

ORIGINAL ARTICLE

Improvements to bronchoscopic brushing with a manual mapping method: A three-year experience of 1143 cases

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Introduction

Conventional flexible bronchoscopy is routinely used for pulmonary disease diagnosis, especially for central lesions. For peripheral pulmonary lesions (PPLs, defined as lesions that are not visible beyond the visual segmental bronchi), the sensitivity of bronchoscopy varies from 16–87% because of the different guiding methods (e.g. C-arm fluoroscopy, electro-

Abstract

Background: Conventional bronchoscopy with brushing alone for diagnosing peripheral pulmonary lesions (PPLs) is of low sensitivity. A manual mapping method was introduced and evaluated in this study, which could be routinely applied with bronchoscopic brushing to improve the sensitivity for malignant PPLs.

Methods: This mapping method involves the bronchoscopist drawing the route with a series of bronchial opening sketches and marking the leading bronchus at every bifurcation point based on thin-section computed tomography. This map is then used to guide bronchoscope insertion for brushing. A cross-sectional study on the evaluation of this method for the diagnosis of malignant PPLs was conducted on patients from July 2010 to June 2013.

Results: The sensitivity for malignant PPLs of conventional brushing, conventional brushing with mapping on a portion of patients, and conventional brushing with mapping method increased from 17.0% to 25.8% to 31.5% ($P < 0.001$), respectively. For lesion sizes over 3 cm, the rate of these three groups increased from 25.1% to 38.6% to 50.9% ($P < 0.001$), respectively. The sensitivity of this mapping method for malignant PPLs was statistically associated with lesion size, lesion character, relationship between the lesion and the leading bronchus, linear distance between the targeted bronchus and the opening of the lobe bronchus, and accessibility ($P < 0.001$, $P = 0.039$, $P < 0.001$, $P = 0.031$, and $P = 0.020$, respectively).

Conclusions: The manual mapping method greatly increased the bronchoscopic brushing sensitivity for malignant PPLs compared to the conventional brushing method. During routine clinical work, it is economical and convenient for guiding bronchoscope insertion.

magnetic navigation bronchoscopy, ultrathin bronchoscopy, endobronchial ultrasound with guide sheath [EBUS-GS], and virtual bronchoscopy navigation), lesion characteristics, the combination of different bronchoscopic sampling procedures, and physician skill.^{1–6} While these technologies or procedures can significantly improve the sensitivity of bronchoscopic brushing in PPL diagnosis, they require special equipment and experienced bronchoscopists and are

expensive or involve radiation exposure. These demands limit their use, especially in developing countries.

Despite its low sensitivity (as low as 16%), brush sampling is routinely performed for PPLs in the Department of Endoscopy, National Cancer Center of China.² By contrast, the use of brushing alone is more rare in the United Kingdom; only 3.1% of physicians use brushing alone for patients with a radiographical mass lesion when the bronchoscopic appearance is normal.⁷ The reasons for these circumstances are complex. First, in addition to providing a final available diagnosis in some patients, conventional bronchoscopy can exclude additional endobronchial tumor manifestations, provide vocal cord function information, and identify anatomic variants. Additionally, the planned surgical approach can be changed after bronchoscopy.⁸ Second, China carries an immense lung cancer burden. The overcrowding of tertiary hospitals, high expectations of physicians in specialized cancer hospitals, high out-of-pocket expenses, and increasing violence against medical workers push doctors to choose low-cost, convenient, and safe examinations to avoid potential medical negligence.⁹ Conventional bronchoscopy plus brushing alone is regarded as a low cost, quick, and practical solution.

Herein, a manual mapping method guiding bronchoscope insertion was introduced and evaluated to improve the sensitivity of bronchoscopic brushing for malignant PPLs.

