## Diagnostic yield of electromagnetic navigational bronchoscopy: A safety net community-based hospital experience in the United States

Sujith V. Cherian, Saranjit Kaur, Siddharth Karanth, Jonathan Z Xian, Rosa M Estrada-Y-Martin

#### Abstract:

Divisions of Critical Care, Pulmonary and Sleep Medicine, McGovern Medical School, University of Texas Health, Houston, TX, USA

### Address for correspondence:

Dr. Sujith V. Cherian, McGovern Medical School, The University of Texas Health Science Center at Houston, 6431 Fannin Street, Houston, TX 77030, USA. E-mail: sujith.v.cherian@ uth.tmc.edu

Submission: 03-07-2020 Accepted: 25-08-2020 Published: 14-01-2021

Access this article online

Quick Response Code:

www.thoracicmedicine.org

10.4103/atm.ATM\_388\_20

**INTRODUCTION:** Electromagnetic navigational bronchoscopy (ENB) is an excellent tool to diagnose peripheral pulmonary nodules, especially in the setting of emphysema and pulmonary fibrosis. However, most of these procedures are done by interventional pulmonologists and academic tertiary centers under general anesthesia. Studies evaluating the diagnostic utility of this tool in safety-net community hospitals by pulmonologists not formally trained in this technology are lacking. The objective was to evaluate the diagnostic yield of ENB done in such a setting and its associated complications.

**METHODS:** Retrospective chart review of consecutive ENB procedures over 5 years from 2014, since its inception in our institution-a safety-net community based hospital was performed. Multiple variables were analyzed to assess their impact on diagnostic yields.

**RESULTS:** After exclusion criteria were applied, 72 patients with 76 procedures were eventually included within our study, with an overall 1-year diagnostic yield of 80.2%. Sensitivity for malignancy was 73% and negative predictive value of 65%. Primary lung cancer was the most common diagnosis obtained, followed by tuberculosis (TB). The overall complication rates were low, with only 1 patient (1.3%) requiring hospitalization due to pneumothorax needing tube thoracostomy. No deaths or respiratory failures were noted within the cohort. The only significant variable affecting diagnostic yield was forced expiratory volume in 1 s. The presence of emphysema did not affect diagnostic yield.

**CONCLUSIONS:** ENB is safe and feasible with a high diagnostic success rate even when performed by pulmonologists not formally trained in interventional pulmonology in low resource settings under moderate sedation.

#### Keywords:

Electromagnetic navigational bronchoscopy, lung cancer, moderate sedation

Lung cancer accounts for >25% of all cancer related deaths in the world. Early diagnosis is essential, and presentation either in the form of solitary peripheral pulmonary nodules (PPN) or lung masses are not uncommon. With the advent of low-dose computed tomography (CT) scans as part of cancer screening, community

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms. physicians, and pulmonologists are having to deal with a significant number of these cases on a daily basis in the US. Indeed in the National Lung Screening Trial; lung nodules were seen in at least 39% of participants of which 72% required further investigation.<sup>[1]</sup> Size is an independent predictor for malignancy in PPN (in the range of 64%–82% with PPN >2 cm).<sup>[2]</sup> Many other imaging characteristics may help ascertain the risk of malignancy while approaching

How to cite this article: Cherian SV, Kaur S, Karanth S, Xian JZ, Estrada-Y-Martin RM. Diagnostic yield of electromagnetic navigational bronchoscopy: A safety net community-based hospital experience in the United States. Ann Thorac Med 2021;16:102-9.

For reprints contact: WKHLRPMedknow reprints@wolterskluwer.com

DOI:

Website:

these pulmonary nodules; however, a significant number of PPN has an intermediate risk of malignancy (5%-65%) for which further investigation either in the form of bronchoscopy or CT-guided transthoracic needle aspiration (TTNA) is recommended.<sup>[3]</sup> Conventional bronchoscopy with biopsies has low sensitivity in diagnosing these lesions, and perform extremely poorly when nodules are located in the outer third of the lung and especially when <2 cm in diameter.<sup>[4,5]</sup> While CT-guided TTNA is highly sensitive in diagnosing malignancy in these lesions, many of them are in the vicinity of significant emphysema, blebs<sup>[6]</sup> - all of which pose a significant risk of pneumothorax (in the range of 25%)<sup>[7]</sup> – which could be life-threatening, especially given the poor lung reserve in many of these patients. Along these premises, image-guided bronchoscopy has assumed a vital importance as it represents the least invasive method to approach PPN and masses with significantly less complications, and is endorsed by the National Comprehensive Cancer Network Guidelines for the diagnosis of non-small cell lung cancer.<sup>[8,9]</sup>

