American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Radiologic Management of Thoracic Nodules and Masses**

Variant 1: **60-year-old man who underwent screening coronary artery CT scan. An incidental 1.5 cm nodule was noted in his right upper lobe. The lesion was smooth, and there was no associated adenopathy. He has no known risk factors for lung cancer.**

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	7	If the patient has significant risk factors, biopsy would be even more indicated.
FDG-PET whole body	7	
Follow-up imaging only	6	The size of the nodule is disconcerting, regardless of the other characteristics.
Surgical lung biopsy/resection	3	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 2: **55-year-old woman presented to emergency department with shortness of breath. CT pulmonary angiogram was negative for pulmonary embolism, but demonstrated incidental 1.5 cm nodule in left lower lobe. The lesion was smooth, and there was no associated adenopathy. She has a 70-packs-a-year smoking history and evidence of significant chronic obstructive pulmonary disease (COPD) on her chest CT.**

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	8	
FDG-PET whole body	8	
Surgical lung biopsy/resection	5	
Follow-up imaging only	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 3: **58-year-old man with a newly diagnosed colon carcinoma. Three pulmonary nodules, ranging up to 2 cm in diameter, noted on staging CT of the chest. At least one of the lesions demonstrates a lobulated appearance.**

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	8	
FDG-PET whole body	8	
Surgical lung biopsy/resection	3	Typically reserved for patients in whom percutaneous biopsy cannot be performed, or in patients with a negative percutaneous biopsy.
Follow-up imaging only	3	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

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Variant 4: **72-year-old woman with a positive PPD and abnormal chest radiograph. On CT scanning, bulky (up to 3 cm) mediastinal adenopathy is noted throughout the mediastinum (pretracheal, subcarinal, aortopulmonary window). The nodes do not demonstrate calcifications or necrosis. There are no associated pulmonary nodules.**

Treatment/Procedure	Rating	Comments
Endoscopic/bronchoscopic biopsy	8	
Percutaneous mediastinal biopsy	5	Consider if bronchoscopic biopsy fails, and the mediastinal biopsy can be safely performed percutaneously.
Surgical mediastinal biopsy/resection	4	Might be appropriate depending on local percutaneous/bronchoscopic biopsy expertise and accessibility of the nodes by nonsurgical approaches.
Follow-up imaging only	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 5: **66-year-old man with a long smoking history and an abnormal chest radiograph obtained for congestion. A follow-up CT demonstrates a 3 cm pulmonary nodule in the lingula and mediastinal adenopathy (up to 2 cm) in the pretracheal and subcarinal regions, as well as left perihilar (up to 2 cm) adenopathy.**

Treatment/Procedure	Rating	Comments
Endoscopic/bronchoscopic mediastinal biopsy	8	Depends on local expertise.
FDG-PET whole body	8	
Percutaneous lung biopsy	7	
Percutaneous mediastinal biopsy	6	Depends on local expertise and accessibility of the nodes by percutaneous approach.
Surgical pulmonary nodule biopsy/resection	3	
Follow-up imaging only	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 6: **35-year-old man with 1.0 cm smooth-walled noncalcified nodule in right middle lobe incidentally seen on CT after minor motor vehicle trauma. He has no known risk factors for lung cancer.**

Treatment/Procedure	Rating	Comments
Follow-up imaging only	8	
Percutaneous lung biopsy	3	
FDG-PET whole body	3	
Surgical lung biopsy/resection	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

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Variant 7: **54-year-old woman presented to emergency department with pleuritic chest pain has a 3 cm lobular mass involving the left pleura associated with rib erosion.**

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	8	
FDG-PET whole body	8	
Surgical pleural biopsy/resection	5	Depends on accessibility by percutaneous approach. Surgical biopsy may be appropriate, however resection is not likely possible.
Follow-up imaging only	1	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 8: **62-year-old man with persistent 1.5 cm ground glass nodule noted on an initial CT scan and a follow-up 3-month CT scan. He has no smoking history and no recent respiratory infection.**

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	7	
Surgical lung biopsy/resection	6	Biopsy depends on local percutaneous expertise. Surgical resection may be performed following percutaneous biopsy.
FDG-PET whole body	5	Broncho-alveolar carcinoma is often PET negative.
Follow-up imaging only	5	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

