Pictorial Essay

Ultrasound-Guided Percutaneous Biopsy of Pulmonary Nodules and Masses: an Alternative to Computed Tomography

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Abstract
Pulmonary nodules and masses are traditionally biopsied under computed tomography (CT) guidance. Ultrasound remains underrated as a guidance method for lung biopsies. It can be employed to target pleural-based lung lesions. Specific contraindications include: mechanical ventilation, contralateral pneumonectomy, uncooperative patient and uncontrollable cough. Post-procedural care should include vital signs check, pain assessment and complication evaluation. Because of the location of the lesions that are accessible to ultrasound-guided biopsy, complications such as pneumothorax and parenchymal bleeding are less frequent than in CT-guided biopsies. In this article, we discuss basic concepts for proper patient selection, planning and safe performance of ultrasound-guided pulmonary nodule biopsy.

Keywords
Biopsy. Pulmonary nodule. Interventional radiology. Ultrasound.

Introduction

Imaging-guided percutaneous biopsy of pulmonary nodules (PN) has become an essential tool in oncologic evaluation, staging and treatment planning[1,2]. Since the first report of this technique in 1976, there have been great advances in the development of both biopsy instruments and imaging equipment.[3]

Computed tomography (CT) is the modality of choice for guiding biopsies of central PNs or those surrounded by aerated lung. However, all throughout history, it has also been used for peripheral PNs with pleural contact. Ultrasound as a guidance for pulmonary biopsies remains underutilized, even for lesions with good acoustic window. Ultrasound has some advantages over CT: lack of ionizing radiation, real time visualization of the biopsy needle, portability and lower cost as guidance method[4-7]. Moreover, color Doppler enables assessment of blood flow and discrimination of vessels within the target lesion[8,9].

The aim of this article is to list indications, contraindications, discuss patient selection, describe the procedure technique and provide some examples of the use of ultrasound as a guidance method for PN biopsy.

Indications

Percutaneous biopsy is indicated for indeterminate pulmonary nodules or masses in patients with or without known cancer, particularly in solitary nodules with suspicious morphology (lobulated margins) with presence of growth on regular follow-up scans. Collection of specimens is used for the detection of mutations, for example the epidermal growth factor receptor (EGFR) gene, to be able to use targeted therapy. Thus, detection of other mutations in metastatic PNs is possible, with the same therapeutic goal. Percutaneous biopsy is also useful for obtaining samples for laboratory testing (culture) in cases of suspected infection[3,10,11].

Pulmonary lesions approachable with ultrasound guidance are those with pleural contact (Fig. 1)[4,12].

Contraindications

General contraindications include non-correctable coagulopathy and lack of a safe access[13]. Specific contraindications include mechanical ventilation, contralateral pneumonectomy, uncooperative patient and uncontrollable cough. Relative contraindications include pulmonary artery hypertension, severe lung disease (chronic obstructive pulmonary disease, pulmonary fibrosis) or heart failure[3,14].

Ultrasound has limitations inherent to the method: visualization may be hampered by posterior acoustic shadowing artifacts such as air or calcium[12]. Therefore, biopsies cannot be performed under ultrasound guidance when there is aerated lung between the margin of the target lesion and the pleura (Fig. 2)[4,12,15].

Patient selection

All patients must be previously evaluated by CT or positron emission tomography (PET/CT). Knowledge of the location of the PN is essential for safe planning of the procedure as well as for choosing the guidance method[2,7]. In patients with imaging consistent with primary pulmonary lesion and secondary lesion in another organ or lymph node, biopsy of the metastatic site may be performed for diagnosis and staging[3]. Other

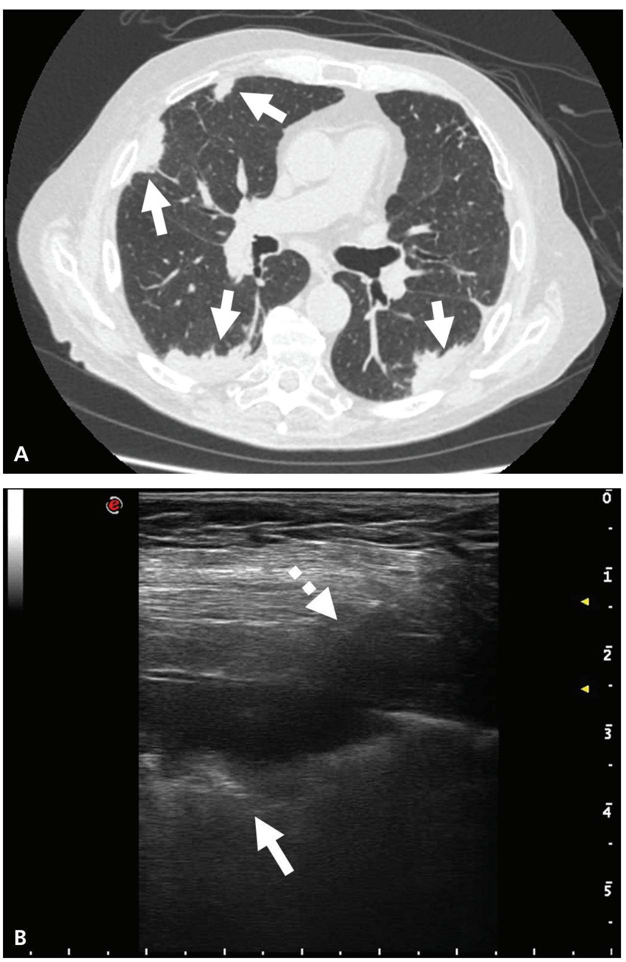

Figure 1. *73-year-old man under evaluation for constitutional symptoms.* ***A:*** *CT imaging shows patchy consolidations with irregular margins, which are in contact with the pleura (arrows).* ***B:*** *Ultrasound-guided biopsy of right subpleural pulmonary consolidation (arrow) using an 18 G Franseen needle (striped arrow) introduced directly. Final diagnosis: IgG4-related lung disease with superinfection by Staphylococcus capitis.*