Electromagnetic navigation bronchoscopy (ENB) displays images of the tracheobronchial tree, which aids the bronchoscopist to guide specialized endoscopy tools to lung targets, i.e., PPN or lung mass. Moreover, it has been used to place fiducial markers for stereotactic radiation therapy as well as pleural dyes for identification during surgery.<sup>[9,10]</sup>

Various factors have been reported in several retrospective cohort studies to affect the diagnostic yield of ENB including the presence of bronchus sign, size of the lesion, lesion location, concurrent use of radial endobronchial ultrasound, user experience, and volume as well as the use of general anesthesia.<sup>[9]</sup> To date, close to 50 different studies on the diagnostic utility of ENB, including the multicenter prospective NAVIGATE study,<sup>[11]</sup> have been published with a reported diagnostic yield in the range of 67%-84%.<sup>[9]</sup> The NAVIGATE study also corroborates to these studies with a reported sensitivity to detect malignancy of 69% and a 1 year diagnostic yield of 73%. The majority of studies including the NAVIGATE study have involved academic centers, higher volume centers (>5 procedures/month) and have been performed under general anesthesia by interventional pulmonologists or interventional pulmonology (IP) fellowship trained physicians. In fact, within the NAVIGATE study, 81% of the procedures were performed under general anesthesia, and only 7.9% of the procedures were performed in low volume centers (defined as 0-4/month) with a trend toward lower success in these centers as well.<sup>[11]</sup> Moreover, the American College of Chest Physicians has recommended the use of ENB to diagnose suspicious PPN if equipment and "expertise" is available.<sup>[12]</sup>

Studies, therefore involving the use of ENB by pulmonologists not formally trained in interventional pulmonologists and in low volume settings under moderate sedation are lacking. Consequently, the feasibility of this technology in such centers and developing countries is questionable. Being a safety net community hospital without easy access to general anesthesia services, we sought to evaluate the diagnostic yield of ENB in our setting by performing a retrospective cohort study of all patients who underwent ENB within our institution and evaluating diagnostic yield, factors affecting the yield and risk of complications.

#### Methods

All patients undergoing ENB between August 2014 and January 2020 were identified by a prospectively maintained database at Lyndon Baines Johnson (LBJ) hospital, which is a safety net community hospital within Harris county, Texas and staffed by physicians of University of Texas Health, Houston. All procedures were performed with the super-Dimension ENB system (Minneapolis, MN) under moderate sedation with informed consent. Olympus video bronchoscopes (Olympus, Tokyo, Japan) with a 2.8 mm working channel were used for all cases. The Institutional Review Board at UT Health-McGovern medical school and LBJ hospital approved the study (HSC-MS-18-0512).

Retrospective chart review of electronic medical records was performed on these patients on whom the following variables were collected: patient demographics, size, location, sedation used, complications, presence of CT-bronchus sign, distance from pleura, proximity to bulla/bullae and tools used for diagnosis (biopsy forceps, cytology brushings, needle aspiration, core biopsy with GenCut and bronchoalveolar lavage).

All of the procedures were performed together by two board certified pulmonologists along with a fellow-in training under moderate sedation. The ENB procedure comprised of three distinct phases: planning, registration, and navigation. During the planning phase, a previously acquired CT scan of the chest was uploaded into a planning software to create a three-dimensional axial, coronal, and sagittal reconstructions of the patient's airway anatomy, thus creating virtual bronchoscopy images at which time registration points in the patient's bronchial system and target lesions are marked. During the registration phase, locatable navigable guide (LNG) catheters were used with conventional bronchoscopes to mark airway anatomy that correlated with the same positions marked on the previously acquired CT images. During the navigation phase, with the patient lying on a board that emits electromagnetic waves an electromagnetic field is created during which time

#### Results

virtual reconstructed images are adjusted in real-time as the locatable navigation guide is moved within an extended working channel (EWC) towards the target lesion. Once the position of EWC (which is usually placed within a distance of 1 cm from the target based on virtual bronchoscopic images) was confirmed on fluoroscopy (if possible based on size), the locatable guide was removed and bronchoscopic sampling instruments were passed through the EWC and samples obtained under fluoroscopic guidance.

