Review Article

Role of electromagnetic navigational bronchoscopy in pulmonary nodule management

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Abstract: The incidence of pulmonary nodules and lung cancer is rising. Some of this increase in incidence is due to improved pick up by newer imaging modalities. However, the goal is to diagnose these lesion, many of which are located in the periphery, by safe and relatively non-invasive methods. This has led to the emergence of numerous techniques such as electromagnetic navigational bronchoscopy (ENB). Current evidence supports a role for these techniques in the diagnostic pathway. However, numerous factor influence the diagnostic accuracy. Thus despite significant advances, more research needs to be undertaken to further improve the currently available diagnostic technologies.

Keywords: Pulmonary nodule; electromagnetic navigational bronchoscopy (ENB); lung cancer; peripheral lung nodule

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Introduction

Peripheral pulmonary nodules (PPN) are common incidental findings (1). Due to modern imaging techniques, their incidence is on the rise. Computed tomography (CT) is approximately 3 times more sensitive than plain chest radiography (CXR) in identifying peripheral nodules, with the increasing use of CT scanning resulting in an overall increase in the incidence of nodules. Lung cancer is associated with high mortality and morbidity rates and is the leading cause of cancer death in both men and women in United States. The detection of lung cancer at an early stage has potential benefits by offering improved outcomes—when lung cancer is detected at an early stage and is localized, the 5-year survival rate increases to 53.5% compared to 16.6% when detected at a late stage (2,3). The National Lung Cancer Screening Trial (NLST) compared CT to CXR for the detection of lung cancer and demonstrated a 20% reduction in lung cancer mortality in the CT screening arm. Overall the detection of nodules generated multiple additional investigations; 72.1% of patients underwent further diagnostic evaluation (4). However, the majority of peripheral nodules are not malignant; approximately 1% of nodules in the high-risk NLST population were ultimately diagnosed with malignant disease. Overall this has led to an increased incidence of small lung nodules; most of which are less than 1 centimeter (cm). Therefore, surveillance remains an important challenge for primary physicians and pulmonologists alike. Lung cancer frequently presents late and with an advanced stage resulting in a poor 5-year survival. Screening of high risk individuals has the potential

to diagnose disease at an earlier stage with overall improved outcomes. However, this has resulted in both diagnostic and management dilemmas and has created a need for a diagnostic tool with high success rates and safety profile.

In this paper we review an emerging modality, electromagnetic navigational bronchoscopy.

Electromagnetic navigational bronchoscopy (ENB)

Technique

ENB has emerged as a diagnostic tool to improve on the yield of current conventional techniques. It combines conventional and virtual bronchoscopy to enable the guidance of bronchoscopic instruments to target areas within the peripheral lung parenchyma. These areas are frequently beyond the reach of standard fiber optic bronchoscopy. In essence, ENB consists of: (I) a low-dose electromagnetic field created around the patient; (II) software that creates a three-dimensional (3D) virtual bronchial tree; (III) a sensor device with navigational capacity that can be located within the magnetic field; (IV) an interface to display the position of the sensor within the field and input desired target location; (V) an extended working channel (EWC) that enables accurate placement of ancillary bronchoscopic tools, such as brush, biopsy forceps etc. into the target lesion.

ENB is divided into two phases. Firstly a planning phase where thin-slice protocol CT is performed prior to the procedure. The images are analyzed by the software and this produces a virtual road map of the bronchial tree in preparation for the second phase, i.e., the navigational phase.

The locatable guide (LG) is continuously sensed in real time by the magnetic field as it is navigated to the point of interest within the bronchial tree. The reconstructed virtual anatomy helps direct the scope via a suggested route for navigation. The software constantly displays the distance from the lesion. The process of matching the CT images to the patient's real life anatomy (CT to body divergence) is called registration accuracy; this is measured as an Average Fiducial Target Registration Error (AFTRE) and should be less than 5 millimeters (mm). An AFTRE greater than 5 mm signifies unacceptable discrepancy and will lead to reduced navigational accuracy (5). Once sufficient data is available to match the patient's anatomy to the CT images, the LG is advanced on the pre-planned pathway. The progress and location of the LG is displayed in six simultaneous views as chosen by the operator. Finally, when the target site is reached the EWC is locked, the LG is removed and a variety of ancillary tools can be passed through the EWC to obtain samples—for example needle aspiration, brush biopsy, and forceps.

