Image-guided percutaneous transthoracic biopsy in lung cancer — Emphasis on CT-guided technique

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Summary Image-guided percutaneous transthoracic core biopsy especially with CT guidance is playing an increasing role in the diagnosis and management of lung cancer. The recent advances in the specific chemotherapy and novel targeted therapy and the increasing need for specific diagnosis of tumor histopathologic subtypes have direct impact on the radiologists performing lung biopsy and important implications for the biopsy technique. Close cooperation between radiologists and referring physicians with understanding of the technical aspects of the biopsy procedure can help clinicians make appropriate referrals for this procedure and understand the significance and limitations of the results. Additionally, the appropriate management of complications can limit morbidity related to the biopsy procedure.

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Introduction

Percutaneous transthoracic core biopsy is an accepted and widely used method of establishing the etiology of lung masses. It is thought to have been developed by Leyden in 1883 in order to diagnose pneumonia. The technique was extended to the diagnosis of cancer from the 1930s onwards [1]. The development of high resolution imaging modalities, biopsy needle designs and cytologic methods have a direct impact on radiologists performing lung biopsies and have led to more widespread use of the technique afterwards.

Patients with suspected lung cancer need a tissue diagnosis, which can be obtained with either a fine-needle aspiration technique or core biopsy, providing cytological and histopathologic specimens, respectively. The recent advances in the specific chemotherapy and novel targeted therapy [2] and the increasing need for specific diagnosis of tumor histopathologic subtypes and molecular markers [3] have led to increasing need for more amount of tissue. Compared with aspiration cytology, core biopsy is preferred and superior to aspiration because it can obtain multiple larger samples for both cytological and histological diagnosis [3,4] and molecular analysis [5,6]. Many radiologists around the world are well trained in obtaining fine-needle aspiration of lung lesions. However, core biopsy requires careful manipulation and special attention to prevent or reduce procedure related complications. In this article, we share our experience, concepts and techniques regarding image-guided percutaneous transthoracic lung biopsy with emphasis on CT guidance and coaxial technique for obtaining core biopsies of lung lesions.

Indications

As with any interventional procedure, the potential benefits of core biopsy must outweigh the risks; and in each case the technique should be considered likely to affect patient management. Typically, percutaneous transthoracic core biopsy is performed in patient with indeterminate pulmonary nodule or mass to confirm or refute the presence of malignancy, and where malignancy is confirmed, to characterize the tumor further. Other indications include mediastinal mass, pulmonary nodules with a known extrathoracic malignancy, perihilar mass after failed or negative bronchoscopy, postoperative or postradiation changes, suspected recurrent disease and infectious consolidation.

Contraindications

Previous pneumonectomy and other instances of a single lung, suspected hydatid cyst or vascular malformation are absolute contraindications to percutaneous transthoracic lung biopsy. Relative contraindications include coagulopathy, anticoagulant therapy, significant pulmonary arterial hypertension, severe lung disease (respiratory failure − mechanical ventilation, severe obstructive lung disease, and severe emphysematous disease), large bullae, or inability of the patient to cooperate.

Imaging modality of guidance

The percutaneous transthoracic core biopsy of lung lesions can be performed using fluoroscopic, ultrasongoraphic (US) or computed tomography (CT) guidance. Choice of the imaging modality is determined by the size and location of the lesion, availability of imaging systems, and local expertise and preference. Chest CT is required prior to the biopsy to determine the biopsy technique as the lesion depth and its relation to ribs, mediastinum, fissures and vessels can be determined to plan a biopsy route and technique [7].

Fluoroscopy has represented the historic and traditional imaging modality for percutaneous biopsy [8,9]. Its main advantages are low cost, short procedure time, and real-time visualization of the needle advancement. It can be used for the peripheral and large lesions. However, the disadvantages of fluoroscopy include difficulty in accessing central lesions and avoidance of bullae and vascular structures in the needle pass [9,10]. Although fluoroscopy is available in most institutes, it is used less frequently at present.

US is most often used imaging modality for accessing the peripheral, pleural-based lesions producing acoustic window as ultrasound beam does not pass through air. It allows real-time visualization with multiplanar capability of the needle advancement, allowing accurate placement of the needle [11,12]. It is a safe with no radiation, quick, and low-cost modality [11]. It should be used whenever possible and appropriate [13].

