Lung, Pleural, and Mediastinal Biopsies: From Preprocedural Assessment to Technique and Management of Complications

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Abstract

Biopsies of the lung, pleura, and mediastinum play a crucial role in the workup of thoracic lesions. Percutaneous image-guided biopsy of thoracic lesions is a relatively safe and noninvasive way to obtain a pathologic diagnosis which is required to direct patient management. This article reviews how to safely perform image-guided biopsies of the lung, pleura, and mediastinum, from the preprocedural assessment to reviewing intraprocedural techniques, and how to avoid and manage complications.

Keywords
- interventional radiology
- percutaneous
- lung biopsy
- pleural biopsy
- mediastinal biopsy

Percutaneous biopsy of the lung, pleura, and mediastinum is an important step in the workup of thoracic lesions. Image-guided percutaneous biopsy of thoracic lesions is a noninvasive and relatively safe method to obtain a pathologic diagnosis which is essential in directing patient management.

Preprocedural Assessment

Lesion Assessment

One of the first steps when a request has been placed to perform a percutaneous thoracic biopsy is to review the patient's imaging to assess if the lesion is amenable to image-guided sampling. For lung lesions, there is a definite relationship between nodule size and risk of malignancy.[1] Studies have shown that diagnostic accuracy declines in proportion to decreasing lesion size[2] and that the diagnostic yield is lower in lesions smaller than 1.5 cm,[3] which can be attributed to the technical difficulty in sampling smaller lesions. However, the diagnostic yield also decreases in larger lesions, reportedly lesions over 5.0 cm, due to necrosis.[3] To avoid sampling necrosis in these larger lesions, positron emission tomography–computed tomography is a valuable adjunct tool for preprocedural planning to assess for areas of viable tissue that can be targeted for sampling to increase the diagnostic yield (►**Fig. 1**).[4–6] Similarly, increased pleural thickness is associated with higher diagnostic yield in pleural biopsies (►**Fig. 2**).[7] Lesion size does not seem to be a factor in the diagnostic yield of mediastinal mass biopsies.[8]

Another consideration is the location of the lesion. For lung biopsies, percutaneous image-guided biopsy is well suited for peripheral lesions, while bronchoscopy is preferred for central or perihilar lesions. If there are extrapulmonary sites of disease, biopsy of these lesions should be considered to more accurately stage the disease. Another advantage of image-guided percutaneous biopsy as compared with an endobronchial approach is the ability to use larger gauge coaxial needles which can provide more robust tissue samples, particularly in cases of lymphoma where larger amounts of tissue are needed as fine needle aspiration biopsy (FNAB) is not sufficient for subtyping lymphoma (►**Fig. 3**).

Patient Selection

Once a patient is deemed a good candidate for percutaneous biopsy, a thorough preprocedural assessment is required.

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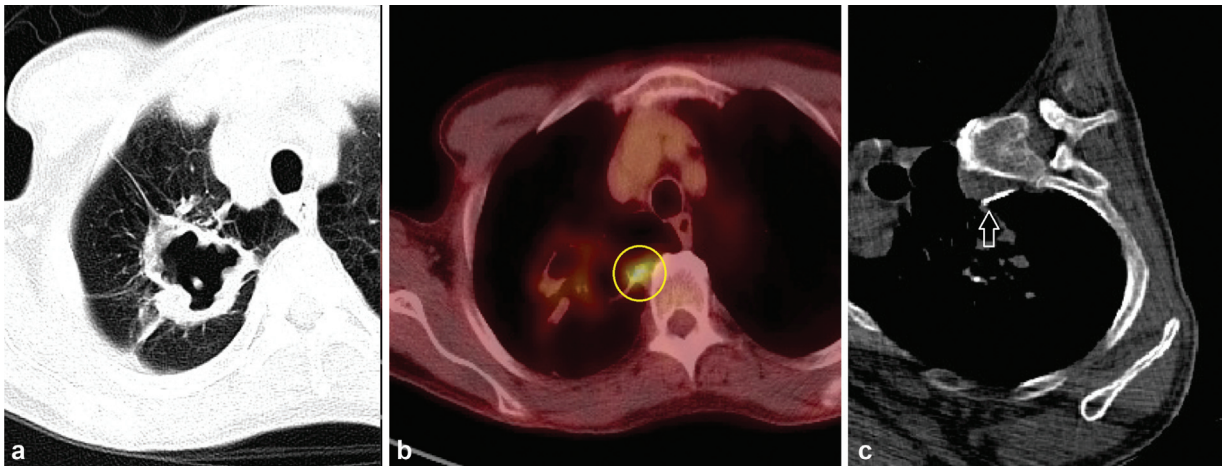

Fig. 1 A 67-year-old with a cavitary right upper lobe mass (**a**) underwent PET-CT that showed FDG uptake in the medial component of the mass (**b**, circle), which was then targeted for the biopsy (**c**; arrow—needle tip). Pathology revealed nonnecrotizing granulomas.

