

CIRSE Guidelines on Percutaneous Needle Biopsy (PNB)

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Introduction

Image-guided percutaneous needle biopsy (PNB) has proven to be a safe and effective procedure, and it became a common procedure representing an essential step for diagnosis and treatment planning in many situations.

Compared to open or excisional biopsy, image-guided percutaneous biopsy is less invasive and can be proposed as an outpatient service in the majority of cases.

However, success of PNB is strictly related to proper patient selection, preparation and post-procedural management as well as adequate procedural planning and monitoring.

Moreover, in the era of personalized cancer therapy, role of PNB is evolving since biomarker status today is guiding therapeutic decisions in many solid tumours, not only at initial diagnosis but also at the time of progression. Biological specimens are also becoming mandatory in many clinical trials. This new role of PNB implies a more intense involvement of interventional radiologists (IRs) in multidisciplinary discussions and clinical trial design, and it involves a deeper knowledge of molecular testing requirements, with concurrent development of new imaging guidance tools for the identification and localization of the most adequate target [1].

This document reviews current literature and provides Standards of Practice for image-guided PNB in different organs, with the exception of breast biopsy whose peculiar features deserve a separate dissertation.

Definitions

PNB is defined as insertion of a needle into a suspected lesion or an organ for the purpose of obtaining tissue or cells for diagnosis. The procedure is performed under guidance of imaging techniques such as ultrasound (US), fluoroscopy, computed tomography (CT) or magnetic resonance imaging (MRI), cone beam CT (CBCT) and positron emission tomography CT (PET-CT). The imaging technique adopted depends on the lesion type and location, patients' compliance, technique availability and operators' preferences.

PNB includes fine-needle aspiration biopsy (FNAB) and core biopsy (CB). FNAB is the use of a thin, hollow needle (18–25 gauge) able to extract cells for cytological evaluation by aspiration and in some cases small tissue pieces for histological examination. CB is the use of a hollow needle (9–20 gauge) [2] with a cutting and/or capturing

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mechanism that allows the extraction of a piece of tissue for histological evaluation.

Technical success of PNB is defined as the procurement of sufficient material to establish a diagnosis and/or guide treatment decisions.

Clinical success of PNB is defined as the outcome of patients depending on the results of biopsy, in term of appropriateness of medical or surgical management according to specific guidelines (e.g. selection for oncologic targeted therapies, active surveillance as an alternative to invasive treatment).

Complications are stratified on the basis of their outcome (see “Appendix”) [3]. Major complications result in hospital admittance (for outpatient procedures) or prolonged hospitalization (for in-patient procedures), unplanned increase in level of cares, permanent sequelae or death. Minor complications result in no sequelae; they may require therapy or a short (generally overnight) hospital stay [3].

Pre-Procedural Imaging Evaluation

The vast majority of cases who are referred to PNB have undergone at least one pre-procedural cross-sectional and/or functional study, including US, CT, MR or positron emission tomography CT (PET-CT), depending on the clinical issue. Careful review of the images by an IR is mandatory for the success of a PNB [4]. Indication to PNB should be discussed with the referring physicians, including the type of biopsy (core biopsy for histology versus FNAB for cytology), taking into account the clinical needs and the procedural risks. In particular cases, indications to biopsy and/or alternative ways to obtain a diagnostic specimen may be discussed within multidisciplinary boards. It is essential to confirm the indications for PNB, to identify the optimal target and to question the differential diagnoses, thus helping the subsequent pathological assessment. Pre-procedural images allow procedural planning, including the selection of the most proper imaging guidance (with or without contrast injection to better detect the lesion), patient’s position, access routes, needle type and trajectory, scheduled number of samples. Finally, imaging may enable the identification of potential contraindications and risks of PNB, anticipating possible complications (for instance, when the target lesion is adjacent to organs at risk of bleeding).

A written report of the pre-procedural evaluation is suggested as a part of the PNB procedure.

Indications and Contraindications to PNB

Indications for PNB include, but are not limited to, the following:

- To establish the nature of diffuse parenchymal disease;
- To obtain material for microbiological analyses in suspected or known infections;
- To establish the benign or malignant nature of a suspected tumour;
- To classify a malignancy (including immunohistochemistry (IHC) evaluation);
- To stage a patient with known (or suspected) malignant tumours elsewhere;
- To obtain material for molecular analysis.

Image-guided PNB is a relatively non-invasive procedure; thus, the absolute contraindications are rare and include:

- Lack of a safe access;
- Non-correctable coagulopathy;
- Refusal of consent.