Types

Currently there are two distinct systems that use ENB. Both systems are based on the same basic principal and consist of an initial planning phase with few minor variations. The i-Logic (Covidien, Mansfield, MA, USA) system generates the magnetic field via a board that is placed underneath the patient and the sensors are maneuverable. The i-Logic LG is available in various angles that is mounted on the EWC. The second commercially available system, the SPiNDrive (Veran Medical Technologies, Inc., St Louis, MO, USA) utilizes a magnetic field over the patient. The sensor system is built into the various instruments that are mounted on the EWC, thus allowing direct navigation of the biopsy instrument. In addition, this system has a sensor pad that allows additional imaging enhancements to compensate for respiratory movement, which in theory, at least, allows for better bronchoscopic navigation.

Current evidence

In a small retrospective chart review ENB led to a diagnosis in 77% of lesions where standard bronchoscopic biopsies were unsuccessful. In this study, nearly half (49%) of the lesions were identified as malignant, mostly non-small cell lung cancer (NSCLC) (6). In a larger retrospective study of 248 patients, the i-Logic system had a comparatively lower diagnostic yield of 55.7% for peripheral lesions (mean size 2.1±1.4 cm standard deviation (SD) and 70% for lymph nodes that were 1.8±0.9 cm (7).

An open-label, prospective, single-group, controlled clinical study with 15 patients demonstrated a 69% diagnostic yield. In this study the majority of these lesions were diagnosed as NSCLC (8). The average size of the lesions was 3.35±1.10 cm (9). Similar results were replicated in a larger study (89 patients) by Eberhardt *et al.* This study reported a 67% (P=0.42) diagnostic accuracy using ENB. They also noted a significantly higher yield in diagnosing lesions in the right middle lobe, 88%. These results were independent of the size of lesion (10). Consistent with the previous studies Seijo *et al.* showed a similar diagnostic yield of 67% in 34 of 51 patients with indeterminate pulmonary lesions (IPN). This study had a smaller median size of the

nodules at 2.5±1.0 cm, a median distance from the pleural surface of 11 mm and a positive bronchus sign in 74% patients. A higher diagnostic accuracy was seen in lesions with a positive bronchus sign, 79% versus 31% respectively. The sensitivity and specificity of ENB for malignancy in this study were 71% and 100% respectively (11). Gildea *et al.*, obtained a higher diagnostic accuracy compared to the preceding studies. The diagnostic accuracy was reported at 80.3% overall. However, it should be highlighted that only 57.0% of these lesions were less than 2 cm in diameter and the mean distance to the center of targeted peripheral lesions was 0.9 cm. The diagnostic yield was not significantly affected by lesion size or AFTRE (P=0.1701). A final diagnosis of malignancy was obtained in 74% of cases via ENB, with the most common diagnosis being NSCLC (12). ENB produced a diagnosis in 25 (62.5%) out of 40 cases. The diagnostic yield of ENB was significantly greater when data registration accuracy was less than 4 mm (77.2% and 44.4% respectively, P=0.03). The mean lung lesion diameter was 23.5±1.5 mm and depth from the visceral-costal pleura was 14.9±2.0 mm (5).

A recent meta-analysis of 15 trials with a total of 1,033 nodules found a definitive diagnosis was obtained in 64.9% [95% confidence interval (CI): 59.2–70.3%] procedures. The sensitivity to detect cancer was 71.1% (95% CI: 64.6–76.8%), with a negative predictive value of 52.1% (95% CI: 43.5–60.6%) (13).