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Summary of Literature Review

Lung cancer causes more deaths than the next three most common cancers combined (colon, breast, and prostate). An estimated 162,460 deaths from lung cancer occur in the United States each year, and the incidence of the disease is rising [1]. The diagnosis of lung cancer carries a very poor prognosis: the expected 5-year survival rate for all patients in whom lung cancer is diagnosed is 15.5% (compared to 64.8% for colon cancer, 89% for breast cancer, and 99.9% for prostate cancer). Early diagnosis is vital and significantly improves survival rates. The 5-year survival rate approaches 50% in patients in whom the disease is detected when still localized [2]. However, only about one in four lung cancer cases is diagnosed at an early stage [2].

Metastatic disease to the lungs can occur with virtually any primary malignancy. Diagnosis of such metastases allows for appropriate treatment and prognostication of patients with the disease. Although diffuse metastatic disease to the lungs typically mandates systemic treatment such as intravenous chemotherapy, some primary tumors such as sarcomas may metastasize solely to the lungs, and surgical resection may be curative [3].

Cases in which lung cancer is diagnosed at an early stage are typically asymptomatic, further delaying diagnosis. Solitary pulmonary nodules represent the most typical radiographic presentation of early lung cancer, and multiple pulmonary nodules may be the first sign of malignancy in a patient without a prior diagnosis. Biopsy of pulmonary nodules therefore allows for a tissue diagnosis of malignancy and, in some cases, staging of the primary tumor. Diagnosis by less invasive means may also preclude more invasive surgical procedures performed for diagnosis; this is particularly important in this high-risk patient population [4]. For example, findings from positron emission tomography/computed tomography (PET/CT) have been shown to reduce the number of futile thoracotomies and the total number of thoracotomies [5].

Due to the nature of this document, its discussion of biopsies centers on percutaneous approaches. Since percutaneous biopsies are now typically considered as a first-line procedure, there is a severe paucity of recent literature directly comparing percutaneous to other approaches (eg, surgical, video-assisted thoroscopy, bronchoscopy with or without fluoroscopic guidance). The reader should keep these other approaches in mind, and on a case-by-case basis based on anatomy and clinical presentation should determine whether or not nonpercutaneous approaches should be seriously considered.

Pulmonary Nodules

Most biopsies in the thorax will be performed for pulmonary nodules. These nodules may be solitary or multiple; in the latter case, metastatic disease or an infectious etiology is more likely than a primary lung cancer. Initial clinical evaluation, including known risk factors for lung cancer, is necessary before biopsy is attempted. There are several published guidelines for the management of small pulmonary nodules detected on CT scans, the most widely cited of which is supported by the Fleischner Society [6]. Many nonradiologists use "pulmonary nodule calculators" to estimate the pretest probability of malignancy for any given solitary pulmonary nodule. By inputting several clinical and radiologic risk factors that increase the likelihood of malignancy (eg, age, smoking history, size and morphology of the nodule), a calculation is performed that gives the probability of malignancy for a patient presenting with a solitary pulmonary nodule. The American College of Chest Physicians recommends the use of pulmonary nodule calculators when determining the diagnostic and/or treatment algorithm to be undertaken for patients presenting with solitary pulmonary nodules. These calculators are widely available on the internet.

There is a distinct paucity of evidence in the literature directly comparing biopsy techniques across multiple specialties. Methods by which biopsies may be obtained include percutaneous biopsy with imaging guidance, mediastinoscopy with biopsy, bronchoscopy-guided

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transbronchial biopsy, video-assisted thorascopy, endoscopic ultrasound transesophageal biopsy, or open surgical biopsy. The location of the nodule (eg, subpleural, paramediastinal, subcarinal, endobronchial) significantly affects the likelihood of success of one form of biopsy compared to another.

Patients in whom biopsies are performed are often considered to be at high risk for complications from the procedure. These risks (eg, pneumothorax, bleeding, and bronchopleural fistula) are largely due to the poor underlying pulmonary reserve and high incidence of chronic obstructive pulmonary disease (COPD) in this patient population. Patients should be counseled before the procedure regarding the significant risks associated with their biopsy.