The relative contraindications include all those conditions that increase the risk of complications. They should be promptly recognized and, when possible, corrected. They include:

- Coagulopathies;
- Inability of patient to cooperate (general anaesthesia may be considered);
- Significant comorbidities (i.e. haemodynamic or respiratory instability);
- Pregnancy (mainly if ionizing radiation exposure is required).

Patient Preparation

Patient clinical assessment and preparation are critical for a success of PNB. Before the procedure, special attention should be paid to the review of relevant medical history, medications and laboratory data [5].

Baseline vitals should be monitored before and during the procedure, particularly in moderate- and high-risk biopsies.

Evaluation of Bleeding Risks and Correction of Coagulopathy

The evaluation of coagulation status is essential. When possible, antiplatelet/anticoagulation medications should be discontinued before the procedure, in particular for biopsies with moderate or significant risk of bleeding. When a cessation is problematic, risks and benefits should be carefully evaluated [6], and patients should be informed of potentially increased risk of bleeding. Recommendations for bleeding risk evaluation and management in PNB

according to the Society of Interventional Radiology (SIR) and the Guidelines of the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) [7] are summarized in Table 1.

Over the last years, new oral anticoagulants (NOACs) have become widely available. They are divided into two classes: oral direct thrombin inhibitors and oral direct factor Xa inhibitors. The main advantage of NOACs is the predictable anticoagulant effect at fixed doses without a need of routine monitoring. However, they lack of a reliable method to monitor anticoagulant activity and of an effective antidote. Management of NOACs before biopsy should be individualized based on drug type, procedure type, patient's clinical conditions and renal function. In general, NOACs should be withheld for 1–2 days before moderate- and high-risk biopsies and restarted 24 h after the procedure (Table 1) [8].

Informed Consent

Informed consent should be obtained directly from the operator who will carry out the procedure, following national laws and Institutional forms. The patients must be fully informed of the indications and benefits as well as of

the risks and adverse events. Alternative options, when available, should be discussed. Finally, the procedure must be described thoroughly, including the need for peri-procedural medications, such as anaesthetics [4]. Whenever possible, the operator should meet the patient in advance. A written consent must be obtained in all moderate- and high-risk PNB, preferably 24 h prior the procedure.

Peri-procedural Medications

A peripheral venous access (18–20 Gauge) should be obtained before the procedure, to ensure an immediate intravenous access in case medications or transfusions are required [5], except for very superficial biopsies (e.g. thyroid FNAB), depending on the operator's preference.

Patients should be fasting for 4–6 h prior to the procedure, in particular when sedation is needed.

The need for sedation should be carefully evaluated. Sedation should be considered to increase patient's comfort and safety, on the basis of lesion location, procedure complexity, patient's compliance and comorbidities. General anaesthesia is recommended for children and for totally non-collaborating patients. While light sedation or anxietyolysis can be managed safely by IRs and trained

Table 1 Recommendations for bleeding risk evaluation and management [7, 8]

	Low (category 1)	Moderate (category 2)	High (category 3)
<i>Risk of bleeding</i>			
Type of PNB	Superficial (thyroid, lymph nodes)	Lung, chest wall, intraabdominal	Renal
<i>Laboratory tests</i>			
INR	Recommended for patients receiving warfarin or liver disease	Recommended	Routinely recommended
aPTT	Recommended for patients receiving intravenous unfractionated heparin	Recommended for patients receiving intravenous unfractionated heparin	Recommended for patients receiving intravenous unfractionated heparin
Platelet count	Not routinely recommended	Not routinely recommended	Routinely recommended
Haematocrit	Not routinely recommended	Not routinely recommended	Routinely recommended
<i>Management</i>			
INR	>2.0: threshold for treatment	Correct to <1.5	Correct to <1.5
aPTT	No consensus	No consensus	Stop or reverse heparin for values >1.5 × control
Platelet count	Transfusion for counts < 50,000/μL	Transfusion for counts < 50,000/μL	Transfusion for counts < 50,000/μL
Haematocrit	No recommended threshold for transfusion	No recommended threshold for transfusion	No recommended threshold for transfusion
Clopidogrel	Withhold for 5 days before the procedure	Withhold for 5 days before the procedure	Withhold for 5 days before the procedure
Aspirin	Do not withhold	Do not withhold	Withhold for 5 days before the procedure
LMWH	Withhold one dose before the procedure	Withhold one dose before the procedure	Withhold for 24 h or up to two doses
New oral anticoagulants	Do not withhold	Withhold for 2–3 days before the procedure	Withhold for 3 days before the procedure

INR International Normalized Ratio, aPTT activated partial thromboplastin time, LMWH low molecular weight heparin

nursing staff, the administration of drugs for moderate and deep sedation should be reserved to personnel with knowledge and experience according to national legal regulations [9], such as anaesthesiologists or, on the basis of local policies, by IRs with appropriate training and certification.