Other routinely used techniques such as standard flexible bronchoscopy have a much lower diagnostic yield when compared to ENB (15% *vs.* 54%) when sampling peripheral lung lesions less than 2 cm. However the yield of bronchoscopy improves the closer the lesion is to the hilum (9).

The ENB has been compared to other technologies in a large randomized controlled trial. This study had three arms comparing ENB, radial probe-endobronchial ultrasound (RP-EBUS), and a combined ENB and RP-EBUS arm. A total of 120 patients were recruited, of which 118 had a definitive histological diagnosis and were included in the final analysis. The diagnostic yield of the combined procedure (88%) was greater than EBUS (69%) or ENB alone (59%; P=0.02). Of importance, the combined procedures yield was independent of lesion size or lobar distribution (14). In another series by the same authors, the diagnostic yield was much higher (93% *vs.* 48%) when the lesion could be identified by RP-EBUS after navigation to the area with ENB (15). A similar study evaluated ENB and peripheral EBUS (pEBUS) alone and in combination. The average diameter of the lesions was 27 mm with an average distance of 20 mm from the pleural surface. The combination of pEBUS and ENB identified lesions in 93% (56/60) cases compared to 75% (45/60) cases with pEBUS alone (P=0.001). The overall diagnostic yield was 50%, however, in this study the diagnostic yield did not significantly improve with addition of ENB over pEBUS alone (26/60 *vs.* 30/60; P=0.125). This low diagnostic rate is unusual given the high success rate in identification of the lesions, 93% (16). These results suggest that combining traditional techniques with ENB may overcome some of the limitations of the technologies and therefore may allow pulmonologists to achieve a more accurate diagnosis.

Other potential applications

This technology may have several other applications including the placement of fiducial markers, guidance for trans-tracheal and trans-bronchial biopsy and bronchoscopic pleural dye marking for localization of lesions pre-surgery. The placement of brachytherapy catheters and markers for radiotherapy has become increasingly useful in the management and the treatment of inoperable lung cancer. This allows for precise delivery of treatment with minimization of side effects to the surrounding healthy lung parenchyma. This role of ENB was validated in a case series which demonstrated that eight of the nine patients (89%) had successful deployment of fiducial markers, and importantly seven markers were located directly within the tumor. Of a total of 39 placed markers, 35 of these remained in place at 10 days (17). In another study with 43 patients, 39 cases had the markers in or on the lesion at the time of surgery (90.6%). The mean displacement was 1.67 cm (SD: 1.15 cm) and the mean tumor size 2.78 cm (SD: 1.46 cm) (18).

In another study with 234 markers placed, it was demonstrated that ENB guided placement of coil spring fiducial markers had better retention rates, with lower complication rates compared to linear fiducial markers (19). Similar safety and efficacy results with the deployment of brachytherapy catheters into inoperable lung cancer via ENB has also been demonstrated (20,21). ENB has also used to place pleural dye markers to allow lesion location at the time of minimal invasive surgery. Krimsky *et al.* showed that 81% of the patients had visible dye marker at the time of surgical wedge resection and there were no cases requiring conversion to an open procedure (22). This reduced the conversion rates from a typical 50% with conventional thoracoscopies and reduced the procedural time (23).

Safety

The overall safety of ENB is superior to conventional techniques for the evaluation of the IPN. A variety of complications have been reported; however the majority of these are minor including hypoxemia or bleeding. To date, no deaths have been reported in the literature. In a large retrospective study, the overall complication rate was 3.20%, with 1.27% of the total 266 patients developing a pneumothorax, making this the commonest complication of ENB (6). In a large meta-analysis with a total of 1,033 IPN, pneumothorax was seen in 3.6% cases, of which 1.6% required chest tube placement (13). This data has been validated by numerous studies with a reported incidence of pneumothorax ranging from 0–10% (5,6,11,14,24).

The safety of ENB has been demonstrated in patients with implantable defibrillators and pacemakers. No cases of fatal arrhythmia or disruption in pacemaker function has been reported (25).

