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REVIEW ARTICLE

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Transthoracic ultrasound-guided biopsy in the hands of chest physicians – a stepwise approach

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ABSTRACT

Background: The evaluation of patients with lung lesions is challenging. The nature of the lesion can be determined by pathological evaluation of biopsies. The pulmonologists will be met by increasing demands with regard to biopsy techniques including ultrasound-guided transthoracic needle biopsy (US-TTNB).

Objective: The aim of this paper is to present the pulmonologist to a systematic step-by-step guide for performing US-TTNB and to assess the evidence for this approach.

Method/results: Indications, contraindications and a step-by-step guide for the techniques used when performing US-TTNB are presented, and major complications and handling of these are described.

Conclusion: US-TTNB performed by pulmonologists is a safe and feasible procedure.

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Lung lesions; transthoracic needle biopsy; ultrasound; ultrasound-guided transthoracic needle biopsy; UL-TTNB; UL-TTNAB

Background

The evaluation of patients with lung lesions is challenging. First, the cause of the lesion must be determined, and second, in the case of malignancy, it is crucial to determine the correct stage. The advanced computed tomography (CT) technique has had a major influence on the detection of suspected malignant lung nodules [1]. Both smaller and increasing numbers of nodules can now be detected because of improvement in scan resolution [2,3] and screening for lung cancer with CT is gaining ground. The correct diagnostic determination of the pathology of these nodules is imperative since the distinction between malignant and benign nodules is essential for treatment planning [4]. Of these reasons, it is obvious, that we in the future can expect referral of both a larger number of patients and smaller and smaller nodules. Additionally, the increased use of markers and genotyping warrants an increase in the quality and amount of tissue obtained when performing invasive procedures. In other words, the pulmonologists will be met by increasing demands with regard to biopsy techniques including ultrasound-guided lung biopsy.

Centrally located lung lesions and mediastinal lymph nodes can be biopsied with the use of bronchoscopy or endosonography. However, these techniques are not feasible or nondiagnostic in a substantial proportion of patients, especially in the absence of endobronchial abnormalities or absence of tumor close to trachea or esophagus. Transcutaneous thoracic biopsy is often useful for peripherally located lung lesions. Transthoracic biopsy can be performed CT-guided (CT-TTNB), fluoroscopy guided or ultrasound guided. Ultrasound-guided transthoracic needle biopsy (US-TTNB) performed by pulmonologists is a safe procedure with a very low risk of complications [5] and is to be preferred especially if the alternative is diagnostic surgery. The procedure is in many centers an integrated part of the overall invasive program performed solely by pulmonologists [5].

The aim of this paper is to present the pulmonologist to a systematic step-by-step guide for performing US-TTNB and to assess the evidence for this approach.

Ultrasound-guided biopsy

US-TTNB has an acceptable diagnostic yield [6–10] and is a cost-effective alternative to CT-guided biopsy [11–15]. The complication rate is generally lower than for CT-guided biopsies [5,16]. Ultrasound-guided biopsies should

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thus be preferred whenever a lesion can be visualized by the use of ultrasound. However, a lesion in the central part of the lungs or peripheral but with no contact to the visceral pleura, will not be visualized with ultrasound due to the ultrasound wave's reflection in air between the lesion and the visceral pleura.

In patients with pleural effusion of unknown cause, the combination of diagnostic thoracentesis and US-TTNB with pleural biopsy has been demonstrated to be able to diagnose more than 90% of the patients [17]. The combination of these two modalities should thus be performed prior to considering thoracoscopy. US-TTNB can be used to obtain tissue from a variety of structures such as the chest wall, parietal pleura, lung, diaphragm and anterior and upper mediastinum. Additionally, the technique can be used to obtain tissue from extrathoracic structures such as supraclavicular and cervical lymph nodes.