Prophylactic antibiotics are not routinely administered for PNB, since the risk of contamination is low when the procedure is performed under sterile conditions. However, antibiotic prophylaxis can be indicated in immunocompromised patients and when targeting any potentially infected lesion or transgressing non-sterile anatomical structures (e.g. transcolic biopsies). There is no specific indication on type of antibiotic, and there is no clear demonstration of superiority of long-course (3 days) over short-course (1 day) treatments, or that the use of multiple drugs may be superior to the single-drug regimen [10]. Recent studies have supported the role of targeted antibiotic prophylaxis selected on the basis of rectal cultures obtained before transrectal biopsy, to reduce the incidence of infections [11]. Generally, prophylaxis should start before the procedure.

Patient Positioning

Patient is positioned according to the selected image-guided modality and access route, in a comfortable and stable position.

Patient positioning can be extremely useful in difficult procedures to move mobile structures away from the target and the biopsy tract. Moreover, patient stability might be particularly relevant when a navigation system is adopted.

Patients with respiratory compromise and severely obese patients should be evaluated carefully when a prone position is selected since they may experience breathing difficulties. When position implies the patient's visualization of the needle insertion (for instance, chest biopsies in supine position), more effort should be made in carefully describing all the manoeuvres to the patient before the procedure, to reduce anxiety and patient's movements.

Imaging Localization of the Access Site

Once the patient is correctly positioned, the lesion and access route must be fully visualized by the selected imaging guidance [12].

Selection of an access route is critical to ensure success of PNB. Generally, the route should be as short as possible and should avoid all risky structures (lung fissures and bullae, large vessels, neural structures, biliary tree, bowel, renal sinus, etc.). In specific situations, a longer route is recommended; in subcapsular liver lesions, a longer tract with intervening normal liver parenchyma reduces the risk

of hemoperitoneum; accordingly, in subpleural lesions, a longer oblique intraparenchymal needle path may facilitate the manoeuvre and increase technical success [13].

The site of skin puncture is marked, and the distance from the skin puncture site to the target is measured to select the correct needle length. Under CT and MR guidance, the angle of access route can be measured, to guide needle insertion.

In specific situations, intravenous contrast media injection (including contrast-enhanced US, e.g. for isoechoic liver or renal tumours) is required to visualize the lesion or the surrounding structures before PNB [14]. If the use of iodinated contrast media during the procedure is foreseen, pre-procedural evaluation of renal function is essential and the risk of contrast-induced nephropathy and allergy should be assessed, together with a potential need for prophylactic medication [5].

Respiratory motions must be taken into consideration when planning the access route, and patients should be instructed according to the operator's needs. In general, the lesions should be localized during the normal breathing to reduce the variability of deep breath-holds.

Skin Disinfection and Local Anaesthesia

Sterility is of paramount importance to avoid infectious complications. Once the access site is identified, the skin is cleaned and carefully sterilized using the standard technique [9, 12]. The boundaries of the skin preparation should be wide enough to allow for possible adjustment of the entry site. The area around the access site is covered with sterile drapes. Local anaesthetic (usually 10–20 mL of lidocaine 1–2%) is injected along the planned needle path. In case of a larger needle size (or coaxial introducer), a few millimetres skin incision is made using a scalpel blade.

Attention has to be paid to the operator's sterility as well (hygienic hand wash, decontaminated or disposable gown and sterile gloves) and the equipment decontamination, particularly in case of the US guidance (use of disposable transducer covers and sterile ultrasound gel) [9]. Whenever available, the biopsy instruments should be disposable, single-use items; otherwise, they should be submitted to machine decontamination and sterilization.

Equipment Specifications

1) Staffing issues

All procedures must be performed by a qualified IR physician with documented knowledge of risks and benefits of the procedure, imaging anatomy, imaging and monitoring equipment and radiation safety [15]. IR should have

access to all required supplies and personnel to safely perform the procedure and ensure prompt treatment of complications [16]. The team performing the procedure should also include trained nursing staff and radiological technologists [15]. When required, anaesthesiologists should be in charge of sedation [15]. In any case, emergency access to qualified acute care support should be guaranteed [16].