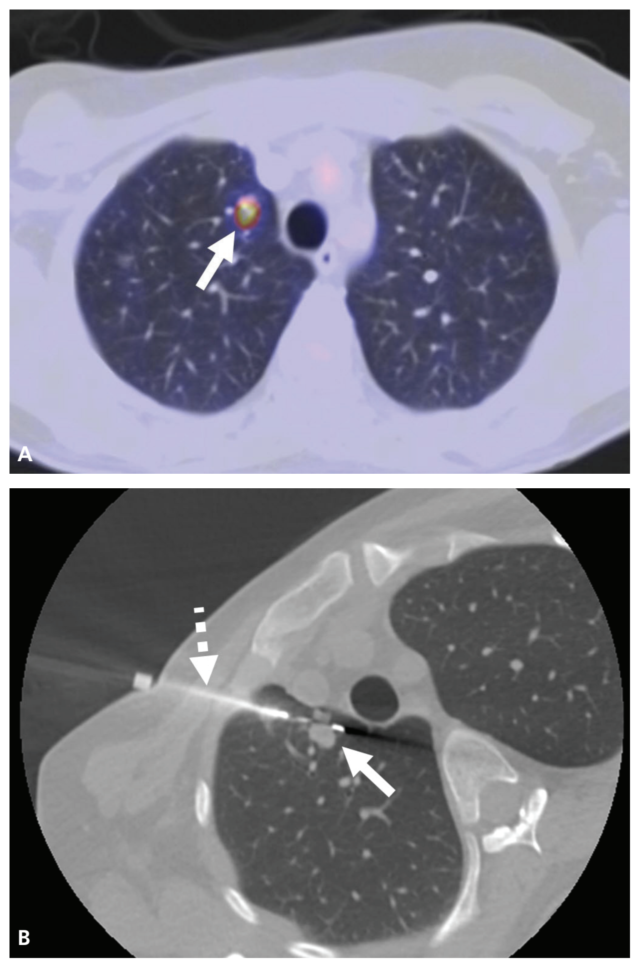

Figure 2. *42-year-old woman with previous history of right breast cancer under follow-up.* ***A:*** *PET/CT fusion imaging shows hypermetabolic right pulmonary nodule (arrow).* ***B:*** *CT-guided biopsy (striped arrow) of known nodule (arrow) performed with a semiautomated 18-gauge cutting needle using a coaxial technique. Procedure performed with the patient placed in a right lateral decubitus position. Final diagnosis: HER2/neu-negative breast carcinoma.*

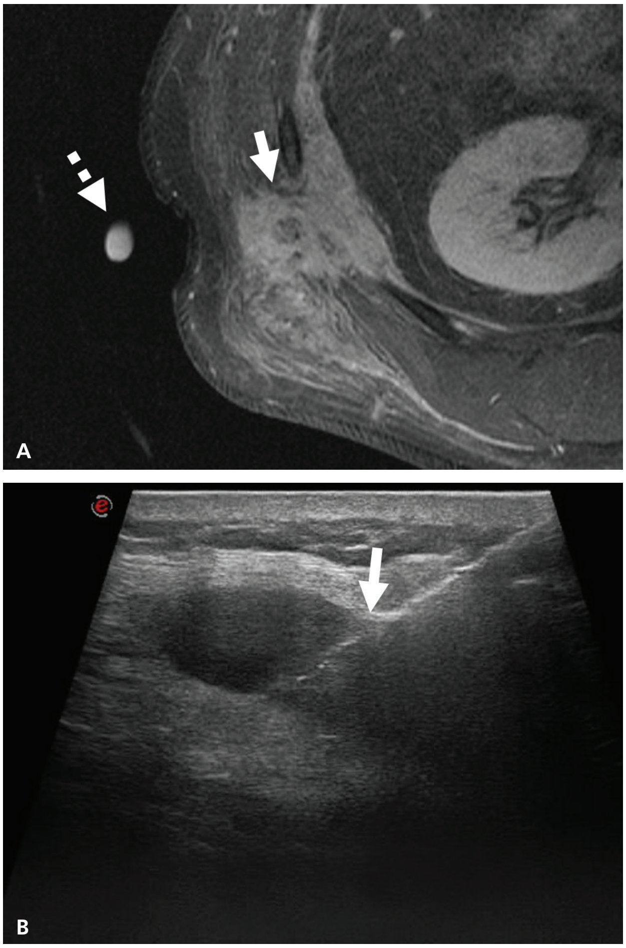

Figure 3. *61-year-old man evaluated for suspected relapse of epithelial mesothelioma.* ***A:*** *Axial fat-saturated T1-weighted magnetic resonance imaging (MRI) with intravenous contrast shows a mass of irregular margins with a contrast enhancement from the thoracic wall to the subcutaneous tissue (arrow); note the skin marker in the region of interest (striped arrow).* ***B:*** *Ultrasound-guided biopsy of hypoechogenic mass with a semiautomated 14-gauge core needle introduced directly (arrow). Final diagnosis: epithelial mesothelioma.*