ENB was considered diagnostic if a definite diagnosis was obtained with histological, cytological or microbiological samples (i.e., malignancy, TB with positive acid-fast bacilli), without the need for any additional diagnostic procedures. Nonmalignant or indeterminate results (i.e., inflammation, necrosis, lymphocytes, hemorrhage, and granulomas) were counted as ENB diagnostic yield successes if supported by follow-up imaging showing stability, resolution, or at least partial clearing (at least 50%). Moreover, if benign nature was confirmed either with surgery or TTNA; then ENB was considered diagnostic as well. However, if additional imaging showed increased nodule size, new lymphadenopathy, or metastatic disease or if a clinical decision was made to pursue further treatment such as radiation/ chemotherapy; then, the procedure was considered non-diagnostic. Furthermore, if ENB was indeterminate and either TTNA or surgery showed a definitive diagnosis; then, ENB was considered as false negative.<sup>[11]</sup>

CT bronchus sign was defined as the presence of bronchus directly leading to the target lesion. Distance from pleura was calculated from center of nodule to parietal pleura from a location where interventional radiology would attempt a transthoracic lung biopsy.<sup>[13]</sup> Ground glass opacities were defined as focal nodular areas of lung attenuation through which normal parenchymal structures such as airways, vessels could be easily defined.

All the variables were collected and entered into the data collection forms by fellows in training (SK and JX), which were independently reviewed and confirmed by both attending pulmonologists (SVC and RMEYM).

#### **Statistical analysis**

The data were analyzed using Stata MP version 15. The data for diagnostic versus nondiagnostic ENB were compared using a *t*-test and Wilcoxon rank-sum test for continuous variables and Chi-square test and Fisher's exact test for categorical variables. The data were sorted by the date of bronchoscopy, and analysis for the association of experience on successful bronchoscopies was performed among the first 30 patients and the last 30 patients. P < 0.05 was considered statistically significant.

A total of 81 procedures were performed consecutively on 77 patients in a 5-year period. Patients without a definite diagnosis who were lost to follow-up (3 patients) and did not have a follow-up visit in 6 weeks (2 patients) after the procedure were excluded, as there was no follow-up imaging in these patients. Thus, a total of 76 procedures done on 72 patients were eventually included in the study.

#### Subject, lesion, and procedural characteristics

Given that we are a safety-net hospital, the majority of patients served are uninsured patients and the indigent population of Houston. Thus, the majority of the cases were in African-American (43%) and Latin American patients (37%) [Table 1]. The average age of patients was 61.5 years  $\pm$  4 years (21–83 years) with an almost similar number of procedures done in men and women. The median size of the lesion was 3 cm in diameter. The mean forced expiratory volume in 1 s (FEV1) of patients was 1.7 L, 69% of predicted. Moreover, close to half of the cases (47%) had a diagnosis of COPD or emphysema on imaging. The most common location of the lesion biopsied was in the right upper lobe (34%), followed by the left upper lobe (19.7%). More than half of the nodules (65%) were either abutting the pleura (29%) or within 2 cm of the pleura (36%), with a median distance of 1.4 cm (interquartile range [IQR]-0-2.7 cm). A total of 9 cases (12%) involved nodules in close proximity to a bulla. Consistency of the lesion was solid in the majority of the cases (82%), followed by cavitary in 8% of cases. The CT bronchus sign was present in 70% of the cases.

All of the procedures were done under moderate sedation with intravenous midazolam and fentanyl. The median

## Table 1: Demographics and baseline patient characteristics

Patient characteristics	Number
Age, mean age (IQR)	61.5 (55–65)
Sex (%)	
Female	47.4
Male	52.6
Race (%)	
Asian	2.6
African-American	43.4
Latin-American	36.8
Caucasian	17.1
COPD (%)	
Yes	47.3
No	52.6
Consultation setting (%)	
Outpatient	80.3
Inpatient	19.7

IQR=Interquartile range, COPD=Chronic obstructive pulmonary disease

dosages of midazolam used were 3.5 mg (IQR-2.5–4.75 mg) and fentanyl was 75 mcg (IQR-62.5–100 mcg). Fluoroscopy was used to confirm position of the LNG in all cases and a combination of biopsy tools, i.e., forceps biopsies and brushes, followed by bronchoalveolar lavage were used in the majority of the cases.