Regarding coagulation parameters, as per current guidelines, the INR should be less than 1.5, or should be corrected if above this level. The platelet count should be greater than 50,000/μL, and patients should be transfused if necessary. Plavix should be held for 5 days prior to the procedure; however, patients can continue aspirin. If patients are on a therapeutic dose of low-molecular-weight heparin, one dose should be held prior to the procedure.[9]

Some institutions perform prebiopsy pulmonary function testing (PFT) to assess a patient's ability to potentially withstand an iatrogenic pneumothorax.[10,11] Aspects of the PFT that are evaluated include the forced expiratory volume in 1 second, with absolute values of 0.8 to 1.5 L, or 30 to 50% predicated as minimum thresholds.[10,11] The transfer factor for carbon monoxide is also sometimes evaluated with ideal values between 30 and 50%.[10] Multidisciplinary patient assessment is recommended if PFT values are less than these thresholds.[11] Interestingly, there is no association between PFT results and the risk for developing a pneumothorax[12–15]; therefore, many proceduralists do not routinely assess PFTs prior to the biopsy.

Relative contraindications to percutaneous thoracic biopsies include uncooperative patients, uncorrectable coagulopathy, severe respiratory compromise (e.g., severe emphysema or chronic obstructive pulmonary disease), pulmonary hypertension, and patients on positive pressure ventilation.[4,16]

Procedural Technique

Moderate sedation is routinely used during percutaneous thoracic biopsies, which increases patient comfort as well as reduces the likelihood of extreme motion during the procedure. We routinely use a combination of fentanyl and midazolam for moderate sedation.

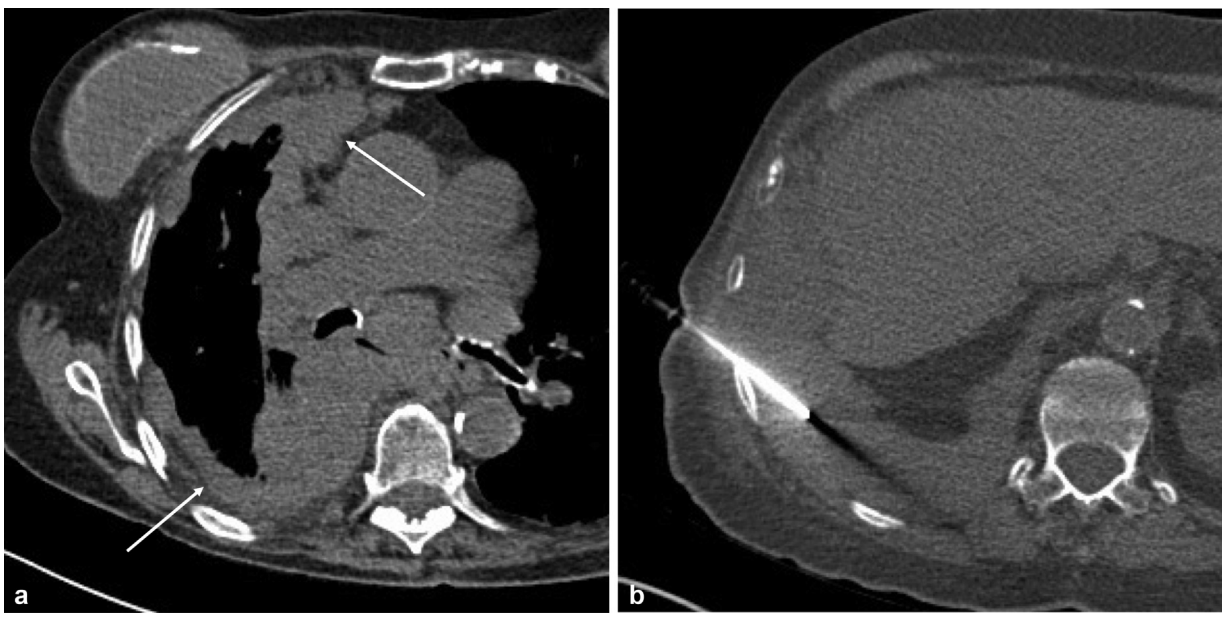

Fig. 2 A 93-year-old man presented with recurrent right pleural effusion and irregular pleural thickening (**a**, arrows). The thickest region of pleural thickening was targeted for biopsy (**b**). Pathology was consistent with mesothelioma.