Success of PNB is finally ensured by the presence of qualified pathologists, adequately informed of PNB indications and relevant medical history. Onsite cytopathologic evaluation of fine-needle aspirations or touch preparations of core samples has the potential to improve PNB diagnostic yield [17].

2) Image guidance

PNB can be performed under US, CT, fluoroscopy, MR, fluoro-CT, cone beam CT or PET-CT guidance. Advantages and disadvantages of the most frequently used image guidance techniques are summarized in Table 2.

The selected imaging modality should allow:

- Complete visualization of all relevant anatomy;
- Sufficient visualization of equipment utilized during the procedure;
- Comfortable patient positioning and operator's manoeuvres;
- Adequate evaluation and management of possible complications (e.g. pneumothorax);
- Limited ionizing radiation exposure (particularly in children and young patients).

To facilitate needle insertion and target visualization during PNB in difficult lesions, new software has become available that allows fusing images obtained from different

modalities, such as CT, MR or PET-CT with real-time US or fluoroscopy [1, 18–20]. Also, optical or electromagnetic navigation systems can be available in some facilities. These systems are able to fuse two or more imaging datasets in real time (*registration*) and display the needle position on the real-time imaging dataset (*tracking*) by using electromagnetic or optical sensors placed on patient and on needle shaft [1, 18–20].

3) Facility

Besides adequate equipment for image guidance, the facility in which PNB is performed must provide [16]:

- *An Area for Patient Preparation and Post-Procedural Monitoring.* This area can be located in the radiology department or in a short-stay unit, with immediate access to personnel and equipment to identify and treat possible complications. The vast majority of PNB is performed as outpatient procedures. However, before the procedure, hospitalization should be considered in fragile patients or when the risk of complications is deemed to be substantially higher.
- *Access to Emergency Resuscitation Equipment.* The facility should provide appropriate equipment for the monitoring of heart rate, cardiac rhythm and blood pressure, an access to emergency resuscitation equipment and drugs, in order to be ready for any possible acute complication [15, 16]. In case of thoracic PNB, aspirator to clear upper airways and equipment for decompression of tension pneumothorax (PNX) must be available. Physicians and nursing staff must be properly trained for the use of this equipment [15, 16]. Equipment and medications should be monitored and inventoried on a regular basis.

Table 2 Imaging techniques for PNB

	Fluoroscopy	Ultrasound	Computed tomography	Magnetic resonance
Real-time imaging	Yes	Yes	Only for CT fluoroscopy	Near real time, with specific sequences
Field of view	Limited	Limited	Large	Large
Visualization of structures and devices	Poor Usually sufficient for bone biopsy Multiplanar visualization	Limited in obese patients and deep lesions Possible interference of surrounding structures	Good In specific situations, contrast media can be injected to detect lesion and vascular structure	Excellent High contrast resolution Multiplanar and three-dimensional visualization
Portability	No	Yes	No	No
Availability	++	+++	++	+
Ionizing radiation	Yes	Absent	Yes	Absent
Procedural time	+	+	++	+++
Costs	++	+	++	+++

- *Access to Laboratory Facilities for Tissue Samples Analysis.* Success of PNB strongly depends on adequate specimen collection and expertise of the local pathologists. Specimen collection and preparation must be appropriate for the clinical question and should be sent to the biopsy facility together with all relevant medical history, to guide microbiological or pathological analysis. Consultation with local laboratory prior to the procedure may be useful in selected cases. Onsite cytopathology assessment is desirable to determine adequacy of sample [17].

4) Procedure

Before the procedure, IRs must check the availability of all required devices [15].

Biopsy Needles

- FNAB needle: thin, hollow needle, 18–25G, able to extract cells for cytological evaluation by aspiration. The most commonly used are the spinal needles and the Chiba needles; when compared with Chiba needles, spinal needles have a thicker wall and smaller lumen, which makes their control somewhat easier. Other FNAB needles have been designed, and they mainly differ for the shape and cutting capabilities of the tip (Westcott, Franseen, Greene, Madayag, Turner needles).
- Tru-Cut needles: hollow needles, 9–20G, for CB, with a cutting mechanism that extract tissue sufficient for histologic analysis; the shape of cores is half-cylindrical and the capture mechanism changes according to the manufacturer and can be partially or fully automatic. Also, how far the cutting needle is advanced, when fired, changes according to the manufacturer and should be taken into consideration when planning the biopsy.
- Full-core needles: for CB, they are able to extract cylindrical cores, capturing them either with a suction mechanism or by a characteristic feature of the tip.
- Screw or helical tip needles: fine or large (10–14G) needles with a peculiar tip, in which the biopsy needle is inserted inside the lesion by rotating the tip and the tissue is captured into an outer cannula.
- Trephine-type needle: large-size needles, used for sclerotic bone lesions; they consist of an outer trocar inserted and left in place into the lesion, to allow multiple passes as for the coaxial technique
- Coaxial needle: used for coaxial technique; hollow needle, 9–19G, depending on the size of biopsy needle. The introducer needle is characterized by a blunt tip to avoid damage to non-target nearby critical structures; it is inserted and left in place after

removing the inner stylet, allowing multiple passes of biopsy needles for multiple specimen collection or combination of FNAB cytology and CB histology from the same access [21].

