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Multidisciplinary approach to thoracic tissue sampling

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Abstract

When choosing the best method to undertake a biopsy of a lesion in the lung or mediastinum, it is important to consider the entire range of possible options, such as surgical, bronchoscopic/endoscopic, and radiologic techniques. Features to be considered include the anatomic location of the lesion, the amount of tissue needed, cost, availability of specific techniques, safety and risks, and expected diagnostic yield/accuracy.

Keywords: *Lung neoplasm; CT-guided biopsy; mediastinal neoplasm; mediastinal lymph nodes; bronchoscopic biopsy; mediastinoscopy; video-assisted thoracoscopic surgery.*

Introduction

Thoracic computed tomography (CT) scans obtained in oncology patients commonly demonstrate abnormalities that require subsequent tissue sampling for disease diagnosis and staging. It is important to choose the most appropriate method of sampling to gain the most information, to maximize patient safety, and to minimize costs. Discussion among members of the multidisciplinary thoracic oncology team is often helpful, to ensure that the most appropriate method is chosen for each individual patient. The aim of this article is to outline the more common methods of tissue sampling and to describe their advantages and disadvantages in relation to one another.

Lung biopsy

Pulmonary parenchymal lesions may be sampled using: conventional bronchoscopic biopsy with or without the added features of endobronchial ultrasound (EBUS) and electromagnetic navigation; CT-guided biopsy; and video-assisted thoracoscopic surgery (VATS).

Bronchoscopic biopsy

Conventional transbronchial needle aspiration biopsy (TBNA) is generally used for central lung lesions, i.e. those no further out than the level of a segmental bronchus, with a bronchial branch leading directly to the lesion. Large parenchymal lesions (at least 2–3 cm in diameter) and endobronchial lesions are best suited for biopsy with this technique. The biopsy is performed under direct vision through the fiberoptic bronchoscope; occasionally fluoroscopy may be used, especially for more distal lesions. TBNA yields cytologic samples; therefore it is generally helpful to have rapid, on site cytological evaluation available. The technique has fair sensitivity (approximately 67%) for lesions larger than 2 cm and poor sensitivity (approximately 33%) for lesions less than 2 cm. The pneumothorax rate is said to be approximately 3%, although in daily clinical practice, this rate is actually almost negligible. An advantage of TBNA is the ability to sample nearby lymph nodes at the same sitting, aiding the staging of a presumed lung cancer. TBNA requires sedation and can be done as an outpatient procedure; a typical charge (in United States dollars (USD)) is approximately $2100.

EBUS is a relatively new technique that can be used in conjunction with conventional bronchoscopic biopsy to enable biopsy of lesions that are adjacent to a bronchus, but do not show a bronchial branch leading into the lesion[1]. The biopsy is performed through the bronchial wall into the adjacent lesion, using a radial or curvilinear ultrasound transducer for guidance; ultrasonographic images can confirm placement of the needle tip in the lesion. Doppler ultrasonography may be used to identify and help avoid adjacent vascular structures during the biopsy. A procedure using TBNA and EBUS costs about $5500 USD.

Another new technique that enhances the capabilities of bronchoscopic lung biopsy is electromagnetic navigation, which is essentially a global positioning system (GPS) for the bronchoscope[2]. Before the procedure, various bronchial landmarks on a CT data set are entered into the computer system; the location of the target nodule is also identified and entered. Subsequently, the patient enters the bronchoscopy suite and lies on a magnetic field generator plate. The pulmonologist uses a location sensor at the tip of the bronchoscope to mark the same internal airway landmarks that were previously identified from the CT data. These two data sets (CT landmarks and bronchoscopic landmarks) are then fused, and the computer system shows the location of the bronchoscopic catheter tip superimposed on the CT images in three planes. The pulmonologist can then steer and watch in real time on the CT map as the bronchoscope is navigated out to the target lesion for sampling. After the expected location of the nodule is reached, EBUS may be used to confirm that the catheter tip is indeed with the nodule, before the sample is obtained. The diagnostic yield of this technique is approximately 70% for peripheral lesions, increasing to 88% with the use of endobronchial ultrasonography. The major complication is pneumothorax, occurring in approximately 5% of procedures. The major advantage of this technique is the ability to sample lesions that are too small and too peripheral to reach using conventional bronchoscopy. A disadvantage is the lack of widespread availability of the technique and the cost (approximately $6200 USD).

