

REVIEW ARTICLE

ELECTROMAGNETIC NAVIGATION BRONCHOSCOPY

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ABSTRACT

Electromagnetic navigation is a novel diagnostic technique which allows bronchoscopic sampling of peripheral pulmonary nodules and mediastinal adenopathy. This technique is compatible with transbronchial biopsy forceps as well as with needle and catheter aspiration, and is therefore quite versatile. Electromagnetic navigation bronchoscopy is an established alternative to conventional computerized tomography (CT) guided fine needle aspiration, mediastinoscopy, endobronchial ultrasound (EBUS) and thoracotomy in a selected group of patients. Its excellent safety profile makes it an especially attractive technique for high risk patients with underlying pulmonary disease or comorbidities unable to undergo surgery or withstand a pneumothorax. Cytological samples obtained by electromagnetic navigation are suitable for molecular analysis, including determination of epidermal growth factor receptor (EGFR), K-ras, and anaplastic lymphoma kinase (ALK) mutations.

Key words: Bronchoscopy, Electromagnetic navigation, Lung Cancer, Biopsy.

INTRODUCTION

The peripheral pulmonary nodule continues to be a frustrating challenge for many bronchoscopists. Transbronchial biopsy, long established as a staple in the work up of a variety of pulmonary diseases including lung masses, infiltrates, and interstitial lung diseases has traditionally failed to achieve reliable yields in the diagnosis of medium-sized and small peripheral nodules. Diagnostic yields for nodules under 2 cm are particularly frustrating, and often do not exceed 30%, particularly if the nodule is located in the distal airways.¹ Results with conventional transbronchial needle aspiration of the mediastinum (TBNA) are somewhat more encouraging, though limited by widely fluctuating results. TBNA yields can be remarkable in centers with extensive experience, but may be frustrating in low-volume centers, or those with less experience with the technique, especially when onsite cytopathological assessment is not available.²

None of the currently established techniques, including fluoroscopy guided transbronchial biopsies and transthoracic fine needle aspiration (TTNA) have improved yields significantly,³ while safety remains a major concern with most, due to the risk of pneumothorax and uncontrolled bleeding. In general, the smaller the lesion, the lower the yield. It seems that only EBUS has afforded the bronchoscopist with a tool apt for the challenge, at least as far as the mediastinum is concerned, although results with peripheral lesions using radial probes are also encouraging.^{4,5,6} It is in this setting that electromagnetic navigation bronchoscopy (ENB) has established itself as an alternative to conventional biopsy methods providing a safe alternative with improved, if not optimal yields, in the diagnostic approach to peripheral pulmonary nodules. ENB is also useful as a guide to mediastinal sampling with a cytology needle, although its role in the work up of mediastinal adenopathy is overshadowed by the growing body of evidence supporting the use of EBUS in this clinical setting.

Success of ENB is based on three distinct characteristics of the technique. Namely: Adequate planning prior to the procedure using a dedicated software and data from a multirow CT scanner, real-time navigational feedback relayed to a computer and hence the operator from the electromagnetic probe, and the virtues of a steerable sensor which can make directed 360° turns along the pathway to the lesion.

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Description of the technique

Several navigational systems are currently or will soon be available worldwide for the diagnosis of peripheral lesions. Published data however relies for the most part on the Superdimension system (superDimension, Inc., Minneapolis, USA), currently known as iLOGIC. The iLOGIC system relies on four basic components which have not changed substantially since the initial technique was described more than a decade ago: an electromagnetic field generated by a board placed directly underneath the patient, a steerable handmade and calibrated electromagnetic probe, a reinforced extended working channel which fits through a therapeutic bronchoscope's 2.8 mm working channel, and the planning and executing software which provides real-time navigational information in a variety of formats, including the traditional CT projections (axial, coronal, and sagittal), phantom and tip views, as well as virtual bronchoscopic views. Some operators prefer to perform the procedure under conscious sedation, as in our case, while others employ general anesthesia. It is in any case imperative that the patient be comfortable as the procedure can take quite some time (>45 min.) and coughing can preclude adequate navigation and/or sampling. At our center we have performed procedures under conscious sedation with a combination of midazolam and fentanyl, but also using propofol, and occasionally general anesthesia employing a laryngeal mask airway or a conventional endotracheal tube.

All candidates for ENB must undergo CT scanning within one month of the procedure, since real-time navigation is based on a virtual reconstruction of the CT images. CT slices and intervals are specific to a given hardware/software combination, and must be saved in the digital imaging and communications in medicine (DICOM) format in order for the planning to proceed correctly. Procedure planning data is saved on a universal serial bus (USB) stick which provides the reference for real-time navigation with the patient lying supine and surrounded by the electromagnetic field.

