Original Article

The introduction of electromagnetic navigation bronchoscopy for the diagnosis of small pulmonary peripheral lesions in an Asian population

Ye Gu[1*], Shanhao Chen[2*], Jingyun Shi[3], Chunyan Wu[4], Zongmei Wen[5], Hong Shi[5], Baomei Wu[1], Xin Xu[6], Hao Wang[1]

[1]Endoscopy Center, [2]Department of Pulmonary Tuberculosis, [3]Department of Radiology, [4]Department of Pathology, [5]Department of Anesthesiology, [6]Medical Affairs Office, Shanghai Pulmonary Hospital, Tongji University, Shanghai China

Contributions: (I) Conception and design: Y Gu, S Chen, X Xu, H Wang; (II) Administrative support: X Xu, H Wang; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: Y Gu, S Chen, J Shi, C Wu, Z Wen, H Shi, B Wu; (V) Data analysis and interpretation: Y Gu, S Chen, J Shi, C Wu, Z Wen, H Shi, B Wu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*These authors contributed equally to this work.

Correspondence to: Dr. Hao Wang. Endoscopy Center, Shanghai Pulmonary Hospital, Tongji University, 507 Zhengmin Road, Shanghai 200433, China. Email: wanghaoshanghai@126.com; Dr. Xin Xu. Medical Affairs Office, Shanghai Pulmonary Hospital, Tongji University, 507 Zhengmin Road, Shanghai 200433, China. Email: xuxinshfk@126.com.

Background: Electromagnetic navigation bronchoscopy (ENB) is emerging as a useful new technique for diagnosing small pulmonary peripheral lesions (SPPLs). However, the accuracy and efficiency of ENB have not been investigated in Asian populations where the differential diagnoses for SPPLs may be different. To analyze this question, this study included patients who received diagnostic ENB followed by surgery for the excision of SPPLs.

Methods: Consecutive patients referred to the Department of Thoracic Surgery, Shanghai Pulmonary Hospital (Tongji University), between May 2014 and April 2015 were recruited. ENB was used to obtain biopsy tissue and make a diagnosis, which was then confirmed by histopathological examination.

Results: The ENB was performed on 84 SPPLs of 78 patients in the study, with four patients having more than one SPPL. It successfully reached and biopsied 81 lesions. The average ENB navigation time was 10.8 minutes (range, 0.5–52 minutes). No mortality occurred, with only two complications (one bleeding and one pneumothorax). The mean diameter of the biopsied SPPLs was 19.0 mm (range, 5.0–30.0 mm). The distance from the sensor probe to the focus was 8.0 mm (range, 1–16 mm). ENB diagnosis had identical results with histopathology examination in 81 lesions (37 lung cancer and 41 non-lung cancer). The sensitivity of ENB was 92.9% (78 out of 84 lesions) in this study.

Conclusions: These data suggested that ENB was an accurate and efficient procedure to sample and diagnose SPPLs in the Asian population. It appeared that ENB had a high percentage of successful results in both navigating and aiding in the diagnosis of SPPLs in the Asian population.

Keywords: Electromagnetic navigation bronchoscopy (ENB); small pulmonary peripheral lesions (SPPLs); efficient; accuracy; complications

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Introduction

The diagnosis of early stage lung cancer, especially small pulmonary peripheral lesions (SPPLs), has great significance for increasing the percentage of operable lung cancer lesions and improving patients' life quality (1). With advances made in diagnostic techniques, the detection rate of SPPLs has gradually increased. The accurate diagnosis of SPPLs, which requires and places a higher demand on pulmonary doctors and techniques, can greatly improve the early diagnosis rate of lung cancer (2). However, the current diagnostic techniques for SPPLs are still far from satisfactory. The main limitations include low accuracy and precision, frequent complications, and the requirement of a large incision.