#### **Adverse events**

Pneumothorax requiring chest tube placement and hospitalization occurred only in 1 case, (1.3%). Any grade pneumothorax occurred in 4 cases (5.2%). Minor bleeding (grade 1)<sup>[14]</sup> occurred in 2 cases (2.6%). There were no deaths or events of respiratory failure noted.

#### **Diagnostic outcomes**

Successful navigation (defined as able to reach within 1 cm of the lesion) was possible in 75 cases (98.6%). The procedure could not be completed in 1 case due to increased agitation. A specific diagnosis with ENB was obtained in 61 cases (80.2%). Among these, ENB was diagnostic on the first attempt in 57 cases (75%), while a repeat ENB was performed in the other cases as CT-guided biopsy referrals were denied due to high risk of pneumothorax in these cases. The diagnosis of malignancy in our cohort with ENB was possible in 48.6% (35 of 72 patients). Of the 37 negative cases (51.4%), 24 were true negative (i.e., either stable on imaging or specific benign diagnosis obtained), 13 were false negative.

Thus, the overall diagnostic accuracy for ENB in our cohort was 80.2%. Sensitivity for malignancy in our study was 72.9% (35/35 + 13) and negative predictive value was 64.8% (24/24 + 13).

In our cohort with diagnostic ENB, primary lung cancer was the most common diagnosis obtained (39%), followed by tuberculosis (5.5%), other diagnoses are listed in Table 2. From the nondiagnostic cases, a specific diagnosis was obtained through CT-guided biopsy in 12 cases, surgical resection in one case, bronchoscopy with EBUS-TBNA in another case (due to the development of mediastinal metastases), one was presumed to be worsening metastases (given increase in number and size of lesions on follow-up imaging). From the nondiagnostic cases, the primary diagnosis was also primary lung cancer (66%). Table 3 shows the remaining cases with other diagnoses.

Further analysis [Table 4] did not show any statistically significant variables affecting diagnostic yield apart from higher FEV1% (nondiagnostic vs. diagnostic - 67% vs. 81%, P = 0.04). The presence of CT-bronchus sign (P = 0.25), size of nodule (<3 cm vs. 3 cm and above; P = 0.6), location of nodule (upper lobe vs. middle lobe/lingula vs. lower lobe; P = 0.72), distance from

## Table 2: Final diagnoses where electromagnetic navigational bronchoscopy was diagnostic

Diagnoses	n
Primary lung cancer	28
Adenocarcinoma	17
Squamous cell cancer	6
Small cell cancer	5
Carcinoid/tumorlets	2
Metastases	2
Lymphoma	2
Organizing pneumonia	2
Hamartoma	1
Tuberculosis	4
Granuloma	2
Nonspecific inflammation/infection with subsequent CT clearing	10
Amyloid	1
Silicosis	1
Atypical cells <sup>a</sup>	2
Total	57

<sup>a</sup>Atypical cells- were reported as mild squamous dysplasia with the lesion being stable on subsequent CT scans/PET-CT scans. PET=Positron emission tomography, CT=Computed tomography

# Table 3: Final diagnoses with nonresolution ofCT findings and nondiagnostic electromagneticnavigational bronchoscopy

Primary lung cancer 10 (13	
, , , , , , , , , , , , , , , , , , , ,	3.1)
Adenocarcinoma 6 (7.	8)
Squamous cell carcinoma 3 (4.	1)
Poorly differentiated NSCLC 1 (1.	3)
Tuberculosis 1 (1.	3)
B-cell lymphoma 1 (1.	3)
Metastases 2 ( 2.6	%)
Fibroinflammatory lesion 1 (1.	3)
Total 15 (19	9.7)

NSCLC=Non-small cell lung cancer

pleura (abutting pleura/<2 cm from pleura vs.  $\geq 2$  cm; P = 0.58), proximity (<2 cm) to bullae (P = 0.68), and presence of emphysema (P = 0.61) were all evaluated which did not show a statistical significant impact on yield of ENB in our cohort. We also evaluated whether diagnostic yield was affected by the learning curves initially (first 30 procedures vs. last 30 procedures; P = 0.77 or first 2 years vs. last 3 years; P = 1.00), which also did not show any significant difference.

