Ther Adv Respir Dis
2016, Vol. 10(4) 295–299
DOI: 10.1177/1753465816637053

Diagnostic yield of electromagnetic navigational bronchoscopy

Mohammed Al-Jaghbeer, Mathew Marcus, Martin Durkin, Franklin R. McGuire and Imran H. Iftikhar

Abstract

Objectives: Peripheral lung nodules (PLNs) are a common and diagnostically challenging finding. Electronavigational bronchoscopy (ENB) is used to increase the diagnostic yield and is considered safe. Multiple factors have been correlated with a better diagnostic yield. We sought to assess the effect of nodule characteristics and prior workup on the diagnostic yield in ENB.

Methods: This was a retrospective chart review of 98 ENB procedures in a community referral center. Two investigators reviewed patients' charts and images independently. Multiple logistic regression analyses was used to determine if factors such as bronchus sign, ground glass opacification (GGO), distance from pleura, prior use of endobronchial ultrasound (EBUS) and positron emission tomography (PET) had an impact on the diagnostic yield.

Results: We evaluated 98 ENBs performed in 92 patients. Most of the lesions were in the upper lobes. The diagnostic yield was 60%. A PET scan was performed prior to ENB in 47% of cases. EBUS was performed in 24% of cases. Bronchus sign was present in 60% of cases and GGO in only 6% of nodules. The odds ratio for diagnostic yield with a bronchus sign was 1.89 [95% confidence interval (CI): 0.83–4.33] and with nodules showing GGO characteristics it was 4.51 (95% CI: 0.51–39.68). Pneumothorax occurred in 6% of cases.

Conclusion: In our cohort, diagnostic yield was 60% with a 6% pneumothorax rate. A suggestive trend for the presence of bronchus sign on computed tomography scan, albeit statistically nonsignificant, as a predictor for improved diagnostic yield needs to be validated in a larger cohort.

Keywords: Electro-navigational bronchoscopy, Lung Nodules, Diagnostic Yield

Correspondence to:
Mohammed Al-Jaghbeer, MD
University of South Carolina, School of Medicine, One Medical Park, Suite 300, Columbia, SC 29203, USA
mohammed.aljaghbeer@palmettohealth.org

Mathew Marcus, MD
Martin Durkin, MD
Palmetto Health Richland, Columbia SC, USA

Franklin R. McGuire, MD, FCCP
Department of Interventional Pulmonology, Frye Regional Hospital, Hickory, NC, USA

Imran H. Iftikhar, MD, FCCP, FACP
Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, The Ohio State University Wexner Medical Center, OH, USA

Introduction

Lung nodules are a common finding on chest X-rays, with a higher incidence on chest computed tomography (CT) scans [Tan *et al.* 2003]. A lung nodule constitutes a possibility of cancer, especially in at-risk populations like smokers [Swensen *et al.* 1997]. The incidence is expected to increase with application of low-dose chest CT for lung cancer screening [National Lung Screening Trial Research Team, 2011]. Bronchoscopy with biopsy has been a diagnostic modality and is applied based on nodule size and patient's risk for malignancy [MacMahon *et al.* 2005]. Peripheral lung nodules (PLN) are more challenging and usually have a lower diagnostic yield on bronchoscopy with transbronchial biopsy [Chechani, 1996]. Electromagnetic navigational bronchoscopy (ENB) was introduced as a modality to increase the diagnostic yield for PLNs with fewer complications [Hautmann *et al.* 2005]. By creating a virtual bronchoscopic image of the airways from a chest CT, ENB helps navigate the steerable sensor probe on the bronchoscope towards the lesion.

Multiple factors have been correlated with a better diagnostic yield. The presence of a bronchus sign was found to correlate with diagnostic yield [Seijo *et al.* 2010]; however, this not been validated in another study [Brownback *et al.* 2012]. The distance between the nodule and pleura was found not to correlate with the diagnostic yield [Jensen

et al. 2012]. Combining endobronchial ultrasound (EBUS) with ENB was also found to increase the diagnostic yield in one study [Eberhardt *et al.* 2007].

Although positron emission tomography (PET) scan is used commonly in the workup for malignancy, its use has not been shown to significantly affect the diagnostic yield of ENB [Chhajed *et al.* 2005]. Ground glass opacification (GGO) is used to classify nodules on chest CT. Their presence has been correlated with better prognosis when compared with solid nodules [Suzuki *et al.* 2006], but it is not known if their presence has an effect on ENB yield.