The emergence of electromagnetic navigation bronchoscopy (ENB) (3-5), a key breakthrough in the diagnosis of SPPLs, provided a solution to this problem. This image-guided localization device could reportedly reach the peripheral lung lesions and obtain biopsy tissues (6,7). Thus far, however, the results, and ramifications of the benefits of ENB are still under debate (8). The accuracy and efficiency of ENB in the diagnosis of SPPLs has not been investigated in Asian populations. Shanghai Pulmonary Hospital (Tongji University), the first hospital in Asia carrying ENB technology, has already diagnosed several cases using ENB. In this study, the performance of ENB in a Chinese population was accessed through a retrospective study.

Methods

Ethical approval, consent and permissions

The protocol of this study was conducted according to the revised Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Shanghai Pulmonary Hospital (Tongji University) (No. 2013-007). Informed consent was obtained from all participants.

Patients

Consecutive SPPL patients from our department who had indications were recruited into this study from May 2014 to April 2015. The conditions of these patients were discussed at department meetings; the decision to proceed with ENB was authorized by the Department Chief. A positive bronchus sign was a prerequisite for our ENB operation. Patients with the following conditions were excluded: (I) myocardial infarction or cardiothoracic surgery within 3 months; (II) hemoptysis within 2 weeks; (III) cardiopulmonary insufficiency; (IV) unstable angina; (V) coagulation disorders; (VI) lesions in the lumen; or (VII) the presence of chest pain.

ENB operation

The protocol followed the recommendations of the manufacturer and a previous report (9). The version number of the SuperDimension system used is 6.1.3. Prior to the ENB operation, a chest CT scan was used to generate a 3D channel. During the initial planning phase, the CT scan data was loaded into the manufacturer's software (SuperDimension). At least five anatomical marks were chosen as the virtual reference points. The operation was performed through a laryngeal mask airway under general anesthesia. The CT images and 3D virtual airways were linked to the controllable probe with the help of the preset landmarks in patient's airways. The steerable guide catheter of SuperDimension was inserted through the working channel of the scope. We monitored the operation through R-EBUS and X-ray and confirmed that the bronchoscopist was at the lesion. If the bronchoscopist did not reach the lesion, two more attempts to reach it were made. After confirming arrival at the lesion, tissue sampling was prepared for biopsy through brush biopsy, biopsy forceps biopsy or fine-needle aspiration biopsy.

To assure accuracy, registration errors were calculated using computer software. These errors represented the radius of the expected difference between the tip of the sensor probe and its expected location in the patient. Further, a navigation error was defined as the discrepancy in the distance between the sensor probe and the lesion. Navigation was deemed successful if the specified distance was less than 10 mm from the lesion.

Clinicopathological features

Confirmation of the final diagnosis was ascertained through a histopathological examination in all cases. Diagnostic yield, lesion size, shape, and location, and complications were documented. The follow-up of all patients was 12 months or more.

Statistical analysis

χ^2 test was used to analyze the associations between the variables. All data were calculated by the SPSS. A P value <0.05 was considered statistically significant.

Table 1 The clinicopathological characteristics of the 78 participants

Variables	Female, n (%)	Male, n (%)
Age		
<30	1 (3.4)	3 (6.1)
31–40	2 (6.9)	5 (10.2)
41–50	3 (10.3)	4 (8.2)
51–60	7 (24.1)	15 (30.6)
61–70	12 (41.4)	14 (28.6)
>70	4 (13.8)	8 (16.3)
Diameter of the lesion (mm)		
1–10	5 (17.2)	1 (2.0)
11–20	15 (51.7)	27 (55.1)
21–30	9 (31.0)	21 (42.9)

The total number of female participants is 29 (37.2%), male participants is 49 (62.8%).

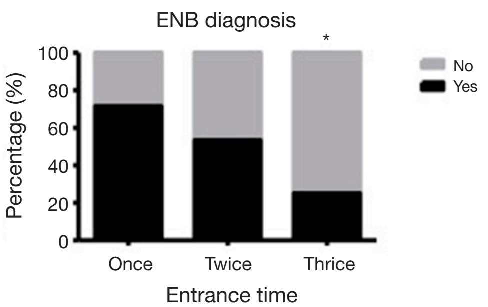

Figure 1 The correlation between the entrance times of ENB and whether it would make a diagnosis. *, P<0.05.

