional bronchoscopy, or were considerably difficult to approach using conventional bronchoscopy were also included. The data for clinical findings, medical histories, laboratory tests (including the coagulation test), electrocardiograms, pulmonary function tests, and for high-resolution CT were available for all patients. All patients gave informed consent prior to the procedures. This protocol was approved by the Shinshu University Ethical Committee (Date of approval: January 8, 2013, approval number: 2170).

2.2. The definition of CT-BS

The PPL–bronchi relationship on chest CT, described as the air–bronchogram sign on CT or CT-BS, was defined as a bronchus leading to or contained within a PPL [5]. In this study, CT-BS 0 indicated no bronchus in proximity to the lesion, CT-BS 1 indicated a bronchus adjacent to the lesion, and CT-BS 2 indicated a bronchus within the range of the lesion (Figure 1). CT-BS 0 was equivalent to a negative CT-BS, and both CT-BS 1 and CT-BS 2 were considered positive [5]. Before CT-guided bronchoscopy, negative and positive CT-BS were identified.

2.3. CT-guided bronchoscopy

All procedures were performed in a designated examination room equipped with the CT apparatus. In cases where CT-guided bronchoscopy was performed by a pulmonologist with more than 6 years' experience in bronchoscopy, one (or more) additional experts supervised the procedures. When a pulmonologist with fewer than 6 years' experience performed the CT-guided bronchoscopy procedure, at least two pulmonologists with more than 6 years' experience supervised and assisted. If a less-experienced pulmonologist could not reach a target lesion, an experienced pulmonologist stepped in to perform the procedure. The protocols for premedication and for monitoring of patients have been previously described [26]. Several different types of flexible fiber optic bronchoscopes (Olympus; Tokyo, Japan) were used through the course of this study: BF-type P240 (5.3-

mm outer diameter, 2.0-mm channel diameter); type 260 (4.9-mm outer diameter, 2.0-mm channel diameter); XP40 (2.8-mm outer diameter, 1.2-mm channel diameter); and, P260F (4.0-mm outer diameter, 2.0-mm channel diameter). A multi-detector CT (Aquilion^{TM} 16; Toshiba; Tokyo, Japan) was used for all procedures, and CT-guided bronchoscopy was performed as previously described [23].

A biopsy was performed following confirmation that the biopsy forceps (under the guide of real-time CT fluoroscopy) were close to or inside the lesion. The physical relationship between the target lesion and the tip of the biopsy forceps (FB-211D, Olympus; Tokyo, Japan) was confirmed by real-time multislice CT fluoroscopy (tube voltage, 120 kV; tube current, 10 mA; rotation time, 0.5 s; slice thickness, 2 mm). The location of the forceps was also recorded after the performance of the biopsy. In situations where the biopsy forceps could not reach the lesion, the steps comprising the approach to the lesion-associated bronchus were repeated. Brushing (BC-202D-2010, Olympus; Tokyo, Japan), curettage (CC-6DR-1, Olympus; Tokyo, Japan), or (rarely) transbronchial needle aspiration (TBNA; NA-1C-1, Olympus; Tokyo, Japan) were performed in cases of biopsy failure. Finally, a bronchial washing was performed using 10 ml of normal saline, and the bronchial lavage fluid was recovered. All the tissues obtained by biopsies were fixed with formalin for histological diagnosis. All materials on the tip of the forceps,

the brush, the curette, or in the aspirate in the transbronchial needle were evaluated by cytology.

2.4. The diagnostic criteria

The definitive diagnoses of malignant and benign PPLs was based on the histopathology of biopsy specimens as evaluated by pathologists. In addition, malignancy was diagnosed through confirmation of the presence of malignant cells in the cytological specimen by pathologists. In all other cases, the PPLs were undiagnosed. In these undiagnosed cases, CT-guided bronchoscopy was repeated, or surgery, TTNA, or follow-up of radiology were undertaken, to facilitate a final diagnosis. All benign lesions were diagnosed using biopsy tissues and were based upon pathological evidence; in the absence of such evidence, lesions were described as undiagnosed.

