






ORIGINAL ARTICLE

Safety and diagnostic performance of pulmonologists performing electromagnetic guided percutaneous lung biopsy (SPiNperc)

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ABSTRACT

Background and objective: Percutaneous lung biopsy for diagnostic sampling of peripheral lung nodules has been widely performed by interventional radiologists under computed tomography (CT) guidance. New technology allows pulmonologists to perform percutaneous lung biopsies using electromagnetic (EM) guided technology. With the adoption of this new technique, the safety, feasibility and diagnostic yield need to be explored. The goal of this study was to determine the safety, feasibility and diagnostic yield of EM-guided percutaneous lung biopsy performed by pulmonologists.

Methods: We conducted a retrospective, multicentre study of 129 EM-guided percutaneous lung biopsies that occurred between November 2013 and March 2017. The study consisted of seven academic and three community medical centres.

Results: The average age of participants was 65.6 years, BMI was 26.3 and 50.4% were females. The majority of lesions were in the right upper lobe (37.2%) and left upper lobe (31.8%). The mean size of the lesions was 27.31 mm and the average distance from the pleura was 13.2 mm. Practitioners averaged two fine-needle aspirates and five core biopsies per procedure. There were

SUMMARY AT A GLANCE

Lung cancer screening has led to the discovery of over 1 million pulmonary nodules each year. New technology allows pulmonologists to perform percutaneous lung biopsies using electromagnetic (EM) guided technology. In this retrospective analysis, we demonstrate that EM percutaneous needle biopsy is safe, feasible and provides an acceptable diagnostic yield.

23 (17.8%) pneumothoraces, of which 16 (12.4%) received small-bore chest tube placement. The diagnostic yield of percutaneous lung biopsy was 73.7%. When EM-guided bronchoscopic sampling was also performed during the same procedural encounter, the overall diagnostic yield increased to 81.1%.

Conclusion: In this large multicentred series, the use of EM guidance for percutaneous lung biopsies was safe and feasible, with acceptable diagnostic yield in the hands of pulmonologists. A prospective multicentre trial to validate these findings is currently underway (NCT03338049).

Key words: lung cancer, bronchoscopy and interventional techniques, pneumothorax, pathology.

INTRODUCTION

The National Lung Screening Trial (NLST) showed a 20% mortality decrease when using low-dose computed

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tomography (CT) screening compared to conventional radiology for the detection of lung cancer.¹ With over 8 million Americans meeting the criteria for lung cancer screening,² accurate and rapid diagnosis of suspicious solitary pulmonary nodules (SPN) is needed. There are over 10 million chest CT scans performed each year in the United States in which an estimated 1.5 million nodules are discovered.^{3–5} This number is expected to increase given the endorsement of low-dose CT scans for lung cancer screening by the US Preventative Services Task Force (USPSTF).^{1,6} Successful diagnosis of an early stage lung cancer gives an opportunity to cure patients of the disease; however, the majority of nodules biopsied will be benign and thus improved minimally invasive techniques are needed to help reduce unnecessary surgery.⁷

The current common procedures used to diagnose SPN are surgical biopsy, percutaneous lung biopsy and bronchoscopy.⁸ Surgical biopsies have a high diagnostic yield, but at the cost of undergoing a more invasive and lengthy procedure under general anaesthesia and a higher morbidity than either of the other two options. Typically, interventional radiologists perform percutaneous lung biopsies under CT guidance, often performing multiple pleural punctures to make a diagnosis in real time. Although diagnostic yield is higher than bronchoscopy alone, this comes at the cost of higher procedural complications. A large population-based study of over 15 000 patients found a 16% pneumothorax rate and a 1% risk of major haemorrhage in patients undergoing a CT-guided lung biopsy.⁹ Although the bronchoscopic yield for SPN historically remains low, some advantages to bronchoscopy include a lower complication rate¹⁰ as well as the ability to stage the disease at the time of diagnosis with mediastinal and hilar sampling using endobronchial ultrasound (EBUS).¹¹

A recent technological advancement, electromagnetic (EM) guided percutaneous lung biopsy, has become available. The system allows clinicians to biopsy an SPN by performing a single percutaneous pass through the visceral pleura under EM guidance alone without the need for real-time CT or fluoroscopic guidance. The procedure is performed under EM guidance that is linked to a CT scan obtained just prior to the procedure.