Results

Patients' information

ENB was performed on 78 consecutive patients during the twelve months specified (*Table 1*). They had 84 SPPLs (four patients had more than one SPPL). Most patients were male. The average age was 53.52 years old (range, 24–82 years). Most lesions were detected in the upper lobes [22 located in the left upper lobe (LUL) and 35 in the right upper lobe (RUL)].

Efficiency

When ENB was applied in clinical practice, its efficiency was the first indicator we wanted to analyze. The ENB navigation successfully reached 81 lesions (39 were reached in the first attempt, 30 lesions were reached after two attempts and 12 needed three tries to reach the lesion during the same operation) of 75 patients. The mean diameter of these lesions was 19±6.16 mm. The number of attempts correlates with whether the ENB procedure would make the diagnosis (*Figure 1*). The diameter of the lesions did not affect the number of attempts. Adequate biopsy samples were harvested after reaching the lesions. The ENB navigation took an average of 10.8 minutes to complete. Timing was more efficient when it succeeded on the first attempt. However, the complications of bleeding and pneumothorax all occurred in groups that needed shorter navigation times. Therefore, whether the ENB procedure would make a diagnosis was not affected by the navigation time (*Figure 2*). The navigation failed in three cases. The distance between the sensor probe and the lesion was 8.02±2.85 mm in average. The sensor probe was mostly located within 8 mm from the lesion. It was affected by the diameter of the lesion. Furthermore, the volume of the lesion did not affect the navigation time, the number of attempts, or the occurrence of complications (*Figure 3*).

Accuracy and safety

The diagnosis accuracy and safety of ENB was another crucial concerns when it was applied in practice. Our results suggested that ENB diagnosis had identical results with histopathology examination in 78 lesions (37 lung cancer and 41 non-lung cancer) (*Table 2*). The sensitivity of ENB was 92.86% (78 out of 84 lesions) in this study. The diagnosis of non-malignant lesions included non-specific inflammation, granuloma gangraenescens, tuberculosis and atypical hyperplasia. The three falsely diagnosed lesions by ENB were fiber connective tissue hyperplasia in the pathological analysis. Complications, including one case of bleeding and one pneumothorax, were reported in two patients.

Discussion

The malignancy rate for small periphery lesions (between 0.8 and 2.0 cm) was previously reported to be approximately 18% (10). Underscoring the potential benefit of the diagnosis and treatment of early stage lung cancer, evaluation of SPPLs highlights the importance of the pulmonologist's early and accurate diagnosis. However, the early and accurate diagnosing process, and the imaging instruments now used are still particularly challenging for clinicians.