CT is the preferred and most common used guidance modality. It is the standard imaging modality for guidance in many institutions as it reveals the anatomic structures and characterizes the lesion. It permits planning a trajectory that minimize passage through aerated lung, bullae, fissures or vessels and that allows possible access to central lesions. Additionally, it has the capability to distinguish necrotic from solid portions of the lesion and to document unequivocally the needle tip within the lesion, a point of major value in the interpretation of absence of malignant cells [14]. The recent advances in spiral CT and fluoroscopy CT permit to biopsy smaller lesion and perform the procedure more quickly in less cooperative patients [8,15—20]. Reported accuracy rates for percutaneous transthoracic CT-guided biopsies range from 64% to 97% [21—24]. A meta-analysis of 19 studies showed an overall sensitivity of 90% (95% CI, 0.88—0.92) for biopsy of pulmonary lesions [25]. A trend toward lower diagnostic accuracy was noted for lesions with less the 1.5 cm in diameter [23].

Needles

Numerous types of biopsy needles with various sizes, tip designs and sampling mechanisms have been used in percutaneous transthoracic core biopsy of the lung [8]. An ideal biopsy needle should minimize pneumothorax and bleeding complications and maximize the tissue specimen obtained.

In our practice, we use automated cutting needles to obtain sufficient tissue amount free of crush injury for histologic evaluation. Two types of automated cutting core biopsy needles have been used. They include side-notch needle and end-cut needle. Choice between these two types is generally a matter of preference and availability.

The end-cut design has several advantages. Most importantly, a full cannular width of tissue is obtained as the entire lumen and almost the whole length of advancement of the needle within the lesion is used to enclose the specimen. In the side-notch biopsy needle, the actual length of the side notch (i.e. specimen) is shorter than the advancement of the needle as only part of the needle lumen (i.e. the volume of the notch) is used to have tissue [26].

Yet another distinction between the types of needles is related to the technique used for obtaining the biopsy as coaxial and single shaft (non coaxial). Each technique has certain advantages compared to the other. However, there is no proof that any type of technique is superior to other types

in terms of diagnostic yield and complication rate [8]. Using the coaxial technique, the needle will be more stable in the chest wall and multiple samples can be obtained with a single pleural puncture which helps in improving the diagnostic yield and reducing the risk of pneumothorax especially with smaller diameter needle [27]. The advantage of the single needle is that it is more flexible. This may help in guiding the needle to the correct location.

The continued refinements in needle design appear to be potential for improved sensitivity and specificity for both benign and malignant diagnosis [28,29].

Biopsy procedure

Planning

After consideration of the patient history and indications for the biopsy, an informed consent is obtained from the patient and the family. The consent should include the discussion of the potential risks and benefits in details.

The baseline chest CT images are carefully reviewed and the procedure is planned based on the size and location of the lesion, availability of imaging systems, and local expertise.

The needle path is chosen considering straight pathway from the skin to lesion. Ideally, the needle should cross the pleura at a 90-degree angle rather than at an oblique angle. The pathway should avoid transversal of bullae, vessels and bronchi. The interlobar fissures are avoided usually as the more pleural surfaces that are crossed, the higher the risk of pneumothorax. In case of more than one lesion is present, the more peripheral lesion is chosen over a deep lesion because less lung will be traversed, decreasing the risk of complications. A lesion in an upper lobe is preferred over one in a lower lobe because of less respiratory excursion in the upper lobes. Necrotic portions of lesions are avoided due to its low diagnostic value and tendency to bleed more than intact tumor.

Patient positioning

Patient position is an important factor in improving the accuracy and safety of the lung biopsy. Consideration of position should be made during biopsy planning as the patient should maintain the same position throughout the entire procedure.

If the target nodule is equally accessible from either prone, supine, or decubitus positioning, the prone position is ideal due to its association with

the least amount of chest wall motion compared with the supine and decubitus positions. Additionally, it allows a more comfortable ''biopsy side down'' supine position during recovery, which may reduce the chance of developing a pneumothorax. Moreover, the prone position prevents the patient from seeing the biopsy needle and that may reduces both patient anxiety and patient movement. The supine position is associated with a moderate amount of chest wall motion, whereas the decubitus position is associated with the greatest amount of chest wall motion

Sedation

Sedation and intravenous analgesic medications are usually not required with the liberal use of chest wall local anesthetic. The pain associated with the procedure is usually limited and momentary, and arises from administration of the local anesthetic and violation of the parietal pleura with the needle. The burning sensation resulting from the administration of local anesthetic can be reduced with adding sodium bicarbonate to raise the pH of local anesthetic.