Methods

Patient enrollment

A cross-sectional study was conducted from July 2010 to June 2013 in the Department of Endoscopy, Cancer Institute and Hospital, Chinese Academy of Medical Sciences. Consecutive

patients who met the following inclusion criteria were enrolled:

- 1 All brushing was conducted by the same bronchoscopist.
- 2 Cytological brushing was collected for each lesion.
- 3 PPL diagnosis was ultimately confirmed by pathological diagnosis (e.g. surgery, computed tomography [CT]-guided transthoracic needle aspiration, and EBUS-transbronchial needle aspiration [TBNA]).
- 4 Patients signed the consent form.
- 5 There were no abnormal findings of the target lung region during routine bronchoscopy.
- 6 Patients had no bronchoscopy contraindications (e.g. allergic reaction to local anesthesia, a bleeding tendency, or serious arrhythmia).

From July 2010 to June 2012, conventional bronchoscopic brushing was performed on 701 patients with PPLs (Group 1). The mapping method was introduced in July 2012 and initially applied to 183 patients with PPLs from July to December 2012 (Group 2). Finally, 168 consecutive patients were prospectively recruited between January 2013 and June 2013 (Group 3), and demographic and clinical parameters potentially related to the sensitivity of the procedure were recorded. During this period, the decision to use brushing with or without mapping depended on the availability of thin-section CT scans. Detailed information on the bronchus is easily missed without thin-section CT scans, and multiplanar reconstruction may be incapable of providing the required information. Therefore, if no thin-section CT scan was available, the patients were enrolled into Group 4 (91 cases; Fig 1).

All patients provided written informed consent. No ethical approval from our research ethics committee was required because patients who underwent this method received the same bronchoscopy and brushing procedure without the

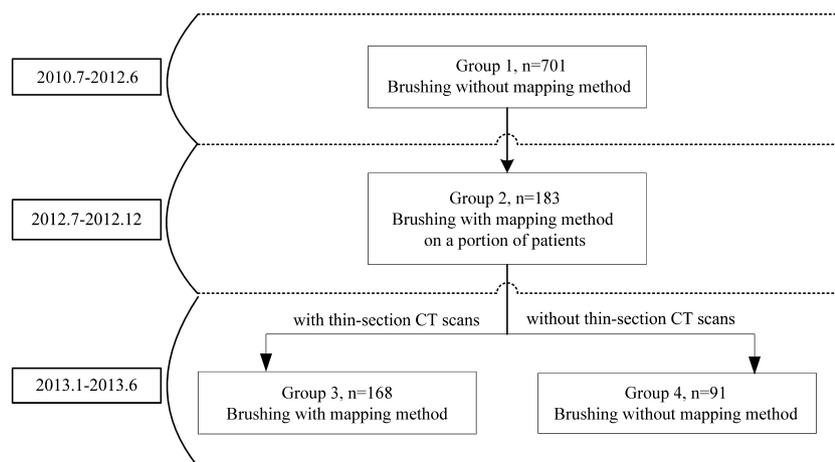


Figure 1 Patient enrollment in the study. Group 1 and Group 4 received conventional bronchoscopic brushing without using the mapping method. Group 3 and a portion of Group 2 received the mapping method. CT, computed tomography.

mapping. The mapping method is just an improvement in choosing the leading bronchus to the lesions. Patients without thin-section CT scans were fully informed of the differences between bronchoscopies with and without thin-section CT scans. In our hospital, the patient may choose whether to undergo thin-section CT.

Mapping method

The manual mapping method involves tracing the bronchial branch status by rolling thin-section CT images continuously, then recording them with a series of bronchial opening sketches, marking the leading bronchus at every bifurcation point. The steps are as follows (Fig 2).

First, the targeted bronchus is identified. The bronchus extending to the lesion is the best choice. If the leading bronchus cannot be identified clearly because the lesion is exces-

sively peripherally located, the accompanying vessels may be helpful for identifying the associated bronchus. If the lesion still cannot be reached because the bronchus or accompanying vessels are too small to recognize, the furthest bronchus or vessel can be used as the target.