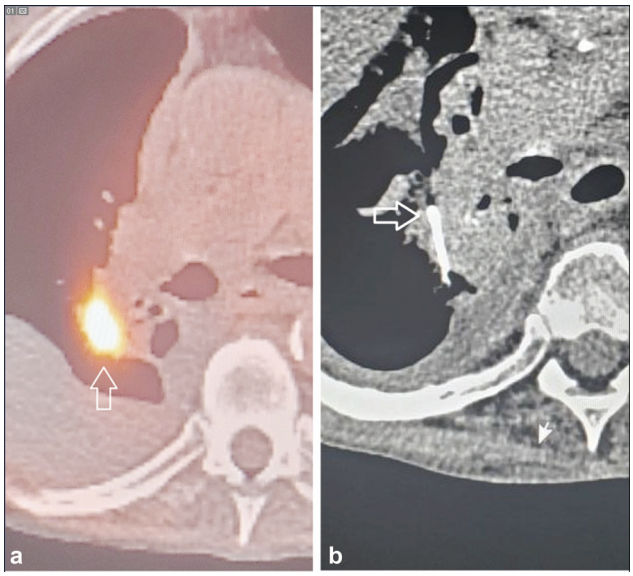

Fig. 3 Patient with a right perihilar mass which was PET-CT avid (**a**, arrow). Bronchoscopic fine needle aspiration biopsy was nondiagnostic. Core biopsy samples were obtained under CT guidance (**b**; arrow—needle tip). Pathology was consistent with squamous cell carcinoma.

If multiple lung lesions are amenable for biopsy, it is typically preferable to target an upper lobe lesion, as there is less respiratory motion in the upper lobes compared with the lower lobes, which will make it easier to target the lesion and reduces risk of pneumothorax.

CT guidance with CT fluoroscopy is usually the modality of choice for image-guided percutaneous lung biopsy, as it allows near real-time visualization of the biopsy needle position, the target lesion, and important structures in between such as the pleura and pulmonary vessels.[4,5,16] We decrease the milliampere seconds (mAs) while using CT fluoroscopy during the procedure to lower radiation exposure to the patient and the operator. While standard CT fluoroscopy for body application uses 50 mA, CT fluoroscopy in the lung can be utilized with lower exposure of 30 mA. Ultrasound (US) can also be used to safely target subpleural/peripheral lesions with the advantage of being more readily available than CT.[17]

Once the lesion for biopsy has been chosen, patient positioning needs to be considered. We suggest placing the patient in a lateral decubitus position (►**Fig. 4**), if tolerable by the patient, with the biopsy side down to decrease motion of the dependent lung and thus decrease the risk of pneumothorax,[18–22] and the operator working from either the front or the back. Another advantage of positioning the patient with biopsy side in the dependent position is decreased spillage of blood to the contralateral lung, if pulmonary hemorrhage occurs. The disadvantage of lateral decubitus positioning is that it can be difficult for patients to remain motionless, and thus supports should be provided as needed. Partial decubitus positioning, which is generally more convenient for patients, can be utilized to obtain the benefits of having the lung in a dependent position (►**Fig. 5**). Moreover, this positioning may open additional accesses for biopsy. Alternatively, supine or prone positioning could be used.

Next, a preprocedural CT scan, usually limited to the region of interest, is performed to localize the lesion. A marking grid could be placed on the patient prior to this scan to landmark. Alternatively, a landmark using the slice of interest on the preprocedural CT with a metallic marker can be utilized.

There are a few principles that should be adhered to when choosing a biopsy trajectory. First, one should choose the shortest path possible to the lesion, as a longer trajectory, usually intra-parenchymal distances of greater than 3 cm, increases the risk of pneumothorax.[19] Also, ideally, the pleura should be transgressed only once, and preferably crossed at a 90-degree angle, with avoidance of the fissures to decrease the chances of a pneumothorax.[19] For subpleural