This platform provides proceduralists the novel capability of performing an algorithmic approach to the procedure to potentially optimize yield and decrease procedural complications by performing EBUS for lymph node staging first in the presence of rapid on-site evaluation (ROSE) and if there is no evidence of nodal involvement, under the same procedural setting, attempt an EM-guided bronchoscopy. The EM-guided bronchoscopy and EM percutaneous lung biopsy can be performed using the same software. If a diagnosis is unachievable with a bronchoscopic approach, the proceduralist can pivot again to perform an EM-guided percutaneous lung biopsy during the same procedural setting. This procedure may take place in a procedure suite or operating room, and adds approximately 20 min to the total procedure time.¹²

The goal of this study was to assess the safety, feasibility and diagnostic yield of pulmonologists performing an EM-guided percutaneous lung biopsy.

METHODS

This was a multicentre, retrospective study on pulmonologist performed EM percutaneous lung biopsies from November 2013 through March 2017. Institutional Review Board approval with waiver of consent was obtained from each of the 10 individual institutions (Institutional Review Board 00116317) prior to initiation of data collection. All patients who received an EM percutaneous lung biopsy were identified using CPT codes (32405 and 10022) and were included in the data analysis. All procedures were performed using the Veran SPiNperc EM guidance system (Veran Medical, St Louis, MO, USA). The outcomes for this study included safety, feasibility and diagnostic yield of this procedure.

All patients were referred to pulmonology for a lung lesion suspicious for cancer, and were scheduled to undergo EM navigational bronchoscopy and EM-guided percutaneous lung biopsy. All patients received a chest CT scan on the day of the procedure with 0.5 mm intervals and 0.67–0.75 mm thickness, with navigational tracking pads (vPAD2, Veran Medical) in place which leads to the creation of a trackable virtual airway map (Veran Medical). Pre-procedure, using the software platform, the physician performing the procedure identified and marked the target lesion and determined where on the chest wall the needle would be placed in order to percutaneously access the lesion. The software then provided the site of entry and trajectory of the needle during real-time EM guidance for the percutaneous approach. All patients were placed under moderate or deep sedation for the bronchoscopy, which was continued throughout the duration of the procedure if EM-guided percutaneous needle biopsy was performed. An EM tip tracked biopsy needle introducer was used under navigational guidance to identify the previously determined entry site. Upon localization of the nodule, an introducer needle was passed through the visceral pleura and a 20-gauge Chiba needle used for fine-needle aspiration followed by a 20-gauge coaxial core biopsy instrument (SuperCore Argon Medical, Frisco, TX, USA) was utilized through the introducer needle to obtain tissue samples. Upon completion of the lung biopsy, the introducer needle was removed and a bandage was placed. The complete details of this procedure have been previously described and are illustrated in Figure 1.¹² Upon completion of the procedure, all patients were evaluated by chest X-ray or thoracic ultrasound for pneumothorax.

Data analysis

Demographic information, including age, sex, race, smoking history and history of lung disease, was collected. Characteristics of the biopsied nodule including location, size, morphology, distance from the pleura and Positron emission tomography scan avidity were collected. The number of tissue samples, adverse events and diagnostics were recorded when available.