Second, the route is traced. Routes beginning from the segmental bronchus and ending at the targeted bronchus should be tracked by continuous rolling thin-section CT images. The route with the clearest accessibility to the lesion is the superior choice.

Third, the route is drawn, and the leading bronchus is marked. Each bronchial bifurcation point of the CT image appears as several bronchial openings under the bronchoscope. Despite the complexity and variation of bronchial branches, the relative spatial position (anterior-inferior, superior-inferior, mediastinal-lateral) and the number of these bronchial openings could be identified by scrolling

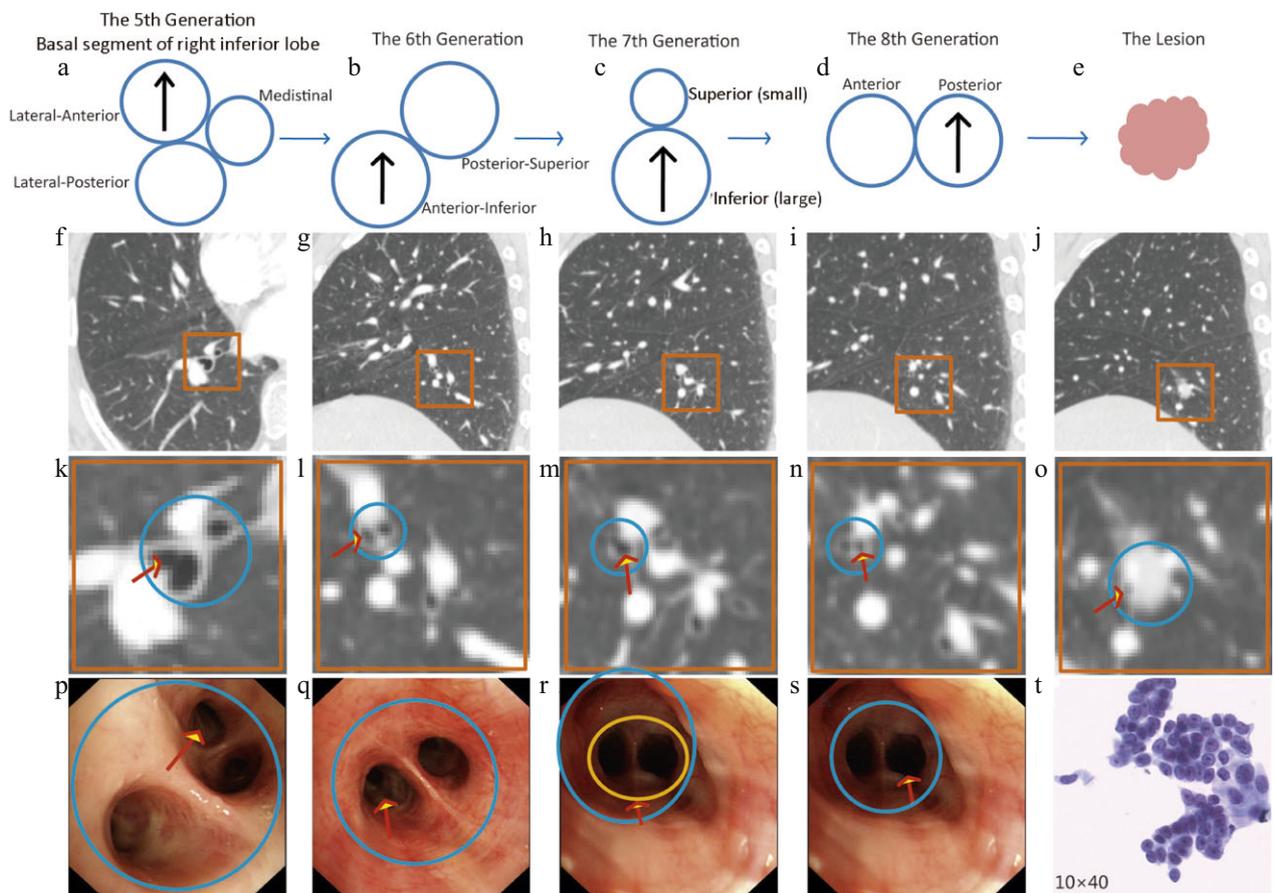


Figure 2 An example of the mapping method is presented with the arrow marking the leading bronchus. After careful image interpretation, the map was drawn from the leading bronchus of the 5th (RB8) to the 8th generation that targeted the lesion (a to e) with a relative spatial position. (a–d) The bronchial opening map of the 5th, 6th, 7th, and 8th generations with the leading bronchus at the relative position (the black arrow marks the leading bronchus along the route), respectively. (e) The lesion located distal to the leading bronchus of the 8th generation of the basal segment of the right inferior lobe. (f–j) The corresponding computed tomography images of (a–e). (k–o) Partially enlarged views of (f–j), respectively. (p–r) Corresponding bronchoscopic images of (a–d), respectively. (t) The cytopathologic result of adenocarcinoma cells.

thin-section CT images up and down, as well as checking the coronal and sagittal views of the multi-planar reconstruction (MPR). In most cases, only one or two directions (e.g. posterior or posterior and anterior) are required for recognizing the leading bronchus. Some details (e.g. the relative opening size of the bronchus, recorded as large-small), might help to differentiate the bronchus. A sketch can be drawn using all of this information, and the leading bronchus along the route must be marked for bronchoscopic insertion.

Finally, a preliminary route map composed of several sketches mimicking the virtual bronchoscopic opening is created.

Bronchoscopy and data collection