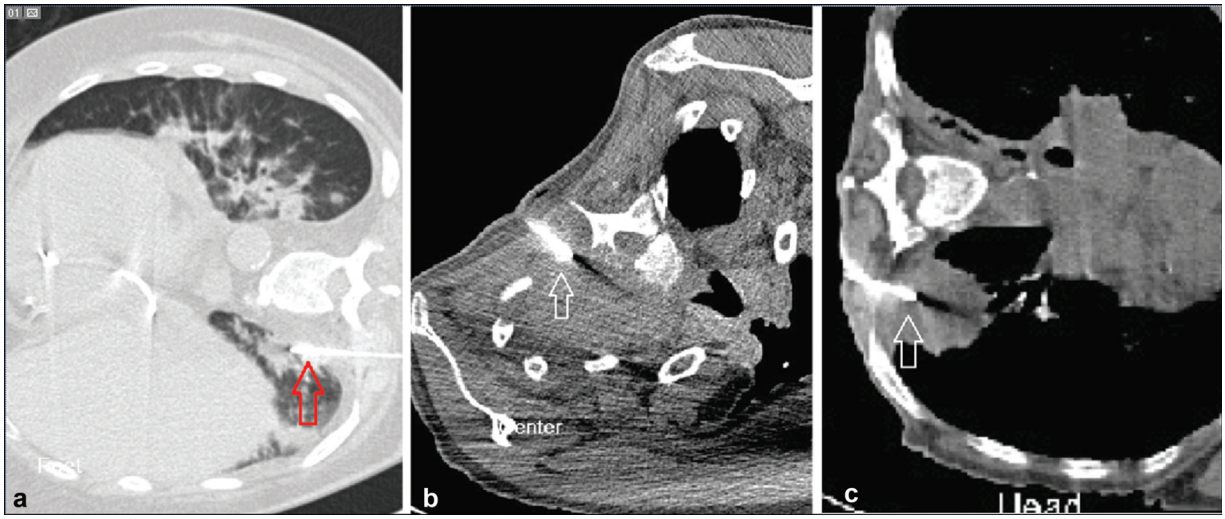

Fig. 4 The lateral decubitus position, with the biopsy side down, helps reduce motion and decreases the risk of an iatrogenic pneumothorax. Examples are shown in a 70-year-old patient with a new right lower lobe pulmonary nodule (**a**; arrow—biopsy needle), an 80-year-old man with a new left upper hemithorax mass post left upper lobectomy for squamous cell carcinoma (**b**; arrow—biopsy needle), and a 75-year-old woman with a left lower lobe mass (**c**; arrow—biopsy needle).

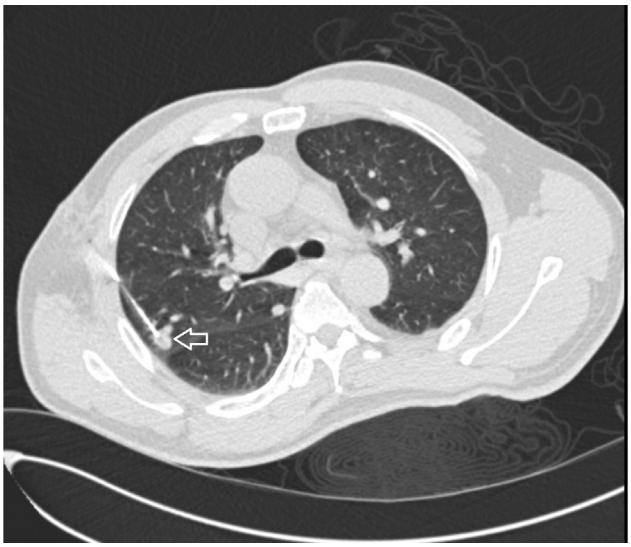

Fig. 5 Partial decubitus position may provide some benefits of decreased motion due to partial effects of gravity, in addition to restricting spread of pulmonary hemorrhage, if it was to occur, to a single lung. Arrow—biopsy needle.

lesions, we try to plan for a trajectory that includes normal lung parenchyma to not lose access/positioning during biopsy needle exchanges and so that the pleura is transgressed only once. Any large bulla should also be avoided.

A preprocedural time-out is required for any interventional radiology procedure, which includes patient verification using two identifiers, verification of the correct procedure, identification of the correct biopsy site, as well as a review of patient allergies, medications, sedation plan, and laboratory tests. An important part of the time-out is to confirm lesion location as well as the number and media for the samples. For example, primary lung cancer now requires a large amount of material for genomic testing in addition to standard histopathological evaluation. We usually obtain at least four core biopsies which are placed in two separate formalin containers. Two to three core biopsies are more than sufficient for metastatic lung lesions, also placed in formalin. However, when lymphoma is in the differential, our protocol includes two to three cores into formalin for histopathological evaluation, two cores in Roswell Park Memorial Institution (RPMI) for flow cytometry, and another two cores for molecular genetics in RPMI for a total of six to seven cores. On the other hand, for culture, the specimen needs to be placed in a sterile container and not formalin.

After prepping the sterile field, and administering superficial and deep local anesthetic, our practice generally uses a 17/18G coaxial system to biopsy lung lesions. We use intermittent CT fluoroscopy to guide our biopsy needle, and try to advance the needle at end expiration during free breathing to make the fluoroscopic images reproducible. Breath-holding can be attempted if the patient is compliant, but in our experience it is not as reproducible as good timing during free breathing. It is important to use the minimum amount of moderate sedation required to optimize free-breathing, and reduce the sporadic respiration rates that can be displayed during sleep.

We suggest advancing the biopsy needle so that the outer stylet is just within the lesion. Studies have shown that the diagnostic sensitivity increases with the higher number of passes performed.[23,24] Our practice does not routinely perform FNAB for lung lesions, as the diagnostic yield is lower than for core needle biopsy particularly in the diagnosis of benign lesions,[3,25,26] despite the higher risk for developing a pneumothorax.[26] Moreover, in the age of precision medicine, core biopsies allow for the characterization of tumor genomics which plays an increasingly important role in patient management. A recent study has shown that obtaining more than two core samples, and submitting samples in two cassettes improved tissue adequacy for molecular testing,[27] the latter of which is part of our routine practice.