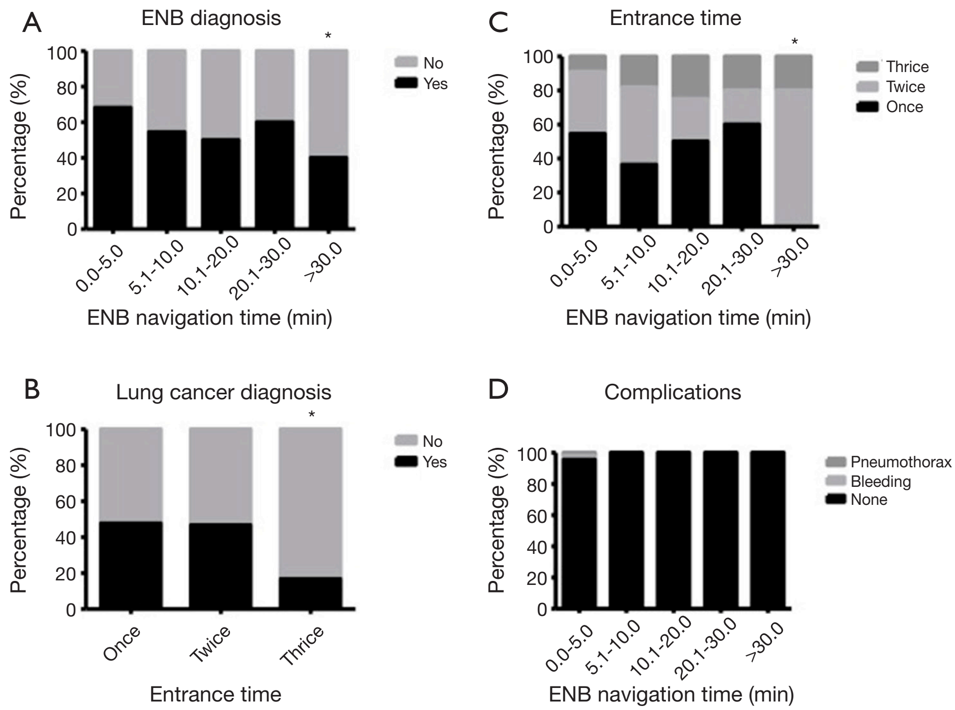

Figure 2 (A,B) The correlation between the navigation time of ENB and whether it would make a diagnosis; (C) the entrance time; or (D) complications caused by ENB. *, P<0.05.

Presently, reaching the lesion and successfully obtaining adequate biopsy tissue samples remains a difficult task. The conventional diagnostic technology, including bronchoscopy, has not been suitable for SPPLs. Currently, suspicious SPPLs are often biopsied using more invasive methods, such as CT-guided aspiration (which increases the risk of pneumothorax) or surgical biopsy. Thus a new, more accurate yet less invasive, diagnostic process is needed.

The introduction of ENB contributes to providing an accurate, navigational and steerable technique to localize small lung lesions. This new technology has been successfully used on animal models since 2003; the first human study was performed in 2005; and to date, over 20,000 procedures have been performed (4,11). During the procedure, ENB-aided diagnostics yielded approximately 75% accuracy and the occurrence of pneumothorax was less than 5% in most studies (12). Thus far, it has become a most suitable assessment tool for SPPLs.

One of the main practical advantages of ENB is the detection of peripheral lesions in upper lobes, which are less detectable through CT scan-guided biopsies. The three greatest advantages of ENB are as follows: (I) it is less invasive; (II) it is more comfortable; and (III) it develops minimal complications. Furthermore, ENB guarantees on-site examination, which significantly improves the accuracy of diagnosis while also decreasing operative time. It is also conducive to improving the skills of the bronchoscopist.

To the best of our knowledge, no report has ever assessed the efficiency and safety of ENB among Asian patients. To answer this question, we designed this study following previously reported instructions (12). Three physicians from our hospital have been using ENB since 2013. It is an efficient and manageable technology. There was no significant difference among operators. We did not set up many thresholds except for a positive bronchus sign in the inclusion criteria. We analyzed both the efficiency and safety of ENB in this study. We were most concerned about the efficiency indicators. We employed ENB procedures deemed medically expedient and efficient. Suspect small lung cancer lesions were difficult to reach by conventional techniques; however, ENB provided a less invasive method to reach and extract sample tissue. In our study, most lesions were accurately determined by the magnetic field of the ENB procedure. ENB diagnosis