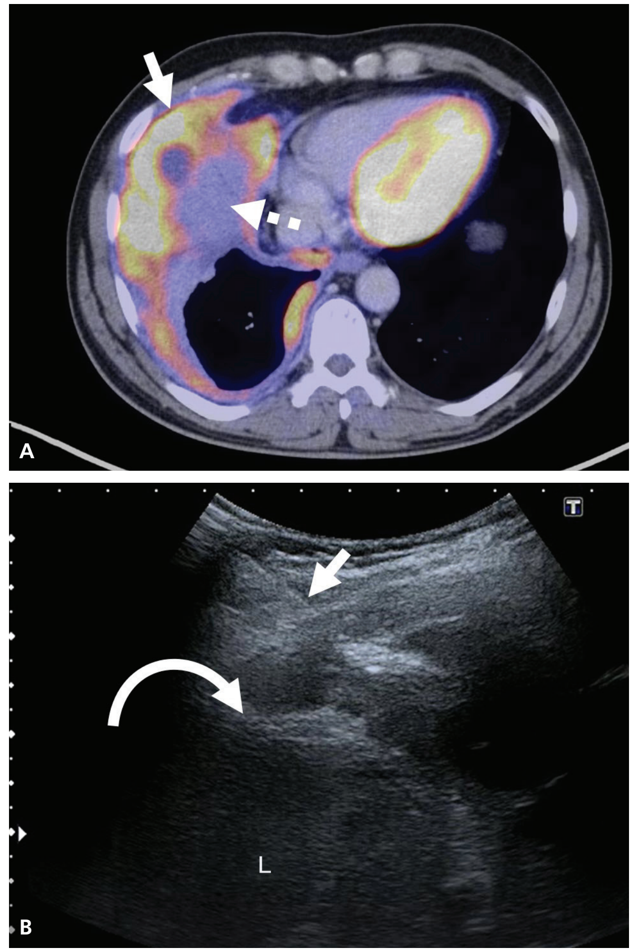

Figure 4. *HIV- and hepatitis C virus-positive 51-year-old man evaluated for pleural thickening in the right lung base.* ***A****: PET/CT fusion imaging shows hypermetabolic pleural thickening (arrow) in contact with the dome of liver (striped arrow).* ***B:*** *ultrasound-guided biopsy (arrow) of pleural lesion performed with a semiautomated 18-gauge core needle using a coaxial technique. Note the hyperechogenic area resulting from the needle cut (arrow), the diaphragm (curved arrow) and the liver (L). Final diagnosis: epithelial mesothelioma.*

lesions that can be biopsied under ultrasound guidance are those located in the thoracic wall (Fig. 3), the pleura (Fig. 4) and the anterior mediastinum (Fig. 5)[7,16].

Interventional procedures of pulmonary lesions surrounded by aerated lung must be performed under CT guidance[4,15-19].

Patients must be provided with clear and understandable information about the complications, specifically mentioning the risk of a pneumothorax as a complication. Obtaining informed consent is a compulsory requirement[1,20].

Coagulation parameters (prothrombin time, activated partial thromboplastin time and platelet count) must be previously tested. Patients with platelet counts below 50,000/µl require transfusion[2,13]. Any anticoagulants should be withheld well in advance before the procedure and international normalized ratios (INR) above 1.5 should be corrected [1]. Consensus guidelines are currently available for the management of these issues[13,21-23].

Anatomical landmarks

It is essential to identify and detect the course of intercostal, internal mammary, subclavian and axillary vessels[1,3,7].

Intercostal vessels usually course along the inferior aspect of the ribs. However, there is great variability in the tortuosity and course of the posterior intercostal artery. Below the scapula, at the paravertebral level, the posterior intercostal artery usually lies in the intercostal space, moving laterally below the superior rib (Fig. 6). Doppler ultrasound may be very helpful to locate this vessel (Fig. 7)[24]. Thus, the posterior intercostal artery lies exposed within the paravertebral space in the first 6 centimeters relative to the spine. Access to the thoracic cavity using the mid-axillary line approach is usually safe. However, when using the paravertebral space approach, the posterior intercostal artery should be identified to avoid injury to this artery[25-27].

When using parasternal approaches, the internal mammary chain can be encountered located lateral to the sternum, on both sides, immediately beneath the costal cartilage (Fig. 8)[28,29].

Subclavian vessels are located over the first rib (Fig. 9). The right subclavian artery arises from the bifurcation of the brachiocephalic trunk, at the level of T1, while the left subclavian artery arises from the aortic arch. The right artery is exclusively cervical in its topography, while the left artery is topographically thoracocervical. The subclavian artery courses medial to lateral towards the outer border of the first rib, where it becomes the axillary artery[30,31].

Needle selection

The decision on which needle to choose is multifactorial. The final decision is usually limited to semiautomated core needles (Fig. 10) or needles for aspiration (Fig. 11)[14,16,20]. Biopsies may be performed directly or using the coaxial technique. The coaxial system reduces the number of pleural punctures performed, as the needle is introduced along a larger-bore introducer needle[14,20].

Technique

An ultrasound must be previously performed to identify the lesion using either a linear or a curvilinear probe. The highest

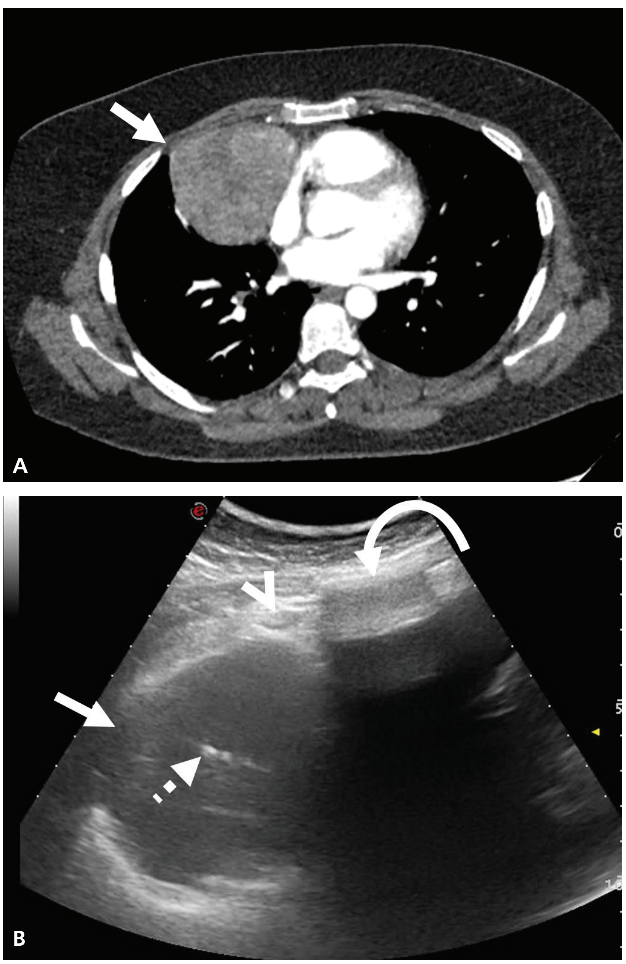

Figure 5. *43-year-old woman evaluated for findings on a chest x-ray ordered for dyspnea. **A:** CT angiography shows anterior mediastinal mass in contact with the thoracic wall (arrow), the heart and the superior vena cava. **B:** ultrasound-guided biopsy of anterior mediastinal mass (arrow) with a 20-gauge Franseen needle introduced directly (striped arrow). Note the internal mammary bundle (arrowhead) and the posterior acoustic shadow related to the breastbone (curved arrow). Final diagnosis: thymoma.*