In this retrospective single center study, we aimed to assess the effect of nodule characteristics (including location, presence of bronchus sign and distance from pleura) and other workup (PET-CT and EBUS) on the diagnostic yield and rate of complications in ENB.

Methods

Data were retrospectively collected by conducting chart reviews of the last consecutive 98 ENB cases performed between February 2008 and September 2014 at Palmetto Health Richland. All procedures were performed with the super-Dimension ENB system (superDimension, Inc., Minneapolis, MN). The procedures were performed under moderate sedation after an informed consent was obtained from each patient. The Institutional Review Board at Palmetto Health Richland approved the protocol (Pro00040638 HS-2509).

Data collected included patient demographics, nodule size (recorded as the largest diameter on axial imaging) and characteristics (in specific presence of bronchus sign and ground glass), lobar location, distance from pleura, use of fluoroscopy, EBUS and pre procedure PET. GGO was defined as focal nodular areas of increased lung attenuation through which normal parenchymal structures such as airways, vessels and interlobular septa can be defined. Bronchus sign was defined as the presence of a bronchus directly leading to the target lesion. Distance from pleura was calculated from center of nodule to parietal pleura from a location where an interventional radiologist would attempt a transthoracic biopsy. Additional data included the final diagnostic outcome and occurrence of pneumothorax (up to 24 hours post procedure). Diagnostic outcome was characterized as either positive-malignant or positive-nonmalignant or negative.

One investigator (M.A.) abstracted data from each patient's medical record. Two investigators (M.A., a pulmonary fellow, and I.H.I., a pulmonologist), independently reviewed each patient's CT images and calculated the distance from pleura, opined on the presence or absence of bronchus sign and ground glass characteristic for each nodular abnormality. Resolution of significant discrepancies was done by a third investigator (M.M., an interventional radiologist). The diagnostic yield was calculated as the number of diagnoses obtained by ENB divided by the total number of procedures multiplied by 100. Analyses were performed in R [R Development Core Team, 2008]. Multiple logistic regression analyses was used to determine if factors such as bronchus sign, GGO, distance from pleura, assistance with EBUS and prior imaging impacted the diagnostic yield. The final model in multiple logistic regression analysis included age, sex, location of mass, whether or not PET was performed, presence of bronchus sign and ground glass opacities, and distance from pleura.

Results

Data from a total of 92 patients was analyzed. The mean age was 64 (range: 31–90) and 50% were females. Average nodule size was 2.6 cm on widest diameter. Most nodules were located in the right upper and left upper lobes (Table 1). PET scan was performed prior to ENB in 47% of cases. EBUS was performed in 24% of cases. Bronchus sign was present in 60% of cases and GGO in only 6% of nodules. The overall diagnostic yield was 60%.

A logistic regression model building process was carried out, using an Akaike information criterion (AIC). The outcome variable was whether a diagnosis (positive-malignant, positive-nonmalignant or negative) was reached or not. Main effect candidate predictor variables were age at procedure, location of nodule, whether or not PET scan was performed, presence of bronchus sign, GGO and distance from pleura. Tests for linearity of the continuous predictors were performed by entering a quadratic term into the model. The final model is shown in Figure 1.

The odds ratio for diagnostic yield with a bronchus sign was 1.89 [95% confidence interval (CI):

Table 1. Baseline characteristics of participants.

***n* (total number of procedures)**	98			
Age (mean ± SD)	64			
Gender (% female)	51			
Nodule lobar location	***n* (98)**	**Distance from pleura (mean ± SD)**	**Bronchus sign (%)**	**Diagnostic yield (%)**
RUL	29	2.8 cm	15/29 (52%)	18/29 (62%)
RLL	15	2 cm	8/15 (53%)	9/15 (60%)
LUL	24	3.1 cm	14/24 (58%)	15/24 (63%)
LLL	15	6.4 cm	11/15 (73%)	7/15 (47%)
RML	10	3.6 cm	9/10 (90%)	7/10 (70%)
Lingula	5	3.2 cm	2/5 (40%)	1/5 (20%)

LLL, left lower lobe; LUL, left lower lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; SD, standard deviation.