However, patients differ in their ability to tolerate the procedure without sedation, which may lower the patient's level of cooperation. Sedation and analgesia are primarily used for anxious and uncooperative patients, selected elderly people who have osteoarthritis or degenerative joint disease and cannot maintained raised arms, lesions adherent to periosteum and chest wall or when the procedure is lengthy.

CT scan parameters

The parameters are related to choice of tube current (mA) and slice thickness. Generally, the lowest dose that allows for evaluation of the needle in relation to the nodule is required. Most of modern CT scanners allow a routine low-dose axial scan with 120 kVp and 40 mA or lower per slice. Radiation dose reduction is important because it is often necessary to perform multiple images through the same tissue volume during the course of the procedure.

The slice thickness is generally chosen in relation to the size of the nodule. The slice thickness should be less than half the diameter of the targeted lesion in order to be certain that a single CT image contains the lesion. In this way contiguous slices will include at least one image that contains no partial volume effects. As a rule of thumb for choosing slice thickness, the following slice thicknesses are chosen; one centimeter or 5 mm for lesions > 3 cm in diameter, 5 mm for

lesion 1—3 cm in diameter, 3 mm for lesions < 1 cm in diameter. A slice thickness of 1 mm then should be chosen for final localization of the needle tip.

Biopsy process

After appropriate patient positioning, a radiopaque marker or grid is placed on the patient's skin over the area of interest. During suspended respiration, a short CT scan of the region of interest is obtained, followed by choosing the appropriate table position and needle trajectory as previously planned. The depth from the skin entry site to the lesion is then measured.

With the use of the gantry laser light to delineate the Z-axis position, and the radiopaque skin marker to reference the X-axis position, the needle entry site is marked with indelible ink on the patient's skin. The skin site is prepped and draped using sterile technique followed by administration of local anesthesia into the skin, subcutaneous tissues, and intercostal muscles.

In our institute, the standard practice is to use coaxial technique for the advantage explained before. We use a 17- or 19-guage introducer needle as guidance with appropriate length depending on the depth of lesion. The automated cutting needle, which can be any needle type, is chosen to be smaller and to matches the introducer needle in length and size to be 18- or 20-guage.

All needle movements and manipulations should be performed with patient's respiration suspended. When advancing the introducer needle, it is important to maintain the same trajectory with each movement, as even slight deviations of the needle at the skin or within the subcutaneous tissues will produce marked deviation at a deeper level. When advancing the needle into the subplural region, it should be done in a rapid thrust to avoid needle tip laceration to the pleura and to avoid the needle slipping into the pleural during breathing later. Additionally, the patient is instructed to breath quietly, remain motionless, and repeat a breath hold of a similar size during needle manipulations throughout the procedure. The needle should be allowed to sway to-and-fro with respiratory motion; not be held or fixed during respiration, as this will lacerate the pleura with each breath.

As needle insertion is considered a dynamic process from skin to the lesion; a short segment CT should performed always to verify the needle angle and tip position based on the last scan (a sequential technique). The needle is then advanced in one motion through the pleura to the prescribed depth.

A smaller automated cutting needle is passed through the lumen of the larger introducer needle and into the lesion. The entire needle shaft should be within the scan plane. If not, additional images above or below the entry site must be obtained. The key to recognizing the true tip of the needle is the identification of an abrupt square tip with a black shadowing artifact arising from it [30]. After needle tip position at the periphery of or within the lesion is confirmed and documented, a tissue sample can be obtained with firing the needle into the lesion during suspended respiration.

Postbiopsy scanning can help in localizing the biopsy direction by visualizing the small hemorrhage in most cases caused by the shock wave of the automated cutting needle [31].

Most operators perform at least two biopsies but more can be obtained based on the lesion characteristic. It is important when using coaxial technique to leave always the inner stylet inside the entry needle as if the tip was in a small branch of a pulmonary vein, it may cause devastating air embolism [32].

In our institution, the standard practice is to seal the biopsy needle track with a hydrogel plug when removing the introducer needle to prevent the air leaks and pneumothorax [33]. As per manufacturer's instructions, the introducer needle tip is positioned at deeper level to the visceral pleura. A hydrogel plug is advanced into the introducer needle which is then removed, leaving the plug behind at the predetermined depth to expand upon contact with moist tissue and fill the track. The seal is airtight. The hydrogel plug resorbs into the body over time.