Considerations for Pleural and Mediastinal Biopsies

There are a few additional considerations for pleural and mediastinal biopsies.

For pleural-based lesions, US or CT could be used for imaging guidance with a meta-analysis showing no difference in diagnostic yield between these modalities.[7,28] For smaller pleural-based lesions, we will typically choose CT guidance to monitor for the development of an iatrogenic pneumothorax. Moreover, core needle biopsy is preferable over FNAB to increase the diagnostic yield (►**Fig. 6**).[29]

For mediastinal lesions, it is important to plan the biopsy trajectory carefully. Careful planning is required to avoid the internal mammillary arteries (IMAs; ►**Fig. 7**), and once within the mediastinum, CT fluoroscopy is judiciously used to avoid the thoracic aorta and pulmonary arteries. Hydrodissection can be used to form a biopsy plane between the IMA and sternum if required. Alternatively, a transsternal approach could be taken, which can be done manually or with the aid of a bone drill (►**Fig. 8**).

Postprocedure Recovery

Once the procedure is finished, patients are asked to rest with the biopsy side down for 1 hour if tolerable. For patients without a pneumothorax on the postprocedural CT, we will monitor for 1 hour. If the patient is asymptomatic and if they score at least a 9 on the post anesthetic discharge score system,[30] then we will discharge the patient home. Studies have shown that a shortened observation period of 2 hours postprocedure without a routine chest radiograph in asymptomatic patients is safe.[31]

Radiology–Pathology Correlation

Our institution runs weekly radiology–pathology rounds, where radiologists review the final pathology of any biopsy performed by our department. For cases where the pathology is indeterminate or discordant with the imaging findings, we will contact the referring provider with our recommendations such as repeat biopsy or obtaining follow-up imaging.

One of the major caveats is a pathology result showing organizing pneumonia. Even though organizing pneumonia exists, similar pathological findings can also be seen adjacent to tumors. Therefore, it is of outmost importance to correlate with the clinical history, imaging findings, and pathological findings to confirm concordance. In case of discordance,

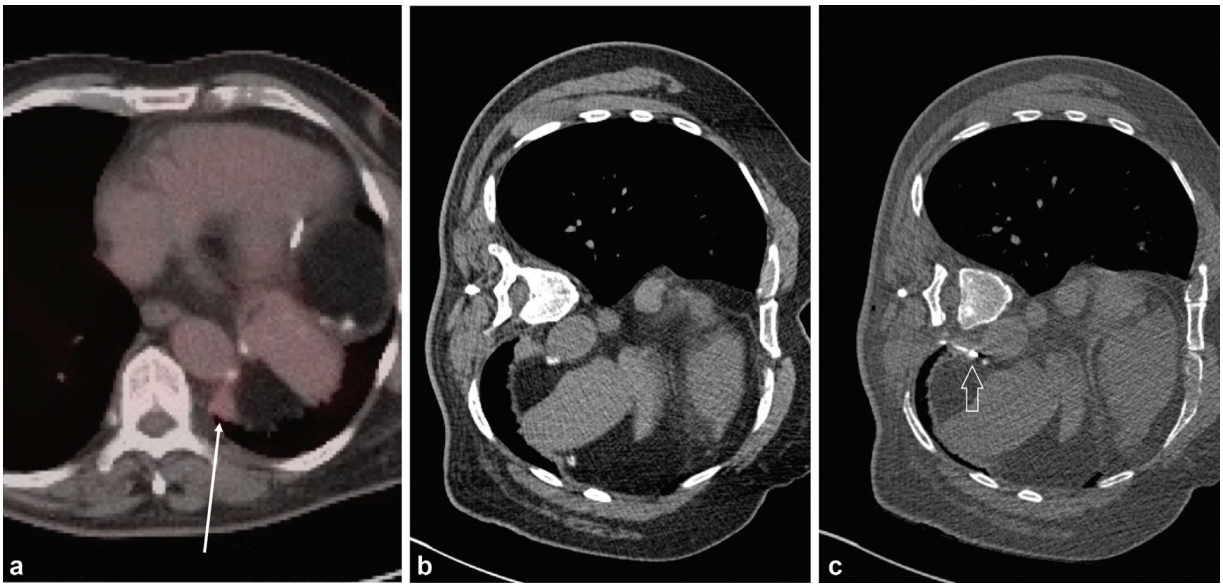

Fig. 6 A 73-year-old with a history of thymoma presents with new left pleural lesion which was mildly avid on PET-CT (**a**, arrow). Biopsy was performed in the left lateral decubitus position (**b** and **c**; arrow—needle tip) avoiding lung. Pathology demonstrated thymoma.