CT-guided biopsy

At many institutions, CT-guided lung biopsy[3] has traditionally been reserved for lesions that are not accessible via bronchoscopic biopsy, due to the relatively high pneumothorax rate for CT biopsies (approximately 20–25%). However, improved current CT biopsy techniques have led to lower pneumothorax rates, and only approximately 2–5% of CT-guided biopsies result in large or symptomatic pneumothoraces that require chest tube drainage. The pneumothorax rate for CT biopsies increases for small nodules and for patients with emphysema. In addition, CT biopsy may be technically difficult for lesions that are near the diaphragm (due to respiratory motion), deep within the lung, subpleural and behind a rib, and/or adjacent to a vital structure. The diagnostic yield for CT biopsy at our large teaching hospital is approximately 80%. Advantages of CT biopsy include lack of need for sedation, ability to obtain core biopsy samples and relatively low cost (~$2600 USD).

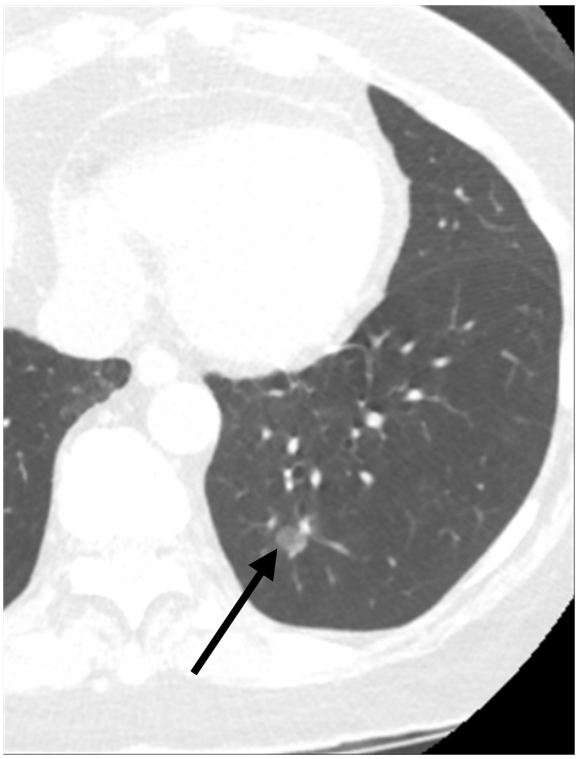

Figure 1 **A 71-year-old female with a growing left lower lobe ground glass nodule at CT (arrow) and a history of previously resected right upper lobe non-small cell lung cancer. CT-guided biopsy was non-diagnostic. The nodule was subsequently marked with indigo carmine dye using bronchoscopy with electromagnetic navigation and then resected using VATS. Histologic analysis revealed bronchioloalveolar cell carcinoma.**

VATS

VATS may be used to sample and perform wedge resection on lesions in the peripheral third of the lung (Fig. 1)[4]. Complications (~5% rate) include prolonged air leak and bloody pleural effusion. If necessary, small and/or deep lesions may be preoperatively marked with dye, radioactive material, microcoils or wires to aid localization at surgery; such marking may be done using CT guidance or bronchoscopic guidance. Advantages of VATS include the ability to sample lymph nodes and pleural lesions at the same sitting. In addition, VATS enables actual lesion resection, rather than just sampling, leading to a large amount of tissue for analysis and potential cure for small cancers. Disadvantages include the

