

Electromagnetic Navigation

Elektromanyetik Navigasyon

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ABSTRACT

Electromagnetic navigation is a novel tool which aids the diagnostic yield of flexible bronchoscopy for peripheral lung lesions and mediastinal lymph nodes. The procedure is safe, effective, and easy and can be performed with or without the use of fluoroscopy. It plays a complementary role with endobronchial ultrasound. It is potentially a helpful tool in improving outcomes from interstitial brachytherapy and cyberknife therapy. Its upfront cost and that associated with the disposable LG could hinder its popularity. Emerging radiological tools, such as "Lung Mapping" may pose a challenge to the technology of EMN.

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ÖZET

Elektromanyetik Navigasyon (EMN), fleksibl bronkoskopinin perifer akciğer lezyonlarında ve mediastinal lenf nodularında tanılabilirliğini arttırmaya yardımcı yeni bir sistemdir. Bu işlem güvenli, efektif ve uygulaması kolay olmakla beraber floroskopi eşliğinde veya floroskopi olmadan da gerçekleştirilebilir. Endobronşiyal ultrasonla beraber tamamlayıcı rol oynar. İnterstisyel brakiterapi ve cyberknife tedavî yöntemlerinin sonuçlarını iyileştirmeye yardımcı olan bir sistemdir. Sistemle beraber tek kullanımlık "yer saptayıcı kılavuzun" maliyetinin yüksek olması popülaritesini engellemektedir. "Akciğer haritalanması" gibi yeni ortaya çıkan radyolojik sistemler ileride elektromanyetik navigasyon ile boy ölçüşebilir.

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INTRODUCTION

Flexible bronchoscopy (FB) is primarily used to sample pathologic lesions involving the tracheobronchial tree as well as lung parenchyma. It is the most commonly performed invasive procedure by pulmonologists. The procedure is frequently used to diagnose the nature of pulmonary nodules (PN). However, when it comes to the nodules located in the peripheral one third of the lung, the procedure is of limited value and establishing the diagnosis remains challenging [1]. Percutaneous needle aspiration of such lesions is frequently marred by pneumothorax requiring chest tube placement and hospitalization in half of the subjects with the complication [2,3]. Obviously, even Video Assisted Thoracic Surgery (VATS) would not be a practical approach in all patients with PN suspected to be malignancy.

Studies have demonstrated that Solitary PNs are seen 1 in 500 chest X-rays and are caused by a variety of conditions ranging from infectious granulomas to lung cancer [4]. Approximately 150,000 new Solitary PNs are discovered each year in the United States and even more

if screening computerized tomography (CT) of the chest is considered [5]. Based on a variety of factors, 10%-70% of these lesions could be malignant [6]. The prevalence of malignancy in PNs depends upon its size and is in the range of: 0%-1% for lesions less than 5 mms in size, 6%-28% for lesions 5-10 mms in size while it is 64%-82% for lesions larger than 20 mms in diameter [6-11].

The diagnostic yield of FB in PNs is limited by its inability to guide endobronchial accessories directly to the lesion. Its diagnostic yield depends on the size and location of the lesion and ranges between 20-84% [12-18]. For PNs less than 20 mms in diameter, the yield is 14% for those located in the outer third of the lung and it increases to 31% for the lesions located in the central two-thirds [19]. If the CT reveals a positive "bronchus sign", the yield of FB increases to 90%; unfortunately not a common occurrence for smaller lesions [20].

Similarly, the diagnostic yield of FB for mediastinal lymph nodes using transbronchial needle aspiration (TBNA) is reported to be between 15-83% [21]. Newer adjuvant technologies such as endobronchial ultrasound



Figure 1. Electromagnetic Location Board placed at the cephalic end of the bronchoscopy table



Figure 2. Microsensor, 8 mm long and 1 mm in diameter

(EBUS) and CT-fluoroscopy [22-26] have been proposed for guiding the tissue sampling to further the yield. Bronchoscopy under CT fluoroscopy has a success rate of 70%, however, the drawbacks of radiation exposure and the necessity of finding CT time for the procedure are considerable [23,26]. On the other hand EBUS technology is demanding, expensive and technically limited as the ultrasound probes can not be easily steered beyond the visible portions of the airways [24,27].