Indications

Proper assessment of both indication and contraindications are important. In some cases, contraindications may overrule the indication. In other cases, another invasive procedure may be more appropriate. Some of the indications for the procedure are as follows (Figure 1):

- Lung: Peripheral mass or nodule of unknown origin
- Mediastinum: Mass in the anterior mediastinum or thoracic inlet
- Pleura: Thickening of the parietal pleura or suspected pleural infection
- Chest wall: Tumor or suspected infection
- Lymph nodes: Suspected malignancy, infection or interstitial lung disease such as sarcoidosis involving infraclavicular/supraclavicular/axillary or internal mammary lymph nodes

Contraindications

The risk of complications must always be balanced against the indication for the procedure, and the pulmonologist must be fully capable of treating any complication immediately. Relative contraindications include coagulopathies, severe decompensated heart failure, unstable angina, symptomatic cardiac arrhythmias, recent myocardial infarction, unstable bronchial asthma, severe impairment of lung function, respiratory failure and severe untreated hypertension. US-TTNB can be performed on patients with mechanical ventilation, but the potential clinical impact of obtaining the biopsy should outweigh the increased risk of pneumothorax and close monitoring is warranted. US-TTNB can be performed immediately after endoscopy, for example, as in combined single-day workup and staging of suspected lung cancer [18].

The patient

Confirmed the patient's identity, and that the patient has received relevant information regarding the procedure,

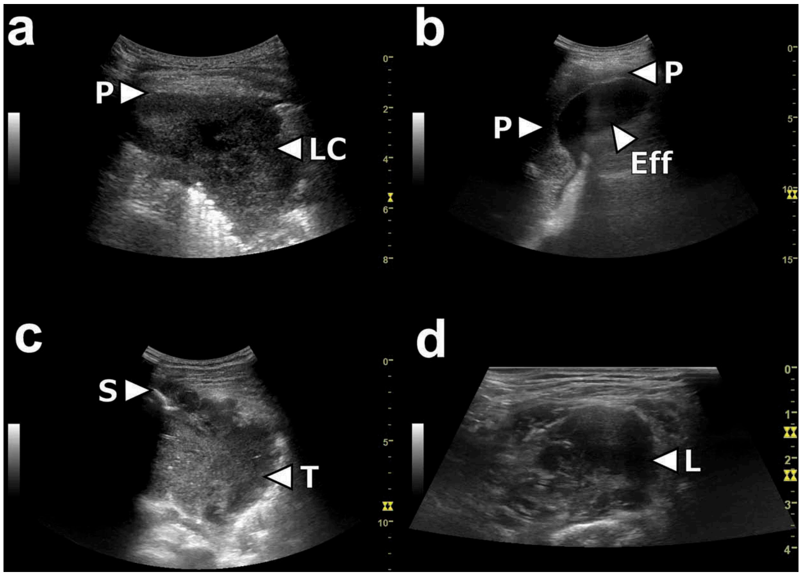

Figure 1. Examples of structures assessable to US-TTNB. (a) A hypoechoic, peripheral lung consolidation (LC) can be seen just below the pleural line (P). (b) A crescent-shaped thickening of the parietal pleura (P) and a pleural effusion (Eff) can be seen. (c) Lateral and profound of the sternum (S) a tumor (T) is present in the anterior mediastinum. (d) An enlarged, ill-defined supraclavicular lymph node (L).

the risk of complications and informed consent has been obtained. Review the indication, available imaging, and make sure to consider any absolute or relative contra-indications. Ensure that you and your staff are prepared to handle all potential complications related to this procedure. Confirm that a pleural drainage system and emergency medications are in the examination room ready for use.

Biopsy needles

Generally, a single-needle technique is used for ultra-sound-guided biopsies. The procedure can be performed using both aspiration needles as well as core biopsy needles (Figure 2). Whether an aspiration needle or a core biopsy needle is chosen for a procedure will depend on the suspected diagnosis (e.g. carcinoma, malignant mesothelioma, lymphoma, infection), lesion characteristics (e.g. size, placement, mobility) and patient characteristics (e.g. comorbidities, medication). The advantage of the core biopsy is the amount of obtained tissue whereas the aspiration needle is less invasive and often easier to use when the lesion is small and mobile. If doubt exists whether a core biopsy needle can be used, or the procedure should be limited to aspiration, a pragmatic approach is to initially perform aspiration biopsies using aspiration needles. If this can be easily performed, core biopsies can be performed subsequently. Such an approach can also be combined with rapid on-site evaluation (ROSE) is available [7].

Coated aspiration needles improving ultrasound visualization are available but these are often expensive. Generally, standard needles used for other purposes (e.g. injection, lumbar puncture, Chiba needle) can be used as less expensive alternatives, reserving the coated needles for more difficult cases. Abrams needle has been demonstrated to have a higher diagnostic yield than conventional cutting needles for the diagnosis of tuberculous pleuritis. If available, the Abrams needle should thus be preferred in a setting in which pleural thickening/pleural effusion due to tuberculosis is more likely than malignancy [19].