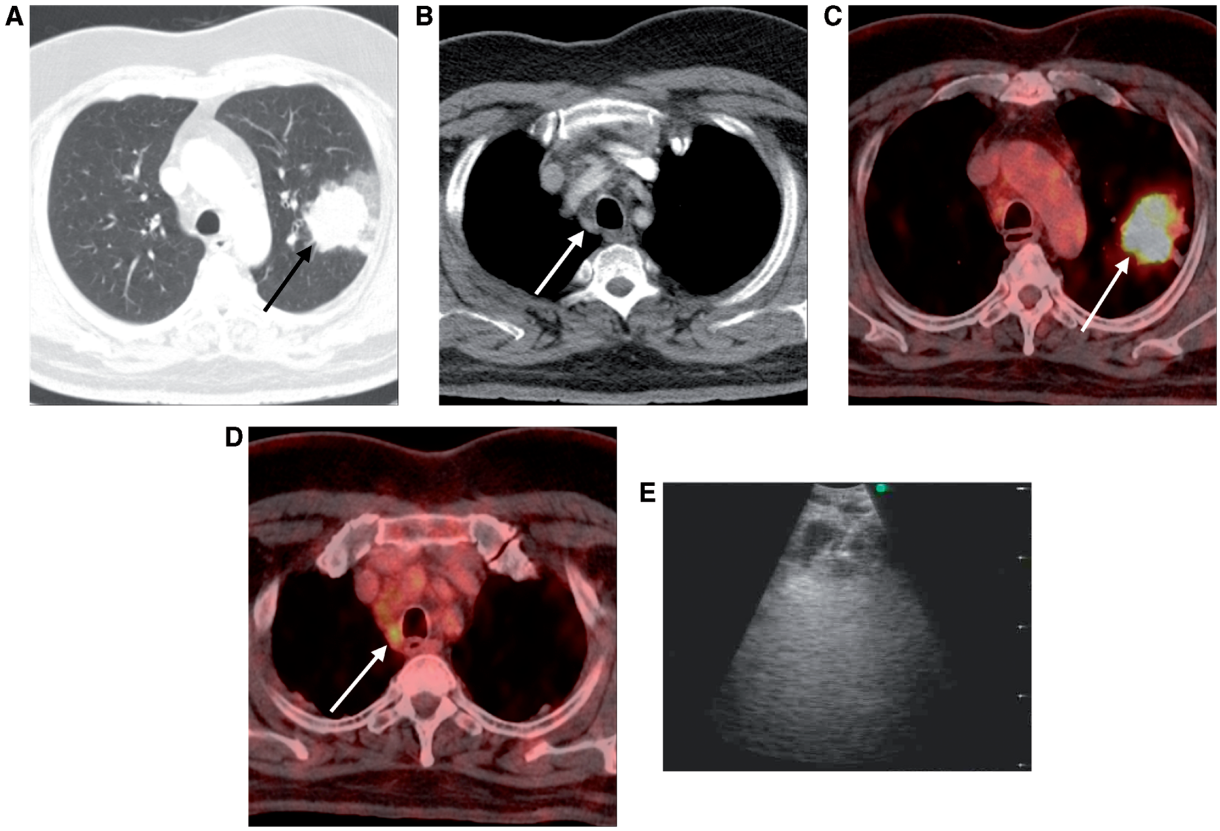

Figure 2 **A 64-year-old man with a left upper lobe mass (arrow, a) and a tiny right paratracheal lymph node (arrow, b) at CT. Both lesions were fluorodeoxyglucose (FDG)-avid at positron emission tomography (PET)/CT (arrows, c,d). TBNA of the lymph node was performed with EBUS guidance (e); the green dot indicates the location where the needle emerges from the bronchoscope. Cytologic analysis revealed non-small cell lung cancer, consistent with unresectable, stage N3 disease. (Figure 2e is courtesy of Douglas Arenberg, MD.)**

need for general anesthesia, possible overnight hospital stay and cost (~$18,000 USD).

Mediastinal biopsy

Mediastinal tissue biopsy may be accomplished using a variety of different techniques including surgical procedures, such as mediastinoscopy, VATS, and Chamberlain procedure; bronchoscopic techniques such as TBNA with or without EBUS; transesophageal endoscopic ultrasound (EUS)-guided biopsy; and CT-guided and ultrasound-guided percutaneous biopsy. Each technique has unique limitations regarding the accessible anatomic range, as described below.