#### **Molecular analysis**

When molecular analysis was requested, the tissue sample was considered adequate in all samples sent (9 cases out of the 35 cases with primary diagnosis as lung cancer); which included testing for EGFR, KRAS, ALK, PD, and PDL-1. However, due to cost constraints, molecular analysis had to be specifically requested by oncology.

Table 4: Variables affecting diagnostic yield in our cor	iort
----------------------------------------------------------	------

Variables	Bronchoscopy successful		Total	P
	No	Yes		
	19	57	76	
Size (cm)				
<3	11	27	38	0.60
≥3	8	30	38	
≤2	5	9	14	0.32
>2	14	48	62	
Distance from pleura (cm)				
Abutting pleura/≤2	11	38	49	0.58
>2	8	19	27	
Proximity to bullae (within 2 cm)				
No	16	51	67	0.68
Yes	3	6	9	
Location of nodule				
R/L lower lobe	7	15	22	0.72
R/L upper lobe	9	32	41	
Lingula/R middle lobe	3	10	13	
Experience				
First 30 procedures	9	21	30	0.77
Last 30 procedures	7	23	30	
Experience (year of procedure)				
First 2 years	4	14	18	1.00
Last 3 years	15	43	58	
CT bronchus sign				
No	8	15	23	0.25
Yes	11	42	53	
COPD/emphysema				
N	9	31	40	0.61
Υ	10	26	36	
PFTs, median (IQR)				
FEV1	1.53 (1.12–2.25)	1.735 (1.335–2.215)	1.7 (1.3–2.24)	0.32
FEV1%	67 (51–69)	81 (57.5–92)	69 (53–89)	0.04
DLCO%	52 (34–78)	67 (35–87)	62 (35–87)	0.40
RV%	143 (118.5–194)	114 (84–140.5)	122 (92–149)	0.11

IQR=Interquartile range, PFT=Pulmonary function test, FEV1=Forced expiratory volume in 1 s, RV=Residual volume, DLCO=Diffusion capacity, COPD=Chronic obstructive pulmonary disease, CT=Computed tomography

#### Discussion

Our study corroborates the findings of other published studies on ENB,<sup>[15-23]</sup> with a diagnostic yield of 80.2%, and a sensitivity of 73% for the detection of malignancy in PPN; with small complication rates (pneumothorax rate of 5.2% and bleeding rate of 2.6%). Out of these, only 1 patient (1.3%) required hospitalization with pneumothorax necessitating tube thoracostomy. Our study represents to the best of our knowledge, the first study evaluating the diagnostic yield of ENB in a safety net hospital done by pulmonologists not formally trained in IP.

The recently concluded NAVIGATE trial reported a 12 months diagnostic yield of 72.9%, with a reported sensitivity and negative predictive value for malignancy at 68.8% and 56.3%, which was similar to the findings in our study as well. A recent meta-analysis involving

40 studies including the NAVIGATE trial showed that ENB had an overall sensitivity of 77% for the detection of malignancy.<sup>[24]</sup> The sensitivity for the detection of malignancy was slightly lower in our study, but as the authors point out in a meta-analysis which included the NAVIGATE study, the sensitivity was positively associated with lung cancer prevalence (66% in their meta-analyses), which was lower in our cohort (48.6%). Two other meta-analyses done all report a diagnostic yield for any diagnosis between 70% and 74%.<sup>[19,20]</sup> In fact, most studies report a diagnostic yield in between 67% and 84%,<sup>[9]</sup> as corroborated in our study as well. Moreover, the complication rates of pneumothorax and bleeding in our study were similar to the other meta-analyses and the NAVIGATE study as well.<sup>[11,19,20]</sup>

