Role of Radiology for Imaging and Biopsy of Solitary Pulmonary Nodules*

Kitt Shaffer, MD, PhD

Both imaging and image-directed biopsy play a major role in evaluating solitary pulmonary nodules. Imaging is used to determine whether the nodule is actually solitary or if multiple nodules are present. Once a nodule has been detected, imaging techniques can be used to characterize the nodule in terms of whether it is likely benign or malignant. As technology has improved, smaller nodules are now more easily detected, which may create a management dilemma. With the advent of video-assisted thoracoscopic techniques, however, sampling of these lesions has become much easier. Once a solitary pulmonary nodule is detected, image-guided biopsy is often considered, which can be undertaken using CT or fluoroscopy. Technical limitations, the location of the solitary pulmonary nodules, and clinical conditions must be considered when determining the role of image-guided biopsy. Other concerns include the role of on-site cytology and the use of more recent technical advances. Image-guided biopsy should be used as part of a multimodality approach to patient management, and decisions should be discussed with the radiologist and other caregivers to determine the cost-effectiveness and safety of the procedure for each patient.

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Abbreviations: FNA = fine-needle aspiration; PET = positron emission tomography; SPN = solitary pulmonary nodules

Imaging plays a major role in the evaluation of solitary pulmonary nodules (SPN) at many points in the patient’s course. A nodule is radiologically defined as a relatively rounded opacity in the lung with diameter < 3 cm. Thus, spiculated irregular masses, large masses, or ill-defined masses are not technically “nodules,” although many of the principles described for the management of SPN may still apply. Likewise, particularly with regard to image-directed biopsy, many of the issues are the same for multiple nodules as for SPN. All SPN should be considered malignant until proven otherwise, and serial chest radiographs for follow-up are not generally recommended except in patients with an extremely low prior probability of malignancy.1 The initial detection of nodules on chest radiographs may be assisted in the future by the addition of computerized detection methods.2–4

Nodule Detection

One of the first points at which imaging can have an impact in patient care is in the determination of whether a solitary pulmonary nodule is indeed “solitary.” This is generally best done with CT, which can detect very small nodules with much higher sensitivity than plain radiographs. MRI is not as sensitive as CT for detecting lung nodules, since spatial resolution of MRI is poorer than with CT. Ultrasound has no role in the detection of lung nodules at present. For the optimal detection of nodules with CT, several technical parameters must be considered. Spiral CT, which can image the entire chest in a single breath, offers obvious advantages in nodule detection, although it does require the patient to hold his or her breath for up to 30 s. This may not be possible in patients with dyspnea or very poor pulmonary function. Collimation is probably best kept at 10 mm, since the use of thinner sections for nodule detection can lower specificity due to the fact that vessels in the lung may become indistinguishable from nodules on very thin sections. Particularly with spiral CT, 10-mm collimation allows very sensitive and specific detection,5 and the data can be reconstructed at various intervals without the need to rescan the patient and expose him or her to additional radiation.

Nodule Characterization

Once a nodule has been detected, CT can also be used to characterize the nodule and help estimate the likelihood of malignancy. Detection of calcification is particularly important, since certain patterns of calcification are associated with a very high likelihood that the nodule is benign. Organized patterns of calcification, such as “popcorn”2 (seen in hamartomas), lamellar concentric rings of calcium, central calcification, or homogeneous dense calcification all carry an extremely low likelihood of malignancy. However, not all nodules that contain calcification are benign. Certain patterns of calcification are considered radiologically “indeterminate,” meaning that they do not increase or decrease the likelihood of malignancy compared to a noncalcified nodule. These indeterminate patterns include stippled fine calcification and eccentric calcification. Detection of calcification when only a small amount is present is not always easy, even with CT. Reference phantoms have been developed to assist in detection of low levels of calcification,6 but these are expensive and cumbersome to use. Dual-energy CT allows detection of low levels of calcification without use of a phantom.7 Presence of fat density within a nodule is also specifically indicative of hamartoma.

The role of IV contrast in the evaluation of SPN is changing. In routine practice, IV contrast is not needed for nodule detection, since nodules inherently stand out from surrounding aerated lung. However, for characterization of nodules, quantitation of degree of enhancement may be useful. This must be done in a controlled manner, with time-activity curves calculated for the nodules to allow...
comparison between precontrast and postcontrast images, and to allow quantification of the percentage change in density with IV contrast. Studies of this technique have shown it to be fairly specific in distinguishing between benign and malignant nodules. Gadolinium-enhanced MRI of SPN may offer similar information.