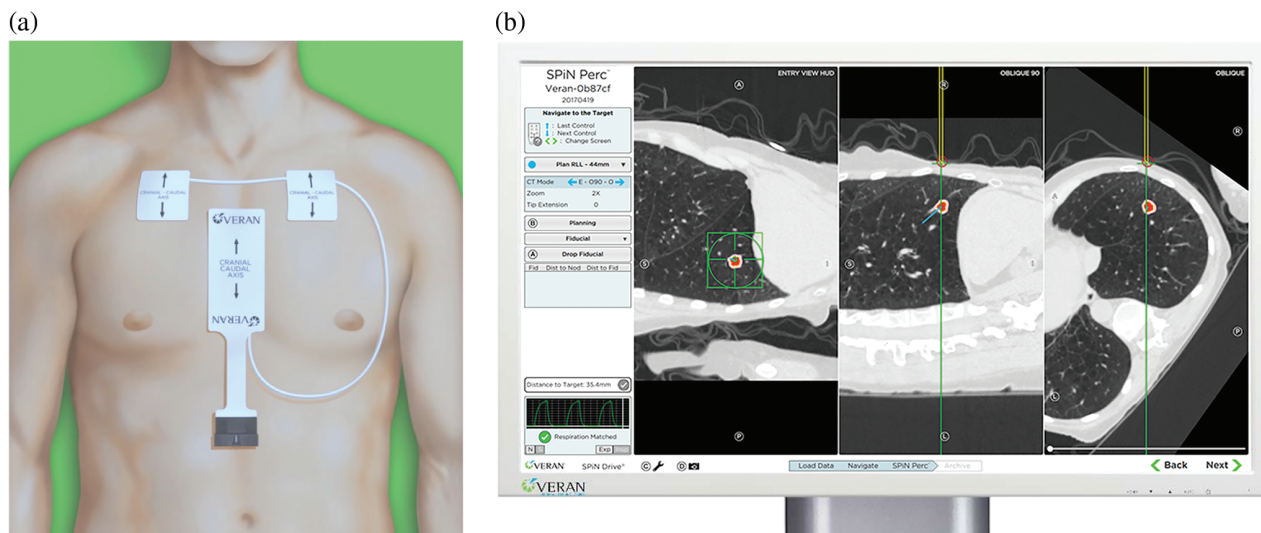


Figure 1 Electromagnetic (EM) navigational trackpad placement and percutaneous lung biopsy planning programme. The panel on the left shows the placement of the tracking pads needed prior to computed tomography (CT) scan to utilize the EM navigational software. These pads can be shifted to the left or the right in order to clear access for the percutaneous lung biopsy. The panel on the right shows the planning screen used prior to performing the transcutaneous needle biopsy. The programme will identify the nodule, which can be optimized by the user, followed by placement of a virtual percutaneous needle. The placement of the needle aids the user in locating the optimal site to perform the percutaneous needle biopsy.

Additional adverse event data were collected, including rates of pneumothorax, site of bleeding, haemoptysis, infection and post-procedure admission. Diagnostic yield data, including adequacy of sample, EM-guided percutaneous lung biopsy and FNA yield, if another procedure was performed and associated yield and final diagnosis were obtained. A biopsy was deemed diagnostic only if there was a definitive neoplastic diagnosis (adenocarcinoma, small cell carcinoma, etc.) or a definitive benign diagnosis (fibrosis, granuloma, etc.) with confirmed radiographic stability up to 1 year. Cellular atypia or lung parenchyma without a confirmed pathologic diagnosis, with or without radiographic stability, was considered incomplete in the final analysis. All patients with incomplete data were excluded from the diagnostic analysis of the statistics.

A large proportion of participants were obtained from a single centre. Because of this, we conducted a secondary analysis comparing this site to the remaining sites pertaining to diagnostic yield and adverse event data. Continuous variables are described using means with SD or range. Dichotomous variables are summarized as simple proportions. Simple t-tests were used to compare populations when necessary. Logistic regression was used to identify potential risk factors for both adverse events and diagnostic yield. A *P*-value of <0.05 was considered statistically significant. All statistics were performed using STATA 14.2 (StataCorp LLC, College Station, TX, USA).

RESULTS

There were 129 patients who received EM-guided percutaneous lung biopsies identified at 10 centres. A consort diagram can be found in Figure 2. Of these centres, seven were academic sites and three

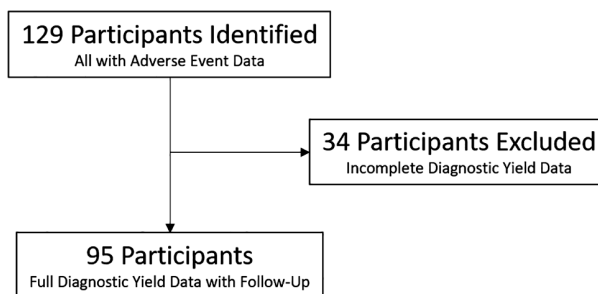


Figure 2 Patient recruitment flow diagram.

community sites. The average age of participants was 65.6 years, and half were females. The baseline characteristics are shown in Table 1.