- Steerable needle: recently introduced; flexible needles that are potentially able to reach targets not accessible using traditional needles. They can be pre-curved or manually deformed. Their role is yet to be assessed.

Sample Aspiration or Capturing

- Syringe (usually 10–30 mL): attached to biopsy needle, it is traditionally used for FNAB. During suction, the needle is oscillated with short “in-and-out” movements. Before withdrawing the needle, the suction has to be discontinued to prevent aspiration of cells from the needle tract.
- Oscillating biopsy needle: used for FNAB; the oscillations associated with suction can increase the sample size.
- Vacuum-assisted biopsy needle: special systems allow the creation of vacuum inside a CB needle to draw long cores of tissue into the centre of the needle.
- Rotating CB needle: the inner needle rotates and oscillates to obtain a uniform tissue sample.

Equipment for Specimen Collection

The equipment required for specimen collection and preparation must be available and prepared before the procedure. This includes, among the others: sterile containers, slides for smears, fixatives and containers with formalin fixative or saline.

Procedural Features and Variations of the Technique

Procedural Steps in US Guidance

Before PNB, a full US examination should be performed to evaluate the target organ and lesion, and plan and measure the access route. Colour Doppler US may be useful to identify relevant vascular structures.

Basic principle of US-guided PNB is to align the scan plane, showing the target, with the needle plane showing the needle during the insertion [9]. Needle can be inserted parallel or perpendicular to the transducer. With the parallel insertion, it is possible to use a freehand or a needle-guided technique, while the perpendicular insertion can only be performed by freehand technique.

The needle-guided insertion consists of a plastic or metal device, with a “channel” for the needle, which is attached to the transducer and is able to provide a computer-generated path to the lesion with a fixed angle. Compared to the freehand technique, the guided technique seems to be faster and more efficient; especially for less experienced operators as it allows almost single puncture, also, for deep targets [22]. However, this technique is limited by a fixed angle, reducing the freedom in needle angulation and manipulation during insertion; thus, the freehand modality is still frequently used, especially by experienced operators [18].

During the insertion, the needle tip should always be clearly visualized as an echogenic complex. Needle tip visualization depends on several factors, such as the needle type and size and scanning angulation, and can be facilitated by simple manoeuvres, such as shaking the needle, moving the stylet within the needle or even injecting a small amount of saline or lidocaine [18]. Particular care should be paid to avoid air injection that may impair the proper visualization of the target area. The puncture should be as rapid as possible, during breath-hold when needed, to reduce damage of organ capsule and bleeding.

Procedural Steps in CT Guidance

A preliminary CT scan is obtained, limited to the volume including the target lesion. When needed, CT can be performed after intravenous contrast media administration to visualize the target and the surrounding structures.

The puncture tract is selected on axial scans or on multiplanar reformations when the path has to be angulated to the z-direction; when a double-angulated puncture is needed, the gantry can be tilted according to the available CT equipment capabilities, to provide images parallel to the direction of the access path. The path length and angle are measured on the CT scan, and the skin access point is marked with the gantry laser, a radiopaque marker (for instance an injection needle) or using a radiopaque grid positioned on the patient before the preliminary CT.

After skin preparation and incision, the needle is advanced into the subcutaneous tissues incrementally to assure proper needle angulation and direction. Using standard CT guidance, operators must leave the CT room to check needle position at each needle’s advancement.

Puncture of risky structures (pleura and solid organ capsule) should be performed in a single deliberate motion directed at the target in a single breath-hold to reduce incidence of complications.

CT Fluoroscopy In CT fluoroscopy, fast images are acquired with reduced spatial resolution, and concurrently

reconstructed and displayed, allowing real-time visualization of the needle advancement.

Compared to conventional CT, if available, CT fluoroscopy represents a valid guiding method that reduces procedural time and number of needle passes, thus resulting in reduced complications [23, 24].