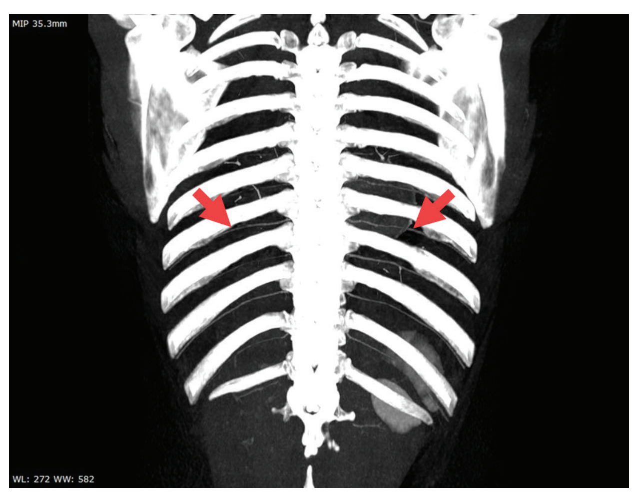

Figure 6. *Coronal maximum intensity projection reconstruction from a diagnostic CT angiography in a 47-year-old woman with a left pulmonary mass found on a chest x-ray ordered for cough. Posterior intercostal arteries are located in the intercostal space at the paravertebral level and below the scapula, then moving below the superior rib (red arrows).*

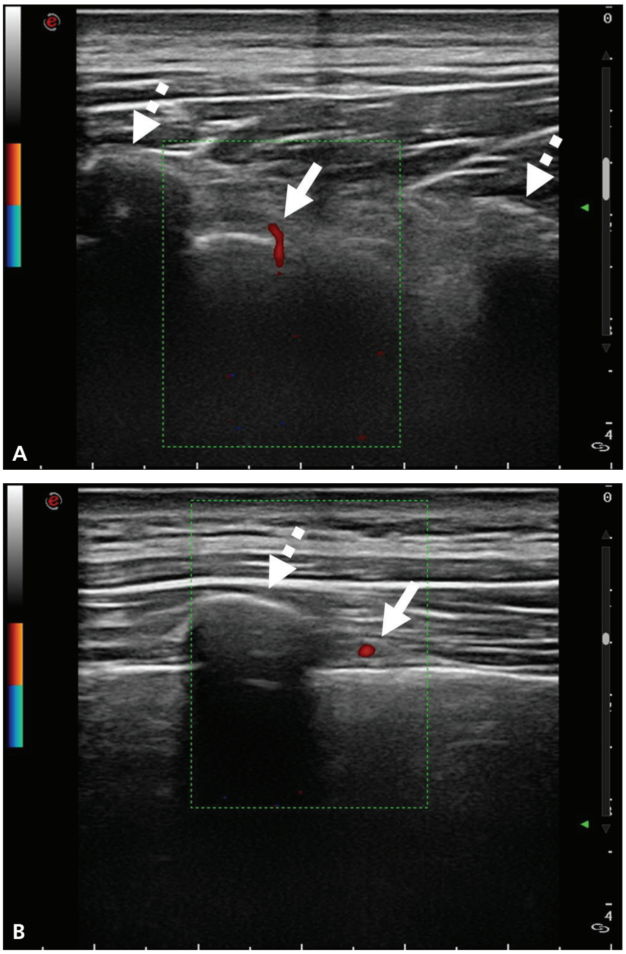

***Figure 7**. 34-year-old male healthy volunteer. Doppler ultrasound performed transversally to the 9th right rib. **A:** 5 cm from the midline, the intercostal artery (arrow) is visualized away from the ribs (striped arrow), coursing in the intercostal space. **B:** 10 cm from the midline, the intercostal artery (arrow) is seen immediately below the superior rib (striped arrow).*

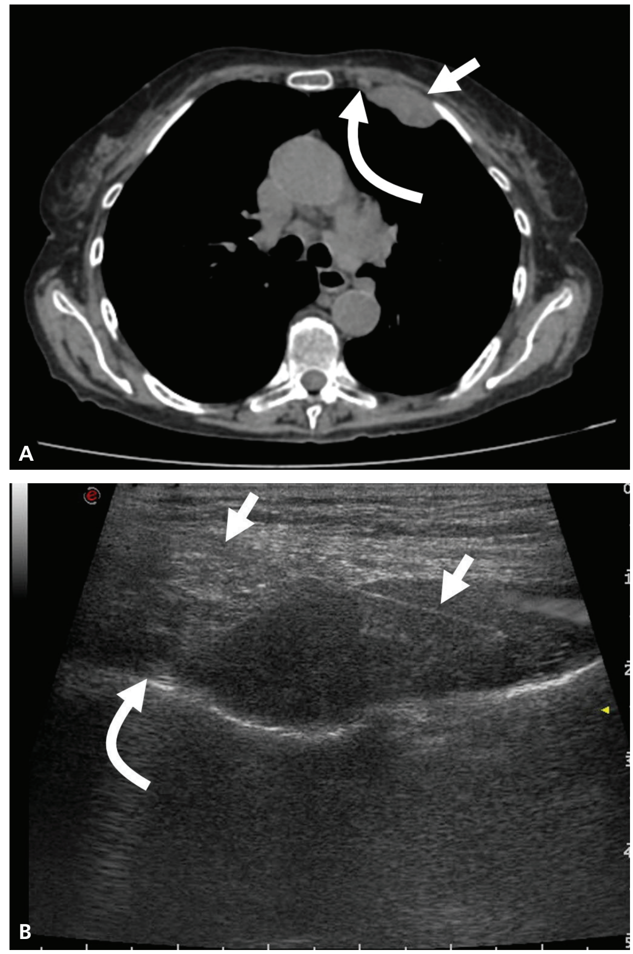

***Figure 8**. 79-year-old woman with a previous history of renal cancer under follow-up. **A:** Chest CT shows the presence of a left pleural mass in contact with the chest wall (arrow), adjacent to the internal mammary chain vessels (curved arrow). **B:** ultrasound-guided biopsy of pulmonary mass performed with an 18-G Franseen needle (arrow) using the coaxial technique. Note the internal mammary bundle adjacent to the lesion (curved arrow). Final diagnosis: clear cell renal cell carcinoma infiltration.*