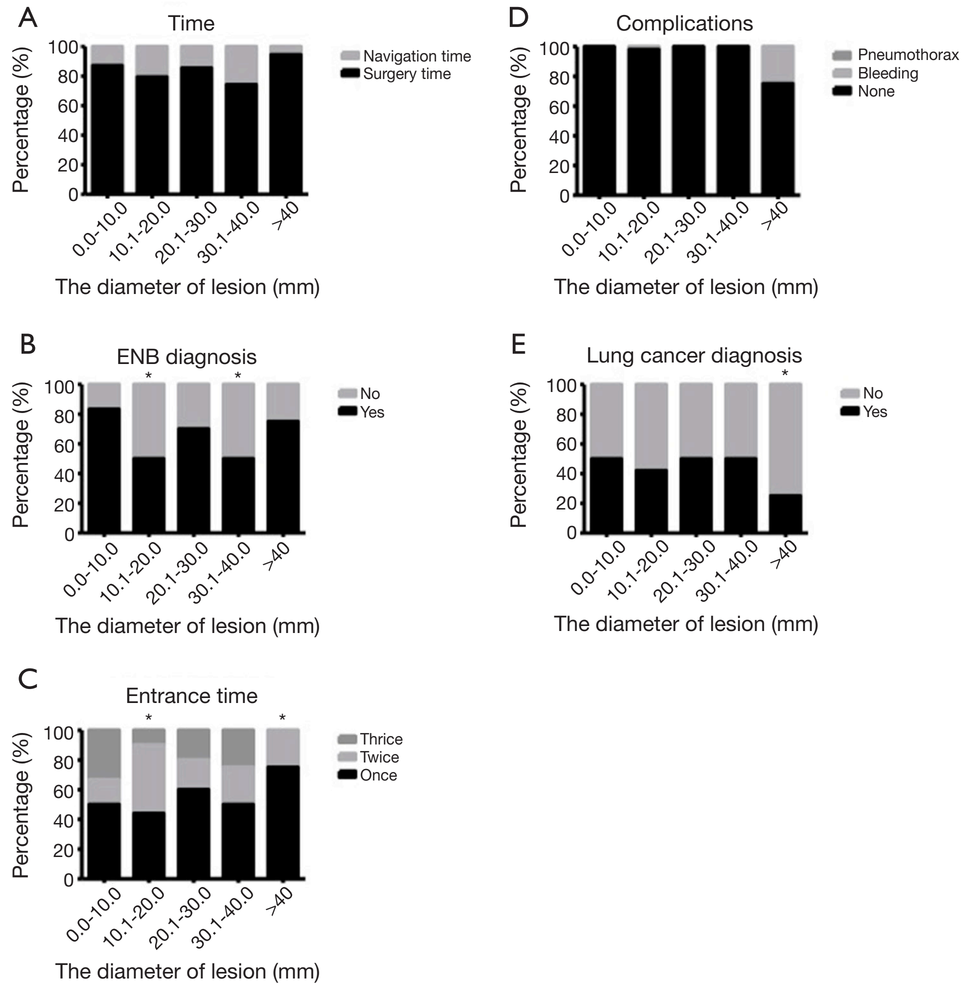

Figure 3 (A) The correlation between the diameter of the lesion and the navigation time; (B) the ENB diagnosis; (C) the entrance time; (D) the complications and (E) the pathological diagnosis. *, P<0.05.

Table 2 The diagnosis of the 78 participants

Diagnosis	Cases
Adenocarcinoma	31
Squamous carcinoma	4
Adenosquamous carcinoma	1
Small cell lung cancer	1
Non-specific inflammation	22
Granuloma gangraenescens	2
Tuberculosis	12
Atypical hyperplasia	5

could be potentially affected by navigation time, attempt frequency, and actual navigation error. In the current study, ENB diagnosis also yielded several non-malignant diagnoses, which were confirmed by pathological examination and followed up.

Effective treatment plans for lung cancer depend on accurate, histologic classification. Presently, lung cancer treatment is based on the histologic subtyping of NSCLC (13,14). Our study strongly suggests that ENB is an outstanding technique that can aid pulmonary physicians in small lung lesions diagnosis. With the assistance of ENB, the samples of 81 lesions were successfully biopsied; normally these are not accessible by routine instruments. Our data also suggested that the diagnostic accuracy of ENB was reliable. It was concordant with the pathological results in 92.86% (78 out of 81) of lesions. The early diagnosis would greatly improve accurate, timely, and successful treatment. In addition to these positive factors, these ENB procedures were deemed satisfactorily safe, which mirrored the previous report (15,16). During the study, only two complications appeared in our participants.

We realize that two factors limited our study: first, our overall actual number of cases was limited; second, the specific groups such as automated implantable cardioverter-defibrillator patients, who also had successful guidance by ENB (17), were excluded. We will continue to monitor the efficiency and safety of ENB in the future.

Conclusions

In conclusion, our experience using ENB indicated that this procedure was both efficient and accurate for the diagnosis of SPPLs. ENB also provided a practicable method for the bronchoscopist to address the SPPLs. Finally, ENB appears to have performed very well in both navigating and aiding in the diagnosis of SPPLs in this Asian population.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The protocol of this study was conducted according to the revised Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Shanghai Pulmonary Hospital (Tongji University) (No. 2013-007). Informed consent was obtained from all participants.

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