Post-biopsy care

After the biopsy is complete, a short CT scan is performed to evaluate patients for immediate complications. If the scan is normal with no significant pneumothorax and the patient is asymptomatic, the patient is transported on a gurney to the designated area for monitoring by the assigned medical staff. The patient should remain recumbent throughout the monitoring period.

Follow-up expiratory chest radiographs are obtained with sitting upright at 1—2 h after biopsy. If the chest radiograph shows no new changes, the patient is discharged. Upon discharge, the patient is asked to abstain from strenuous or weight-bearing activities for 3 days. Additionally, anticoagulants, antiplatelets and non-steroidal anti-inflammatory drugs are not allowed.

Complications

Percutaneous transthoracic core biopsy of the lung is generally associated with higher complication rates compared to solid organ biopsy. Based on published guidelines by the Society of Interventional Radiology, the overall complication rate of percutaneous transthoracic lung biopsies of 10% with threshold success rate of 85% are acceptable [34]. Most complications occur immediately or within the first hour of a biopsy and they can be treated conservatively; often on an outpatient basis [35—37]. Common complications include pneumothorax and hemorrhage. Rare complications include air embolism, vasovagal reaction, cardiac tamponade, and seeding of the tract with tumor.

Pneumothorax

Pneumothorax after CT-guided percutaneous lung biopsy has been reported from 8 to 54%, with an average of around 20% in most large series as CT imaging can detect even very small pneumothorax that may not even be visible on chest radiograph. However, the rate for pneumothoraces requiring treatment with chest tube varies from 5 to 18% [10,35,37—47]. Pneumothorax can occur during or immediately after the procedure, which is why it is important to perform a CT scan of the region following removal of the needle.

Risk factors of pneumothorax after lung biopsy have been identified in the literature with a lot of controversy. The suggested main factors influencing the incidence of pneumothorax are lesion size [42,43], lesion depth [42,44], contact with the pleura [23], the presence of emphysema on CT, transgression of fissures, a small angle of the needle with the thoracic pleura, and multiple repositioning of the needle [48,49].

Various techniques have been proposed to reduce the incidence of a significant pneumothorax but their true efficacy remains unclear and none of them has found widespread acceptance [46,50—53]. Recently, a prospective, multicenter, randomized, controlled clinical study of using an expanding hydrogel lung biopsy tract plug in patients undergoing CT-guided percutaneous transthoracic lung biopsy has shown significant reduction in the rates of pneumothorax, chest tube placement and post-procedure hospital admission [33].

Pneumothorax that is small (<20% lung volume), asymptomatic and stable does not require treatment and conservative management is appropriate. The pneumothorax must be treated when it is

symptomatic, its size exceeds 30% of the lung volume, and/or its size continues to increase. Treatment starts with administrating supplemental nasal oxygen and positioning biopsy side-down if possible. If the biopsy needle is still within the thorax, manual aspiration of the pneumothorax can be attempted [37,54]. If the biopsy needle has been removed and the pneumothorax is large or symptomatic, emergent percutaneous decompression with a needle or catheter is necessary. Choosing a small-bore or large bore catheter depends on the pneumothorax size. As an expiratory upright chest radiograph is usually obtained immediately after biopsy as a baseline, serial chest radiographs are obtained to observe for the recurrence of pneumothorax. An unchanged small pneumothorax at 4 h post-biopsy is unlikely to become larger [55]. If the chest radiographs at 2 and 4 h post-biopsy show a stable small or decreasing pneumothorax and the patient is asymptomatic, the patient can be discharged in accordance with institutional policy. Management specifics vary by institution, but good communication with the referring clinician or appropriate inpatient service regarding patient status and disposition is vital [56].