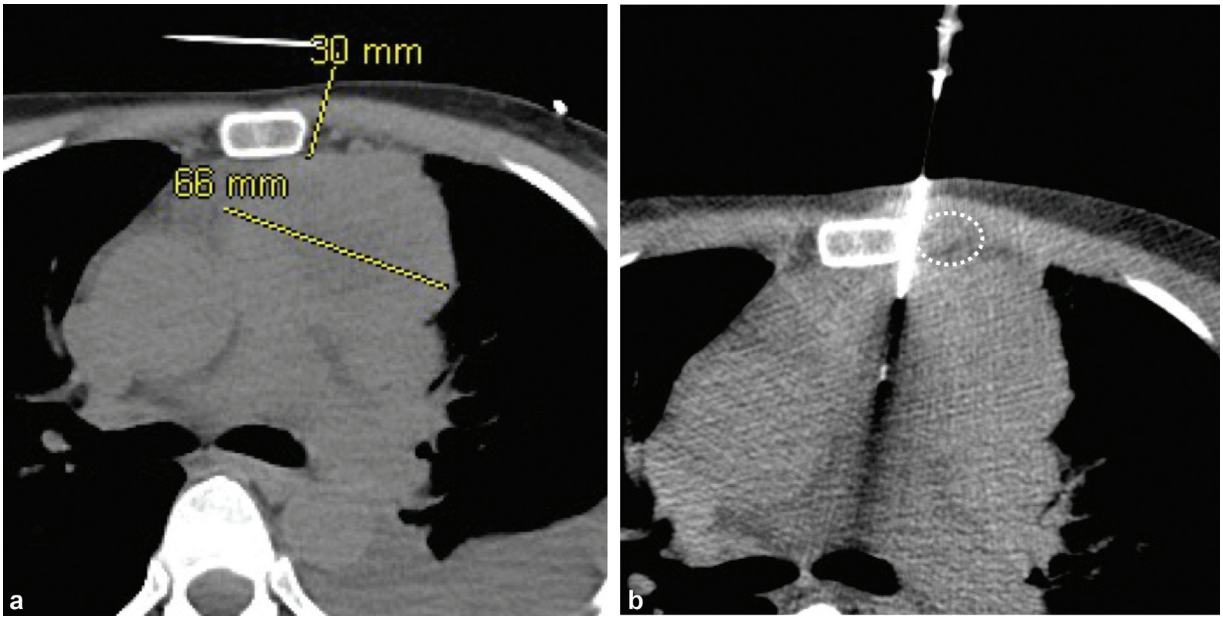

Fig. 7 A 53-year-old patient with an anterior mediastinal mass (**a**). The window between the sternum and internal mammary vessels (dashed circle) is used to safely access the anterior mediastinal mass (**b**).

repeat biopsy with a slightly different approach is likely to be successful (►**Fig. 9**). Therefore, discordant biopsy is *not* an indication for surgical biopsy.

Complications

Complications for lung, pleural, and mediastinal biopsies are similar with pneumothorax and hemorrhage occurring most frequently.

Pneumothorax

Pneumothorax is a common complication of percutaneous thoracic biopsy with an average rate of approximately 26%, with pneumothoraxes requiring a chest tube in the 0 to 15% range.[19] If a pneumothorax is detected during the procedure, once sampling of the lesion of interest is completed, we will retract the coaxial needle to the pleural cavity and aspirate the pneumothorax using a three-way stopcock. If the pneumothorax does not respond to aspiration, recurs, or the patient is symptomatic, a chest tube will be placed. The chest tube can be small (e.g., 8–10 Fr), unless there is a concomitant hemothorax.

Some operators at our institution use a saline tract sealant which was shown in a meta-analysis to decrease the risk of chest drain insertion by ninefold.[32] Other techniques that can be employed to reduce the likelihood of chest drain

