

American College of Radiology ACR Appropriateness Criteria®

Clinical Condition: Needle Biopsy in the Thorax

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	8	Indicated for definitive diagnosis. Associated comorbidities may necessitate a change in the algorithm.
FDG-PET whole body	8	Appropriate for baseline examination and for concomitant disease elsewhere.
Surgical lung biopsy/resection	2	May be appropriate if percutaneous biopsy cannot be safely performed or is nondiagnostic.
Follow-up imaging only	2	
Conservative management (do nothing)	1	
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate		

Variant 2: 55-year-old woman presented to the 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	Indicated for definitive diagnosis. Associated comorbidities may necessitate a change in the algorithm.
FDG-PET whole body	8	Appropriate for baseline examination and for concomitant disease elsewhere.
Surgical lung biopsy/resection	3	May be appropriate if percutaneous biopsy cannot be safely performed or is nondiagnostic.
Follow-up imaging only	1	
Conservative management (do nothing)	1	
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate		

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Clinical Condition:**Needle Biopsy in the Thorax****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	Depends on outcome of PET. May indicate more easily accessible lesions for biopsy.
FDG-PET whole body	8	For staging and baseline exam.
Surgical lung biopsy	2	May be appropriate if percutaneous biopsy is nondiagnostic. Surgical resection may provide improved survival benefit in select cases.
Follow-up imaging only	2	May be appropriate depending on presence of other metastatic disease (eg, liver), stage of the primary tumor, and to monitor response to therapy.
Conservative management (do nothing)	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 4:

72-year-old woman with a positive PPD and abnormal chest x-ray. On CT scanning, bulky mediastinal adenopathy is noted throughout the mediastinum. The nodes do not demonstrate calcifications or necrosis. There are no associated pulmonary nodules.

Treatment/Procedure	Rating	Comments
Percutaneous mediastinal biopsy	8	
Endoscopic/bronchoscopic biopsy	8	May be useful prior to proceeding with mediastinoscopy to see if a definitive diagnosis can be obtained. May be preferred to percutaneous biopsy depending on safety of percutaneous approach.
Surgical (open) biopsy	2	
Follow-up imaging only	2	
Conservative management (do nothing)	1	
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Clinical Condition:**Needle Biopsy in the Thorax****Variant 5:**

66-year-old man with a long smoking history and an abnormal chest x-ray obtained for congestion. A follow-up CT demonstrates a 3 cm pulmonary nodule in the lingula and mediastinal adenopathy in the pretracheal and subcarinal regions, as well as left perihilar adenopathy.

Treatment/Procedure	Rating	Comments
Percutaneous mediastinal biopsy	7	The specifics of node size and imaging window will determine preferable approach in any given patient (lung biopsy vs mediastinal biopsy).
Percutaneous lung biopsy	7	The specifics of node size and imaging window will determine preferable approach in any given patient (lung biopsy vs mediastinal biopsy).
Endoscopic/bronchoscopic mediastinal biopsy	7	May be appropriate with significant comorbidities or if endobronchial lesion is suspected. Depends on institutional expertise.
Surgical (open) mediastinal biopsy	2	Appropriate if unable to obtain diagnosis with other modalities.
Surgical pulmonary nodule biopsy/resection	2	
Follow-up imaging only	1	
Conservative management (do nothing)	1	
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NEEDLE BIOPSY IN THE THORAX

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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, 89% for breast cancer and 99.9% for prostate cancer). Early diagnosis is vital and significantly improves survival rates for patients with lung cancer. 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].

Part 1: 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. Many clinicians 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 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 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

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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 [5].

Characteristics of pulmonary nodules impact the likelihood of malignancy. Morphologic characteristics, such as smooth and well-defined margins and diffuse or central nodular calcifications favor benignancy. Lesions that have a ground glass appearance (rather than solid) are more likely to be benign [6-8]. Other characteristics such as growth rate, dynamic changes on contrast-enhanced helical CT, and uptake of 18F fluorodeoxyglucose (FDG) during positron emission tomography (PET) imaging may help in distinguishing benign from malignant lesions [8]. The likelihood of cancer diagnosis increases with the size of the pulmonary nodule. Nodules larger than 3 cm in diameter are considered pulmonary masses.

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 [9], PET was 97% sensitive and 78% specific. It is important to recognize the limitations of PET. It is best used in patients with nodules larger than 1 cm in diameter. False-negative scans may occasionally occur with malignancies such as well-differentiated adenocarcinomas, bronchoalveolar cell carcinomas, and carcinoid tumors. False-positive lesions may result in patients with tuberculosis, fungal infections, or sarcoidosis.

Transthoracic needle aspiration and biopsy are the mainstay for obtaining tissue for histopathologic diagnosis of pulmonary nodules. Several technical factors may increase the yield or decrease the risk of percutaneous biopsies:

1. Preselection of 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 [9-12].
3. Performing both fine-needle aspiration (FNA) and core biopsies of the same lesion has been shown to increase yield over FNA alone [13], particularly when trying to diagnosis benign nodules.
4. Using a steeper angle of the biopsy needle may decrease the risk of pneumothorax [14].

Percutaneous biopsy is limited in its ability to obtain a specific diagnosis of a benign pulmonary process; yields of 50% or less are expected [15]. Performing both core biopsies and FNA of benign lesions significantly increases the diagnostic yield [16].

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 [5]. 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 those with pneumothoraces. Most postbiopsy complications can be treated conservatively, often on an outpatient basis [17-19]. 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 [20-22]. Patients who undergo percutaneous lung biopsies that yield a definitive malignant diagnosis may or may not go onto therapy. False-positive results occur very rarely. 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.

Part 2: 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.

Radiologic biopsies of mediastinal masses are almost always performed using computed tomography (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 suspected because of the relative lack of 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 [23]. Several approaches have been described including parasternal, suprasternal, and even

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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 compared to radiologic biopsy. Bronchoscopically guided transbronchial FNA [24], endoscopic transesophageal US with FNA [25-28], mediastinoscopy [26], endobronchial US [29], and thoracoscopy [30] may all be used to obtain tissue from mediastinal masses. The indications for radiologically guided versus nonradiologic procedures will vary from institution to institution.

Part 3: 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) depends in large part on the location and size of the lesion, the underlying pulmonary function, adjacent structures, clinical expertise at the particular location, and operator preference.
- In patients with incidentally noted pulmonary nodules that do NOT have a typical appearance 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 larger than 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.

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.

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.

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

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