In addition to problems associated with a relatively high-risk patient population, percutaneous biopsies of pulmonary nodules may be difficult to perform technically. Patients may often have difficulty suspending respirations or may take variable volume breaths, resulting in the target lesion moving in and out of the biopsy plane. Lesions may also be very small or central (deep) in location, making needle placement challenging. For these reasons and others, the failure rate of lung biopsies is relatively high. The Society of Interventional Radiology guidelines for lung biopsy specify that an 85% success rate is acceptable [7].

Characteristics of pulmonary nodules affect the likelihood of malignancy. Morphologic characteristics, such as smooth and well-defined margins and diffuse or central nodular calcifications, favor benignancy. Persistent ground glass and mixed ground glass density nodules have a high rate of malignancy [8-10]. The likelihood of cancer diagnosis increases with the size of the pulmonary nodule, regardless of solid or ground glass density. Nodules >3 cm in diameter are considered pulmonary malignancies until proven otherwise. Other characteristics, such as growth rate, dynamic changes on contrast-enhanced helical CT, and uptake of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) during PET imaging may help in distinguishing benign from malignant lesions [11].

FDG is accumulated in malignant nodules. Benign lesions such as hamartomas and inflammatory nodules do not significantly accumulate FDG. Thus, PET is a valuable tool in evaluation of indeterminate lesions. In one meta-analysis of 1,474 pulmonary nodules [12], PET was 97% sensitive and 78% specific. It is important to recognize the limitations of PET. It is best used in patients with nodules >1 cm in diameter, and false-negative scans may occasionally occur with malignancies such as well-differentiated adenocarcinomas, broncholoalveolar cell carcinomas (BAC), and carcinoid tumors. False-positive lesions may result in patients with tuberculosis, fungal infections, or sarcoidosis.

Transthoracic needle aspiration and biopsy are the mainstays for obtaining tissue for histopathologic diagnosis of pulmonary nodules, and they usually provide adequate tissue quantity for biochemical analysis [13]. Several technical measures may increase the yield or decrease the risk of percutaneous biopsies:

1. Preselecting patients with nodules having high potential for malignancy.
2. Providing on-site analysis of the specimen, rather than placing the specimen in fixative for later analysis, allows for higher diagnostic accuracy [12,14-16].
3. Performing both fine-needle aspiration (FNA) and core biopsies of the same lesion has been shown to increase yield over FNA alone [17], particularly in the diagnosis of benign nodules.
4. Using a steeper angle of the biopsy needle may decrease the risk of pneumothorax [18].
5. Using a 19-gauge or smaller needle [19].

Percutaneous biopsy is limited in its ability to obtain a specific diagnosis of a benign pulmonary process, and yields of 50% or less are expected [20-21]. Performing both core biopsies and FNA of benign lesions significantly increases the diagnostic yield [22]. In addition, some investigators have suggested that multiple larger biopsies (at least three ≥1 cm in length) increases the yield of diagnosis for benign lesions [23].

In certain instances, nonradiologic biopsies of pulmonary nodules may provide higher yields than image-guided procedures. Video-assisted thoroscopic biopsy may have a very high success rates in patients with subpleural nodules, and bronchoscopic biopsy of central intraluminal lesions may also provide better success rates compared to percutaneous biopsy.

Percutaneous lung biopsy is generally associated with higher complication rates compared to solid organ biopsy. The Society of Interventional Radiology has published guidelines stating that an overall complication rate of 10% is acceptable for lung biopsies, compared to 2% for all other organ systems [7]. The most common complication of percutaneous lung biopsy is bleeding (hemoptysis, chest wall, parenchymal); however, the most common complication requiring intervention is pneumothorax (10%-30%). Chest tube insertion is needed in approximately one-third of patients with pneumothoraces. Most postbiopsy complications can be treated conservatively, often on an outpatient basis [24-26]. Embolization of the tract following biopsy using a coaxial system has been described, with embolization agents varying from collagen foam plugs to autologous clot to fibrin glue [27-29]. The risk of chest wall implantation caused by percutaneous biopsy is rare, with reports ranging from 0%-3% [30-31].