Choice of biopsy technique has an impact on the optimal needle length for the procedure. If a freehand technique is used, the length of the needle should generally be at least the distance of the proposed needle path from the skin to the middle of the lesion. If a biopsy guide is used, the length of the biopsy guides channel should be added to the needle length.

The procedure

US-TTNB should be performed with the patient in a position allowing for accurate ultrasound visualization and also is acceptable for the patient (e.g. sitting, supine, prone). Equipment for patient monitoring should be available and used throughout the procedure. Placement of an intravenous access prior to the procedure is recommended, if complications occur. The

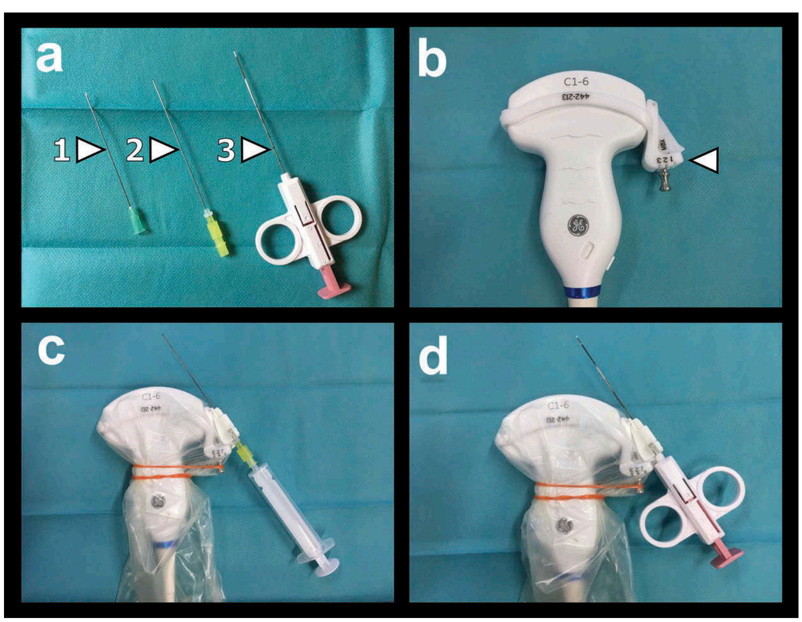

Figure 2. Equipment used for US-TTNB. (a) Examples of biopsy needles: A 21G conventional Chiba needle (1), a 20G coated Chiba needle (2), an 18G cutting needle (3). (b) Ultrasound transducer with a biopsy guide system. This guide system has three different adjustable needle angles. (c) Ultrasound transducer with biopsy guide, sterile covering and a 20G coated Chiba needle and syringe. (d) Ultrasound transducer with biopsy guide, sterile covering and an 18G cutting needle.

authors do not use intravenous sedation or opioids as standard care, but it may be necessary in some cases.

Prior to the procedure lung ultrasound is performed to ensure accurate visualization of the lesion and adequate planning prior to the procedure (e.g. choice of technique, choice of needle) [14]. Presence or absence of lung sliding on the anterior chest surface and presence of pleural effusion should be noted since this information is essential when reassessing the patients for the development of complications following the procedure.

Generally, ultrasound-guided biopsy can be performed using a variety of different techniques. The three most commonly used techniques are described in the following.

Ultrasound identification of puncture site

The use of ultrasound may be limited to identifying an optimal site, angle and depth for performing a transthoracic biopsy. Once these factors have been determined, the biopsy is performed 'blindly' without the direct guidance of ultrasound. No studies have demonstrated whether this technique is inferior to the techniques using direct ultrasound guidance. Despite the lack of studies, real-time visualization of the needle and placement when obtaining the biopsy should be preferred whenever possible.

Transthoracic ultrasound-guided biopsy using biopsy guide

When using a biopsy guide, the biopsy can be performed using real-time visualization of the biopsy needle by the use of ultrasound. Different biopsy guides systems exist and vary depending on the ultrasound system used. When using a biopsy guide, an in-plane (or long axis) technique is used. With this approach, the needle enters the thoracic wall at the side of the probe in the guiding system, and it is possible to visualize the movement of the needle toward the lesion.