2.5 Statistical analysis

Statistical analysis was performed using SPSS 14.0 (SPSS Inc., Chicago, IL, USA) for Windows (Microsoft Inc., Redmond, WA, USA). All quantitative data are presented as mean ± standard deviation. The data were analyzed by Pearson's chi-squared test or Fisher's exact test when the number of cases was less than 5. When univariate analysis showed that a factor significantly affected diagnostic yield, multivariate analysis was performed using multiple logistic regression. A p-value of <0.05 was considered

statistically significant.

3 Results

3.1. Baseline characteristics

The data for CT-guided bronchoscopy of 237 patients with 240 PPLs were reviewed. Three patients demonstrated two PPLs each. There were 127 men and 110 women, and the average age was 67.0 ± 10.4 years (range, 24 to 88 years). The average diameter of the PPLs was 15.4 ± 6.8 mm.

3.2. Factors affecting the diagnostic yield

Age and gender were not significantly associated with diagnostic yield (data not shown). The relationship between diagnostic yield and CT-BS is shown in Table 1. The diagnostic yield for CT-BS 0 lesions (2.9%) was significantly lower than for CT-BS 1 and CT-BS 2 lesions (52.2%) ($p < 0.001$). Thus, further analysis was carried out on the data for PPLs classified as CT-BS 1 and CT-BS 2 only. The diagnostic yield did not differ between lesions of various sizes for both the CT-BS 1 and 2 datasets, indicating that lesion size did not affect diagnostic yield in PPLs with CT-BS 1 or 2 in examination with CT-guided bronchoscopy (Table 2). Therefore, we combined these two groups as ‘positive CT-BS’ for subsequent analysis.

The diagnostic yield for PPLs with positive CT-BS in various lung segments is listed in Table 3. Except for the significantly higher diagnostic yield observed for PPLs in the left S^3 (83.3%, 10 of 12) compared to other bronchial segments (50.3%, 97 of 193) ($p = 0.02$), yields did not differ significantly among the PPLs from different lobes.

The diagnostic yield was significantly lower in PPLs from which lung tissue biopsy specimens were not taken compared to those involving biopsy specimens ($p < 0.01$, Table 4). However, in cases where biopsy specimens were available, the diagnostic yield did not differ significantly between PPLs involving one biopsy specimen and those involving more than one specimen.

Regarding the type of bronchoscope, the thin bronchoscope (BF-type P260F) demonstrated a higher diagnostic yield (66.0%, 31 of 47) compared with all the other types (BF-type 260, BF-type P240 and XP-40) of bronchoscopes (47.6%, 76 of 158, $p = 0.03$). The diagnostic yield for cases using the XP-40 bronchoscope was only 37.8% (14 of 37). This data comprised cases where the XP-40 was utilized either alone or following examinations with conventional bronchoscopes (BF-type P240 and type 260). The yield for cases using XP-40 (37.8%) was significantly lower than the yield for P260F (66.0%; $p = 0.01$).

Although the diagnostic yield was lower in cases involving pulmonologists with

fewer than 6 years' experience than in cases involving pulmonologists with more than 6 years' experience (47.5% [29 of 61] vs. 54.2% [78 of 144]), no significant difference was found (p=0.39).

A multiple logistic regression analysis was performed when univariate analysis showed significant differences. Multivariate analysis revealed that the number of biopsy tissue specimens was an independent factor affecting diagnostic yield. However, the type of bronchoscope and location of lesions did not affect diagnostic yield (Table 5).

3.3. The final clinical diagnosis and complications

The final clinical diagnosis of PPLs with positive CT-BS is shown in Table 6. Complications were observed in 22 (10.7%) of a total of 205 examinations, including moderate bleeding in 13 cases (6.3%), pneumothorax in seven (3.4%), arrhythmia during examination in one case (0.5%), and pneumonia after examination in one case (0.5%). The complication described as moderate bleeding indicated that the bleeding had flowed into the other side of the bronchus. One case of pneumothorax required insertion of a chest tube.

4. Discussion

We assessed factors influencing the diagnostic yield of 240 PPLs examined using CT-

guided bronchoscopy. CT-guided bronchoscopy is valuable for diagnosis of PPLs with positive CT-BS regardless of lesion size. However, obtaining tissue specimens by biopsy was an important factor in the diagnostic yield of PPLs with positive CT-BS. According to our results, negative CT-BS lesions are not eligible for CT-guided bronchoscopy.