The characteristics of the lesions sampled are shown in Table 2. The majority of lesions were located in the upper lobes. There was a mean of one pass of the introducer needle into the target (range: 1–3) performed per patient with the introducer needle. There were two FNA (range: 0–7) and five core (range: 0–10) biopsies taken.

Adverse event data are presented in Table 3. The location of the nodule biopsied was not an independent risk factor for an adverse event (OR: 0.87; 95% CI: 0.67, 1.13). Given these findings, it was excluded from the multivariable analysis. There was no association between the presence of an adverse event and size of the lesion (OR: 0.97; 95% CI: 0.94, 1.01; for each 1 mm increase in nodule size). There was a trend towards increased risk of adverse events seen with increasing distance from the pleura (OR: 1.02; 95% CI: 0.99, 1.05; for each 1 mm increase in nodule size). The presence

Table 1 Baseline characteristics

Characteristic	All patients
Age, mean (range)	65.52 (27–91)
Female sex (%)	50.40
BMI, mean (SD)	26.30 (5.97)
Race (%)	
White	61.24
Black	18.60
Smoking history	
Current (%)	31.78
Prior (%)	51.16
Never (%)	17.05
Pack-years, mean (SD)	28.0 (23.56)
History of COPD (%)	38.76
History of emphysema on CT (%)	55.04

CT, computed tomography.

Table 2 Lung nodule characteristics

Characteristics	All patients
Location (%)	
Right upper lobe	37.21
Right middle lobe	10.85
Right lower lobe	7.75
Left upper lobe	31.78
Left lower lobe	7.75
Lingula	4.65
Size (mm), mean (range)	27.31 (9–140)
Distance from the pleura (mm), mean (range)	13.20 (0–63)

Table 3 Adverse events

Adverse event	Percentage of patients (<i>n</i> = 129)
Overall	29 (22.5%)
Pneumothorax	23 (17.8%)
Requiring chest tube placement	16 (12.4%)
Minor bleeding	2 (1.6%)
COPD exacerbation	1 (0.78%)
Transient hypercapnia	2 (1.6%)
Transient hypoxaemia	1 (0.78%)

of emphysema on CT scan, history of COPD and number of pack-years smoking also did not lead to increased odds of an adverse event. As the size of lesion increased, there was a decreased risk of pneumothorax (OR: 0.95; 95% CI: 0.90, 1.01; for each 1 mm increase in nodule size). There was no association between the number of pleural punctures with the introducer needle and risk of pneumothorax. There was also no association between the number of core biopsies, or FNA, and the risk of an adverse event.

Ninety-five participants had complete data reporting available for diagnostic yield, after excluding patients

Table 4 Diagnoses obtained, electromagnetic percutaneous diagnosis versus all diagnoses

Diagnosis	Percutaneous diagnosis (<i>n</i> = 70)	All diagnoses (<i>n</i> = 95)
Malignant		
Adenocarcinoma	23 (31.9%)	32 (33.7%)
Squamous cell carcinoma	13 (18.1%)	20 (21.1%)
Neuroendocrine	3 (4.2%)	3 (3.2%)
Sarcomatoid carcinoma	2 (2.8%)	2 (2.1%)
Hurthle cell	1 (1.4%)	1 (1.1%)
NSCLC, undifferentiated	1 (1.4%)	1 (1.1%)
Metastases	1 (1.4%)	4 (4.2%)
SCLC	0	1 (1.1%)
Benign		
Fibrosis	6 (8.3%)	6 (6.3%)
Granuloma	6 (8.3%)	8 (8.4%)
COP	5 (6.9%)	5 (5.3%)
Inflammatory	5 (6.9%)	5 (5.3%)
Infection	3 (4.2%)	5 (5.3%)
Hamartoma	1 (1.4%)	2 (2.1%)

NSCLC, Non-Small Cell Lung Cancer; SCLC, Small Cell Lung Cancer.