A fiber optic bronchoscope (BF-260; Olympus; Tokyo, Japan; external diameter, 4.9 mm; channel diameter, 2.0 mm) was introduced via the transnasal route under topical anesthesia. A full airway examination was performed first under white light bronchoscopy. The bronchial tree was examined as far down as possible. If there were no visible abnormalities, the bronchoscopist inserted the bronchoscope according to the map, carefully observed the target bronchus, and then took routine brushings with a disposable endoscopic brush (Endoscopic Cytobrush, Micro-Tech, Nanjing, China). Then, ThinPrep (Hologic, Marlborough, MA, USA) was performed on the brushings for cytopathological diagnosis. The cytological diagnosis, histological type, lesion size, mapping information, age, and gender were recorded.

Results

A total of 1155 PPLs from 1143 patients met the inclusion criteria for enrolment. The final diagnosis of all enrolled PPLs in

each group is listed in Table 1. Overall, 84.5% (977) of the enrolled lesions were malignant (adenocarcinoma was the main type). There were no false-positive cytological diagnoses in the 1155 PPLs. Moreover, 89.5% (1034) of the patients with PPLs received subsequent surgery. A total of 4.6% (53) of the PPLs were finally diagnosed by TBNA, EBUS-GS, EBUS-TBNA, or thin bronchoscopy, and another 5.9% (68) were finally diagnosed by EBUS-TBNA of the metastatic lymph nodes or needle biopsy of other metastases (e.g. supraclavicular lymph nodes and liver). In all, 864 patients with malignant PPLs and 170 patients with benign PPLs received surgery.

Table 2 shows the baseline characteristics and the sensitivity for malignancy of the mapping cases and controls: Group 1 (no mapping method), Group 2 (mapping method on a portion of patients), and Group 3 (mapping method). There was a significant increase in the sensitivity of brushings among these three groups, from 17.0% to 25.8% to 31.5% ($P < 0.001$), respectively. However, the average lesion size significantly decreased from 3.1 ± 1.57 cm to 2.9 ± 1.28 cm to 2.7 ± 1.23 cm ($P < 0.001$), respectively. There was no significant difference between the groups in terms of age, gender, or pathology. For PPLs over 3 cm, the sensitivity for malignant lesions of these three groups was 25.1%, 38.6%, and 50.9% ($P < 0.001$), respectively.