Variables affecting diagnostic yield in ENB have included the presence of CT bronchus sign, lesion location and size, operator experience, size of the lesion, and the type of sedation used for the procedure.<sup>[10]</sup> Seijo et al. reported a significant difference in diagnostic yield with the presence of bronchus sign (79% vs. 31%), which was consistent in the NAVIGATE study as well (78 vs. 67%).<sup>[25]</sup> However, within our cohort, although the diagnostic yield differed between lesions with and without CT-bronchus sign (79% vs. 65%), this did not reach statistical significance. It is moreover pertinent to note that our diagnostic yield even in lesions without the CT bronchus sign was 65%, which was much higher than previously reported studies.<sup>[25]</sup> Similar to the NAVIGATE trial, the location of the nodule (upper lobe vs. middle lobe vs. lower lobes); the diagnostic yield between the locations did not have a statistically significant difference (78% vs. 76% vs. 68%). Similarly, size of the lesion also did not seem to show a statistically significant difference (71% vs. 78% in lesions <3 cm vs. >3 cm, P = 0.60). Moreover, further division into nodules of < 2cm and 2-3 cm also did not show a statistically significant difference (64% vs. 75%, *P* = 0.57).

Operator experience has been noted to affect the diagnostic yield in some studies,<sup>[17]</sup> this was not seen in our cohort (66% vs. 73% in first 30 patients vs. last 30 patients). Moreover, while the moderate sedation has been noted to affect diagnostic yield in a meta-analysis;<sup>[19]</sup> our cohort involved the use of conscious sedation in all the patients with a high diagnostic yield, similar to findings of Bowling et al.<sup>[26]</sup> Our study findings also suggest that ENB can be safely performed in patients with emphysema, and diagnostic yield was not affected by its presence, similar to the NAVIGATE study<sup>[11,27]</sup> and findings of Towe et al.<sup>[28]</sup> Along these lines, proximity to bullae also did not affect diagnostic yield (66% in our study) with no pneumothorax seen in any of these patients. While a trend towards lower diagnostic yield (64.9%) was seen in centers with low procedural volumes (0-4 cases/month) in the NAVIGATE study,<sup>[11]</sup> our study findings show that this factor does not affect the diagnostic yield.

Within our cohort, 43 cases had pulmonary function tests (PFT) available, among whom FEV1% was the only factor, which significantly affected diagnostic yield. In addition, a trend toward lesser diagnostic yield (P = 0.11) was seen in patients with increased residual volume. This may be due to better tolerance for the procedure thus allowing more time to perform a greater number of biopsies, brushes, other sampling procedures and also allowing for more sedation to be administered in patients with less lung dysfunction. This finding was not seen in other studies<sup>[11,28]</sup> including the NAVIGATE study where PFTs were evaluated; however, general anesthesia was used in >80% of procedures in the NAVIGATE study.<sup>[11]</sup> Moreover, among patients with FEV1 <50% (8 cases),

there was a 75% diagnostic yield with ENB, of which one case developed a pneumothorax requiring tube thoracostomy. Thus, ENB was found to be safe with a good diagnostic yield even in patients with severe COPD - including when done under moderate sedation, as in our study.

To date, ENB as a diagnostic tool has not been adopted widely outside the United States. Within the US itself, it is performed primarily in academic centers. Financial costs incurred may be a significant barrier to its adoption elsewhere, outside the US.<sup>[29]</sup> Moreover, the requirement for anesthesia and formal training to do such procedures may represent other barriers. Safety net hospitals have limited resources including anesthesia services, and thus are similar in many ways to hospitals in developing countries/low-income settings. Although the installation of navigational bronchoscopy and further accessories require a considerable financial investment from a hospital perspective, it presents an excellent diagnostic tool for accessing peripheral pulmonary lesions with minimal complications even in patients considered to be high risk such as severe COPD and pulmonary fibrosis with significant economic benefits downstream.<sup>[30]</sup> Within the same context, ENB may be one of the only tools available to approach PPN proximal to bullae, given the findings in our study. CT-guided biopsy in such cases can have disastrous complications with pneumothorax and potentially persistent air leak resulting in prolonged hospitalization with consequent patient morbidity, with resultant significant financial losses for hospitals, in addition. Indeed, in our cohort, out of the nondiagnostic PPNs, CT biopsy done had a 25% (4/12) pneumothorax rate with resultant hospitalization. Apart from diagnosing malignancy, ENB is also an excellent tool to diagnose benign etiologies.<sup>[29]</sup> In fact, the second-most common etiology of PPN in our cohort was tuberculosis, which may be a common etiology in countries outside the US, further suggesting the applicability of our findings in countries outside the US.<sup>[29]</sup> Our study highlights that navigational bronchoscopy can be performed easily even by pulmonologists not formally trained in IP with an excellent success rate in diagnosing benign and malignant conditions with minimal complications. Moreover, it can be safely performed under conscious sedation, including in patients with COPD and bullous emphysema. In addition, the institution of ENB serves as a valuable diagnostic tool in the hands of pulmonologists to access PPN even in low resource settings such as ours; a model which could easily be emulated in many other countries.