with incomplete data as defined in the methods. The overall diagnostic yield of EM-guided percutaneous lung biopsy was 73.7%. A detailed list of diagnoses can be found in Table 4. There was no association between diagnostic yield using EM-guided percutaneous needle biopsy and lesion size (OR: 1.03; 95% CI: 0.99, 1.08) which remained insignificant when analysed as a categorical variable. There was also no association in diagnostic yield and distance from the pleura (OR: 0.99; 95% CI: 0.96, 1.02), anatomical location (OR: 0.92; 95% CI: 0.69, 1.22), number of punctures (OR: 1.80; 95% CI: 0.43, 7.44), number of fine-needle aspirations (OR: 1.06; 95% CI: 0.70, 1.59) or the number of core biopsies obtained (OR: 0.78; 95% CI: 0.57, 1.08). When the lesion was abutting the pleura, there was a diagnostic yield of 85% and a lower pneumothorax rate of 10%. Patients who developed a pneumothorax also had an overall lower diagnostic rate of 63%. When EM-guided bronchoscopic sampling was also performed during the same procedural encounter, the overall diagnostic yield increased to 81.1%.

Fifty-one percent of all procedures were conducted at a single site. When comparing this site to the rest of the locations, where 10 or less cases were performed at each site, there was a higher yield and lower complication rate, although these results did not reach statistical significance. The single site had an 18.1% adverse event rate versus 27% at the remainder of the sites (*P* = 0.23). The single site also had a 15.1% pneumothorax rate versus 20.6% at the remaining sites (*P* = 0.42). Of the patients who had a pneumothorax, 7.6% received chest tubes at the single site, while 17.5% received chest tubes at the remaining sites (*P* = 0.09). There was also a diagnostic rate of 78.4% at the single centre versus 68.1% at the remaining sites (*P* = 0.26).

DISCUSSION

Until the introduction of EM-guided percutaneous lung biopsy, the routine options for percutaneous lung biopsies were performed with CT or ultrasound guidance. CT guidance has been the gold standard for the minimally invasive diagnosis of SPN with a high diagnostic yield but also a high complication rate when compared to bronchoscopy.^{11,13–15} Complication rates of 38.8% for core biopsies and 24% for FNA from radiologists performing CT-guided percutaneous lung biopsy were reported in a recent meta-analysis.¹⁶ Another new approach to diagnosing these lesions includes bronchoscopic transparenchymal biopsies, in which pilot studies have shown to have a diagnostic yield of 83%, although with a higher pneumothorax rate (up to 33%).^{17,18} A combined procedural approach for the diagnosis of pulmonary nodules by attempting a bronchoscopic diagnosis first to limit complications, followed by a percutaneous biopsy if the bronchoscopy is non-diagnostic, may be effective in limiting overall complications and increasing diagnostic yield. However, the feasibility to attempt a combined approach has been limited as few centres have a CT scanner within the bronchoscopy suite and lesions must abut the pleura to allow for adequate visualization under ultrasound guidance.¹⁹ In this study, we show that EM-guided percutaneous lung biopsy was feasible with an acceptable safety profile in the hands of pulmonologists, with diagnostic yields approaching CT-guided biopsies.

We did not identify an association between the number of pleural punctures with the introducer needle and risk of pneumothorax. This is likely due to the low number of participants ($n = 11$) who received greater than one pleural puncture. Of these 11, 3 (27%) suffered a pneumothorax in comparison to the rest of the participants in the study who only received one pleural puncture, with a 17.8% pneumothorax rate. The diagnostic rate of patients who had a pneumothorax was lower, at 63%. This is likely because the pneumothorax would lead to a shift in the nodule, which would likely not be accurately tracked by the software. Similar drops in diagnostic yield are reported in the CT-guided literature.