Real-time guidance and the ability to steer biopsy instruments to the peripheral lesion is critical for a successful FB procedure. Electromagnetic Navigation (EMN) is a novel technology that facilitates approach to peripheral lung lesions as well as mediastinal lymphnodes which are difficult to sample with conventional FB. The following is a concise review on the present day experience with EMN.

What is Electromagnetic Navigation?

The navigation system involves creating an electromagnetic (EM) field around the patient's chest and then directing endoscopic accessories using a micro-sensor placed upon previously acquired CT images. In other words, EMN is an image-guided localization device



Figure 3. Proximal end of the Locatable Guide. Computer wire is connected at the black socket. Red arrow on the rotating knob is positioned in the direction indicated by the navigation system and the handle is squeezed to change the direction of the micro-sensor

which assists in placing endobronchial accessories in the target areas of the lung. The principles and components of the EMN are provided below [27-31].

Electromagnetism

EMN operates on the principles of electromagnetism. The Electromagnetic Location Board (EMLB) produces low frequency EM waves. The board is 1-cm-thick, and 47 x 56 cm in dimension. It is placed under the cephalic end of the bronchoscopy table mattress to produce an EM field over the patient's chest (Figure 1).

A retractable sensor probe, 1mm in diameter and 8mm long is mounted on the tip of a flexible cable Locatable Guide (LG) (Figure 2). This micro-sensor is the main feature of the system. Once placed within the EM field, its position in x, y, z axes as well as in-motion (roll, pitch and yaw) is captured by the EMN system and displayed on the monitor in real-time at a rate of 166 images/second; superimposed upon previously acquired CT images.

Steerable Guide

The LG also has a feature that allows its distal end to be steered in 360 degrees, in 45 degree increments. The terms steerable and locatable guide are used interchangeably. Four separate wires control the movement of the distal end of the probe from the proximal end of the device using a rotating knob and control lever. The LG also provides a socket for connecting a wire, which relays the information from the sensor to the main computer (Figure 3).

Extended Working Channel (EWC)

An adult size flexible bronchoscope usually cannot be advanced beyond the 4th or 5th generation bronchus. Hence, the LG is inserted into a 130-cm-long, 1.9-mm-diameter flexible catheter, serving as a EWC (Figure 4). Once the tip of the bronchoscope is wedged into the segmental bronchus of interest, the LG is advanced along with the EWC under the guidance provided by the navigation system. Upon reaching the desired target, the LG is withdrawn, leaving the EWC in place. Endobronchial accessories are inserted through the EWC to sample the target.



Figure 4. Extended working Channel (blue) with locatable guide in place. Both accessories are navigated to the peripheral lung lesions once the tip of the scope is wedged in place

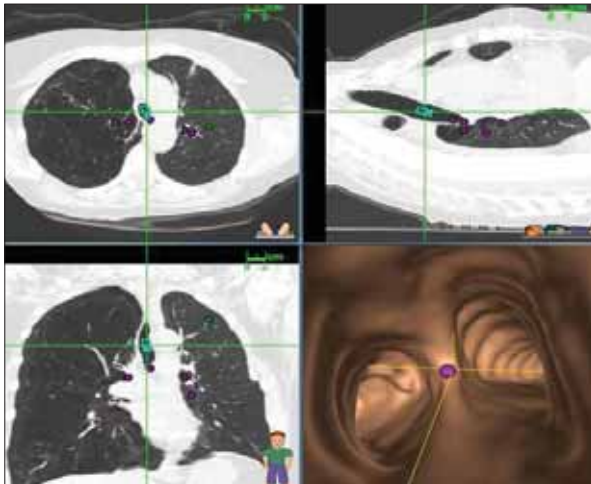


Figure 5. Computer Interphase: Dedicated program on the laptop provides coronal, axial and saggital views of the chest along with virtual bronchoscopy. Planning involves selecting the target (green) and the anatomical landmarks (purple)

Computerized Tomography

To overlay the patient's radiographic information onto the electromagnetic field a high resolution spiral CT scan of the chest is performed (with or without the contrast) using a special protocol. Three millimeter cuts are obtained at 1.5 mm intervals. High resolution protocol adds to the clarity of the images to be created for navigational purposes. The information is gathered in the DIACOM (Digital Imaging Communication in Medicine) format and placed either on a compact disc or directly downloaded on the system's laptop from the CT scanner. This information is used for the "Planning" and "Registration" of the procedure.