Hemorrhage

Hemorrhage is the second most common and the most dangerous potential complication of percutaneous transthoracic lung biopsy. At least to some extent, every percutaneous transthoracic lung biopsy is associated with some degree of hemorrhage. However, it is most often self-limited and resolves spontaneously without treatment. It may occur with or without hemoptysis. Hemorrhage and hemoptysis after percutaneous transthoracic lung biopsy occur in approximately 11% and up to 7%, respectively as reported in most series [38,57]. Unusually blood emerging from the hub of the introducer needle and alveolar hemorrhage identified on the CT scan directly as perifocal ground-glass attenuation in the area of the biopsy or along the needle tract are the only manifestations of bleeding during the procedure but should be considered as clues to the onset of hemoptysis. It is more likely to occur in patients with abnormal coagulation or pulmonary arterial hypertension. Cutting needles especially those are larger than 18 gauge are associated with an increased risk for hemorrhage [10,27,40,58]. Lesion depth especially at greater than 2 cm has been identified as the most important risk factor for hemorrhage [59]. However, other lesions risk factors include size smaller that 2 cm, vascularity, cavitations, presence of enlarged bronchial vessels in the vicinity, and central location [59,60].

If significant hemorrhage occurs, the patient should be placed in decubitus position with the biopsy side down to prevent transbronchial aspiration of blood. However, if the patient is hemodynamically unstable, appropriate supportive management with fluid resuscitation with or without blood transfusion is required. Rarely, bronchial or pulmonary arterial transcatheter embolization is required.

Air embolism

Air embolism is the most severe complications but it is one of the least frequent (0.07%) [61,62]. It occurs when air enters the pulmonary venous system and can lead to systemic air embolism. Air embolism can cause myocardial infarction, arrhythmia, stroke and death. Once air embolism is suspected, the patient should be placed in the left lateral decubitus position or in Trendelenberg position to prevent residual air in the left atrium from entering the cerebral circulation. Supplemental 100% oxygen should be administer and general symptomatic support should be provided [10].

New directions

Randomized evidence suggests that the technique of biopsy should be dropped in favor of image guidance where available in cases of suspected lung lesion, on the basis of higher diagnostic yield. The choice between image guidance modalities is largely dependent on lesion characteristics on CT images and an understanding of which image-guided technique will be safer. Recently, C-arm cone-beam CT (CBCT) with a flat-panel detector system in which a cone-beam X-ray tube and a flat-panel detector are integrated with a C-arm gantry has been developed for interventional purposes [63]. It has both CT and fluoroscopy image capabilities and offers greater flexibility in orientating the detector around the patient than closed CT gantry systems in addition to advanced real-time fluoroscopic and three-dimensional CT capabilities [64]. This image-guided system allows identification of the correct trajectory of the needle to the lesion under real-time fluoroscopic capability and verification of the exact location of the needle tip within the target lesion using the CT capability of the system, thereby improving the diagnostic accuracy and efficacy of biopsy and enhancing the operator's confidence during the procedure. Although there are only few studies about CBCT-guided percutaneous transthoracic lung biopsy, the reported accuracy

and sensitivity were 92% and 94%, respectively, which are comparable CT-guided percutaneous lung biopsy [65].

With the availability of specific chemotherapy and novel targeted therapy for lung cancer, the core biopsy should provide enough material for both diagnosis and specifically subtyping of malignancy. As some of the tumors show histological heterogeneity, particularly with regards to the expression of molecular markers, the core biopsies should be obtained from different parts of the lesion for adequate evaluation of this heterogeneity. Although obtaining multiple samples with using cutting needle and coaxial technique is a potential advantage, substantial advantages regarding sensitivity and specificity need to be demonstrated in subsequent larger studies.

Image-guided percutaneous transthoracic lung biopsy is traditionally and technically performed by specialized radiologists. However, a multidisciplinary approach, including oncologists, radiologists, pathologists, thoracic surgeons, and/or pulmonologists, is required on a local or institutional level to standardize biopsy protocols for obtaining lung tissue with regards to the biopsy technique used, the number of cores obtained and the types of histopathologic tests applied [3]. Such a multidisciplinary approach should be adopted whenever possible as it will help to fulfill emerging diagnostic requirements for the use of novel therapies, avoid thoracotomy and unnecessary costs, limit patient stress and risks associated with repeat biopsies due to inadequate initial obtained samples and optimize patient treatment. Moreover, it will facilitate building local database and inclusion of patients in specific clinical trials.

Conclusion

Image-guided percutaneous transthoracic lung biopsy especially with CT guidance is generally considered safe technique with low complications rate and a high diagnostic yield for lung cancer. Various imaging modalities have been used for guiding the percutaneous transthoracic lung biopsy based on lesion characteristics on CT images and an understanding of which image-guided technique will be safer. Additionally, radiologists should be aware of the increasing need for a specific histolopathologic diagnosis in order to optimize patient treatment of lung cancer with the novel therapies and achieve the most for the patient care.

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