The use of ENB to place fiducial markers is associated with a lower complication rate compared to trans-cutaneous implantation of these devices (26). Thus ENB seems to be well tolerated when compared to other traditional methods. The biggest advantage of ENB over trans thoracic needle aspiration (TTNA) is its superior safety profile. Because the pleural is not breached with transbronchial biopsy, the pneumothorax rates are considerably lower than TTNA ranging between 0% to 10% (11).

Factors influencing outcomes of ENB

The navigation phase during ENB is deemed successful in 90% of cases, yet the overall diagnostic yield remains significantly lower at 70% (7). There are numerous factors that affect this, as discussed below.

A higher CT-body divergence results in a higher AFTRE obviously results in poor virtual visualization of the airway and poor navigation. This reduces the diagnostic yield and leads to higher complication rates. Recently a new i-Logic software update has reduced the need for manual adjustments resulting in automation and a higher registration accuracy. This eliminates the need to mark numerous pre-defined points for alignment of the CT images with the real time anatomy. However no efficacy data is available for this to date.

User technique and patient sedation also play a role in the outcome of ENB. No conclusive data is available regarding the optimal sedation method. There is no statistically significant differences in diagnostic yield reported in two studies performed by Eberhardt *et al.* These studies compared conscious sedation to general anesthesia and reported diagnostic accuracies of 67% *vs.* 76%, P=0.28 and 64% *vs.* 70%, P=0.57 respectively (10,14). Another study showed that inhalational anesthesia could also be used for ENB (15). However these results do not demonstrate superiority of one anaesthetic method over another and therefore the choice of anaesthetic method is determined by patient co-morbidities, operator experience and anaesthetist availability.

However the main factor affecting the outcome are the characteristics of the lesion itself. Lesions located in the right upper or middle lobes have higher diagnostic yield (6). Traditionally these lobes are difficult to examine with conventional bronchoscopy. The presence of a bronchus sign favorably impacts the diagnostic yield. The yield was shown to double from 30% to 60% when a positive sign was present for PPN (27). In a single center study with 51 patients the overall diagnostic yield was 67% in 34 procedures. However sub-analysis demonstrated that the ENB was diagnostic in 79% (30/38) patients with a bronchus sign on CT imaging but only in 4/13 (31%) without an identifiable bronchus sign (11).

As mentioned above, numerous studies of varying sizes have shown that the combination of ENB with other modalities like fluoroscopy or RP-EBUS increase the diagnostic yield as compared to either method alone. A combined procedure raised the diagnostic yield by 29% (14). However despite the increase in diagnosis, this has not been statistically significant in all studies (16).

The location of the nodule is also an important factor in the outcome. It has been shown that the further the lesion is to the periphery, the lower the yield. Central, intermediate, and peripheral lesions were associated with diagnostic yields 82%, 61%, and 53%, respectively. This difference was statistically significant (P=0.05). The diagnostic yield of bronchoscopy was 14% (2 of 14) when lesions were less than 2 cm and peripherally located, as compared to 31% (5 of 16) when lesions were greater than 2 cm and intermediately located (P=0.3) (28). The use of filtered cigarettes has resulted in an increased incidence of peripheral opacities (29). Peripheral lesion less than 2 cm have a lower diagnostic yield compared to lesions greater than 2 cm (30). In a pooled study with similar predetermined cut off sizes, lesions less than 2 cm were associated with a lower diagnostic yield when compared to lesions greater than 2 cm (56.3% *vs.* 77.7%) (31). However another study showed that

the location of the lesions had no further independent effect on the yield of bronchoscopy if the lesions were greater than 2 cm in size. The yield was 28% when the diameter was less than 2 cm compared to 64% if the diameter was greater than or equal to 2.0 cm (P=0.0035) (32). Best results were seen when lesions were greater than 5 cm from the hilum (67% positive yield) (33). The choice of ancillary tools may also affect the performance and accuracy of ENB. When compared to forceps biopsy, catheter aspiration had a higher success rate (22/40 *vs.* 36/40. P=0.035). In this study 75.5% of the samples were diagnostic. However, in lesions not seen with ultrasound, suction catheter was diagnostic in 100% compared to only 33% with forceps biopsy (15). Even with standard bronchoscopy a needle brush (a cytology brush with a needle tip) had a higher diagnostic yield than transbronchial needle aspirate, regular cytology brush or transbronchial forceps biopsy (34).