frequency probe available should be used. Patient positioning will depend on the location of the lesion and may be prone, supine or lateral decubitus to obtain the most direct access. As expected, longitudinal orientation of the probe to the intercostal space offers the best acoustic window for visualization of the target lesion (Fig. 12). Other approaches may include supraclavicular or subcostal access[17,18]. The patient can be given breathing instructions (breath holding or gentle breathing) to achieve better visualization of the target lesion. If there is a likelihood of healthy lung transgression or a risk of pneumothorax, the procedure may be performed in a CT suite to be able to change the imaging modality without transferring the patient (Fig. 13)[16,32]. Subpleural PNs will appear isoechogenic or hypoechogenic relative to the chest wall. The distal margin is usually well-defined and there is posterior acoustic enhancement, since tumors facilitate the passage of ultrasound beams, contrary to the adjacent lung parenchyma. These nodular lesions are associated with an interruption of the echogenic line representing the visceral pleura (Fig. 14). In contrast, pulmonary masses show heterogeneous echogenicity resulting from areas of necrosis or bleeding (Fig. 15)[7,18,33.]

The skin must be disinfected and sterile drapes must be pla-

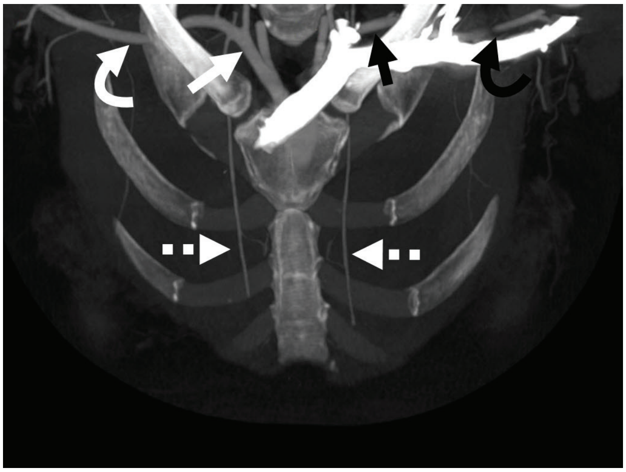

Figure 9. *47-year-old woman with a left pulmonary mass (same patient as in Fig. 6). Coronal oblique maximum intensity projection image shows the course of chest vessels. Note the course of the subclavian artery (arrows), axillary artery (curved arrows) and internal mammary artery (striped arrow).*

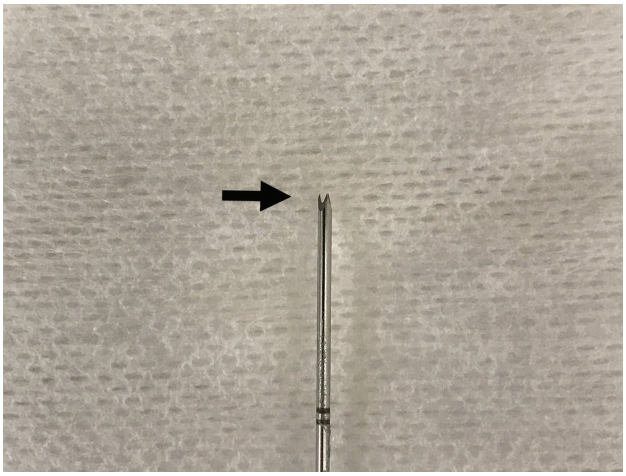

Figure 11*. Picture of the distal end of 18-G Franseen needle for aspiration biopsy, with no inner stylet. The distal end has a trephine type configuration (arrow) for cutting tissue. With this system, specimen is obtained by front cutting.*

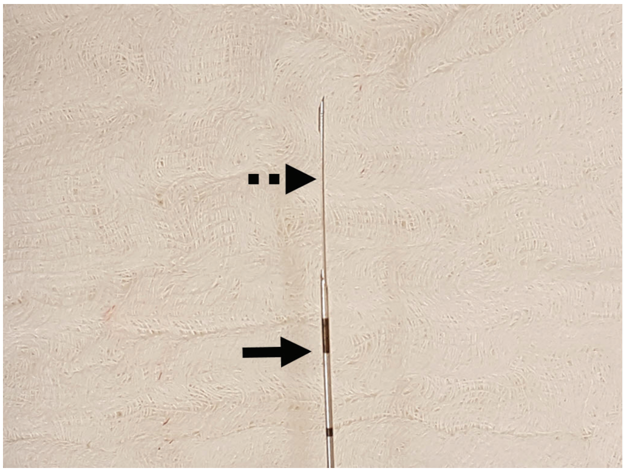

Figure 10. *Picture of the distal end of the 20-G semiautomated needle. The inner stylet has a chamber for drawing the sample (striped arrow). The outer cannula (arrow) is advanced to the distal end when the system is triggered, leaving the tissue drawn in the chamber. With this system, specimen is obtained by lateral cutting.*