Another imaging modality with promise for discriminating between benign and malignant SPN is positron emission tomography (PET). PET scanning has been studied in the setting of SPN and shows good specificity for benign vs malignant etiologies. False-positives, however, can occur in SPN with inflammatory components, such as anthrosilicotic nodules and some infectious nodules. PET is still an expensive procedure and not readily available, but it may play a larger role in future nodule evaluation. While PET is expensive, if it prevents unnecessary surgery it may actually be cheaper in the long run.

Detection of Small Nodules

As CT technology has improved, smaller nodules are now more easily detected. We are now faced with the common occurrence of very tiny subpleural nodules, sometimes called “ditzels,” which would probably not have been visible on older CT scans. Many of these are benign in etiology, such as granulomas or intrapulmonary lymph nodes. Most typically, intrapulmonary lymph nodes are 1 to 2 mm in diameter and are located in the posterior basal subpleural portions of the lungs. Biopsy is not cost-effective for all of these lesions. However, since they are so small, they are generally indeterminate in terms of imaging criteria, with no detectable calcification, and they are too small to be imaged with PET or sampled by percutaneous biopsy. This is a management dilemma with no clear solution. Several studies have shown that a significant proportion of these ditzels are metastatic disease in patients with known malignancies. This suggests that management of ditzels must be tempered by consideration of the patient’s history of any malignancy with propensity to metastasize to the lung. With the advent of video-assisted thoracoscopic techniques, sampling of these lesions is much easier for patients than in the past.

Differential Diagnosis of SPN

The differential diagnosis of SPN is usually between malignancy, benign tumor, and infection. In most studies, the incidence of malignancy in SPN ranges from 50% to 75%. Among patients with initial imaging suggesting cancer who were later found to have an infectious diagnosis, almost all had SPN as an initial imaging finding. Overall, in a 3-year retrospective study, only 1% of patients with SPN ultimately had an infectious final diagnosis (mainly fungal infections followed by mycobacterial or other bacterial infections). These percentages may be altered in areas endemic for fungal infections or tuberculosis. Noninfectious benign etiologies for SPN include rheumatoid nodules, hamartoma, plasma cell granuloma, anthrosilicotic nodule, and sarcoidosis. Unusual causes include parasitic infections, intrapulmonary Castleman’s disease, and inflammatory pseudotumor.

Biopsy

Once a solitary pulmonary nodule is detected with no clear benign features on any imaging study, the next step is often the consideration of image-guided biopsy. Two main imaging modalities, CT and fluoroscopy, can be used for this procedure, and each has certain advantages. CT allows better planning of the needle path and safe biopsy of lesions located in proximity to vascular structures or nerves. Fluoroscopy allows real-time monitoring of the needle course and is often easier in patients who are less cooperative with breath-holding, since the needle can be directed into the lesion even if the patient is breathing. Fluoroscopic biopsies are often faster, since no delays are introduced while waiting for images to be reconstructed and displayed. Ultrasound offers many of the same advantages as fluoroscopy, but cannot be used to direct biopsy of most lung nodules, since air in the lung parenchyma blocks ultrasound beams. However, ultrasound can be used to guide biopsy of peripheral lung lesions. In the future, MRI may play a more of a role in directing lung biopsies, with development of open configuration magnets that allow more rapid evaluation of needle position.

Technical Concerns

Certain technical limitations must be kept in mind when considering image-directed biopsy or fine-needle aspiration (FNA) of lung nodules. In order to minimize the risk of pneumothorax, which is the main complication of FNA, the smallest possible gauge of needle should be used (generally 21 gauge or 22 gauge). Larger-caliber core biopsy needles can also be used for lung lesions, particularly those abutting pleura. Many FNA needles have compartments along their distal side walls that are designed to allow collection of the maximum amount of tissue while aspirating through the needle and moving it back and forth within the lesion. This aspiration technique will not work if the lesion is so small that the needle side compartment cannot be kept within the lesion while the needle is being moved. Overall, diagnostic success is low in lesions <1 cm in diameter. The risk of pneumothorax is also increased with increased lesion depth from pleura and decreased lesion size.