The yield for positive CT-BS lesions has been reported to be higher than that for negative CT-BS lesions using conventional bronchoscopy [5,27]. Gaeta et al. [7] reached a similar conclusion and suggested that when a lesion has a positive CT-BS, an endobronchial approach is recommended rather than TTNA, which might incur more complications. The yield for PPLs with positive CT-BS has also been reported to be higher than for PPLs with negative CT-BS with other bronchoscopy modalities, such as EBUS-GS [28, 29] and electromagnetic navigation bronchoscopy [30]. Our result is in agreement with previous CT-guided bronchoscopy studies showing that the yield for lesions with positive CT-BS or CT artery sign (a pulmonary artery leading to a lesion) is higher than for lesions with negative CT-BS [24, 25]. Thus, we strongly recommend evaluating the CT-BS status of PPLs before CT-guided bronchoscopy. Diagnostic procedures other than CT-guided bronchoscopy, such as TTNA, might be appropriate for the diagnosis of negative CT-BS lesions. EBUS is an adjunctive method for bronchoscopy and in widespread use for the diagnosis of PPLs. One feature of EBUS is that the

diagnostic yield of cases in which the probe approaches the inside of the lesion is significantly higher than in cases when the probe approaches adjacent to the lesion on EBUS-GS [31]. This result differs to that obtained with CT-guided bronchoscopy. Our study showed no difference of diagnostic yield between CT-BS 1 and 2. A prospective study is necessary to understand the relationship between diagnostic yield and the characteristics of PPLs through a comparison of the CT-guided bronchoscopy and EBUS methods.

An increase in the number of tissue specimens obtained from PPLs is reported to be associated with a higher diagnostic yield [32]. The results reported in the present study are consistent with this observation. Thus, the diagnostic yield was statistically higher in PPLs from which one or more tissue specimens had been collected than in PPLs with no specimens. In addition, PPLs with three specimens on biopsy tended to be associated with a higher diagnostic yield than PPLs with one or two specimens. According to American College of Chest Physicians' guidelines [14], the yields concerning PPLs from transbronchial biopsy, brushing, bronchial washing, and TBNA are 57%, 54%, 43%, and 63%, respectively. Although TBNA showed the highest yield among these four methods, the result should be interpreted with caution, since studies of TBNA have employed only small sample sizes. Furthermore, despite the fact that TBNA might produce a higher

diagnostic yield, it is not preferred in our institute. This is due to concerns about pneumothorax developing during TBNA while the needle is advanced to the PPLs. Under CT fluoroscopy, the tip of the needle cannot be followed in real time while the needle is advanced to the target lesion, and thus the risk of pneumothorax is increased.

The diagnostic yield for PPLs that are less than 20 mm is markedly lower using conventional bronchoscopy according to several previous reports [11, 12, 14]. In contrast, according to our results, lesion size did not affect diagnostic yield for PPLs when using CT-guided bronchoscopy. In agreement with the results presented here, evidence has been published that supports the proposal that diagnostic yield is independent of lesion size in CT-guided bronchoscopy examination [24]. Although Matsuno et al. [25] report that the diagnostic yield is lower in lesions ≤15 mm in diameter (69.4%) compared to lesions >15 mm in diameter (84.6%), no significant difference was found. Moreover, for PPLs less than 15 mm in diameter, the diagnostic yield was significantly higher in examinations with CT-guided bronchoscopy than in examinations with conventional bronchoscopy [23]. For PPLs with positive CT-BS, CT-guided bronchoscopy was also preferable to TTNA for the diagnosis of PPLs less than 20 mm. Again, this is especially true in patients who could not tolerate the severe complications potentially arising from TTNA, such as pneumothorax.