Among patients who were recruited in the first half of 2013, 93 PPLs of 91 patients were allocated into Group 4. There was no significant difference between Group 3 and Group 4 in age, gender, pathology, or lesion size ($P = 0.994$, $P = 0.545$, $P = 0.848$, and $P = 0.948$, respectively). Although the bronchoscopic brushing sensitivity did not differ significantly between Group 3 and Group 4, more PPLs were diagnosed, with sensitivities of 31.5% and 19.7%, respectively.

The factors associated with the sensitivity for malignant PPLs using mapping were analyzed in Group 3 using

Table 1 Final diagnosis of enrolled PPLs

	Group 1 (pn = 701, ln = 706)	Group 2 (pn = 183, ln = 183)	Group 3 (pn = 168, ln = 173)	Group 4 (pn = 91, ln = 93)
Malignant	595	163	143	76
Primary lung cancer	577	157	141	76
Adenocarcinoma	450	125	123	67
Squamous cell carcinoma	77	21	12	5
Small cell lung cancer	19	4	1	4
Large cell lung cancer	6	1	1	0
Other types of lung cancer†	15	3	4	0
Unclassifiable malignant	10	3	0	0
Metastatic lung tumor‡	18	6	2	0
Benign disease§	111	20	30	17

†Other types of lung cancer, such as neuroendocrine, sarcomatoid and adenosquamous carcinomas, and mesothelioma. ‡Metastatic lung tumor from breast, rectal, and cervical cancers; lingual, esophageal, and hepatic carcinomas; and lymphoma. §Benign disease, such as tuberculosis, organizing pneumonia, non-tuberculous granulomatous inflammation, pneumonia, hamartoma, pulmonary sequestration, and atypical adenomatous hyperplasia. ln, lesion number; pn, patient number; PPLs, peripheral pulmonary lesions.

Table 2 Baseline characteristics and the sensitivity for malignant lesions in the three groups

	<3 cm			>3 cm			Total			P-value
	Group 1 (pn = 398, ln = 403)	Group 2 (pn = 118, ln = 118)	Group 3 (pn = 111, ln = 114)	Group 1 (pn = 292, ln = 292)	Group 2 (pn = 63, ln = 63)	Group 3 (pn = 57, ln = 59)	Group 1 (pn = 701, ln = 706)†	Group 2 (pn = 183, ln = 183)‡	Group 3 (pn = 168, ln = 173)	
Age, year	58 ± 10.1	58 ± 10.1	57 ± 10.5	59 ± 10.2	61 ± 11.3	59 ± 10.1	59 ± 10.2	59 ± 10.6	58 ± 10.4	0.460
Gender male, n (%)	209 (52.5%)	58 (49.2%)	53 (47.7%)	193 (66.1%)	36 (57.1%)	33 (57.9%)	409 (58.3%)	96 (52.5%)	86 (51.2%)	0.131
Pathology										0.186
Malignant	334 (82.9%)	104 (88.1%)	90 (78.9%)	251 (86.0%)	57 (90.5%)	53 (89.8%)	595 (84.3%)	163 (89.1%)	143 (82.7%)	
Benign	69 (17.1%)	14 (11.9%)	24 (21.1%)	41 (14.0%)	6 (9.5%)	6 (10.2%)	111 (15.7%)	20 (10.9%)	30 (17.3%)	
Lesion size	2.0 ± 0.58	2.1 ± 0.58	2.0 ± 0.56	4.5 ± 1.34	4.3 ± 1.04	4.1 ± 0.91	3.1 ± 1.57	2.9 ± 1.28	2.7 ± 1.23	0.018
Sensitivity	11.10%	19.20%	20.00%	25.10%	38.60%	50.90%	17.00%	25.80%	31.50%	0.000

†Lesion size information was lacking for 11 patients in Group 1; ‡Lesion size information was lacking for two patients in Group 2. ln, lesion number; pn, patient number.

univariate logistic regression. The sensitivity for the 143 malignant PPLs were statistically significant with respect to the larger lesion size, solid appearance, cut-off sign at the targeted bronchus, shorter distance from the lesion to the opening of the lobar bronchus, and clear accessibility ($P < 0.001$, $P = 0.039$, $P < 0.001$, $P = 0.031$, and $P = 0.020$, respectively; Table 3).