The location of the solitary pulmonary nodule can affect the likelihood of success with FNA. Lesions that are nearer the pleura are generally easier to sample. Lesions that are in the lower lobes may be harder to sample if the patient is unable to hold his or her breath in a consistent manner, particularly for CT-guided FNA, since the basilar portions of the lungs move the most with breathing. This is less of a limitation for fluoroscopically guided FNA. The risk of pneumothorax increases when a fissure must be crossed in order to reach a lesion. Thus, certain nodules positioned such that the only possible needle path crosses the major or minor fissure may have a high risk of associated pneumothorax. Lesions surrounded by bullae carry the same high risk of pneumothorax. In fact, COPD has been associated with an overall increased risk of pneumothorax during FNA. This risk increased as the FEV1 decreased in one study, although results are controversial. Some lesions may be inaccessible due to
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Clinical Concerns

Certain clinical conditions should also be kept in mind when considering image-guided FNA of lung lesions. Patients who are taking aspirin should have bleeding time checked before the procedure, and if prolonged, the risk of serious bleeding may necessitate other measures, such as delay of the procedure until the effects of the aspirin are reversed. Routine CBC count, prothrombin time, and partial thromboplastin time are sometimes checked before FNA. If microbiologic culture is needed, some of the specimen must be added to various culture media in a sterile manner. It is important during the procedure to suspend respiration at all times when the needle is being moved, to minimize the size of the pleural tear that is produced and to decrease the risk of pneumothorax.

On-Site Cytology

The utility of on-site cytologic examination is somewhat controversial. Initial studies suggested that having a cytologist examine the specimen immediately could increase the success rate for the procedure. Other articles have suggested that this is not necessary if enough samples are collected. However, more samples require a longer procedure, more discomfort for the patient, and a higher risk of pneumothorax. At our institution, a cytologist is routinely on site during the procedure, and a quick-prep slide is examined after each pass to determine the adequacy of the sample and whether more tissue will be needed. The cytologist also helps with slide preparation, which may also ensure that the most information is obtained from each sample. It is important to plan prior to the procedure exactly what specimens are needed, since some techniques (e.g., immunohistochemical studies) may require slightly different specimen handling. In addition, if microbiologic culture is needed, some of the specimen must be added to various culture media in a sterile manner before preparation of the cytologic slides.

Technical Advances

Some new technical advances may lead to more accurate FNA diagnoses. The addition of core biopsy with an automated biopsy device to routine FNA may increase specific benign diagnoses. In a study of 50 patients, the accuracy of benign diagnoses increased from 31% with FNA alone to 68% with core biopsy, although the addition of core samples did not increase the accuracy of malignant diagnoses.

Role of FNA

The role of FNA is best examined as part of a multimodality approach to patient management, and decisions about FNA should be discussed with the radiologist and other caregivers to determine if the procedure will be cost-effective and safe in each individual patient. Many surgeons do not require preoperative FNA diagnosis before planned resection of a solitary pulmonary nodule, since a nondiagnostic result will not prevent resection, and a malignant result will not alter the surgical approach. In fact, in patients with no contraindication to surgery, resection may be cheaper overall than initial bronchoscopy or FNA. Rarely, a specific benign diagnosis may be made (e.g., hamartoma) that may preclude surgery, but in most cases, the results are nonspecific. Since the sample is usually cytologic rather than a core of tissue, architectural histologic information is not available from an FNA sample and may further limit the ability to reach a specific benign diagnosis. The role of FNA is also unclear in cases of multiple pulmonary nodules, where determination of the primary site may have important effects on further treatment options, but may also require larger tissue samples for immunohistochemical analysis than can be easily obtained with FNA.

Summary

The solitary pulmonary nodule is a common clinical problem, and radiology plays a significant role in the detection and characterization of these lesions. The determination that the lesion is indeed solitary, the detection of any specific benign patterns of calcification, the analysis of an enhancement pattern to assess the likelihood of malignancy, and the guiding of FNA to reach a specific diagnosis all depend on careful evaluation of imaging studies and consultation among radiologists, surgeons, and oncologists.

References

1 Lillington GA. Management of solitary pulmonary nodules: how to decide when resection is required. Postgrad Med 1997; 101:145–150