The relationship between the diagnostic yield and the location of lesions is unclear. In this study, PPLs in the left apical anterior segment of the upper lobe (S^3) showed a higher diagnostic yield than lesions in other segments, possibly because the bronchoscope was more easily advanced to the left B^3 than to posterior segments as a result of the anatomical angles of the bronchus. In addition, movement of the diaphragm during breathing might have less influence on the left B^3. A lower diagnostic yield has previously been reported for PPLs in the apical segment, basal segments, and the S^6 [11, 24, 31], and a higher yield has been reported for PPLs in the right middle lobe and the left lingular segment [28].

The present analysis revealed that a higher diagnostic yield was obtained with the thin bronchoscope (P260F) compared to other types of bronchoscopes. Prior to the introduction of the thin bronchoscope into our hospital, conventional bronchoscopes (BF-type P240 or BF-type 260) were widely used. When the conventional bronchoscope could not reach or could not select the bronchial branch to the target lesion, a switch was made to the ultrathin bronchoscope (XP-40). After the thin bronchoscope was introduced, we initially followed the same procedure. Thus, when the thin bronchoscope could not reach the target lesion, we switched to the ultrathin bronchoscope (this occurred in two cases). Use of an ultrathin bronchoscope in combination with virtual bronchoscopic navigation

(VBN) has been reported to produce a diagnostic yield of 81.6% (31 of 37) for PPLs less than 30 mm in diameter [33]. Using the ultrathin bronchoscope in combination with CT-guided bronchoscopy and VBN, the yield for PPLs less than 20 mm in diameter was 66% (56 of 85) [24]. This is higher than the reported yield for PPLs less than 20 mm using the conventional bronchoscope [14]. However, several drawbacks with use of the ultrathin bronchoscope have been reported. Because of the small working-channel diameter, the resulting poor suction might make it difficult to remove blood for a clean field of view (when bleeding from bronchus occurs) or to obtain a sufficient amount of tissue [34]. Other drawbacks include low conduction of torque from the bronchoscopist's fingertips at the operating portion to the tip of the bronchoscope, and excessive flexibility of the ultrathin bronchoscope itself, which is sometimes accompanied by a poor manipulation capability when inserting to peripheral locations [35].

Oki et al. [36] reported that a bronchoscope thinner than the P260F (outer diameter of the tip of the scope, 4.0 mm) but thicker than the ultrathin bronchoscope could be inserted into significantly more peripheral bronchial areas compared to the ordinary bronchoscope. The P260F was widely used in our institute and is categorized as a thin bronchoscope. The higher diagnostic yield obtained may be the result of an adequately sized outer diameter that contributed to a good manipulation capability and a larger

working channel (compared to the ultrathin bronchoscope) with adequate enough suction to yield sufficient tissue specimens. The diagnostic yield produced by the thin bronchoscope, P260F, was similar (66.0%) to that in other reports (62.2% - 78.4%) [23-25]. For cases in which the XP-40 was used, diagnostic yields were lower than in cases with P260F. However, the diagnostic yield with XP-40 is difficult to estimate since, as mentioned earlier, multiple bronchoscopes were used in these examinations. Therefore, in the present study, our comparison of the yield using P260F versus other types of bronchoscopes represents a best estimate. The diagnostic yield for cases involving XP-40 (37.8%) is certainly lower than that reported in other studies using ultrathin bronchoscopes [35, 37-39]. The number of biopsy specimens taken was typically two or three in our study (with a maximum of six), which was lower than the number taken in other studies using ultrathin bronchoscopes [35, 37, 38]. This difference may be related to the lower reported diagnostic yield observed with XP-40. Finally, many of the lesions investigated with XP-40 might have been those that other types of bronchoscopes could not reach.

CT-guided bronchoscopy requires proficiency. For example, extensive training is required for the manipulation of an ultrathin bronchoscope. Furthermore, because a pulmonologist remains standing for long periods of time behind the CT gantry, difficulty

maintaining a good posture may arise, and this may impact user proficiency. New, less-experienced pulmonologists cycle through every year in an educational hospital, and this may complicate the relationship between total diagnostic yield and proficiency. It has previously been reported that conventional bronchoscope operator skill affected the diagnostic yield [40]. In this study, the experience of pulmonologists did not affect the yield. This is probably because the procedures reported in our study were supervised by experienced pulmonologists at all times.