Planning the procedure, getting there, and obtaining a sample

An adequate reconstruction of the patient's virtual bronchial tree based on the acquired CT images is essential for the procedure to be successful. Virtual reference points must be registered prior to the intervention in order for the hardware to understand the location of the steerable probe within the electromagnetic field, and therefore provide precise information in real time to the bronchoscopist during the procedure. Generally, the chosen reference points are easy to access and sufficiently spread out for the system to be able to determine accuracy and divergence when comparing the virtual tree with the patient's real bronchial tree. The main carina and interlobar carinas are often the best choices. Patients who have undergone pneumonectomy are especially challenging, as all reference points must reside in one hemithorax. Also, one or several targets are chosen during registration, in order for the system to be able to provide real time information regarding the remaining distance to a target during the procedure, much as one chooses a starting point and destination with a global positioning system (GPS) device in a car. Instead of relying on a satellite, the probe's position and movement are sensed within the electromagnetic field by three external sensors placed on the patient's chest wall. As in GPS navigation, several way points can be selected during registration in order to guarantee that a chosen route is leading to the target rather than away from it. Recent software improvements allow for the automatic generation of potential pathways to the target, which the operator must approve during registration and may be useful during real time navigation.

Essential data regarding the patient's airways, registration points, and targets are relayed to the hardware during the procedure by a USB storage device which has saved registration information during planning. During the procedure the bronchoscopist must first identify and register the selected reference points by touching them with the tip of the probe and pressing a foot pedal. The system then calculates the registration error known as divergence or AFTRE, and asks the operator for approval in order to commence navigation. In general, a divergence of 4 mm or less is considered optimal, although many experts will proceed with a mean divergence of 5-6 mm. If the divergence is too high, the system may recommend registering anew a given reference point which it believes to be the cause of a large error in registration. Once registration is complete, the extended working channel and the probe are simultaneously advanced through the airways. The appropriate turns are made using a hand-held device either by trial and error, or following a pre-determined pathway selected by the computer and approved during planning by the bronchoscopist. This process continues until the target is reached or the probe is close enough

for sampling to begin. The operator can toggle to different views during navigation in order to understand the position of the probe within the patient's thoracic cage, and be able to anticipate the next turn or adjustment in the probe's position which may bring the latter closest to the selected target. The system will inform the bronchoscopist at all times of the relative distance from the tip of the probe to the center of the target and its position in 3 dimensions. One must bear in mind that the location of the probe is reflected on the monitor's screen within a virtual world based on the patient's original CT scan slices. Any significant change in the position or size of the target as may happen when pleural fluid shifts within the pleural space in a patient with a pleural effusion, or a pneumothorax resulting from the sampling itself will lead to significant "undetectable" shifts in the target's position and therefore failure to obtain a diagnosis. This is why the CT scan used for planning must be recent, in order to avoid sampling error. The patient's movement, as long as it is within the electromagnetic field is accounted for by the system, since the external sensors move with the patient. However, breathing can be a problem, especially when a lesion is adjacent to the diaphragm or close to the interlobar fissures, as neither the static CT images obtained during planning nor the system itself can account for respiratory movement.

Navigation is much more straightforward when the target is a mediastinal lymph node, as registration error affects the peripheral airways more than the central airways, and one always has visual feedback regarding the probe's location when attempting to locate a lymph node in close proximity to the trachea or mainstem bronchi. Traditional landmarks are also helpful in this respect. Such landmarks do not exist beyond the central airways. Either way, once the target is reached, the extended working channel is fixed and the probe withdrawn. A sampling instrument is then advanced and either biopsies, needle or catheter aspiration are performed in order to obtain a representative sample of the lesion or lymph node. As with conventional TBNA, rapid onsite cytopathology assessment is highly recommended. Some centers use fluoroscopy in order to make small adjustments in the probe's position, but no single study has demonstrated a benefit regarding yield of this technique. We never use fluoroscopy in this setting.

Indications for ENB

ENB is indicated in the diagnosis of peripheral pulmonary nodules or masses, as well as mediastinal adenopathy, although patient selection must bear in mind the costs associated with the procedure. The extended working channel and the probe itself are not reusable and can be quite expensive because the latter is calibrated by hand. Also, the procedure is more time consuming than conventional bronchoscopy. In general, most experts rely on ENB for patients at greater risk for complications related to alternative procedures such as surgery or CT guided TTNA. The risk of pneumothorax, for example, is much lower with ENB than with TTNA. The procedure is best reserved for patients with medium sized nodules (2.5 cms) or small lymph nodes not amenable to conventional TBNA. ENB is also helpful in the diagnosis of lesions located in a "no man's land" beyond the reach of the conventional diagnostic bronchoscope, but yet relatively far from the pleural surface (> 2 cm).

Contraindications to ENB

Contraindications to ENB are no different from those contemplated for conventional bronchoscopy, with the exception of special considerations regarding the electromagnetic field. In this regard, patients with pacemakers or implantable defibrillators have been traditionally eschewed, although a growing body of evidence supports the use of ENB in this setting, as untoward events have not been reported in this patient population.