Shortcomings

While the theory behind ENB remains robust, several challenges still need to be addressed before the widespread adoption of this technology. The first animal trials of ENB were performed in 2003, however, over the past decade only a few randomized controlled trials have been undertaken. There remain numerous unanswered questions about the exact place of ENB in the diagnostic algorithm for IPN. Important questions remain unanswered including when to choose ENB over TTNA for diagnosing PPNs and whether ENB is useful after failed RP-EBUS.

Multiple studies have shown that there is a discrepancy between the navigation success rate and the final diagnostic yield of the ENB procedure. A better understanding of this inconsistency is imperative. The presence of a bronchus sign positively affects the diagnostic yield of ENB. This requires further study and may help to reduce the gap between the navigational phase and the diagnostic yield. A better understanding of this may help in selecting the appropriate patients for ENB thus reducing health care costs. Currently the cost of ENB is high and its use is limited to specialized centers. Dale *et al.* showed that ENB has an additional cost of $3,719 for each biopsy when compared to CT-guided biopsy. Additionally, ENB is associated with an increased rate of video-assisted thoracopic surgery (VATS) procedures, increasing indirect costs related to ENB (35). It should be noted that the LGs and EWCs are single use only, whereas the RP-EBUS probe can be reused as many as 100 times. However the cost-effectiveness of ENB has yet to be published.

Currently the use of ENB is limited to specialized centers as it requires a well-functioning team, numerous pieces of equipment and software. The procedure itself is technically complex requiring significant skills and experience. A learning curve exists which effects successful navigation and yield. This has been studied and the diagnostic yield compared to level of skill has been reported. Consecutive patients were placed into three groups (A, B, C) based on the chronological time they had their procedure. Both PPNs and mediastinal lesions were targeted with an average target size of 23±12 mm. The diagnostic yield of groups A, B and C was 58.8%, 87.5%, and 93.3% respectively, leading to the conclusion that numerous procedures need to be done before obtaining procedural proficiency (36). Conversely, another study found no difference in diagnostic yield between the first 13 and final 13 procedures as well as the first 7 and last 7 procedures performed by two different operators who performed 26 and 14 consecutive procedures respectively (5). Thus simulation training as well as hands-on training in the operating rooms is required to maximize the diagnostic capabilities of ENB. Also, this is an evolving technology where software and hardware updates are constantly occurring. The latest i-Logic software performs automatic registration. However this algorithm has not yet been studied. Thus, as new steering mechanisms, LGs and software become available, their safety and efficacy will need to be restudied which may in turn hinder widespread adoption.

Emerging techniques

Virtual navigational bronchoscopy (VNB)

VNB is a method for the guidance of a bronchoscope to peripheral lesions. It provide additional guidance for the bronchoscopist, assisting in the selection of an appropriate course through the bronchial tree. Data from the CT images is used to construct a 3D bronchial tree and a roadmap is created to the preset lesion. Numerous views are available along with the ability to rotate the images in almost any plane or direction. VBN can be utilized pre or during the procedure. Intra procedural use often requires an additional operator, but the advanced guidance system allows the bronchoscope to be readily guided to the target in a short time. Therefore appropriate use of VBN may increase the selection of appropriate pathways and reduce the chance of user error (37). Currently there are

two systems commercially available; the Bf-NAVI System (Olympus) and the LungPoint System (Broncus Medical, Mountain View, CA, USA). Currently more data is available on the former system, however only the lung point system is currently available within the United States. A meta-analysis showed a diagnostic yield of 72% when utilizing VNB; however, this data was mainly extrapolated from the Bf-NAVI system (30). In a study done to evaluate the Bf-NAVI system, biopsy forceps could be advanced to the lesion in 33 of the 38 lesions (86.8%) and a definitive diagnosis was possible for 31 lesions (81.6%) (38).

