



Editorial

Interventional Pulmonology and Solitary Pulmonary Nodule

Neumología intervencionista y nódulo pulmonar solitario

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Interventional pulmonology (IP) is an evolving field with substantial technological progress during the past decade. These advances should be accompanied by efforts to validate their use in different patient populations and improve patient care.

An area of significant progress and novel challenges is the diagnosis and management of solitary pulmonary nodules (SPN).

The identification of solitary pulmonary nodules in large lung cancer screening studies range from 8% to 51%, with prevalence of malignancy from 1.1% to 12%.¹ The National Lung Cancer Screening Trial (NLST) showed that early detection of lung cancer, had a 20% reduction in mortality in the low dose CT (LDCT) arm as compared to CXR.² Furthermore, a LDCT was positive in 24% of screening studies, requiring further diagnostic procedures.³ Unfortunately, for SPNs of less than 2 cm, the sensitivity of conventional bronchoscopy is low at approximately 34% and the yield is probably influenced by the distance from the hilum, air bronchus sign and the lobe or subsegment where the lesion of interest is located.⁴ CT-guided transthoracic needle aspiration (CT-TTNA) has a high diagnostic yield for SPNs, particularly in the upper lobe lesions and in close proximity to the pleura. However, this approach is associated with frequent incidence of pneumothorax (20–25%) with approximately 7% of patients requiring insertion of a chest tube. Additionally, in patients with bullous lung disease or lesions that are distant from the pleura, the diagnostic accuracy for TTNA drops to 60% or less when the needle path length exceeded 40 mm.^{4,5} In an attempt to minimize the risk of the percutaneous approach that traverses the pleura, several bronchoscopy-guided technologies such as: electromagnetic navigation bronchoscopy, virtual bronchoscopy, radial probe endobronchial ultrasound, and ultrathin bronchoscope with guided sheath have been developed to improve the diagnostic yield of transbronchial biopsy for SPNs diagnosis. A meta-analysis of studies published before 2010 showed that the pooled diagnostic yield of guided bronchoscopy using one or a combination of the above modalities was 70% with a pneumothorax rate of 1.5%.⁶ Nevertheless, the yield was 61% for those lesions <2 cm vs 82% for those

>2 cm and 79% with a bronchus sign vs 31% without a bronchus sign.⁶

However, the variable yields in some of the navigation bronchoscopy studies have raised concerns about the applicability of these results in clinical practice outside of academic institutions. In an attempt to answer this question, the NAVIGATE investigators enrolled 1390 patients in North America and Europe to determine the safety and diagnostic yield of EMN in academic and non-academic settings. The 2-year study is ongoing and the safety analysis at 30 days showed a pneumothorax rate of 3.2%.⁷

Recently, a novel bronchoscopic trans-parenchymal nodule access (BTPNA) has been developed to reach pulmonary lesions regardless of not having an airway leading into the lesion. The Archimedes Virtual Bronchoscopy Navigation System (Broncus Medical, Mountain View, CA, USA) reconstructs CT data into a 3D model that provides a guide map for the insertion of the sheath. During the actual procedure, a hole is created in the airway wall using a needle at the point of entry. This is followed by a dilating balloon, and advancing the sheath through parenchymal tissue in a straight line to the nodule under real-time fluoroscopy data. Ultimately allowing for repeat sampling of the SPN. Two recent pilot studies in humans (total of 18 patients) suggested that BTPNA was feasible in creating an airway exit point and tunneling to the target lesion through the parenchyma with adequate biopsy obtained in 83% of the cases.^{8,9} Two patients developed pneumothorax in one study with one requiring chest tube drainage.^{8,9}

Another novel diagnostic tool, the electromagnetic guided transthoracic needle aspiration (ETTNA) (Veran Medical Technologies Inc, St Louis, MO, USA) has been developed to allow bronchoscopists to perform percutaneous needle biopsies. This device uses an electromagnetic field to track sensors at the tip of the instruments in relation to a CT-based image of the patient's anatomy. A recent pilot study of 24 patients showed that ETTNA was feasible in 96% of cases with a diagnostic yield of 83%. The yield increased to 87% with navigational bronchoscopy and to 92% when combined with linear probe EBUS/TBNA and navigational bronchoscopy. Given the percutaneous nature of this technology and traversing the pleura, it has resulted in a pneumothorax rate of 21% in the only small study published to date.¹⁰

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In the last couple of months, the appearance of robotic technology in bronchoscopy has opened yet another area of research. Robotic bronchoscopy has a few advantages over other platforms. In theory, it should allow access to visual inspection of peripheral lung nodules that are in proximity to the pleura, it should enable the physician to perform the procedure at a distance from the patient, and it should minimize the limitations of the hand-held bronchoscope for complex navigation in convoluted paths. These theoretical advantages, when coupled with better imaging technologies such as cone-beam CT, uncover new applications for the interventional pulmonologist.