EBUS is an adjunct modality for bronchoscopy and is in widespread use in the diagnosis of PPLs. The diagnostic yield with EBUS is reported to be 62% to 77% [29, 31, 41-43]. EBUS is also associated with fewer complications, and the dose of radiation exposure during X-ray fluoroscopy is within the allowable range [44]. However, EBUS cannot generally aid in the visualization of a ground glass opacity (GGO) detected during the CT scan. Indeed, GGO lesion imaging by EBUS requires a highly skilled operator. In contrast, imaging ability with CT fluoroscopy is independent of imaging characteristics such as the solid nodule and GGO lesion. Even with lesions that are invisible on X-ray fluoroscopy, CT imaging can easily depict the spatial relationship between the tip of the forceps and a target lesion. GGO lesions with positive CT-BS might present a good application for CT-guided bronchoscopy. An investigation of the relationship between

GGO lesions and diagnostic yield using CT-guided bronchoscopy is an issue for future study.

In our institute, we previously tried to utilize the software in the CT system to create VBN images. However, we abandoned this effort because the software could not provide accurate images of the peripheral bronchus, and too much effort and time were required to compensate for the peripheral bronchus that the software could not delineate. In addition, since the provided CT images from other institutes were not always digitized in the first few years of our study, we did not utilize the software to create VBN images for the not digitized CT images. We have already started to assess the value of CT-guided bronchoscopy combined with VBN.

5. Conclusion

Obtaining tissue specimens on biopsy was an important factor in estimating the diagnostic yield of PPLs with positive CT-BS in our examination of CT-guided bronchoscopy. While lesion size did not affect the diagnosis of PPLs with CT-guided bronchoscopy, it was concluded that negative CT-BS lesions were not good candidates for examination. A combination of CT-guided bronchoscopy and VBN is desirable to increase diagnostic

sensitivity and decrease radiation exposure providing greater benefit and less harm for the patients undergoing CT-guided bronchoscopy.

Conflict of interest

The authors have no conflicts of interest.

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Figure caption

Figure 1 Classification of CT-BS.

CT-BS = CT-bronchus sign.

a, CT-BS 0: There is no bronchus in proximity to the nodule (arrowhead); *b, CT-BS 1*: There is a bronchus (arrow) that contacts the nodule (arrowhead); *c, CT-BS 2*: There is a bronchus (arrow) in the nodule (arrowhead).

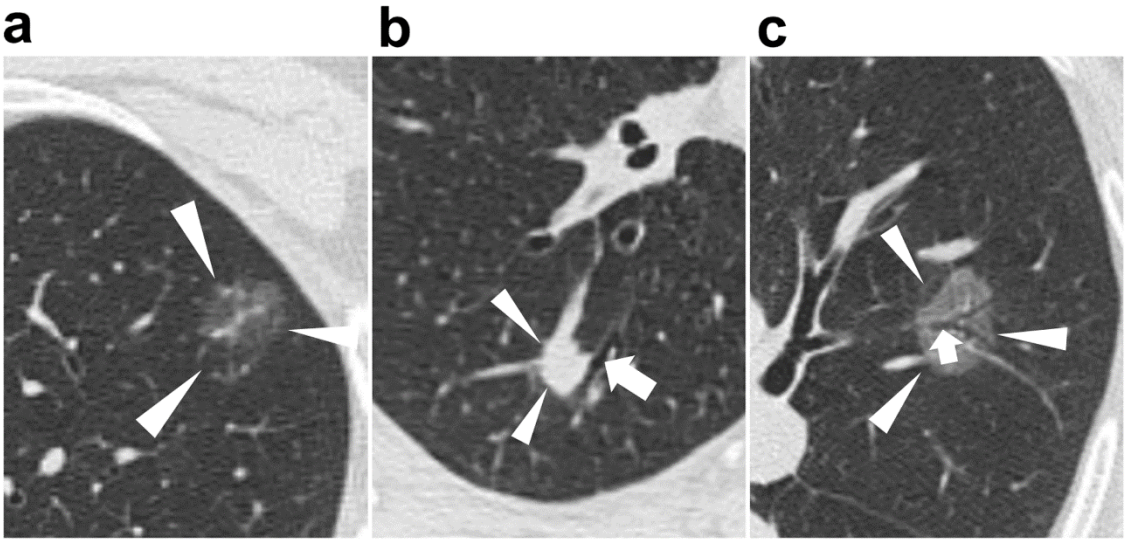

Table 1 The diagnostic yield for PPLs by types of CT-BS.