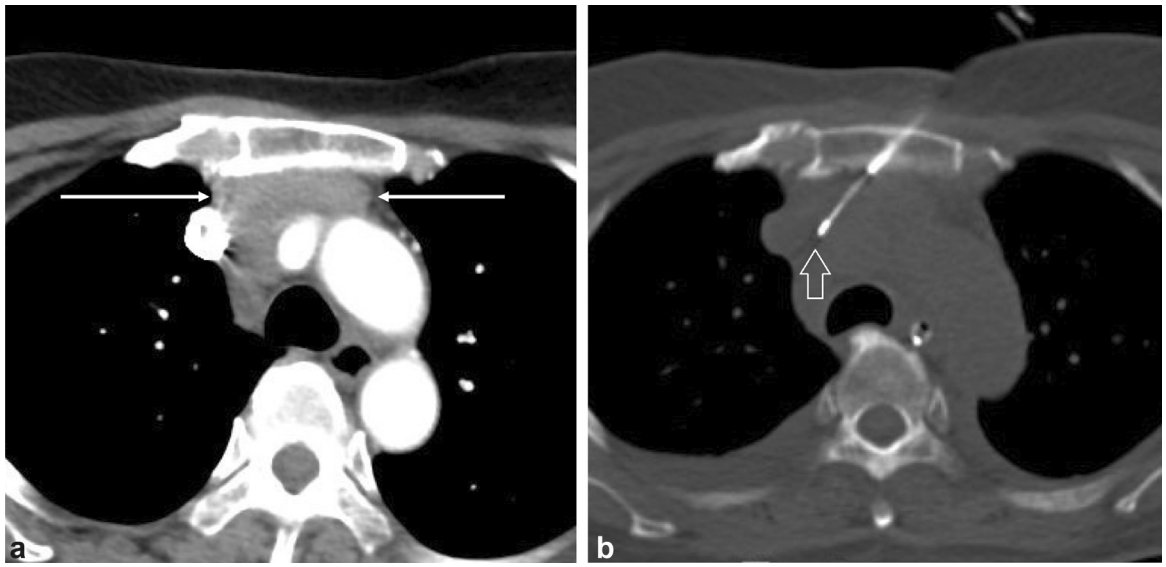

Fig. 8 A 57-year-old patient with myasthenia gravis presented with an anterior mediastinal mass (**a**, arrows). Transsternal approach was utilized with an 11G coaxial bone biopsy set through and an 18G soft-tissue biopsy was obtained (**b**; arrow—18G needle).