CT fluoroscopy can be continuous or intermittent. When continuous CT fluoroscopy is used, CT images are acquired continuously during needle advancement, thus exposing operators and patients to high radiation doses [23–26]. As opposite, in intermittent CT fluoroscopy, the operators stand at the side of the gantry where a pedal is available to acquire CT images; the operators’ radiation dose becomes minimal or null, since the gantry width is generally enough to block the vast majority of the radiation dose.

Procedural Steps in Uncommon Guidance

MR Guidance MR guidance can be extremely useful for lesions not detectable with other imaging modalities [27]; it is gaining increasing acceptance for specific indications, such as breast and prostate lesions [28, 29]. Special non-magnetic alloy needles are needed for MR-guided PNB.

Procedure steps are similar to those described for CT guidance (patient positioning and immobilization, access identification, monitoring of needle advancement). However, technical complexity of MR guidance relies mostly on the understanding of the used MR equipment and sequences that influence the visualization of the target and the puncture needle [30]. In fact, susceptibility artefacts, with apparent widening of the needle and reduced visualization of the surrounding structure, are more prominent when using higher MR field strengths, lower sampling bandwidth and rapid gradient-echo sequences. Thus, when the target is small and close to risky structures, using turbo spin-echo sequences and setting the frequency-encoding axis parallel to the needle shaft may allow artefact reduction.

There are several methods used to guide the procedure. Freehand and stereotactic techniques are suited for open magnets systems when the operator has direct access to the patient. In the freehand technique, short TR/short TE gradient-echo sequences allow real-time monitoring of the procedure with a possibility of scanning the patient in one or multiple orthogonal planes. In close-bore systems, when the radiologist has a limited access to patient, augmented reality and image fusion techniques have been developed [20, 31]; their major limitations are, however, represented by movement mismatches that may occur between pre-procedural image registration and the time of the actual needle insertion.

PET/CT PET/CT has been proposed to guide PNB in the setting of metabolically active lesions not evident using other images modalities, or located within areas of necrosis, fibrosis or atelectasis [32]. Since FDG uptake is not specific for cancer, strict collaboration with nuclear medicine physicians is mandatory for a proper interpretation of PET/CT in order to increase PNB success.

PET/CT guidance can be performed either using a conventional CT scanner by registering pre-procedural PET/CT images with intraprocedural CT scans or using the CT elements of the integrated PET/CT system. In the latter situation, operators' radiation exposure may be consistent, representing a major drawback of the technique.

PNB Techniques

1) Coaxial technique

A guide needle, larger than the biopsy needle (typically 9–19G), is advanced under image guidance, reaching the edge of the target. The inner stylet is removed, with the operator's finger placed over the lumen to prevent air aspiration. A biopsy needle is then introduced into the guide needle coaxially. This technique allows the collection of multiple specimens in a single puncture [33] and may prevent possible tumour cells seeding along the needle tract by re-inserting the inner stylet of the coaxial needle before removal [34, 35]. In order to biopsy different portions of the target, position of the guiding needle can be modified by manual steering; side exiting guide needles are also available.

Compared to the non-coaxial method, the coaxial technique does not increase the rate of complications [36, 37]. Moreover, in specific situations such as in transperineal prostate biopsy, it can reduce procedural time and procedure-related pain [38].

2) Tandem technique

A small gauge needle is first introduced into the lesion under image guidance. A second biopsy needle is then advanced parallel to the first reference device. This system has the disadvantage of requiring multiple punctures.

3) Fine-needle aspiration biopsy (FNAB)

FNAB uses a small, hollow (18–25G) needle with inner stylet. Once in place, the stylet is removed, a syringe (usually 10–30 mL) is attached to the biopsy needle, and cells are aspirated oscillating the needle either manually or automatically to increase the sample size. Before withdrawing the needle, suction has to be discontinued to prevent aspiration of cells from the needle tract.

4) Core needle biopsy (CB)

For CB, the needle (9–20G) has a cutting edge able to extract tissue for histologic analysis, with different mechanisms:

- *Tru-Cut needles* are composed of an outer cannula and inner notched trocar, in which a tissue specimen is cut, trapped and withdrawn. Before introducing the needle, the inner trocar is withdrawn into the outer cannula. Once the needle is in place, the trocar is advanced and its correct position is checked. The cutting system is then activated according to the manufacturer's indications. The inner trocar can be advanced manually or automatically, whereas the outer needle is usually moved automatically. The notched trocar containing the specimen is withdrawn into the outer cannula, before removal of the device.
- In the so-called *full-core biopsy needles*, after inserting the needle with the inner trocar up to the lesion margin, the outer cutting cannula is manually or automatically pushed into the pathologic tissue, and the core can be harvested by rotating/torquing the needle tip or using another capture/trapping cannula system.
- In more recently designed *screw or helical needles*, the tip is introduced through the outer cutting cannula, engaging the lesion by using a clockwise motion. Sample is collected by advancing the outer cutting cannula forward over the biopsy needle tip.