This mapping method initially took a bronchoscopist with 10 years of experience approximately 10–15 minutes to finish the map; after approximately 30 cases, the mapping procedure usually took five minutes. Bronchoscopy with this mapping method extended the examination time by only two to three minutes for checking the route and was well tolerated by all patients. No serious complications were observed, except for one case with about 30 mL bleeding, which was controlled by endoscopic hemocoagulase spraying.

Discussion

Our study focused on the advancement of conventional bronchoscopic brushing sensitivity using a mapping method for the diagnosis of malignant PPLs without fluoroscopic guidance or a transbronchial lung biopsy (TBLB) during daily clinical work. In our study, the sensitivity of bronchoscopic brushing alone was 17%. Similarly, a retrospective cohort study showed a diagnostic yield of 17% on non-visible lesions by brushing.² After the introduction of the manual mapping method, brushing sensitivity had greatly improved to 31.5% for malignant PPLs, especially for lesions over 3 cm (sensitivity increased to 50.9%). With this mapping method, the sensitivity of conventional bronchoscopic brushing for malignant PPLs is comparable to previous studies using C-arm fluoroscopy (35.4%).² Furthermore, we also found that while the average lesion size decreased, the diagnostic sensitivity of malignant PPLs increased for Group 3. A higher sensitivity was observed in Group 3 compared to Group 4, while no significant differences were presented. This finding might have been a result of the limited number of cases, while the improved understanding of correct positioning and ability may also have benefitted Group 4 patients, even without the mapping method, to some extent. This improvement was mainly a result of the mapping method, as it could increase the chance to reach the lesions with the guidance of bronchoscopy procedures.

The core of the manual mapping method is the translation of thin-section CT information to the endoscopic route. In China, communication between medical specialists is poor or non-existent.⁹ Bronchoscopists usually perform the examination with an isolated, general CT report and then perform bronchoscopic brushing at roughly selected segmental or subsegmental bronchi, which may be inaccurate even at the subsegmental bronchus level.¹⁰ This type of almost “blind brush” approach may result in low sensitivity. Furthermore,

Table 3 Logistic regression analysis of factors associated with the sensitivity for malignant PPLs with regard to mapping

Characteristic	Brushing positive PPLs/total malignant PPLs	P value
Symptom		0.49
Negative†	26/78	
Positive‡	17/61	
Smoking Status		0.723
Smoking	16/51	
Non-smoking	25/84	
NA§	2/4	
Lesion location from the hilum		0.371
Peripheral 1/3	20/76	
Intermediate 1/3	16/43	
Central 1/3	9/24	
Lesion location by bronchopulmonary segment		0.511
Left upper lobe	12/32	
Left lower lobe	6/21	
Right upper lobe	10/45	
Right middle lobe	5/12	
Right lower lobe	12/33	
Lesion size, mm		<0.001
≤20	4/46	
>20 and ≤30	14/44	
>30	27/53	
Lesion character		0.039
Solid nodule	44/109	
Mixed GGN	1/22	
GGN	0/12	
Relationship between lesion and targeted bronchus		<0.001
Cut-off	42/80	
Penetration	2/24	
Outside	0/4	
Deduction according to the vessel	1/35	
Linear distance between the targeted bronchus and the opening of the lobe bronchus, mm		0.031
≤50	20/47	
>50 and ≤70	21/65	
>70	4/31	
Relationship between edge of tumor and pleura		0.374
Connected with	24/84	
Apart from	21/59	
The utmost visible bronchus opening		0.115
≤5 th generation	10/42	
=6 th generation	13/45	
=7 th generation	9/31	
≥8 th generation	13/25	
Accessibility		0.020
Clear	45/110	
Unsatisfied¶	0/33	