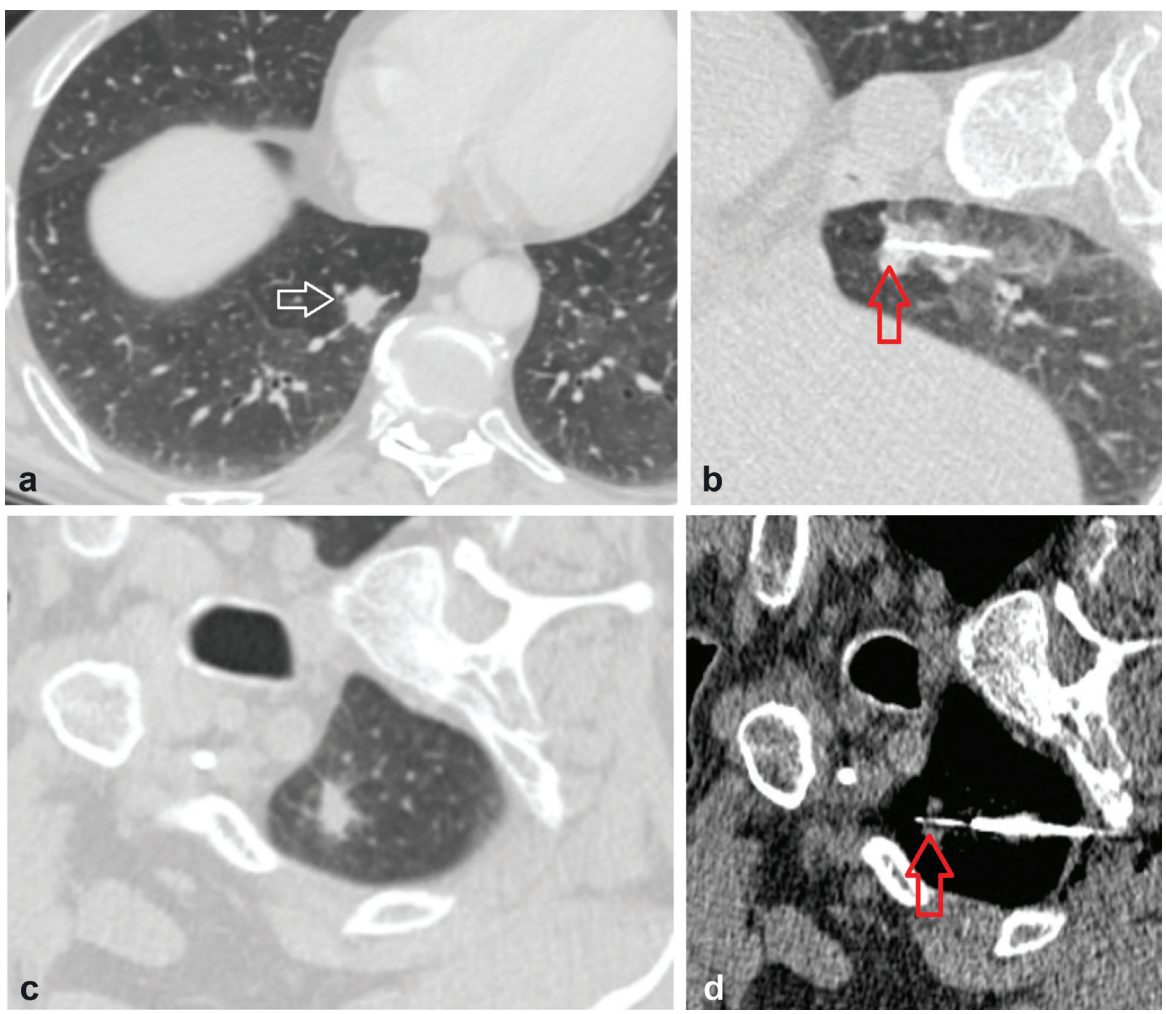

Fig. 9 A 61-year-old patient with chondrosarcoma presented with new pulmonary nodules (example shown in **a**, arrow). Percutaneous biopsy was performed (**b**; arrow—needle tip) in the right lateral decubitus position with pathology demonstrating organizing pneumonia. This was determined to be discordant with imaging and clinical characteristics and therefore a biopsy of a different pulmonary nodule (**c**) was performed (**d**; arrow—needle tip) which showed metastatic chondrosarcoma.

placement are to rapidly roll the patient biopsy-side down following the procedure, using a tract plug, or sealing the tract with a blood patch.[32–34]

Most pneumothoraxes occur immediately; however, delayed pneumothoraxes can also develop afterward, even up to 14 days postprocedure.[35,36] Female sex, the absence of emphysema, upper lobe location, and an increased number of pleural punctures are independent risk factors for the development of a delayed pneumothorax.[35,36] Delayed pneumothoraxes are clinically significant, as these patients are at a higher risk of needing a chest tube.[35,36]

In terms of postprocedure instructions, many centers will instruct patients to avoid scuba diving or flying for at least 72 hours post-biopsy; however, one study has shown that air travel can be safe in patients with pneumothoraxes as soon as 24 hours post-biopsy.[37]

Risk factors that increase the likelihood of pneumothorax include longer lesion depth ($\geq$3 cm), smaller lesion size ($\leq$4 cm), lesions without pleural contact, emphysematous lungs, larger needle gauge ($\geq$18G), crossing fissures or bulla, multiple pleural punctures, and operator's experience.[35,38,39]

Pulmonary Hemorrhage and Hemoptysis

Pulmonary hemorrhage is another commonly encountered complication. This manifests on imaging AS perilesional ground-glass opacities. It is therefore critically important for the biopsy needle to be well positioned within the lesion of interest on the first pass because needle repositioning when pulmonary hemorrhage develops becomes nearly impossible due to obscuration of the underlying lesion, with the operator having to estimate lesion location based on landmarks.

The rate of pulmonary hemorrhage during biopsy has been reported in the 30 to 65% range.[40,41] Hemoptysis occurs much less frequently at approximately 2 to 10%.[40,42] Most cases of hemoptysis are self-resolving with hemoptysis requiring intervention seen in 0.1 to 1.6% of cases.[40,42,43] Risk factors for high-grade pulmonary hemorrhage include female sex, older age, emphysema, coaxial technique, non-subpleural location, lesion size of 3 cm or smaller, and subsolid lesions.[38,40]

Air Embolus

Air embolus is an extremely rare complication with an estimate incidence of 0.08%, but it is clinically important to recognize due to its significant morbidity and mortality. A systematic review showed that 32% of patients with symptomatic air embolus survived with sequelae or passed away.[44] Strategies to avoid air embolus include always occluding the biopsy needle, for example, with the inner stylet, saline, or the operator's finger.[16]

Most patients who develop air embolus are immediately symptomatic with the most common symptoms including loss of consciousness, cardiac-related symptoms such as chest pain, or neurological symptoms such as motor weakness, dysarthria, and convulsions.[44] If a systematic air embolsu is identified, the procedure should be immediately terminated and the patient placed in a left lateral decubitus Trendelenburg position, which is associated with favorable outcomes, to prevent air from passing from the right heart into the pulmonary arteries.[44] 100% supplemental oxygen should also be applied to decrease the air's nitrogen content. Air embolus can occur in any of the arterial or venous vasculature; however, air in the coronary arteries or intracranial spaces is associated with unfavorable outcomes.[44]

Conclusion

Percutaneous image-guided biopsy is a relatively safe and accurate procedure to obtain a tissue diagnosis of thoracic lesions. In the age of precision medicine, core biopsies are increasingly performed to allow for characterization of tumor genomics, which plays an important role in patient management. Preprocedural planning is critical to promote safety of the procedure and avoid complications. Evidence-based strategies to avoid complications can be readily implemented during percutaneous biopsy to promote the safety of this procedure.

Disclosures
The authors have no grants, disclosures, or any other conflicts of interests to declare.

Conflict of Interest
None declared.

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