Patients who undergo percutaneous lung biopsies that yield a definitive malignant diagnosis may or may not undergo therapy. False-positive results are very rare. Patients with definitive benign diagnoses can be managed conservatively, although false-negative results may occur in a minority of patients. Patients who do not have either a definitive malignant or benign diagnosis need close

follow-up, surgical referral, or repeat biopsy (either percutaneous or by other means). Death from percutaneous lung biopsy is extremely rare but may occur from systemic air embolism.

Mediastinal Nodes and Masses

Mediastinal masses may arise without a concurrent intraparenchymal pulmonary mass and may represent metastatic disease. Definitive diagnosis by biopsy is vital in that it may significantly change the treatment options or may preclude the need for exploratory surgery. The best method of biopsy largely depends on the location of the mass and the proximity of adjacent structures.

Image-guided biopsies of mediastinal masses are almost always performed using CT guidance. The lack of an acoustic window prevents the use of ultrasound (US), unless the mass extends to the pleural surface or invades the chest wall. Real-time CT guidance, however, may be more difficult than expected because of its relative poor visualization of vascular structures on unenhanced CT. In select instances, the use of iatrogenic saline windows (so-called "salinoma") may be helpful in decreasing the incidence of postbiopsy pneumothorax by moving the pleural surface away from the needle path [32]. Several approaches have been described, including parasternal, suprasternal, and even trans-sternal. Awareness of the internal mammary vessels is crucial in safely performing a parasternal approach.

Nonradiologic mediastinal mass biopsy may be safer and have higher yields than radiologic biopsy. Bronchoscopically guided transbronchial FNA [33], endoscopic transesophageal US with FNA [34-37], mediastinoscopy [35], endobronchial US [38], and thoracoscopy [39] may all be used to obtain tissue from mediastinal masses. The indications for image-guided versus nonradiologic procedures will vary from institution to institution.

Pleural Biopsies

Pleural biopsies can be separated on the basis of whether the region of interest is a focal mass or a diffuse process. Biopsies for diffuse processes, such as tuberculosis, are frequently done without imaging guidance. Biopsies for focal pleural-based mass lesions can frequently be performed with US guidance, particularly in the presence of a pleural effusion. Due to the paucity of evidence in the literature, complication rates are impossible to determine; however, it is anticipated that the risk of pneumothorax will be somewhat lower than that demonstrated with intraparenchymal biopsies.

Summary

Intraparenchymal pulmonary nodules:

- The choice of modalities (percutaneous with imaging guidance, bronchoscopy, video-assisted thoroscopy, mediastinoscopy, or open surgical) depends in large part on the location and size of the lesion, the underlying pulmonary function, adjacent structures, clinical expertise at the particular practice, and operator preference.
- In patients with incidentally noted pulmonary nodules that do NOT have an appearance typical of malignancy (eg, nodule has smooth borders, calcification, does not invade surrounding structures) and no known risk factors, conservative follow-up with imaging is more appropriate than biopsy.
- PET imaging is very sensitive for nodules >1 cm in diameter; however, there is a relatively high rate of false negatives. PET may be particularly helpful during follow-up of patients postintervention and for assessing patients for distant metastatic disease.
- Increased diagnostic yield is expected when core biopsy is performed in addition to FNA.
- Slide fixation at the time of FNA improves diagnostic yield compared to placing the specimen in a fixative for later cytopathologic evaluation.
- Most complications can be treated using percutaneous techniques, and many can be treated on an outpatient basis.
- Delayed pneumothorax is known to occur, but is a rare complication.

Mediastinal masses/adenopathy:

- In select patient populations, image-guided percutaneous FNA and biopsy may provide the highest diagnostic yield in the safest manner.
- Nonradiologic biopsies (eg, mediastinoscopy with biopsy, bronchoscopic or endoscopic US-guided transbronchial or transesophageal biopsy) may provide a safer alternative to percutaneous biopsy.

Pleural biopsies:

- Pleural biopsies for diffuse disease (eg, tuberculosis) can typically be performed without imaging guidance.
- Biopsies of focal pleural masses can be performed safely with either CT or US guidance.

Many of the diagnostic, surgical, and interventional procedures described here are highly specialized. Their availability and utility vary by institutional and operator experience.

Supporting Document(s)

- ACR Appropriateness Criteria® Overview
- Evidence Table

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