†Chief complaint negative: the peripheral pulmonary lesions (PPLs) were found by physical check-up or preoperative examination of other diseases.
‡Chief complaint positive: cough, stuffiness of the chest, chest pain, blood-stained sputum, shortness of breath, backache, cervical mass, and lower limb pain.
§NA: missing smoking information. ¶Unsatisfied: mapping was deduced by the accompanying vessels or the condition of the furthest bronchus, or the vessel that was recognized as the target because the bronchus or accompanying vessels were too small to recognize to reach the lesion. GGN, ground glass nodule.

while MPR can show high-resolution anatomy imaging of the bronchus and the exact location of PPLs, it is difficult to mentally reconstruct a sequence of the airway that reaches the lesion.¹¹ By this mapping method, the generated two-

dimension map shows information about the actual relative position, allowing the bronchoscopist to recognize the route easily, thereby increasing the chance of reaching the peripheral lesions. Although the bronchoscope might rotate while

being advanced, this type of rotation could be undone by withdrawing the bronchoscope or by referring to the adjacent familiar bronchial position. Thus, this mapping method is a convenient way to improve bronchoscopic brushing for malignant PPLs.

Lesion size, location, and CT bronchus signs are known predictors of positive samples, and our results were consistent with these predictors.^{2,12–14} Unsatisfactory accessibility, when the mapping was deduced by the accompanying vessels or the furthest bronchus, or the vessel was recognized as the target because the bronchus or accompanying vessels were too small to recognize to reach the lesion, meant that the final mapping location was further away from or inconsistent with the lesion. This type of inaccurate positioning caused low sensitivity. Generally speaking, the mapping method is especially suitable for cases with larger, solid-appearing lesions, cut-off signs at the targeted bronchus, lesions nearer to the lobar bronchial opening, and clear accessibility.

Although the mapping method increased sensitivity compared to bronchoscopic brushing alone, other methods can achieve higher sensitivities. For example, virtual bronchoscopy navigation provides better automation and objectivity and can achieve a higher diagnostic yield, from 62.5–84.4%, with a shorter examination time.^{15–18} However, this advanced technology is quite limited in China, and the cost also restricts its routine application. Chinese physicians treat an increasing number of patients and perform more bronchoscopies each year.¹⁹ With data revealing the mortality benefits of lung cancer screening by low-dose CT, bronchoscopists will also be challenged with more PPLs.²⁰ It is neither practical nor economical to perform bronchoscopies guided with navigation systems on all PPLs. This manual method is a quick, low cost, and practical method for improving bronchoscopic brushing without the use of expensive navigation systems.

There are some shortcomings to this mapping method. First, compared to navigation software, the automation of this method is insufficient, and the efficiency of this method depends largely on the bronchoscopist's skill. Training could solve this issue. Second, this study was not randomized. However, enrollment in Group 3 was random to a certain extent, as patients were grouped by the availability of thin-section CT scans. Third, to eliminate a skill bias, the same senior bronchoscopist with 10 years of diagnostic bronchoscopy experience performed diagnoses on all enrolled PPLs. However, the performances of this mapping method among different bronchoscopists merits further study. Additionally, this mapping method requires high-quality CT images and a specific workstation to consult the MPR, which some Chinese hospitals do not possess. Despite these limitations, this mapping method is convenient and inexpensive and could also be used to assist EBUS-GS and TBLB for guiding bronchoscope insertion if a navigation instrument is not available.

Conclusion

In conclusion, this proposed mapping method greatly increased the bronchoscopic brushing sensitivity for malignant PPLs, with convenience and low cost. During routine clinical work, it could be helpful for the guidance of bronchoscope insertion.

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Disclosure

No authors report any conflict of interest.

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