Figure 6. Navigation: Position of the micro-sensor in relation to the lesion is seen on coronal, sagittal and the axial views of the chest. Target lesion depicted as a green dot in all views. Lower right hand corner "Tip View": Orange ring and the red arrow represent the rotating knob and help steer towards the lesion

Computer Interphase

The Electromagnetic Navigation system requires use of two separate computers, a laptop with a dedicated program for "Planning" and a main system computer used for "Registration" and "Navigation".

Upon receiving the CT chest information the laptop program provides images of the chest in coronal, sagittal and axial fashion as well as in virtual bronchoscopy. These images are used to select the target as well as endobronchial anatomical landmarks ("Planning") (Figure 5). This information is uploaded into the system's main computer using an external memory device. The main computer software and the monitor allow the bronchoscopist to view the reconstructed CT images of the patient's anatomy once again in coronal, sagittal and axial views together with superimposed graphic information depicting the position of the LG as well as pre-identified anatomical landmarks and position of the target lesion. In addition, the computer also provides the "tip-view" (view from the micro-sensor), which helps steer the LG to the lesion by turning the rotation knob on the handle (Figure 6).

PROCEDURE

The procedure of EMN is performed with the following steps:

(1) Computerized Tomography Imaging

A spiral CT scan of the chest (4-liner, collimation 1mm, increment 1mm, table feed 6mm/s, 120 kVp, 70 mA) is performed using the conventional breath-hold technique in all patients with the protocol as described above, in a DIACOM format.

(2) Planning

The digitized information from the CT scan is downloaded into the software of the dedicated laptop. This information is now used to reconstruct graphic axial, coronal and sagittal views of the chest and virtual images of the bronchial tree. Between 5 and 7 prominent anatomic landmark "fiducial targets" (main carina, the right and left upper lobe carina, the middle lobe carina, and in some cases the lower lobe branching etc.) are

marked as "coordinates" on the virtual bronchoscopy image which are automatically depicted on corresponding CT images as well. The center of the target lesion is also identified and labeled in a similar fashion (Figure 5).

(3) Registration

The information gathered during the planning stage is uploaded into the system's main computer using an external memory device. FB is performed in the bronchoscopy suite where the EMN system is pre-calibrated for its surrounding metallic objects. The procedures can be performed either under general anesthesia or moderate sedation. Once the patient is placed on the examination table, three reference electrodes are fixed on the chest wall for compensation for respiratory, body or cough related movements. FB is performed in a usual fashion. The LG is inserted via the working channel of the scope. The radiological landmarks (fiducial targets) selected on the virtual bronchoscopy images are identified in-vivo and touched with the tip of the LG to register their location in the system's main computer to establish Radiographic-Anatomic alignment. Registration of all the above information into the computer software automatically synthesized a navigation scheme to approach the lesion with precision. Accuracy of navigation depends upon this Radiographic-Anatomic alignment, also referred as "average fiducial target registration error" (AFTRE); which defines registration quality. The AFTRE can be corrected by repositioning the misplaced landmark or by eliminating that with the greatest deviation. The registration error of 5 mm or less can be considered acceptable.

(4) Real-time Navigation

Following a successful registration, the scope with the LG in place is advanced towards the segmental bronchus of interest. The lesion is represented as a green dot on the "tip-view" portion of the system's monitor. The three-dimensional CT images are also displayed for the corresponding CT slice according to the actual position of the sensor. Once the flexible bronchoscope is wedged into the specific segmental bronchus, the LG and the EWC are steered to the target under the guidance of the 3-dimensional CT images, especially following the "tip-view" orientation. As the LG gets closer to the lesion, the green dot continues to get larger in a relative fashion. Once the LG reaches the location closest to the target, EWC is fixed at the proximal end of the biopsy channel of the scope by a special locking mechanism and the LG is withdrawn. A fluoroscopy can also be performed in an antero-posterior view to confirm that the LG has reached the desired area before its removal. Then the accessories such as biopsy forceps, transbronchial aspiration needle and endobronchial brush or endobronchial ultrasound probe can be inserted via EWC for either further confirmation or to obtain a tissue specimen.