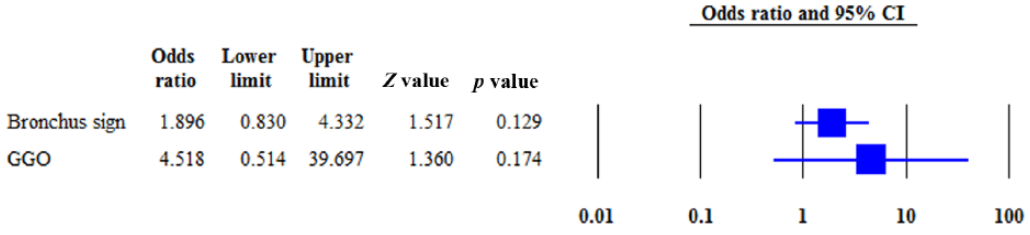

Figure 1. Final model of odds ratio for prediction of diagnostic yield.
CI, confidence interval; GGO, ground glass opacification.

0.83–4.33) and with nodules showing GGO characteristics it was 4.51 [95% CI: 0.51–39.68]. Table 1 summarizes the diagnostic yield based on location of nodules, presence of bronchus sign and GGOs. Pneumothorax was seen in 6% of the cases.

Discussion

The 60% overall diagnostic yield in our study is comparable with what is reported in most studies [Jensen *et al.* 2012; Eberhardt *et al.* 2007; Makris *et al.* 2007]. None of the variables studied were predictive of diagnostic yield, although the presence of bronchus sign narrowly eluded statistical significance. Seijo and colleagues in a study of 51 consecutive patients undergoing ENB showed a diagnostic yield of 67% with the presence of bronchus sign as predictive of higher diagnostic yield [Seijo *et al.* 2010]. Fluoroscopic guidance was used in 100% of ENB procedures in our study.

ENB using superDimension does not allow respiratory gating as 30–40% of nodules move >2cm in upper lobes and >4cm in lower lobes with diaphragmatic excursion [Chen *et al.* 2015]. Therefore using fluoroscopic guidance allows for better navigation. In a study where ENB was used without fluoroscopic guidance, the diagnostic yield was 59% overall and 29% in the lower lobes which was attributed to navigation error [Eberhardt *et al.* 2007]. Navigation in the lower lobes is susceptible to error due to diaphragmatic movement during breathing. The diagnostic yield for lesions in the lower lobes in our study was also comparatively lower (right lower lobe 57%, left lower lobe 40% *versus* right upper lobe 62% and left upper lobe 70%). Moreover, the location of pulmonary lesions on full inspiratory planning chest CT does not reflect the actual position of these lesions at the time of bronchoscopy [Chen *et al.* 2015].

In our study EBUS was not performed to confirm placement of ENB probe. In studies where EBUS was used diagnostic yield was improved. Herth and colleagues who showed a diagnostic yield of 70% when EBUS was utilized even though navigation with radial EBUS was successful in 89%

(48/54) of the cases [Herth *et al.* 2006]. Yamada and colleagues showed a diagnostic yield of 67% with the use of a radial ultrasound probe with higher yields when the probe was situated within the nodule rather than adjacent to it (88% *versus* 61%) [Yamada *et al.* 2007]. Asano and colleagues reported a diagnostic yield of 84.4% when virtual navigational bronchoscopy was combined with ultrathin bronchoscopy and radial probe EBUS [Asano *et al.* 2014]. Radial ultrasound provides real-time confirmation for the placement of the guide catheter in or near the nodule. New ENB systems are now being utilized that not only allow for real-time confirmation of target lesions with simultaneous use of EBUS and navigation, but also use a 0.5–3.0 mm slice thickness inhalation and exhalation CT scan protocol for increased accuracy and mapping of target lesions.

All ENB procedures in our study were performed with the availability of rapid onsite cytologic evaluation (ROSE). ROSE has been shown to improve the diagnostic yield of transbronchial aspirates as it leads to fewer biopsies, and in a way provides confirmation of catheter placement when the correct tissue being sampled returns diagnostic on preliminary histological exam [Baram *et al.* 2005]. The pneumothorax rate in our study was 6%. The overall safety of ENB is comparable with that of standard bronchoscopy and better than CT-guided needle biopsy [Leong *et al.* 2012].

Several points limit the generalizability of our findings. This was a single center experience with a limited number of cases. ENB was performed in moderate sedation without rigid bronchoscopic intubation technique or general anesthesia. We also did not evaluate navigation error in our study which was due to the retrospective nature of our study.