Limitations of the procedure

Several limitations must be taken into account. Cost is a major concern, since the procedure is clearly more expensive than some of the alternatives. Also, nodule size can be a problem if the nodule is particularly small, i.e., less than 8 mm in size. Some targets, such as those located near the diaphragm or the interlobar fissures are harder to reach, while lesions without a visible bronchus sign on CT are also less amenable to ENB as will be explained later. There is an obvious learning curve which must be taken into account, as well as procedural time constraints. Also, the bronchoscope used must have a 2.8 mm channel in order to allow for the extended working channel to pass through it. Biopsies remain small in size and may not be representative of the nodule in a substantial amount of patients. Finally, it is generally best to avoid patients with pacemakers or other implantable devices with which the electromagnetic field might interfere. Patients with prior pneumonectomies, central airway stenoses, and

those with moderate to large pleural effusions must also be considered as potentially poor candidates for ENB. If a pneumothorax is suspected during the procedure, the latter must be terminated since precision in such patients is irretrievably lost, even if the pneumothorax is relatively small and clinically insignificant.

DISCUSSION

A growing body of evidence has established ENB as a reliable and safe alternative to CT guided TTNA and other more invasive procedures in the diagnostic approach to the peripheral pulmonary nodule and mediastinal adenopathy. Its precision and safety were demonstrated in a seminal Cleveland Clinic study.⁷ In that study, mean nodule size was less than 23 mm, and mean lymph node size less than 29 mm. Diagnostic yields were 74% and 100% respectively. Only two pneumothoraces were seen in a total of 60 patients and navigation times were relatively short (7 and 2 minutes respectively). Other studies have shown similar results.⁸

Although no prospective head-to-head comparison has been undertaken in this setting, most experts agree that the diagnostic yield of ENB is significantly higher than what can be expected from conventional bronchoscopy in the diagnosis of peripheral nodules. One of the first studies to evaluate the performance of the superDimension system, reported a diagnostic yield of 70%.⁹ Interestingly, diagnostic yields in that study remained stable for nodules less than 2 cm in size. Another study showed modest improvements in yield with growing size, although not as impressive as those typically seen with conventional bronchoscopy. In that study, overall diagnostic yield was 63% for nodules with a mean size of 23 mm.¹⁰ Most readers will agree that conventional transbronchial biopsies are limited by nodule size. Such biopsies, even with the use of fluoroscopic guidance, are size-dependent.

Considerable uncertainty remains regarding fluctuating yields, and especially the obvious disparity seen in ENB between navigational success and diagnostic yield. Meta-analysis of existing data might help clarify why, despite reaching 90% of peripheral nodules, reported ENB diagnostic yields do not generally exceed 70%. Various authors have sought to identify the cause of this frustrating disparity. Fluoroscopy does not seem to make much of a difference as evidenced in some of the initial ENB studies.¹⁰ The presence of a bronchus sign on the planning CT was very significant in one prospective study and probably accounts for an important part of the discrepancy. In that study, the diagnostic yield of ENB for nodules with a visible bronchus sign was 79%, well above the reported yield of 31% for lesions without an identifiable bronchus sign.¹¹ Other authors have identified a large divergence or registration error as the culprit,¹⁰ and still others believe that the sampling tool may be at fault.¹²

A multi-modality approach combining navigational bronchoscopy with radial endobronchial ultrasound may be the solution. A well designed prospective trial enrolling 120 patients showed a remarkable yield employing a combination of EBUS and ENB.¹³ Patients in that study were assigned to one of three study arms: navigation using endobronchial ultrasound only, ENB only (ENB), or the combined procedure. Yield rates were 88% for the combined procedure compared with 69% for the ultrasound navigation only and 59% for the ENB only groups. The diagnostic yield of the combined approach was independent of lesion size or lobar distribution. In that study, the improved yield was attributed to ultrasound guided repositioning of the probe following successful navigation to the lesion. Such findings are in consonance with those reported by experienced radial ultrasound probe experts, showing that relatively small fluctuations in the probe's position with respect to the lesion (adjacent vs inside the lesion) can have remarkable consequences for the diagnostic yield.¹⁴ Finally, it should be noted, that samples obtained with ENB are amenable to molecular analysis, including EGFR, KRAS, and ALK mutations.¹⁵ Such analysis is crucial to the modern use of chemotherapeutic agents.

CONCLUSION

Despite some obvious limitations, ENB has found its place in the armamentarium of the advanced diagnostic tool set available to bronchoscopists worldwide. Its versatility and excellent safety profile make it an attractive alternative to CT guided TTNA and surgery. Future therapeutic applications of this technology may well make it feasible for a diagnosis and treatment of the peripheral nodule to be performed during one single procedure.

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