	No. of diagnosed	No. of lesions	Yield (%)
CT-BS 0	1	35	2.9**
CT-BS 1	39	87	44.8
CT-BS 2	68	118	57.6

CT-BS = CT-bronchus sign.

** $p<0.001$ compared to other groups.

Table 2 The diagnostic yield for PPLs with positive CT-BS by various lesion sizes.

Lesion size, mm	No. of diagnosed	No. of lesions	Yield (%)
≦ 10	16	36	44.4
10 < size ≦ 15	35	72	48.6
15 < size ≦ 20	32	58	55.2
20 < size ≦ 25	13	23	56.5
> 25	11	16	68.8
Total	107	205	52.2

Lesion size showed no significant difference in the diagnostic yield.

Table 3 The diagnostic yield for PPLs with positive CT-BS in various lung segments.

Segment	No. of diagnosed	No. of lesions	Yield (%)
rt S^1	13	27	48.1
rt S^2	14	27	51.9
rt S^3	6	13	46.2
rt S^4	4	8	50.0
rt S^5	2	3	66.7
rt S^6	3	10	30.0
rt S^7	0	1	0.0
rt S^8	5	8	62.5
rt S^9	5	12	41.7
rt S^{10}	3	5	60.0
lt S^{1+2}	12	26	46.2
lt S^3	10	12	83.3
lt S^4	3	4	75.0
lt S^5	2	3	66.7
lt S^6	13	22	59.1
lt S^8	9	10	90.0
lt S^9	2	7	28.6
lt S^{10}	1	7	14.3
Total	107	205	52.2

rt = right; lt = left.

Table 4 The diagnostic yield for PPLs with positive CT-BS by the number of biopsy specimens.

The number of biopsy specimens	No. of diagnosed	No. of lesions	Yield (%)
None†	7	38	18.4
1	17	34	50.0*
2	34	59	57.6**
3	32	44	72.7**
4 or more (max 6)	17	30	56.7*
Total	107	205	52.2

† Obtaining cytological specimens by brushing, curettage, and transbronchial needle.

* $p<0.01$ compared to none of tissue specimens.

** $p<0.001$ compared to none of tissue specimens.

Table 5 Multivariate analysis of factors affecting the diagnostic yield for PPLs with positive CT-BS.

Variables	Odds ratio	95% CI	P value
More than one lung tissue specimen obtained by biopsy	5.64	2.33-13.66	<0.001
The type of bronchoscope†	1.69	0.82-3.45	0.15
The location of lesions††	3.29	0.69-15.75	0.14

CI = confidence interval.

† P260F vs others.

†† The left S3 vs other segments.

Table 6 The final clinical diagnosis of the patients with PPLs with positive CT-BS.

		CT-guided bronchoscopy	VATS	Retry CT-guided bronchoscopy	TTNA	Follow-up CT scan*	Unknown	Total
Malignancy		91	57	10	1	0		
	Primary lung cancers	82	55	9	1			
	adeno	71	51	8	0			
	squamous	8	2	1	0			
	non-small	1	2	0	1			
	small	2	0	0	0			
	AAH	2	0	0	0			
	Metastatic cancers	5	2	1	0			
	MALT lymphoma	2	0	0	0			
Benign		16	1	1	0	3		
	Granuloma	0	1	0	0			
	Organizing pneumonia	1	0	1	0			
	Inflammation	11	0	0	0			
	Hamartoma	1	0	0	0			
	IgG4 related respiratory disease	2	0	0	0			
	Sarcoidosis	1	0	0	0			
Total		107	58	11	1	3	25	205

AAH = atypical adenomatous hyperplasia; MALT lymphoma = mucosa-associated lymphatic tissue lymphoma; VATS = video-assisted thoracic surgery; TTNA = transthoracic needle aspiration.

* These cases were clinically diagnosed as benign, reflecting the obvious reduction of the lesion volume.