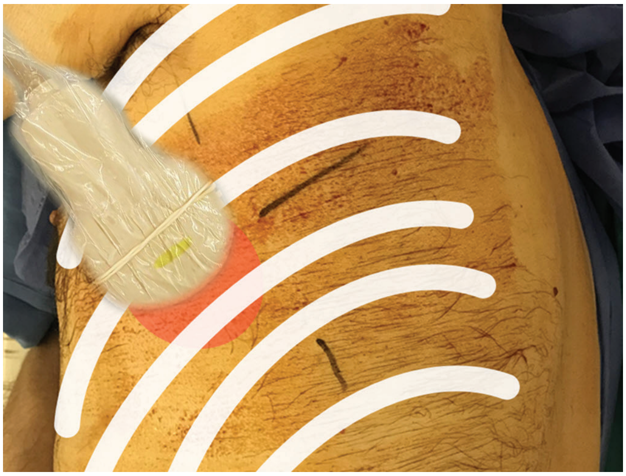

Figure 12. *Picture and schematic representation of preprocedural planning of ultrasound-guided biopsy of pulmonary nodule. The probe must be aligned with the intercostal space seeking to obtain the best acoustic window for visualization of the target lesion (red oval). White lines represent the ribs and black ink marks on the skin aid in rapid localization of the target.*

ced (Fig. 16). Skin preparation is performed with 10% povidone-iodine and, in the event of allergies, with a mixture of 2% chlorhexidine gluconate and 70% ethyl alcohol. Local anesthesia will be administered to the skin, soft tissue and pleural surface. Biopsy may be performed with a needle-guide attachment or a freehand approach. Needle guides are easier to use for less experienced operators; however, this approach limits the trajectory of the needle to a pre-established angle[16,17,20]. Our team uses the freehand technique, with a sterile cover for the probe, advancing the needle within the plane of imaging entering through one of the sides of the probe. This technique gives us freedom to choose the angles of access to the target and enables us to change the angles during the procedure as needed. We usually do not use the out-of-plane approach for these cases.

It has been demonstrated that the presence of a pathologist during the procedure reduces the amount of material needed to establish a diagnosis, thus increasing the effectiveness of the procedure[14,34,35.] Core biopsy has been shown to have slightly higher diagnostic effectiveness compared to fine needle aspiration, with sensitivity and specificity values of 89% and 97%, respectively. However, Coley et al.[36] concluded that fine needle aspiration and core biopsy show comparable results at the time of molecular testing of the tissue.

Postprocedural monitoring

Patient recovery takes place in the observation ward. The patient rests on a stretcher, lying with the puncture site down, although this position remains controversial[14,37] Postprocedural pain is recorded using a numeric rating scale. Postprocedural care includes vital signs monitoring (heart rate, blood pressure, oxygen saturation) for 1-6 hours. Abrupt movements, coughing and talking must be discouraged. The length of the observation period will be adjusted according to the characteristics and complexity of the procedure. Imaging

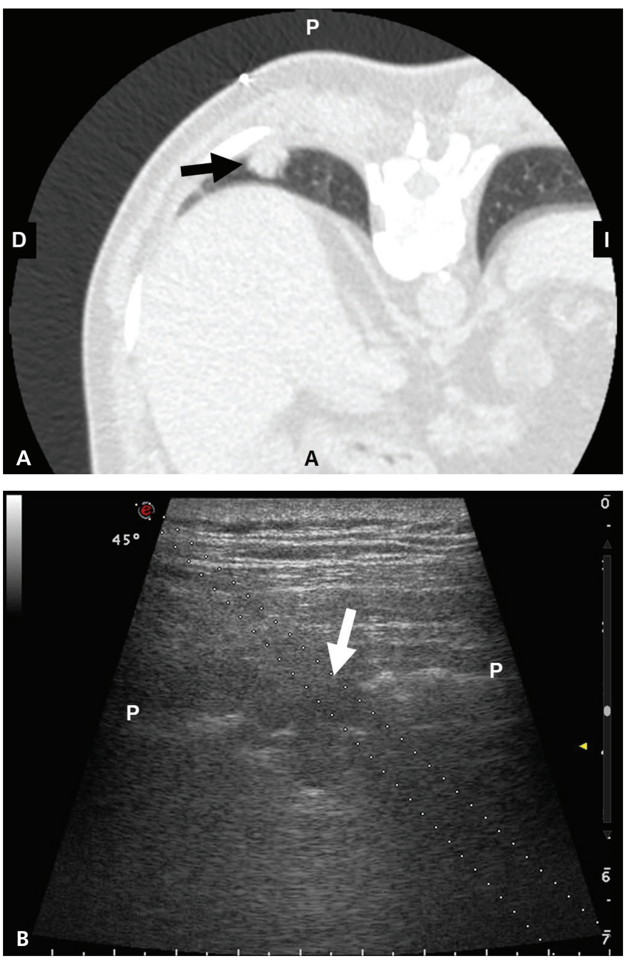

Figure 13. *73-year-old man with hearing impairment, under evaluation for pulmonary nodule. Because of the region mobility and the patient's hearing impairment, the ultrasound-guided biopsy was planned to be performed in the CT suite.* ***A:*** *CT for biopsy guidance: pulmonary nodule with pleural contact (arrow) in the right lung base; note ancillary skin marker for additional reference.* ***B:*** *ultrasound as main imaging guidance modality for biopsy of small mobile nodule (arrow). Pleural echogenic line (P).*