Mediastinoscopy

Conventional (cervical) mediastinoscopy entails insertion of a rigid metal tube anterior to the trachea, via an incision at the sternal notch[5]. Whole lymph nodes or large tissue samples can be obtained with this procedure and sent for histological analysis; the large tissue samples may be particularly useful when excluding malignancy, due to minimization of sampling errors. The only areas accessible to conventional mediastinoscopy include the upper and lower paratracheal and subcarinal regions (excluding the posterior subcarinal space); lymph nodes in other regions of the mediastinum cannot be sampled with mediastinoscopy. The procedure requires general anesthesia and may necessitate an overnight hospital stay. Morbidity is quite low (<0.5%) and includes left recurrent laryngeal nerve injury, pneumothorax and bleeding. The technique has high sensitivity (80–90%) and negative predictive value (NPV) (~90%) for diagnosing metastatic disease from lung cancer. Contraindications include: previous mediastinoscopy and previous treatment with chemotherapy and radiation therapy, because of the development of mediastinal adhesions and fibrosis; severe cervical arthritis leading to limitations in hyperextension of the neck; and cutaneous tracheostomy. The outpatient charge for mediastinoscopy is approximately $15,400 USD at our institution.

VATS

Mediastinal VATS enables sampling of lymph nodes only in the aortopulmonary window, anterior paraaortic,

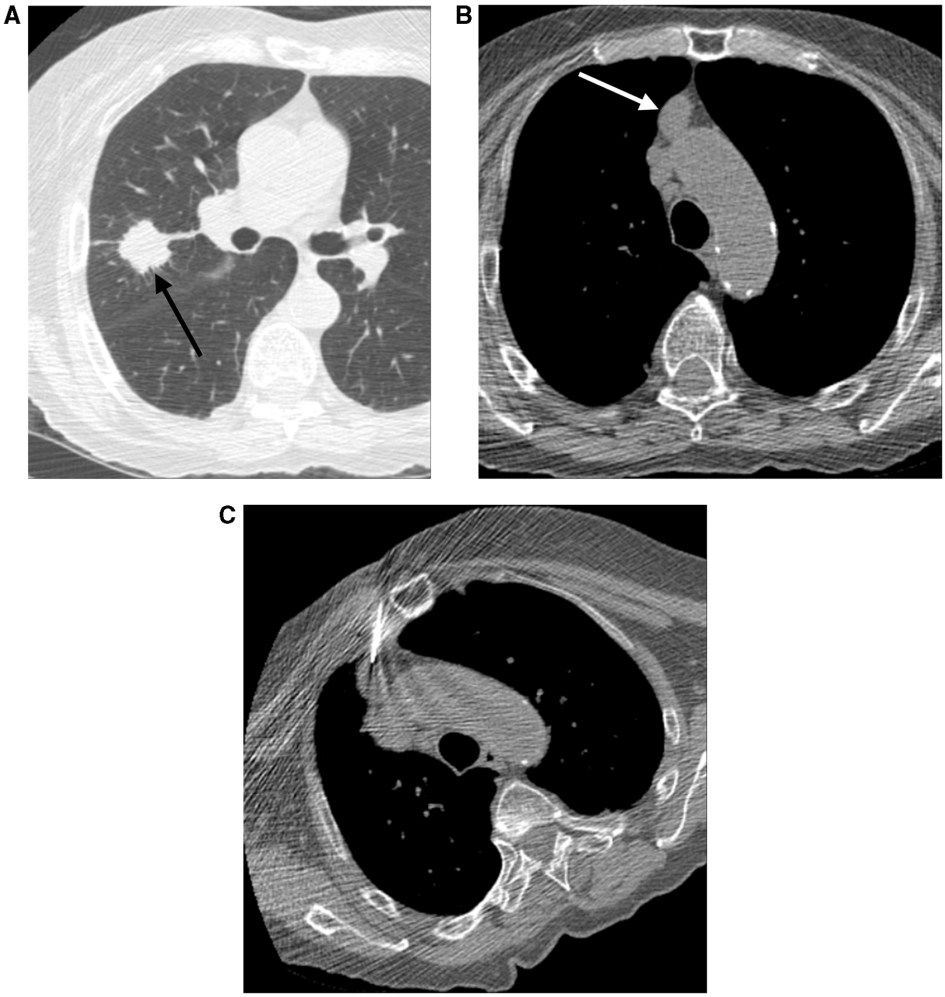

Figure 3 **An 82-year-old woman with a spiculated right upper lobe nodule (arrow, a) and an enlarged anterior mediastinal lymph node (arrow, b) at CT. CT-guided biopsy of the lymph node (c) revealed non-small cell lung cancer.**

subcarinal, paraesophageal, and inferior pulmonary ligament regions[4]. Advantages and disadvantages of the technique are as described above, in the section on lung biopsy.