RESULTS

A number of studies have been published establishing effectiveness of the EMN [27-37] (Table 1).

Schwarz et al. [28] performed the first animal trial to determine the practicality, accuracy and safety of the real time EMN in locating peripheral lung lesions in a swine model. The study proved that EMN was accurate when added to the standard bronchoscopy to assist in reaching peripheral lung lesions. Artificially created lung lesions were sampled without difficulty or complications, using conventional accessories.

Becker et al. [27] published the results of a pilot study in humans. They obtained biopsies of the peripheral lesions under the guidance of EMN in 30 adults. Evaluation was possible in 29 patients; definitive diagnosis was established in 20 patients (69%). EMN added 9 minutes of time to the bronchoscopy procedure. There was one pneumothorax requiring chest tube insertion. They concluded that EMN is feasible and safe as an aid to obtaining biopsies of peripheral lung lesions.

Hautmann et al. [30] performed a prospective evaluation of an EMN system for the diagnosis of peripheral infiltrates or solitary PNs. In all of the pulmonary infiltrates and solitary PNs, the navigation system was able to guide the sensor tip to the center of the lesion, despite some being undetectable by fluoroscopy. All the lesions were reached by EMN and tissue was sampled successfully for the histological examination. The biopsy results in three of five solitary PNs were positive for carcinoma, whereas normal lung tissue was obtained in the two remaining cases. All "masses" were positive for carcinomas. Biopsy results for infiltrates were diagnostic in five cases. In the remaining three, histological findings were nonspecific. There were no complications. Overall, EMN was well-tolerated and proved to be safe and useful in localizing small and fluoroscopically invisible lung lesions with an acceptable level of accuracy.

Schwarz et al. [29] also performed a human study following their animal trial on unreachable peripheral lung lesions (15-50 mm in size) under EMN guidance. The diagnostic sensitivity of the procedure was reported as 69%. This success rate was felt to be due to the road map created by the navigation system, which reduced trial and error attempts during the use of endobronchial accessories. No complications were reported.

A prospective, single center, pilot study was conducted by Gildea et al. [31] to determine the ability of EMN to sample peripheral lung lesions and mediastinal lymph nodes. Sixty subjects were enrolled and the diagnostic yield was 74% for the peripheral lesions and 100% for mediastinal lymph nodes. A diagnosis was obtained in 80.3% of bronchoscopic procedures with EMN. The lesions were accessed in all subjects. Two patients developed pneumothorax. There was no significant relationship between diagnosis and the size or location of the peripheral lesions or lymph nodes.

Prospective studies were undertaken by Makris et al. [32] and Eberhardt et al. [33] to determine the yield of EMN without using fluoroscopy in the diagnosis of peripheral lung lesions. The diagnostic yield was found to be 67% and 62.5% respectively and was independent of

Table 1. Diagnostic yield of EMN aided FB

Reference	Technique	N	Size (mm) Range or mean	Diagnostic yield (%)	AFTRE (mm) (mean±SD)	Procedure Duration (min)	Flouro	PNX % (n)
Becker (27)	EMN+ flouro	29	12-106	69	RE:6.1±1.7	NT:7.3 RT:2	+	3.3 (1)
Hauttman (30)	EMN+flouro	16	22±6	Not given	4.2	NT:+3.9min	+	0
Schwarz (29)	EMN+flouro	13	15-50	69	NE:5.7	TPT:46min	+	0
Gildea (31)	EMN+flouro	58	PL:22.8 LN:28.1	PL:74% LN:100%	RE:6.6±2.1 NE:9±5	RT:3±2 NT:7±6 TPT:51±6	+	3.4 (2)
Wilson (36)	EMN+flouro +ROSE	248	PL:2.1 LN:1.8	70-86%	RE:0.5±0.02	Not given	+	1.2 (3)
Makris (32)	EMN	40	23.5	62.5	RE:4±0.15 NE:8.7±0.8	Not given	-	7.5 (3)
Eberhardt (33)	EMN	89	24	67	RE:4.6±1.8 NE:9±6	RT:3.2±2.3 NT:4.5±3.4 TPT:29.9±6.5	-	2.2 (2)
Eberhardt (35)	EMN+EBUS	40	26	88	Not studied	Not studied	-	6* (3)
Lamprecht (37)	EMN+PET -CT+ROSE	13	30	76.9	Not studied	TPT:60	-	0