Until the implementation of EM-guided percutaneous lung biopsy, the only options for percutaneous lung biopsies were CT-guided and ultrasound-guided. CT-guided lung biopsy has been the standard for minimally invasive diagnosis of SPN, and has been shown to have a higher diagnostic yield than bronchoscopy alone.^{11,13–15} We have shown that EM-guided percutaneous needle biopsy is not only safe, but also has a diagnostic yield that may approach CT-guided percutaneous needle biopsies. Combining the use of EM-guided percutaneous lung biopsy with EM navigational bronchoscopy increased our diagnostic yield to 81.1%. Conceptually, this not only provides overall improved diagnostic yield over bronchoscopy alone, but also leads to a decrease in overall pneumothorax rates by limiting the percutaneous approach to only those cases where ROSE is non-diagnostic for the bronchoscopic phase of the procedure. Further increases in yield and

decreases in complications may also be seen with integration of EBUS with ROSE as the initial procedure but prospective validation is warranted.

Practitioner training is another important aspect of all procedures. With proper training on how to use the navigational software and equipment, coupled with expert teaching, competency in EM-guided percutaneous lung biopsy significantly increases.²⁰ This is demonstrated by our analysis showing that experts, who performed at a single centre with the highest volume of EM-guided percutaneous lung biopsies, had a higher diagnostic rate and lower complication rate than their counterparts. By undergoing appropriate training, the provider is able to better manipulate the angle of entry into the lesion, interpret the respiratory variation and limit their technique to a single pleural puncture.

There are limitations to this study. The study was retrospective, limiting us to data available by chart review. In addition, patients were identified by CPT codes showing that a patient received an EM percutaneous lung biopsy; this referral bias was not controlled for. Although this was a multicentre retrospective chart review, many of the physicians had limited experience with EM-guided percutaneous lung biopsy. All but one site performed under 10 procedures, and 51.2% of the participants included were seen at a single large academic centre, which also limits the generalizability. This highest volume single centre had a lower pneumothorax rate, 15% (7.6% chest tube rate), as well as a higher diagnostic yield (78.4%), although not statistically different from the pooled diagnostic yield and pneumothorax rate from the remaining centres. This leads us to believe that as centres perform more EM-guided percutaneous lung biopsies, there will be increased safety and diagnostic yield. In addition, 32% of the lesions diagnosed were confirmed benign thus reducing potential surgical complications by limiting benign resection rates. Lastly, we only received complete diagnostic data for 95 (74%) subjects. Given the retrospective nature of this study, it was difficult to obtain follow-up data on patients, and we elected to include only complete data in order to report the current true results.

Although the pneumothorax rates were lower than many reported studies on CT-guided percutaneous lung biopsies, there was an overall chest tube rate of 12.4%, which is higher than some reported studies in patients undergoing CT-guided biopsy. Our lower pneumothorax rate, in comparison to CT-guided biopsies, may be a function of imaging modality used to diagnose pneumothoraces. CT-guided biopsies verify the presence or absence of a pneumothorax using the CT scanner which is highly sensitive to diagnosing a pneumothorax, where the patients in this series were diagnosed using a combination of chest X-rays and thoracic ultrasound. Despite this, when adjusting for risk factors related to pneumothorax, we found that the highest volume single centre had a lower pneumothorax rate, 15% (7.6% chest tube rate), as compared to the entire study cohort. This leads us to believe that as centres perform more EM-guided percutaneous lung biopsies, there may be an overall decrease in pneumothorax rates. The authors also hypothesize that the clinicians in this study may also have had a lower

threshold to place chest tubes in the setting of a newer technique in conjunction with the use of minimally invasive small-bore chest tubes (8Fr or 14Fr) in all cases reported. No patients in the study suffered from a prolonged air leak.

In this study, we show that an EM-guided percutaneous lung biopsy approach yields a high diagnostic rate with minimal safety concerns and the added benefit of using a combined bronchoscopic and percutaneous staged approach to pulmonary nodule diagnostics in a single procedural setting. A prospective multicentre trial to validate these findings is currently underway (NCT03338049).²¹

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Disclosure statement

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Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CPT, current Procedural terminology; CT, computed tomography; EBUS, endobronchial ultrasound; EM, electromagnetic; FNA, fine needle aspiration; ROSE, rapid on-site evaluation; SPN, solitary pulmonary nodule.

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Supplementary Information

Additional supplementary information can be accessed via the *html* version of this article at the publisher's website.

Visual Abstract Electromagnetic guided transthoracic needle biopsy is safe, feasible and has high diagnostic yield