State-of-the-Art Modalities for Peripheral Lung Nodule Biopsy

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KEYWORDS

• Peripheral pulmonary nodules • Electromagnetic navigational bronchoscopy • ENB • Radial ultrasound • Solitary pulmonary nodule • Lung cancer

KEY POINTS

- Lung nodules are being increasingly detected, particularly with lung cancer screening with low-dose computed tomography.
- Although the vast majority of lung nodules are benign, many often require tissue diagnosis.
- Several modalities to obtain diagnostic tissue from peripheral lung nodules are available.
- Bronchoscopic modalities such as radial ultrasound and electromagnetic navigational bronchoscopy are being increasingly used because of their superior safety profile and improving diagnostic yield.
- Although these modalities continue to become more advanced, newer and complementary technologies appear promising.

INTRODUCTION

A solitary pulmonary nodule is defined as a single, well-demarcated radiographic opacity measuring less than 3 cm in diameter, and is surrounded by lung tissue. It may be solid, subsolid, or ground glass. Solitary pulmonary nodule is a specific clinical entity with fairly well-known risk-ascertainment clinical prediction tools. Multiple pulmonary nodules can be an entirely different clinical problem. Peripheral pulmonary nodules (PPN) pose significant diagnostic challenges to pulmonologists because, unlike endobronchial lesions, there is lack of direct visualization of PPN during bronchoscopy that results in unsatisfactory reach of diagnostic instruments to the nodule. Conventional bronchoscopy and transbronchial biopsies have a low sensitivity (14%–63%) for diagnosing malignant lesions.[1,2] The yield is particularly low (30%) for PPN less than 2 cm in diameter.[1,2]

With the advent of low-dose computed tomography (CT) lung cancer screening, pulmonologists are expected to dedicate a significant portion of their practice dealing with PPN. The National Lung Cancer Screening Trial demonstrated lung nodules in at least 39% of the participants, of which 72% required further investigation.[3] PPN greater than 2 cm in diameter may carry risk of malignancy in the range of 64% to 82%.[4] Although several characteristics of a nodule may determine the probability of a nodule being malignant or benign, none of them can be conclusive on their own, except perhaps complete calcification. Comparison with prior images is extremely helpful, but older images may not always be available.

Although several modalities of performing biopsy of PPN are available, each has its own pros and cons. For instance, CT-guided transthoracic needle biopsy of PPN has a higher sensitivity for

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Clin Chest Med 39 (2018) 125–138
https://doi.org/10.1016/j.ccm.2017.11.007

malignant lesions (up to 90%) compared with bronchoscopic techniques; it is also fraught with higher complication rates (24% in some studies). This article reviews the techniques, diagnostic abilities, and limitations of commonly used modalities available for PPN biopsy and briefly describes promising innovations in this area (Fig. 1).

CONVENTIONAL BRONCHOSCOPY

Conventional transbronchial biopsy for diagnosis of peripheral lung nodules has been almost phased out. Although it is true that larger lesions may well be successfully sampled with traditional transbronchial lung biopsy with fluoroscopy, the challenges with smaller, particularly peripheral lesions are obvious. Although conventional bronchoscopy is still an excellent tool for endobronchial lesions, its diagnostic sensitivity for smaller nodules (<2 cm) in the periphery of the lung is dismal. A review of literature suggests the diagnostic yield of conventional bronchoscopy for PPN is 43% to 65%, much less for smaller peripheral lesions, about 14% to 31%.[5] Table 1 provides a summary of key studies over a 20-year period from 1967 to 1995 with little improvement in diagnostic yields over time, particularly for small nodules. Even extending CT fluoroscopy, conventional bronchoscopy does appear to improve the yield.[6]

Newer advanced technologies such as electromagnetic navigational (EMN) bronchoscopy have replaced conventional bronchoscopy in the diagnosis of peripheral lung nodules.

RADIAL PROBE ULTRASOUND

Radial probe endobronchial ultrasound (RP-EBUS, Olympus Medical Systems, Tokyo, Japan) is a technology that uses ultrasound properties to provide a minimally invasive modality to visualize the airways structure and the lung parenchyma. Originally intended to visualize the airway and mediastinal structures, RP-EBUS is now mainly used to visualize and sample PPN. It consists of a miniature ultrasound probe (20–30 MHz) with a rotating tip that allows a 360° view of the target lesion (Fig. 2A). It is one of the very few image-guided modalities for diagnosis of PPN that offers real-time confirmation of the PPN. The probe may be threaded through the working channel of a flexible bronchoscope, and given its small diameter, it can be advanced all the way to the periphery of the lung. The RP-EBUS image of normal lung parenchyma has a "snowstorm" appearance, whereas a solid lesion had a dark and "solid" appearance (Fig. 2B, C). However, RP-EBUS does not possess the ability to sample the target lesion by itself. The RP-EBUS has to be retracted and the biopsy instruments passed in its place. Given the difference in caliber and flexibility between RP-EBUS and the biopsy tools, it is not always possible for the biopsy tools to retrace the same path traversed by the RP-EBUS. To overcome this challenge, a guide sheath (GS) (also called extended working channel – EWC) is first threaded into the working channel of the bronchoscope through which the RP-EBUS is passed. After the RP-EBUS reaches the target lesion, the GS is then advanced over the RP-EBUS and positioned just

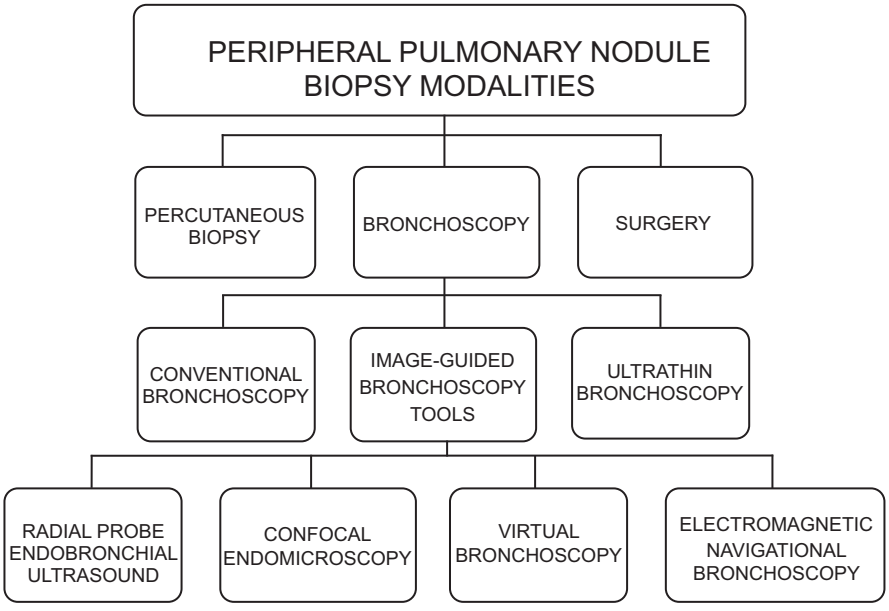

Fig. 1. Currently available PPN biopsy modalities.