EMN: Electromagnetic navigation, ROSE: Rapid On-site Examination, EBUS: Endobronchial Ultrasound, PL: Peripheral lesions, LN: Lymph nodes, RE: Registration Error, NE: Navigation Error, NT: Navigation Time, RT: Registration Time, TPT: Total Procedure Time
iyileştirmeye AFTRE: Avarage fiducial target registration error, PNX: Pneumothorax * When only EMN was done

lesion size. There were 3 and 2 incidents of pneumothoraces, respectively. The EMN yield was found to be 77.2% if AFTRE was less than 4mm [32]. Diagnostic yield was lower for the upper lobe lesions probably due to the acute angle of the corresponding bronchus as well as for the lower lobes, probably related to the diaphragmatic movement [33]. Both studies concluded that EMN can be used as a stand alone procedure (without fluoroscopy) without compromising diagnostic yield or increasing the risk of pneumothorax.

It has also been established by a prospective, randomized trial that a combination of EBUS and EMN improves the diagnostic yield of FB in peripheral lung lesions without compromising safety [35]. In this particular study, 72% of all 118 patients recruited had a positive diagnostic yield via FB. Combined EBUS/EMN had a significantly higher diagnostic yield of 88% compared to that of EBUS (69%) and EMN (59%) alone. Another finding was that the diagnostic yield from the lower lobes was significantly lower, consistent with the previous study by Eberhardt [33]. The improved yield of the joint procedure was ascribed to combining the ability of EBUS to directly visualize the peripheral lung lesions with the precise navigation capabilities of EMN. The overall pneumothorax rate was 6 % (7 patients) and 6.3 % (5 patients) when EMN was used. Four of the 7 patients required a chest tube placement. Although this combination provides a higher diagnostic yield compared to either one of them alone, the issues of cost and training need to be addressed.

A retrospective, single center study was carried out to evaluate the diagnostic yield of bronchoscopy, guided

by EMN plus the Rapid On-Site Evaluation (ROSE) of the cytology specimens [36]. Of 248 subjects, 65% received a definitive malignant or non-malignant diagnosis on the day of the procedure. During the follow-up 12 patients (5%) were confirmed to be free of malignancy and 8 patients (3%) were confirmed as having malignant disease. 67 patients (27%) were lost for follow up (Inconclusive). Thus, on the day of the procedure in 173/248 (70%) of all patients, correct information was gathered. If all inconclusive cases are treated as non-diagnostic (worst case scenario) the yield was 70%, but if all inconclusive cases were treated as diagnostic (best-case scenario), the estimate was 97%. The diagnostic yield probably ranged between 70-97% based upon the assumptions made regarding the outcome of the cases that had an inconclusive diagnosis on the day of the procedure. In this particular study, pneumothorax was encountered in 3 patients and a few other minor complications, yet none of the latter was related to the use of EMN. It was concluded that the combination of EMN and ROSE can provide a better diagnostic yield in patients with a peripheral lung lesions.

Recently; the combination of EMN, PET-CT and ROSE were further studied for the routine diagnostic work-up of peripheral lung lesions [37]. EMN was performed in 13 subjects, where the PET-CT scans were the part of the diagnostic workup. In 76.9% of the patients EMN resulted in a definitive diagnosis. No pneumothorax or any other complications related to the procedure was encountered. In patients with peripheral lung lesions, EMN in combination with ROSE and prior PET-CT was shown to be safe and highly effective.