Improved access to malignant lung nodules in patients with significant comorbidities and limited pulmonary reserve has opened the possibility of pursuing ablation and providing local therapy.¹¹ Percutaneous ablative techniques including cryotherapy, radiofrequency ablation and microwave ablation have encountered variable success but significant complication risks including pneumothorax and hemorrhage.¹² Now the possibility of using flexible probes and delivering such energies bronchoscopically is enticing. Photodynamic therapy for peripheral lung nodules is also being evaluated as a potential treatment option. The possibility for bronchoscopists to address the considerable number of patients who have limited treatment options is inspiring. Moreover, these ablative techniques are far-reaching in their application and can be used for stage I bronchogenic carcinomas, oligometastatic disease and oligoprogressive disease.¹³

We envision the future as a one-stop-shop bronchoscopic approach, where we can first stage by sampling the mediastinum and hilum, then navigate to the peripheral nodule for diagnosis, and lastly treat by ablating the tumor using different types of energies.

In conclusion, significant progress has been recently accomplished in diagnostic and therapeutic techniques for SPNs. These new technologies appear to be promising but await further clinical studies to confirm safety and efficacy in a broader population. Each of these technologies will require independent testing for safety,

efficacy and generalizability before they can be widely used. Likewise to medications that require independent safety and validation, new bronchoscopic technologies will also require thorough testing before widespread implementation.

References

1. Patel VK, Naik SK, Naidich DP, Travis WD, Weingarten JA, Lazzaro R, et al. A practical algorithmic approach to the diagnosis and management of solitary pulmonary nodules: Part 1: Radiologic characteristics and imaging modalities. *Chest*. 2013;143:825–39.
2. National Lung Screening Trial Research Team Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365:395–409.
3. Aberle DR, Abtin F, Brown K. Computed tomography screening for lung cancer: has it finally arrived? Implications of the national lung screening trial. *J Clin Oncol*. 2013;31:1002–8.
4. Hergott CA, Tremblay A. Role of bronchoscopy in the evaluation of solitary pulmonary nodules. *Clin Chest Med*. 2010;31:49–63.
5. Cham MD, Lane ME, Henschke CI, Yankelevitz DF. Lung biopsy: special techniques. *Semin Respir Crit Care Med*. 2008;29:335–49.
6. Wang Memoli JS, Nietert PJ, Silvestri GA. Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. *Chest*. 2012;142:385–93.
7. Khandhar SJ, Bowling MR, Flandes J, Gildea TR, Hood KL, Krinsky WS, et al. Electromagnetic navigation bronchoscopy to access lung lesions in 1,000 subjects: first results of the prospective multicenter NAVIGATE study. *BMC Pulmon Med*. 2017;17:59.
8. Herth FJ, Eberhardt R, Sterman D, Silvestri GA, Hoffmann H, Shah PL. Bronchoscopic transparenchymal nodule access (BTPNA): first in human trial of a novel procedure for sampling solitary pulmonary nodules. *Thorax*. 2015;70:326–32.
9. Harzheim D, Sterman D, Shah PL, Eberhardt R, Herth FJ. Bronchoscopic transparenchymal nodule access: feasibility and safety in an endoscopic unit. *Respiration*. 2016;91:302–6.
10. Yarmus LB, Arias S, Feller-Kopman D, Semaan R, Wang KP, Frimpong B, et al. Electromagnetic navigation transthoracic needle aspiration for the diagnosis of pulmonary nodules: a safety and feasibility pilot study. *J Thorac Dis*. 2016;8:186–94.
11. Harris K, Puchalski J, Sterman D. Recent advances in bronchoscopic treatment of peripheral lung cancers. *Chest*. 2016.
12. Lu Q, Cao W, Huan L, Wan Y, Liu T, Cheng Q, et al. CT-guided percutaneous microwave ablation of pulmonary malignancies: results in 69 cases. *World J Surg Oncol*. 2012;10:80.
13. Kim C, Hoang CD, Kesarwala AH, Schrupp DS, Guha U, Rajan A. Role of local ablative therapy in patients with oligometastatic and oligoprogressive non-small cell lung cancer. *J Thoracic Oncol*. 2017;12:179–93.