5) Puncture site compression or embolization

Direct manual compression of the puncture site for seconds to minutes is required to prevent bleeding.

When using the coaxial technique, puncture site plugging has been proposed, particularly in procedures at higher bleeding risk [39] and to reduce the rate of PNX [40, 41]. The biopsy needle is removed and the embolic material is injected through the guiding needle, embolizing the biopsy site and the needle path and avoiding non-target structures. Usually, embolization is performed using gel-foam slurry of plugs that are pushed either using saline injection or using the inner needle. Some authors have proposed the use of 1–3 ml of saline or autologous blood clot to seal the needle tract in lung biopsy [42, 43]. Since the guiding needle should be kept in place for the shortest time possible to avoid injuries of nearby structures, it is recommended to select and prepare the embolic material in advance.

Specimen Collection and Preparation

FNAB The specimen is smeared on glass slides and fixed according to institutional pathology laboratory preference (air-dried smears, ethanol or methanol fixed smears and

smears fixed with coating spray containing ethanol and polyethylene glycol are all common practices).

CB Specimens may be placed in saline or 10% formalin depending on institutional pathology laboratory preference. In general, for histopathological examination the specimen is fixed in formalin, while for bacteriological analysis the sample is sent in saline for culture.

All samples must be correctly labelled and sent to the laboratory together with all relevant medical information [5].

Post-Procedural Care

Immediately after the procedure, patient has to be imaged for potential immediate complications using the same imaging modality used for PNB guidance.

In US-guided procedures, further X-ray or CT examinations may be required when PNB or bleeding is suspected.

The vast majority of complications occur within 4–6 h following PNB. Thus, clinical observation, pain evaluation, using standard numeric rating scales, and vital signs monitoring are required for 1–6 h following the procedure, depending upon its location and complexity. Blood count check is recommended in procedures at higher risk of bleeding.

Imaging control (whether US, X-rays or CT) should always be obtained and documented before discharge.

When discharged, patient must be fully informed about post-procedural care, potential late complications and their symptoms, be provided with guidance for initial management and prompt access to appropriate care [5].

Analgesics (typically, paracetamol or NSAIDs) are prescribed when needed. Also, topical local anaesthetic creams or sprays may be useful for local, superficial pain.

When indicated, clinical and imaging follow-up should be scheduled at the time of discharge [5].

Follow-Up

Result of PNB should be evaluated and discussed by the multidisciplinary team involved in patient's management, including a referring physician, an IR, a pathologist and, when indicated, a surgeon and/or a microbiologist to define subsequent treatment and/or follow-up [15].

When biopsy results do not show a diagnostic, a repeated biopsy should be considered, simultaneously discussing different approaches, techniques or guidance modalities. Also surgical biopsy should be discussed among the possible options.

Results of PNB and of the multidisciplinary discussion will be finally communicated to the patient with a most proper modality, according to the Institutional policy [5].

Outcome

Procedural features, outcomes and complications of PNB in different anatomical districts are summarized in Supplementary tables [14, 44–63].

a. Effectiveness

Overall reported diagnostic technical success rate of PNB ranges from 70 to 96% [44]; however, it varies greatly depending upon the size and location of the target, benign or malignant nature of the lesion, number of samples obtained, availability of an onsite cytopathologist, IRs' and pathologists' experience, equipment availability. The Society of Interventional Radiology (SIR) quality improvement guidelines for PNB suggested using a threshold of 70–75% for the technical success rate for internal auditing [44].

Clinical success of PNB can be measured as the usefulness of the procedure in terms of improvement of patient care determined by the result of biopsy, including quality of life (QoF). As examples, in the era of personalized cancer care, selection of patients for targeted or immune-targeted therapies as well as recruitment in clinical trials can be a favourable outcome of PNB. Similarly, PNB reaches its clinical goal when surveillance is chosen as an alternative to the active treatments on basis of a diagnosis of low-grade malignancy in selected patients (e.g. prostate or renal cancer in elderly patients).

b. Complications

PNB is usually considered a minimally invasive and safe procedure, with a procedure-related mortality rate lower than 0.05%.

Complications are divided into major and minor (“Appendix”) and into generic (common for all biopsies, such as bleeding, infection, perforation, unintended organ injury and tract seeding) and organ specific (such as pneumothorax, haemoptysis, air embolism, haematuria).