COMPLICATIONS

Pneumothorax is the most common complication encountered with the use of EMN and occurs in the range of 0-6% [27,31-33,35,36]. In the published studies related to EMN, 16 patients have developed pneumothorax. Four of these patients needed chest tube drainage, while in the remaining 12 it resolved spontaneously. Theoretically the rate of pneumothorax could be affected by AFTRE, as an error of even a few millimeters could be crucial in these small peripheral lesions, especially if the fluoroscopic guidance is not utilized.

Self-limiting bleeding may be encountered in some cases [27, 36]. It is believed that the EWC also facilitates the tamponading of the bleeding by allowing the scope to remain wedged at the subsegmental bronchus throughout the process [31,35].

There is also a possibility of EWC being dislodged from its primary site during sampling of the tissue, requiring repeat navigational stage of the procedure [31]. Use of fluoroscopy during the sampling of the tissue can help identify the problem. In a single case, repeated insertion and removal of biopsy forceps perforated the EWC [33].

Limitations:

We believe that the major obstacle to the wide spread use of the EMN is its cost and the need for expensive disposable LG and EWC. Medical economics will certainly limit its use in developing and third world countries.

FUTURE

EMN is a promising technology not only in diagnosing the peripheral lung lesions and mediastinal lymph nodes, but also may provide a means for therapeutic interventions for the treatment of lung cancer.

Recent advances in minimally invasive thoracic surgery have renewed an interest in the role of interstitial brachytherapy for lung cancer [38-41]. One of the studies has described the principles of navigated brachytherapy for treatment of a medically inoperable peripheral non-small cell lung cancer patient [41]. A right upper lobe lesion was treated with external-beam radiotherapy and navigated endoluminal brachytherapy. After successful localization of the lesion, EBUS was performed and a brachytherapy catheter was placed within the tumor. After the application of high-dose-rate brachytherapy, EBUS and CT demonstrated a partial, while histology showed a complete remission of the tumor. This finding advocates that navigated brachytherapy for peripheral pulmonary tumors not responsive to conventional treatment is achievable [41].

Studies have demonstrated that a minimally invasive robot-assisted (MIRA) lung brachytherapy system produced results that are equal to or better than those obtained with VATS and comparable to results with open surgery for peripheral, malignant lung lesions [40]. Following these findings, an integrated system involving modified EMN, EBUS and MIRA is being evaluated for

brachytherapy for the peripheral lesions. It appears that EMN with an improved robotic controller may help to perform minimally invasive robot-assisted lung brachytherapy, which may have a better outcome than standard VATS [39].

Sterotactic radiosurgery (Cyberknife) is a treatment option for patients who are medically unfit to undergo lung tumor resection [42]. This technology has been complemented by more targeted chemotherapeutic regimens, novel methods of administering more accurate and more concentrated doses of radiation therapy, and innovative local excisional methods. For an exact tumor ablation, Cyberknife requires fiducial marker placement in or near the tumor. In the past this was carried out via the transthoracic route under CT guidance with an obviously high risk of pneumothorax. When the fiducials are placed via standard bronchoscopy, they have a tendency to dislodge [43]. In a single study, a total of 39 fiducial markers were successfully deployed in 8 of 9 patients using EMN guidance without any complication [44]. This finding supports the notion that EMN can be used to deploy fiducial markers for Cyberknife radiosurgery safely and accurately. Larger, prospective and randomized studies are still needed before definite conclusions can be reached.

We believe that such uses of EMN will continue to flourish in the future.

SUMMARY

Electromagnetic navigation is a novel tool which aids the diagnostic yield of flexible bronchoscopy for the peripheral lung lesions and mediastinal lymph nodes. The procedure is safe, effective, and easy and can be performed with or without the use of fluoroscopy. It plays a complementary role with endobronchial ultrasound and has a potential to be a helpful tool in improving outcomes from interstitial brachytherapy and cyberknife therapy. Its upfront cost and that associated with the disposable LG could hinder its popularity. Emerging radiological tools, such as "Lung Mapping" may pose a challenge to the technology of EMN [45].

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