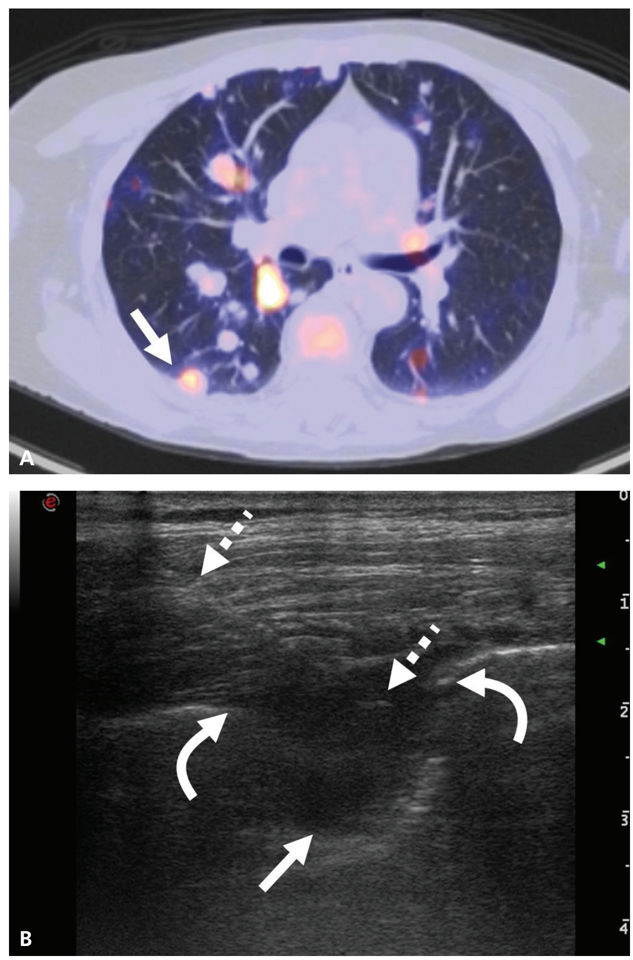

Figure 14. *61-year-old woman with previous history of endometrial cancer under follow-up.* ***A:*** *PET/CT fusion imaging shows hypermetabolic pulmonary nodule (arrow) with pleural contact. Note other nodules, some of them hypermetabolic, scattered around both lungs.* ***B:*** *Ultrasound-guided biopsy of subpleural nodule (arrow) using an 18 G Franseen needle (striped arrows) introduced directly. Note the interruption of the pleural echogenic line (curved arrows). Final diagnosis: poorly differentiated adenocarcinoma of endometrial origin.*

monitoring is crucial for an early detection of complications and it may be performed with CT or radiographs[3,7,13].

Complications

The most common complications are pneumothorax and bleeding. Pneumothorax has a variable incidence, reported at approximately 26% for CT guidance, with an incidence of 3-17% for pneumothorax requiring chest drainage[38-40]. For ultrasound-guided biopsies, self-limited pneumothorax has been reported in 5.8-7% of cases (Fig. 17)[4,17]. Ultrasound has a limited role in quantifying the size of a pneumothorax. However, it is useful for detecting this complication, which causes a loss of visceral pleural movement that is visible on ultrasound.[7]

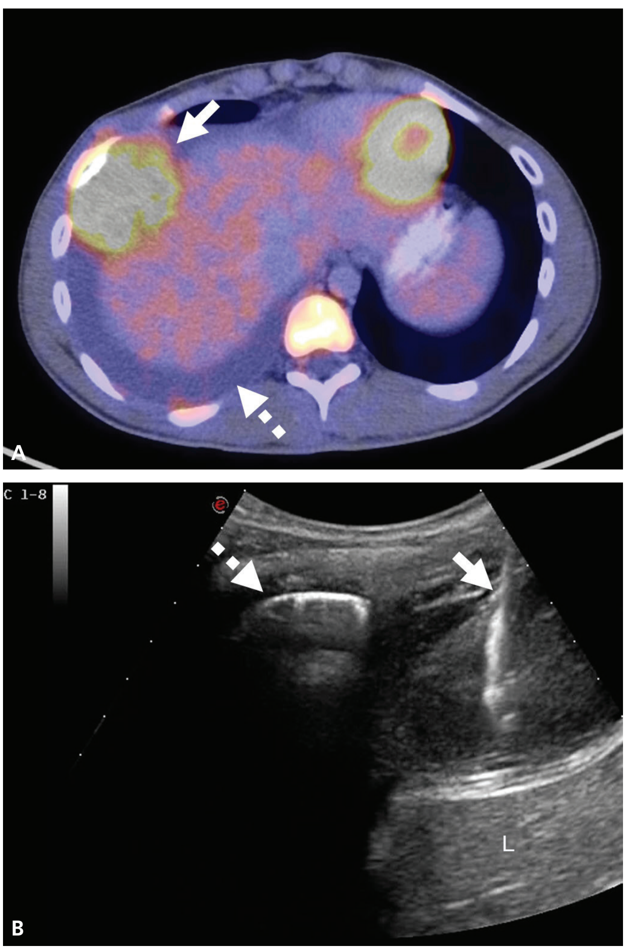

Figure 15. *16-year-old male under evaluation for the presence of a lung base mass found when the patient presented with chest swelling.* ***A:*** *PET/CT fusion imaging shows hypermetabolic pulmonary nodule (arrow) in contact with the pleural wall, with associated pleural effusion (striped arrow).* ***B:*** *ultrasound-guided biopsy of pulmonary mass (arrow). Note the echogenic line corresponding to the visceral pleura (striped arrow) and the liver (L). Needle used: coaxial semiautomated 18 G needle (arrow). Final diagnosis: BCOR-CCNB3 fusion sarcoma.*

Figure 16. *Picture and schematic representation of preprocedural planning of ultrasound-guided biopsy of pulmonary nodule. The operative field allows adequate space for handling the probe according to previous marks (black ink). The while lines represent the ribs and the red oval represents the target lesion.*

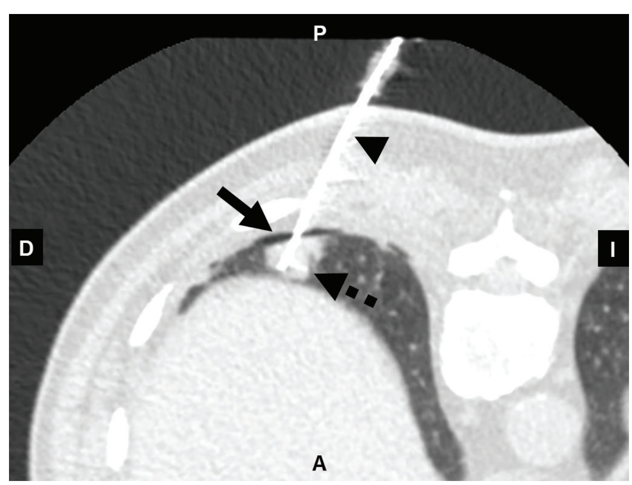

Figure 17. *73-year-old man with hearing impairment, under evaluation for pulmonary nodule (same patient as in figure 13). CT as ancillary guidance modality for pulmonary nodule biopsy (striped arrow) with laminar pneumothorax (arrow) impeding ultrasound guidance. Needle used: coaxial semi-automated 20 G (arrowhead). Final diagnosis: piece of mature cartilaginous tissue, scarce detritus and fibrous tissue with no atypical cells.*