The major limitations of our study are in its inherent retrospective nature. As images were reviewed earlier, selection bias pertaining to cases with the CT bronchus sign would have added to the diagnostic success of the study. Moreover, ours is a single-center study, where the same team comprising of two pulmonologists, nurses, bronchoscopy technicians performed all of the bronchoscopies and who were thus well versed with the procedure; which may not be reproducible in all centers; thus limiting the generalizability of the study. Moreover, navigation error was not evaluated and ROSE was not performed in any of the ENB procedures. In addition, as mentioned above, given that a significant proportion of our cases included benign nodules including infection, our study findings may not apply to primary lung cancer centers. However, our study remains one of the few studies evaluating ENB in a community-based safety net hospital with a large indigent population base and scarce resources.

#### Conclusions

ENB is an excellent diagnostic tool, which can be safely instituted and performed within community hospitals with minimal resources with high success rates. Moreover, operator experience or frequency of procedures does not significantly affect diagnostic yield. Furthermore, it is a safe procedure with a low complication rate even in patients with severe emphysema, COPD and in fact maybe the best procedure to access PPN proximal to bullae. Future multicenter studies involving the use of this technology in similar settings and developing countries should be performed to evaluate the diagnostic success and applicability of this technology.

#### **Financial support and sponsorship** Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

#### **References**

- National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, *et al.* Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365:395-409.
- Wahidi MM, Govert JA, Goudar RK, Gould MK, McCrory DC; American College of Chest Physicians. Evidence for the treatment of patients with pulmonary nodules: When is it lung cancer? ACCP evidence-based clinical practice guidelines (2<sup>nd</sup> edition). Chest 2007;132:94S-107S.
- 3. Ost DE, Gould MK. Decision making in patients with pulmonary nodules. Am J Respir Crit Care Med 2012;185:363-72.
- Popovich J Jr., Kvale PA, Eichenhorn MS, Radke JR, Ohorodnik JM, Fine G. Diagnostic accuracy of multiple biopsies from flexible fiberoptic bronchoscopy. A comparison of central versus peripheral carcinoma. Am Rev Respir Dis 1982;125:521-3.
- Baaklini WA, Reinoso MA, Gorin AB, Sharafkaneh A, Manian P. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest 2000;117:1049-54.
- 6. Spyratos D, Papadaki E, Lampaki S, Kontakiotis T. Chronic

obstructive pulmonary disease in patients with lung cancer: Prevalence, impact and management challenges. Lung Cancer (Auckl) 2017;8:101-7.