In a prospective non-randomized trial there was no significant increase in diagnostic yield when comparing RP-EBUS alone to VNB and RP-EBUS (80.0% *vs.* 84.2%), however the time required to determine biopsy position was significantly lower in the VNB and RP-EBUS arm (5.54±0.57 *vs.* 9.27±0.86 min, P<0.01) (39). A larger study showed that VNB assisted bronchoscopies resulted in a higher diagnostic yield when compared to the non VBN assisted group (80.4% *vs.* 67.0%; P=0.032). This study also showed a shorter time to sample collection (40). The most recent randomized-controlled trial enrolled 334 patients to undergo either VNB with fluoroscopy versus standard bronchoscopy with fluoroscopy. No overall difference in diagnostic yield was identified, but subgroup analysis revealed that VNB improved the diagnostic yield in the right upper lobe, peripheral third of the lung and in patients with lesions invisible on CXR (41). The lack of real time guidance is a major drawback of VNB, however the addition of RP-EBUS resulted in an increased diagnostic yield, from 88% to 93% (42).

Optimistic results have been obtained on the LungPoint system as well. In non-human and phantom studies VNB was shown to have superior ability to localize lesions and select the correct pathway to the lesion (37,43). In a human study, in 14 of 25 cases (56%) the lesions could be reached and the overall diagnostic yield was 80% (all patients with a visualized lesion obtained a diagnosis) (42).

Although VNB technology remains attractive, current literature does not support its widespread adoption at this point. Further study is required with this technology to justify its widespread use in clinical practice.

Bronchoscopic trans-parenchymal nodule access (BTPNA)

Just like ENB, the software of BTPNA creates a virtual pathway to the lesion. However it is not limited by failure of the bronchoscope reaching the nodule. The software associated with BTPNA generates a straight line from the airway to the lesion. This trans parenchymal approach is possible due to a balloon catheter equipped guide sheath. In an animal study, 13 tunnels were created with an average length of 32.3 mm (range, 24.7 to 46.7 mm). No major complications were reported including pneumothorax (44). Recently a newly FDA approved trans bronchial device was studied by Bolton *et. al.* In a porcine model the cross country trans bronchial access (Covidien, Plymouth, MN, USA) was compared to the existing endoscopic needle with a balloon dilator (FleX Needle, Bronchus Medical, Inc.). There were no significant microscopic changes on post mortem examination and there were no signs of pneumothorax. Overall 34 of the 36 (94%) device deployment sites had no intra-operative bleeding, with both the test device and the comparator device having one case each. These results suggest that the device was successful in creating an airway exit point and tunneling to the target lesion via the parenchyma with no greater risk compared to a sham device (45).

Conclusions

The current evidence regarding the safety and higher diagnostic yield supports a role for ENB. In addition, ENB used in conjunction with other modalities further improves diagnostic accuracy. Thus it allows pulmonologists to sample lesions previously thought to be too small or too peripherally located. However its cost, operational expertise and learning curve have limited its widespread use. Further research and refinement of its software is needed to overcome these major drawbacks. Ongoing studies will further clarify the role of this promising technology in contemporary practice. However, despite these challenges ENB holds great potential for a wide range of clinical applications, both diagnostic and therapeutic, compared to current, conventional techniques.