Chamberlain procedure

A Chamberlain procedure is also known as a left median sternotomy or anterior mediastinotomy[5]. An incision is made at the left second-third intercostal space, adjacent to the sternum. Tissue biopsy is then done under direct vision. The only areas accessible via a Chamberlain procedure are the aortopulmonary window and anterior paraaortic lymph node stations. The procedure requires general anesthesia and a possible overnight hospital stay. Outpatient charges for this surgery are about $20,000 USD.

Bronchoscopic biopsy

Mediastinal lymph nodes may be sampled using TBNA; this is sometimes called a Wang needle biopsy. With this procedure, a needle is passed through the wall of the central airway into the adjacent lymph node. For lymph nodes touching or nearly touching the outer airway wall, the biopsy can be done blindly, i.e. using only internal airway anatomic landmarks for guidance. This technique is commonly performed for bulky subcarinal and lower paratracheal lymph nodes, usually yielding a cytological specimen, and with sensitivity and NPV approaching ~75%. For lesions that do not touch the outer wall of the airway and/or are not bulky, EBUS may facilitate TBNA by providing real-time ultrasound guidance during needle insertion; accessible lymph node regions include the upper and lower paratracheal, subcarinal and hilar stations[6]. Successful sampling of small lymph nodes may be accomplished using TBNA with EBUS, and sensitivity and NPV approach approximately 88% (Fig. 2)[7]. Advantages of TBNA with EBUS over mediastinoscopy include: the ability to restage the mediastinum after previous chemoradiotherapy or previous mediastinoscopy (with mediastinal adhesions); the ability to reach posterior subcarinal lymph nodes and hilar

lymph nodes; decreased morbidity due to the use of sedation rather than general anesthesia; and substantially lower costs (see charges for bronchoscopic lung biopsy techniques, above).

EUS-guided biopsy

EUS-guided biopsy enables sampling of lymph nodes adjacent to the esophagus in the upper, mid and lower thorax, generally yielding a cytologic sample. The procedure is performed on an outpatient basis using conscious sedation. Morbidity is low (~0.5%), including rare instances of mediastinitis or bleeding. Sensitivity of diagnosing metastatic disease from lung cancer is approximately 90%[8]. The technique is also commonly used to diagnose regional nodal metastases in patients with esophageal cancer, and can be used to diagnose other diseases such as sarcoidosis or lymphoma. Advantages of the technique include the ability to biopsy lesions in the upper abdomen at the same sitting. Outpatient charges are approximately $2300 USD.

CT-guided biopsy

CT-guided mediastinal biopsy[9] is not routine at most institutions; it can be technically difficult due to the proximity of the lesion to vital structures and is generally reserved for large lesions. Possible approaches include parasternal, trans-sternal, paravertebral, subxiphoid, and suprasternal notch routes (Fig. 3). The technique is minimally invasive, yields cytologic or histologic samples, generally requires no sedation and is relatively inexpensive (approximately $2600 USD).

Ultrasound-guided percutaneous biopsy

Ultrasound-guided percutaneous biopsy is an excellent method for sampling non-palpable lymph nodes in the supraclavicular, lower cervical and sternal notch regions. It is minimally invasive, yields cytologic or histologic samples, generally requires no sedation and is relatively inexpensive (approximately $2200 USD). In addition, it does not entail the use of ionizing radiation.

Conclusion

When choosing the best method to obtain a biopsy of a lesion in the lung or mediastinum, it is important to consider the entire range of possible options that are offered throughout the institution by specialists in surgery, pulmonary medicine, gastroenterology and radiology. Features to be considered include the anatomical location of the lesion, the amount of tissue needed, cost, availability of specific techniques, safety and risks, and expected diagnostic yield/accuracy.

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