Bleeding may appear as parenchymal hemorrhage, hemoptysis, hemothorax, chest wall hematoma or mediastinal hematoma. The rate reported for bleeding is 4-27%, with the presence of alveolar hemorrhage being a common finding of little clinical significance. Hemothorax is an uncommon complication (Fig. 18) and clinically significant hemothorax is rare (Fig. 19). The risk of bleeding increases with the target lesion depth[2,15,38,39]. Consequently, under ultrasound guidance, the risk of parenchymal bleeding has been reported to be about 1%[17]. The size of the target lesion has been evaluated as an independent risk factor for bleeding. However, results have been discrepant[41-43]. The prevalence of parenchymal bleeding or hemothorax decreases with appropriate preprocedural planning, which allows avoiding injuries to the pulmonary, intercostal, internal mammary, axillary or subclavian vessels[2,3,38]. Mild alveolar hemorrhage has been suggested to reduce the risk of pneumothorax by sealing the needle track, thus preventing air from leaking into the pleural cavity[2].

Air embolism is a rare but potentially life-threatening complication[38,44]. Avoiding injuries to vessels and reducing the time the stylet is removed from the needle during the procedure would be very helpful[13,38].

Tumor seeding along the needle track has an incidence below 0.1% and no definitive risk factors have been identified for this complication[38,39].

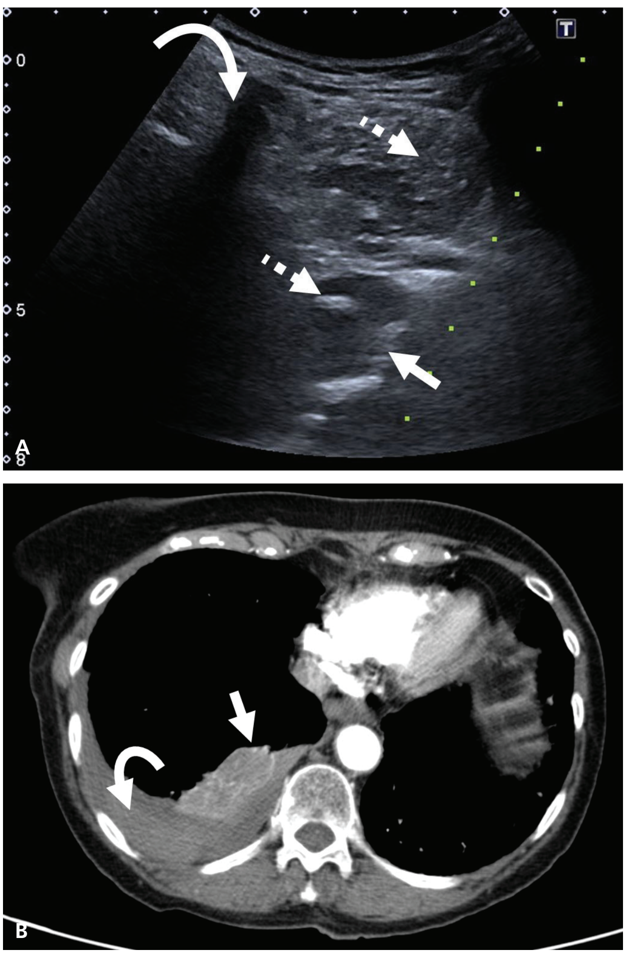

__Figure 18.__ 77-year-old ex-smoker woman under evaluation for pulmonary mass in the right lower lobe. __A:__ ultrasound-guided biopsy of right pulmonary mass (arrow) performed with a semi-automated 20 G core needle using a coaxial technique (stripped arrow). Note the posterior acoustic shadow caused by the spinous process (curved arrow). __B:__ CT angiography with intravenous contrast 2 hours post-procedure shows heterogeneous pleural effusion consistent with hemothorax (curved arrow). Note the (hypervascular) enhancement of the biopsied nodule (arrow). This was an imaging finding with no hemodynamic impact. Final diagnosis: high-grade small-cell neuroendocrine carcinoma.

Conclusion

Ultrasound is a good alternative to CT as guidance method for biopsying pulmonary nodules and masses in selected patients, with high diagnostic yield and low rate of complications.

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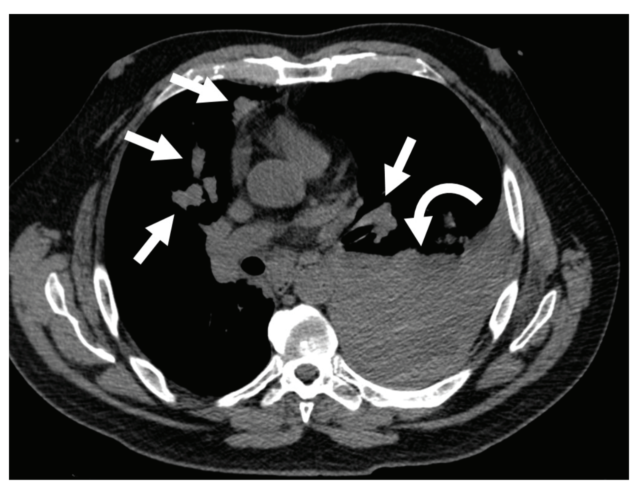

__Figure 19.__ 60-year-old man under evaluation for pulmonary nodules detected on CT scan in the setting of constitutional symptoms. Follow-up CT one hour after percutaneous biopsy of the pulmonary nodule, ordered for hemodynamic decompensation. Note the pulmonary nodules (arrows) and the left hemothorax (curved arrow). This complication required drainage by video-assisted thoracoscopy, which confirmed an intercostal arterial injury. The patient made good progress.

Conflicts of interest

The authors declare no conflict of interests.

Ethical responsibilities

Protection of human subjects and animals. The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

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