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Footnote

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References

1. Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet 1999;354:99-105.
2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013;63:11-30.
3. Humphrey L, Deffebach M, Pappas M, et al. Screening for Lung Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation [Internet]. Cited Oct 30, 2015. Available online: http://www.ncbi.nlm.nih.gov/pubmed/?term=24027793
4. National Lung Screening Trial Research Team, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365:395-409.
5. Makris D, Scherpereel A, Leroy S, et al. Electromagnetic navigation diagnostic bronchoscopy for small peripheral lung lesions. Eur Respir J 2007;29:1187-92.
6. Mahajan AK, Patel S, Hogarth DK, et al. 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.
7. Wilson DS, Bartlett RJ. Improved Diagnostic Yield of Bronchoscopy in a Community Practice: Combination of Electromagnetic Navigation System and Rapid On-site Evaluation. J Bronchol 2007;14:227-32.
8. Schreiber G, McCrory DC. Performance characteristics of different modalities for diagnosis of suspected lung cancer: summary of published evidence. Chest 2003;123:115S-128S.
9. Schwarz Y, Greif J, Becker HD, et al. Real-time electromagnetic navigation bronchoscopy to peripheral lung lesions using overlaid CT images: the first human study. Chest 2006;129:988-94.
10. Eberhardt R, Anantham D, Herth F, et al. Electromagnetic navigation diagnostic bronchoscopy in peripheral lung lesions. Chest 2007;131:1800-5.
11. Seijo LM, de Torres JP, Lozano MD, 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.
12. Gildea TR, Mazzone PJ, Karnak D, et al. Electromagnetic navigation diagnostic bronchoscopy: a prospective study. Am J Respir Crit Care Med 2006;174:982-9.
13. Gex G, Pralong JA, Combescure C, et al. Diagnostic yield and safety of electromagnetic navigation bronchoscopy for lung nodules: a systematic review and meta-analysis. Respiration 2014;87:165-76.
14. Eberhardt R, Anantham D, Ernst A, et al. Multimodality bronchoscopic diagnosis of peripheral lung lesions: a randomized controlled trial. Am J Respir Crit Care Med 2007;176:36-41.
15. Eberhardt R, Morgan RK, Ernst A, et al. Comparison of suction catheter versus forceps biopsy for sampling of solitary pulmonary nodules guided by electromagnetic navigational bronchoscopy. Respiration 2010;79:54-60.
16. Chee A, Stather DR, Maceachern P, et al. Diagnostic utility of peripheral endobronchial ultrasound with electromagnetic navigation bronchoscopy in peripheral lung nodules. Respirology 2013;18:784-9.
17. Anantham D, Feller-Kopman D, Shanmugham LN, et al. Electromagnetic navigation bronchoscopy-guided fiducial placement for robotic stereotactic radiosurgery of lung tumors: a feasibility study. Chest 2007;132:930-5.
18. Harley DP, Krimsky WS, Sarkar S, et al. Fiducial marker placement using endobronchial ultrasound and navigational bronchoscopy for stereotactic radiosurgery: an alternative strategy. Ann Thorac Surg 2010;89:368-73; discussion 373-4.
19. Schroeder C, Hejal R, Linden PA. Coil spring fiducial markers placed safely using navigation bronchoscopy in inoperable patients allows accurate delivery of CyberKnife stereotactic radiosurgery. J Thorac Cardiovasc Surg 2010;140:1137-42.
20. Becker HD, Harms W, Debus J, et al. Brachytherapy of inoperable peripheral lung cancer guided by electromagnetic navigation and endobrochial ultrasound: feasibility study and confirmation by long-term results at two centers. Chest 2009;136:2S.
21. Bedekar AR, Kerley JM, Ochran T, et al. Successful treatment of peripheral lung cancers utilizing high dose iridium 192 (HDIR) brachytherapy guided by electromagnetic navigation bronchoscopy (ENB) and radial endobronchial ultrasound (REBUS). Chest 2007;132:516.
22. Krimsky WS, Minnich DJ, Cattaneo SM, et al. Thoracoscopic detection of occult indeterminate pulmonary nodules using bronchoscopic pleural dye