When performing lung ultrasound prior to the biopsy procedure, the optimal biopsy angle is determined and chosen as the ultrasound preset. The biopsy handle is attached to the ultrasound transducer. The angle of the biopsy handle is adjusted so it corresponds with the biopsy angle chosen as the ultrasound preset (Figures 2 and 3). Ultrasound gel is applied to the transducer.

The operator uses sterile gloves. The skin of the biopsy area is cleansed using an antiseptic fluid. Once the fluid has dried a sterile dressing can be applied to ensure that no contamination of the puncture site occurs during the procedure.

The transducer is then placed in a sterile plastic bag.

The sterile part of the biopsy handle can now be attached to the transducer. An adapter corresponding to the needle size (G) is placed in the biopsy handle. Sterile ultrasound gel is applied to the transducer.

The biopsy site is scanned using the sterile transducer. Once the optimal biopsy path has been identified a local anesthetic can be injected using ultrasound guidance. When injecting the local anesthetic one should note whether the needle path is still optimal for the subsequent biopsy procedure. The largest amount of the local anesthetic should be applied to the skin and parietal pleura. Once the local anesthetic has had some time to induce analgesia the biopsy procedure can be performed. If a core biopsy is performed, a small skin incision is made to facilitate the needles penetration of the skin. The optimal biopsy site is once again identified using the transducer. Great care should be made in order to ensure that no vessels, nerves, aerated lung or other vital structures are located in the needle path. Whenever possible, a needle path

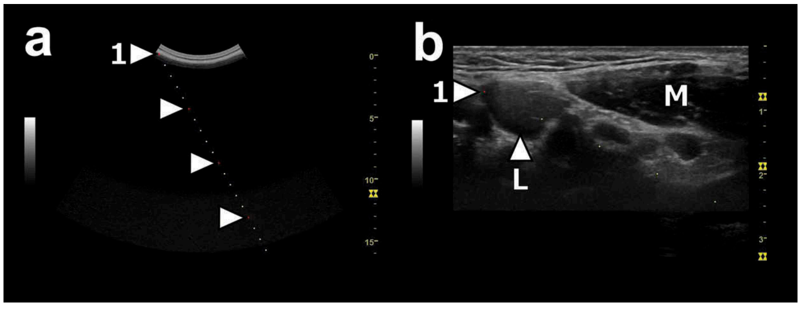

Figure 3. Needle guidance on the ultrasound screen. (a) Needle biopsy guide for a given predefined angle can be seen as yellow dots on the ultrasound screen. The distance between two dots corresponds to 1 cm. A red dot (arrows) is present for every 5 cm. (b) Ultrasound image of the supraclavicular region. Muscle tissue (M) and a lymph node (L) can be seen. The needle biopsy guide has been switched on. If the transducer is being held in this position and a needle is inserted, the tip of the needle should enter the lymph node after having been inserted approximately 5 cm into the guide system as the red dot (1) is located just within the node.

just above a rib should be chosen in order to minimize the risk of making a lesion of an intercostal artery.

Once the optimal site has been identified, the transducer is held fixed in this position. The biopsy needle is then introduced in the biopsy guide and gently advanced toward the lesion of interest. When the needle is advanced one should notice signs of immediate complications (e.g. pneumothorax). When the needle is in the lesion, the biopsy can be performed and the needle gently removed afterward (Figure 4). Additional biopsies can be performed repeating the procedure described.

If the biopsy site is not fixed and moves in synchrony with the patients breathing, the procedure has to be performed in coordination with the patients breathing. Prior to the biopsy procedure, it is determined which part of the breathing fazes are optimal for the biopsy. The patient is instructed on how to breathe and hold their breath at the ideal time for the biopsy. The maneuver is briefly trained with the patient in order to ensure that the patient has understood the instructions. The biopsy procedure is then performed as described as above, the difference being when the biopsy needle is introduced. The needle is advanced until the needle tip is located in the chest wall a few mm from the parietal pleura. The patient then holds his/her breath as trained. The biopsy needle can briefly be advanced and the biopsy performed with subsequent rapid withdrawal of the needle. The patient is then allowed to begin breathing again. When using an aspiration needle, aspiration is performed while the needle tip is within the relevant structure. There is no evidence regarding the ideal number of passes within the target lesion when aspirating. If possible we use an approach as is recommended for the endobronchial ultrasound with 10–15 passes. The number of passes has to be reduced if the lesion is mobile and the patient is only shortly able to hold his/her breath. Most core biopsy needles a single pass is sufficient in order to obtain the biopsy. As mentioned above, ROSE can be used for US-TTNB [7] where available but is not a requirement.