In summary, we have shown a diagnostic yield of 60% and low complication rate at a small tertiary level hospital where all procedures were done using ROSE and fluoroscopy. Baring the presence of bronchus sign on CT scan, which fell slightly short of statistical significance possibly due to low power of the study, none of the other variables studied were predictive of an improved diagnostic yield.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

Asano, F., Eberhardt, R. and Herth, F.J.F. (2014) Virtual Bronchoscopic Navigation for Peripheral Pulmonary Lesions. *Respiration* 88: 430–440.

Baram, D., Garcia, R. and Richman, P. (2005) Impact of rapid on-site cytologic evaluation during transbronchial needle aspiration. *Chest* 128: 869–875.

Brownback, K., Quijano, R., Latham, H. and Simpson, S. (2012) Electromagnetic navigational bronchoscopy in the diagnosis of lung lesions. *J Bronchology Interv Pulmonol* 19: 91–97.

Chechani, V. (1996) Bronchoscopic diagnosis of solitary pulmonary nodules and lung masses in the absence of endobronchial abnormality, *Chest* 109: 620–625.

Chen, A., Pastis, N., Furukawa, B. and Silvestri, G. (2015) The effect of respiratory motion on pulmonary nodule location during electromagnetic navigation bronchoscopy, *Chest* 147: 1275–1281.

Chhajed, P., Bernasconi, M., Gambazzi, F., Bubendorf, L., Rasch, H., Kneifel, S. *et al.* (2005) Combining bronchoscopy and positron emission tomography for the diagnosis of the small pulmonary nodule ⩽3 cm. *Chest* 128: 3558–3564.

Eberhardt, R., Anantham, D., Ernst, A., Feller-Kopman, D. and Herth, F. (2007) Multimodality bronchoscopic diagnosis of peripheral lung lesions: a randomized controlled trial. *Am J Respir Crit Care Med* 176: 36–41.

Hautmann, H., Schneider, A., Pinkau, T., Peltz, F. and Feussner, H. (2005) Electromagnetic catheter navigation during bronchoscopy: validation of a novel method by conventional fluoroscopy, *Chest* 128: 382–387.

Herth, F., Eberhardt, R., Becker, H. and Ernst, A. (2006) Endobronchial ultrasound-guided transbronchial lung biopsy in fluoroscopically invisible solitary pulmonary nodules: a prospective trial. *Chest* 129: 147–150.

Jensen, K., Hsia, D., Seijo, L., Feller-Kopman, D., Lamb, C. and Berkowitz, D. (2012) Multicenter experience with electromagnetic navigation bronchoscopy for the diagnosis of pulmonary nodules, *J Bronchology Interv Pulmonol* 19: 195–199.

Leong, S., Ju, H., Marshall, H., Bowman, R., Yang, I., Ree, A. *et al.* (2012) Electromagnetic navigation bronchoscopy: a descriptive analysis. *J Thorac Dis* 4: 173–185.

MacMahon, H., Austin, J., Gamsu, G., Herold, C., Jett, J., Naidich, D. *et al.* (2005) Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. *Radiology* 237: 395–400.

Makris, D., Scherpereel, A., Leroy, S., Bouchindhomme, B., Faivre, J., Remy, J. *et al.* (2007) Electromagnetic navigation diagnostic bronchoscopy for small peripheral lung lesions. *Eur Respir J* 29: 1187–1192.

National Lung Screening Trial Research Team (2011) Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 365: 395–409.

Seijo, L., de Torres, J., Lozano, M., Bastarrika, G., Alcaide, A., Lacunza, M. *et al.* (2010) 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* 138: 1316–1321.

Suzuki, K., Kusumoto, M., Watanabe, S., Tsuchiya, R. and Asamura, H. (2006) Radiologic classification of small adenocarcinoma of the lung: radiologic-pathologic correlation and its prognostic impact. *Ann Thorac Surg* 81: 413–419.

Swensen, S., Silverstein, M., Ilstrup, D., Schleck, C. and Edell, E. (1997) The probability of malignancy in solitary pulmonary nodules. Application to small radiologically indeterminate nodules. *Arch Intern Med* 157: 849–855.

Tan, B., Flaherty, K., Kazerooni, E. and Iannettoni, M. American College of Chest Physicians (2003) The solitary pulmonary nodule. *Chest* 123: 89S–96S.

Yamada, N., Yamazaki, K., Kurimoto, N., Asahina, H., Kikuchi, E., Shinagawa, N. *et al.* (2007) Factors related to diagnostic yield of transbronchial biopsy using endobronchial ultrasonography with a guide sheath in small peripheral pulmonary lesions. *Chest* 132: 603–608.