marking. J Community Hosp Intern Med Perspect 2014;4.
23. Suzuki K, Nagai K, Yoshida J, et al. Video-assisted thoracoscopic surgery for small indeterminate pulmonary nodules: indications for preoperative marking. Chest 1999;115:563-8.
24. Lamprecht B, Porsch P, Pirich C, et al. Electromagnetic navigation bronchoscopy in combination with PET-CT and rapid on-site cytopathologic examination for diagnosis of peripheral lung lesions. Lung 2009;187:55-9.
25. Khan AY, Berkowitz D, Krimsky WS, et al. Safety of pacemakers and defibrillators in electromagnetic navigation bronchoscopy. Chest 2013;143:75-81.
26. Kupelian PA, Forbes A, Willoughby TR, et al. Implantation and stability of metallic fiducials within pulmonary lesions. Int J Radiat Oncol Biol Phys 2007;69:777-85.
27. Naidich DP, Sussman R, Kutcher WL, et al. Solitary pulmonary nodules. CT-bronchoscopic correlation. Chest 1988;93:595-8.
28. Baaklini WA, Reinoso MA, Gorin AB, et al. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest 2000;117:1049-54.
29. Wynder EL, Muscat JE. The changing epidemiology of smoking and lung cancer histology. Environ Health Perspect 1995;103 Suppl 8:143-8.
30. Wang Memoli JS, Nietert PJ, Silvestri GA. Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. Chest 2012;142:385-93.
31. Steinfort DP, Khor YH, Manser RL, et al. Radial probe endobronchial ultrasound for the diagnosis of peripheral lung cancer: systematic review and meta-analysis. Eur Respir J 2011;37:902-10.
32. Radke JR, Conway WA, Eyler WR, et al. Diagnostic accuracy in peripheral lung lesions. Factors predicting success with flexible fiberoptic bronchoscopy. Chest 1979;76:176-9.
33. Cortese DA, McDougall JC. Biopsy and brushing of peripheral lung cancer with fluoroscopic guidance. Chest 1979;75:141-5.
34. Wang KP, Britt EJ. Needle brush in the diagnosis of lung mass or nodule through flexible bronchoscopy. Chest 1991;100:1148-50.
35. Dale CR, Madtes DK, Fan VS, et al. Navigational bronchoscopy with biopsy versus computed tomography-guided biopsy for the diagnosis of a solitary pulmonary nodule: a cost-consequences analysis. J Bronchology Interv Pulmonol 2012;19:294-303.
36. Bansal S, Hale K, Sethi S, et al. Electromagnetic navigational bronchoscopy: A learning curve analysis. Chest 2007;132:514b.
37. Dolina MY, Cornish DC, Merritt SA, et al. Interbronchoscopist variability in endobronchial path selection: a simulation study. Chest 2008;133:897-905.
38. Asano F, Matsuno Y, Shinagawa N, et al. A virtual bronchoscopic navigation system for pulmonary peripheral lesions. Chest 2006;130:559-66.
39. Oshige M, Shirakawa T, Nakamura M, et al. Clinical Application of Virtual Bronchoscopic Navigation System for Peripheral Lung Lesions. J Bronchology Interv Pulmonol 2011;18:196-202.
40. Ishida T, Asano F, Yamazaki K, et al. Virtual bronchoscopic navigation combined with endobronchial ultrasound to diagnose small peripheral pulmonary lesions: a randomised trial. Thorax 2011;66:1072-7.
41. Asano F, Shinagawa N, Ishida T, et al. Virtual bronchoscopic navigation combined with ultrathin bronchoscopy. A randomized clinical trial. Am J Respir Crit Care Med 2013;188:327-33.
42. Eberhardt R, Kahn N, Gompelmann D, et al. LungPoint--a new approach to peripheral lesions. J Thorac Oncol 2010;5:1559-63.
43. Merritt SA, Gibbs JD, Yu KC, et al. Image-guided bronchoscopy for peripheral lung lesions: a phantom study. Chest 2008;134:1017-26.
44. Silvestri GA, Herth FJ, Keast T, et al. Feasibility and safety of bronchoscopic transparenchymal nodule access in canines: a new real-time image-guided approach to lung lesions. Chest 2014;145:833-8.
45. Bolton W, Krimsky W, Mattingly J, et al. Performance Of A Novel Off-Airway Access Tool For Peripheral Lung Navigation In A Porcine Lung Model. Available online: http://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2015.191.1_MeetingAbstracts.A3064

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