Transthoracic ultrasound-guided biopsy using freehand technique

Real-time ultrasound-guided biopsy can also be performed using a freehand technique. When using this technique, the needle is advanced without the use of a biopsy guide. The advantage of being a more flexible choice of angle and needle path when introducing the needle as well as an option to choose from different biopsy techniques such as in-plane or out-of-plane technique. The major disadvantage of the free-hand technique is that the operator needs to have highly trained three-dimensional sense of where the needle is placed and integrate this sense with the information obtained on the ultrasound image. This is generally easier when performing biopsies of superficial structures (e.g. supraclavicular lymph node) and more difficult with more deeply located structures (e.g. lung consolidation). When used for transthoracic biopsies, the technique should generally be reserved for physicians that have more extensive experience in transthoracic ultrasound-guided biopsies and who masters the technique using a biopsy guide.

Supplementary color Doppler can be used to visualize intercostal arteries, other vessels near the lesion, and in some cases central necrotic areas in the targeted lesions. However, the movement of the thoracic wall and lungs during the procedure can be a challenge when adding Doppler [20].

Handling of the biopsies

It is imperative that the operator knows exactly how to handle the biopsies with regard to the pathologist´s requirements for both cytological assessment,

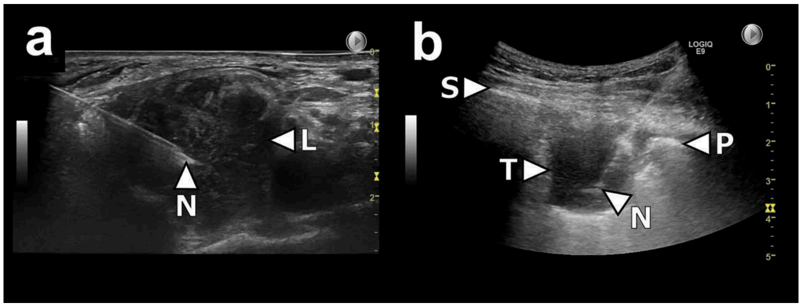

Figure 4. Examples of US-TTNB procedures. (a) US-TTNB of a supraclavicular lymph node (L). A 21G Chiba needle was used (N). (b) US-TTNB of a small lung tumor (T). The tumor can be seen between the sternum (S) and the pleural line (P). A 18G cutting needle (N) was used for the procedure.

immunohistochemistry and mutation analyses. Even the most perfect biopsy procedure is meaningless if the samples are not handled correctly.

After the procedure

Once the biopsy procedure has been performed, lung ultrasound is once again performed to rule-out complications (e.g. pneumothorax, hemothorax, intrapulmonary bleeding). Ultrasound or chest x-ray is performed after 1 h.

US pictures of the prebiopsy lung ultrasound examination, the biopsy procedure and the postbiopsy lung ultrasound examination should be stored for documentation purposes, and for use in case of difficulties in the interpretation of the biopsy result or the need for an additional biopsy procedure.

If the patient within 1 h of the biopsy procedure has no signs of complications, the patient can be discharged from the outpatient clinic. The patient should receive instructions on how to act in the case of developing symptoms of complications within the first 24 h following the biopsy procedure.

Complications

Pneumothorax is one of the most common complications to transthoracic lung biopsy, sonographic this is visualized with absence of lung sliding, and confirmed with the diagnostic sign; lung point. Additionally, a pneumothorax must be suspected if the lesion suddenly is not visual after performing a biopsy.

Pneumothorax after CT-guided transthoracic lung biopsy occurred in between 18.8 and 25.3% when the biopsies were performed with a fine needle and core biopsy, respectively, in a recent meta-analysis [21] but only in 2.5% (95%CI 0.03–4.6%) of US-TTNB cases [5]. Approximately half of the patients who develop an iatrogenic pneumothorax, placement of a chest tube is necessary. Lung ultrasound or chest x-ray should be performed 1 h after the procedure as approximately 90% of pneumothoraxes are detected during this time [15,22,23].