- Heerink WJ, de Bock GH, de Jonge GJ, Groen HJ, Vliegenthart R, Oudkerk M. Complication rates of CT-guided transthoracic lung biopsy: Meta-analysis. Eur Radiol 2017;27:138-48.
- 8. Network. NCC. Non-Small Cell Lung Cancer, Version 2.2018. NCCN Clinical Practice Guidelines in Oncology; 2018.
- 9. Mehta AC, Hood KL, Schwarz Y, Solomon SB. The evolutional history of electromagnetic navigation bronchoscopy: State of the art. Chest 2018;154:935-47.
- Kalanjeri S, Holladay RC, Gildea TR. State-of-the-art modalities for peripheral lung nodule biopsy. Clin Chest Med 2018;39:125-38.
- 11. Folch EE, Pritchett MA, Nead MA, Bowling MR, Murgu SD, Krimsky WS, *et al.* Electromagnetic navigation bronchoscopy for peripheral pulmonary lesions: One-year results of the prospective, multicenter NAVIGATE study. J Thorac Oncol 2019;14:445-58.
- Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3<sup>rd</sup> ed.: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e142S-e165S.
- Al-Jaghbeer M, Marcus M, Durkin M, McGuire FR, Iftikhar IH. Diagnostic yield of electromagnetic navigational bronchoscopy. Ther Adv Respir Dis 2016;10:295-9.
- 14. Folch EE, Mahajan AK, Oberg CL, Maldonado F, Toloza E, Krimsky WS, *et al.* Standardized definitions of bleeding after transbronchial lung biopsy: A Delphi Consensus Statement From the Nashville Working Group. Chest 2020;158:393-400.
- Eberhardt R, Anantham D, Herth F, Feller-Kopman D, Ernst A. Electromagnetic navigation diagnostic bronchoscopy in peripheral lung lesions. Chest 2007;131:1800-5.
- Gildea TR, Mazzone PJ, Karnak D, Meziane M, Mehta AC. Electromagnetic navigation diagnostic bronchoscopy: a prospective study. Am J Respir Crit Care Med 2006;174:982-9.
- Lamprecht B, Porsch P, Wegleitner B, Strasser G, Kaiser B, Studnicka M. Electromagnetic navigation bronchoscopy (ENB): Increasing diagnostic yield. Respir Med 2012;106:710-5.
- Mahajan AK, Patel S, Hogarth DK, Wightman R. Electromagnetic navigational bronchoscopy: An effective and safe approach to diagnose peripheral lung lesions unreachable by conventional bronchoscopy in high-risk patients. J Bronchology Interv Pulmonol 2011;18:133-7.
- Wang Memoli JS, Nietert PJ, Silvestri GA. Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. Chest 2012;142:385-93.
- Gex G, Pralong JA, Combescure C, Seijo L, Rochat T, Soccal PM. Diagnostic yield and safety of electromagnetic navigation bronchoscopy for lung nodules: A systematic review and meta-analysis. Respiration 2014;87:165-76.
- Jensen KW, Hsia DW, Seijo LM, Feller-Kopman DJ, Lamb C, Berkowitz D, *et al*. Multicenter experience with electromagnetic navigation bronchoscopy for the diagnosis of pulmonary nodules. J Bronchology Interv Pulmonol 2012;19:195-9.
- 22. Sun J, Xie F, Zheng X, Jiang Y, Zhu L, Mao X, *et al.* Learning curve of electromagnetic navigation bronchoscopy for diagnosing peripheral pulmonary nodules in a single institution. Transl Cancer Res 2017;6:541-51.
- 23. Pearlstein DP, Quinn CC, Burtis CC, Ahn KW, Katch AJ. Electromagnetic navigation bronchoscopy performed by thoracic surgeons: One center's early success. Ann Thorac Surg 2012;93:944-9.
- 24. Folch EE, Labarca G, Ospina-Delgado D, Kheir F, Majid A, Khandhar SJ, *et al.* Sensitivity and safety of electromagnetic navigation bronchoscopy for lung cancer diagnosis: Systematic review and meta-analysis. 2020;23:S0012-3692(20)31502-6. doi: 10.1016/j.chest.2020.05.534. Epub ahead of print. PMID: 32450240.
- 25. Seijo LM, de Torres JP, Lozano MD, Bastarrika G, Alcaide AB,

Lacunza MM, *et al*. Diagnostic yield of electromagnetic navigation bronchoscopy is highly dependent on the presence of a Bronchus sign on CT imaging: Results from a prospective study. Chest 2010;138:1316-21.

- Bowling MR, Kohan MW, Walker P, Efird J, Ben Or S. The effect of general anesthesia versus intravenous sedation on diagnostic yield and success in electromagnetic navigation bronchoscopy. J Bronchology Interv Pulmonol 2015;22:5-13.
- Towe CW, Nead MA, Rickman OB, Folch EE, Khandhar SJ, Perry Y, *et al*. Safety of electromagnetic navigation bronchoscopy in patients with COPD: Results from the NAVIGATE study. J Bronchology Interv Pulmonol 2019;26:33-40.
- Towe CW, Ho VP, Kazakov J, Jackson T, Perry Y, Argote-Greene LM, *et al.* Severe chronic obstructive pulmonary disease is not associated with complications after navigational bronchoscopy procedures. Ann Thorac Surg 2017;104:290-5.
- Cheng SL, Chu CM. Electromagnetic navigation bronchoscopy: The initial experience in Hong Kong. J Thorac Dis 2019;11:1697-704.
- Garwood SK, ClenDening P, Hevelone ND, Hood KL, Pidgeon S, Wudel LJ Jr. Navigational bronchoscopy at a community hospital: Clinical and economic outcomes. Lung Cancer Manag 2016;5:131-40.