The treatment of pneumothorax consists of oxygenation and insertion of a pleural chest tube, for example, a 7F tube, followed by aspiration. When defining a management strategy, the size of the pneumothorax is less important than the degree of clinical compromise. The differentiation of a ‘large’ from a ‘small’ pneumothorax is the presence of a visible rim of >2 cm between the lung margin and the chest wall at the level of the hilum. This is easily measured on a chest X-ray, but accurate size is best measured by CT [24–26]. Using lung ultrasound, whether the lung point is located anteriorly or posteriorly to the midaxillary line correlates to a small or large pneumothorax, respectively [27]. Tension pneumothorax is a medical emergency that should be treated immediately with needle decompression followed by pleural drainage without waiting for supplemental x-ray or other investigations.

Bleeding in the lung parenchyma can be seen in approximately 5–15% of CT-guided lung biopsies. Lung parenchymal bleeding following transthoracic biopsies can be diagnosed using lung ultrasound [28] but no diagnostic accuracy studies have been published. It is unknown whether the risk of bleeding following US-TTNB is the same as with CT-TTNB, but might be lower since the needle does not pass normal aerated lung tissue when performing US-TTNB. Lung parenchymal bleeding can manifest as hemoptysis, and is only seen in 1–5% of the patients when the procedure is done CT guided. In a retrospective multicenter study of US-TTNB procedures, hemoptysis was seen in 0.5% (95%CI 0–1.5%) of the patients [14].

The treatment of hemoptysis depend on the severity and may include Tranexamic acid 500–1,000 mg intravenously (non-bolus), placement of the patient in a lateral position with the bleeding lung placed downward giving the nonoperated lung free air access. In the case of severe bleeding with manifest or threatening airway, compromise early aggressive airway management with endobronchial intubation is imperative since this allows access to additional airway management. Bronchoscopy with tamponade and the use of a balloon catheter, treatment of coagulopathies or coiling may be necessary in severe and refractory cases.

Training of the operator

Only a few studies have explored the educational aspects of US-TTNB [29], and there is no evidence on how the most evidence-based or effective educational program should be composed. Since the procedure is a technical hands-on procedure, the authors recommend hands-on training after a theoretic session or sufficient theoretical knowledge obtained from books or papers. The eye-hand coordination, and understanding of needle movement is crucial, no matter which technique is used.

To our knowledge, no phantoms or simulators have been presented in US-TTNB. Looking at other ultrasound-guided biopsy training programs, several phantoms have been created, for example, gelatin blocks with embedded lesions [30–32]. However, a disadvantage in these home-made phantoms is, that they are all static, whereas in US-TTNB the lungs are moving synchronously with the patient's respiration. Further studies are needed to investigate how the most effective training program should be composed, but until these exist the inexperienced operator should, if possible train the technique on phantoms, and always be supervised by an experienced operator until both operator and supervisor find the level of competence sufficient, and know how to handle complications and critically situations. Based on our experience we also recommend that inexperienced operators initially perform US-guided biopsies of structures which are either technically less difficult to biopsy or has a low risk of complications (e.g. large masses, superficial lymph nodes) rather than beginning with technically challenging cases or more high-risk procedures (e.g. mediastinal mass, small mobile lung nodules).

Future perspectives for the pulmonologist

It is raised beyond any doubt that the pulmonologist in the future can expect referral of more patients and patients with smaller lung lesions, since screening for lung cancer is gaining ground. Furthermore, there is an increasing focus on how to provide a fast diagnosis. US-TTNB in the hands of the pulmonologist is an important tool in both respects.

An advantage when the procedure is performed by pulmonologists is that they constantly reassess and adjust the invasive programme including the indication and know exactly when diagnosis including immunohistochemistry, mutation analyses, microbiology and staging of the disease is satisfactory. Moreover, they have close contact with the patient from start to end of the programme and perform all other invasive procedures, meaning that the patients only need to see a single physician. The procedure can be performed rapidly without the patient having to wait for an available time-slot in the radiology department.

Ideally, the implementation of US-TTNB performed by pulmonologists should in the future be based on training and certification including theoretical courses, simulator/phantom-based education and clinical training. The establishment of competence should be based on an objective and valid assessment of all three before the patient is exposed to the operator.

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