SIR quality improvement guidelines suggest a 2% quality improvement threshold for the overall incidence of major complications after PNB [44].

Complications Management

Ideally, all possible complications should be anticipated to allow early recognition and treatment; this implies prompt access to resuscitation equipment and drugs, imaging

techniques, interventional radiology and surgical procedures [16].

Bleeding Significant bleeding (grade 3 or greater) is a rare complication of PNB. In a single-centre, retrospective review of over 15,000 biopsies, Atwell et al. [64] reported 0.5% of cases of significant haemorrhage within 3 months, varying according to biopsy site from 0.7% for the kidney to 0.1% in pancreatic biopsy.

Bleeding can be diagnosed during or immediately after the procedure by imaging or linked to the presence of pain, tachycardia and hypotension. Clinical severity and potential bleeding site should be immediately evaluated, and manual compression should be applied whenever possible. Based on the severity and the localization of the bleeding, assessed clinically and by imaging, following treatments can be considered:

1. Reverse any anticoagulation if required and considered safe;
2. Endovascular embolization for clinically relevant arterial bleeding in solid organs or bowel;
3. Endovascular deployment of covered stents for injured large vessels;
4. Surgery, when endovascular treatment is not feasible or unsuccessful, or for haemodynamically unstable patients.

Infection Severity and location of infection should be evaluated clinically and by imaging. Samples for culture are required for a final diagnosis and treatment with appropriate antibiotics. Drainage should be considered for abscesses and collections.

Perforation The majority of organs tolerate puncture well, with no substantial sequelae. In case of a bowel transgression, close monitoring is required because a risk of peritonitis and prophylaxis may be considered (antibiotic and parenteral alimentation).

Pneumothorax PNX represents a frequent complication of lung biopsy, with a pooled rate reported in a recent meta-analysis of 25.3% for CB and 18.8% for FNAB [65]. However, only a minority of cases require an intervention (5.6% after CB and 4.3% after FNAB) [65].

Several measures can be taken to reduce the incidence of PNX requiring chest. Besides proper patient instructions during the procedure, and an adequate planning of the access site (reducing the number of crosses of pleural surface and avoiding fissurae and bullae) [66], some authors recommend positioning the patient with the puncture side down for at least 1 h immediately after the introducer needle removal after the biopsy that should reduce aeration of the punctured lung. Also, plugging of

the needle tract has been proposed to prevent PNX [40, 41, 43].

When using the coaxial technique, a CT check should be performed prior to the removal of the introducing needle; if PNX develops, the needle can be withdrawn into the pleural space and air can be manually aspirated using a three-way valve and a 50-mL Luer-lock syringe.

Chest tube placement is indicated in symptomatic PNX or when PNX continues to enlarge. A 6- to 9-French catheter is placed under the CT guidance and attached to a one-way Heimlich valve, or to underwater seal drainage device and wall suction. Larger catheters could be used in patients with concomitant pleural effusion. The tube is generally removed after 1–2 days. Chest X-ray should be obtained after chest tube removal.

Air Embolism Air embolism is a rare but potentially fatal complication due to the puncture of a pulmonary vein that causes air to be being sucked in and enter the systemic circulation, subsequently causing ictus, seizures or other neurologic symptoms, coronary ischaemia or cardiopulmonary collapse.

To prevent air embolism, the introducer needle should always be occluded by the inner stylet or a finger, and the patient should avoid coughing and deep breathing during biopsy.

If air embolism occurs, the needle is immediately removed, the patient is placed in a mild Trendelenburg position to avoid cerebral embolization, and 100% oxygen is administered to accelerate bubble absorption [67]. Early hyperbaric oxygen therapy is recommended.

Tract Seeding Tumour seeding occurs when malignant cells are deposited along the needle path. It is a rare, yet catastrophic complication, particularly when it occurs in otherwise potentially curable oncologic patients, such as surgical candidates. The risk of seeding may be influenced by the needle size and the number of needle passes, and it varies according to the tumour type and location.

The risk is negligible after biopsy of intrapulmonary nodules (0.061% in a Japanese review of almost 10,000 percutaneous lung biopsies) [68] and renal tumours (below 0.01%) [69], while it increases in liver biopsies. The reported overall risk of needle tract seeding following biopsy of hepatocellular carcinoma is around 2.3–2.7%, and can be reduced to 0.7–1.4% when combining biopsy with percutaneous ablation in the same session [70, 71]. Needle tract seeding becomes a major issue when dealing with colorectal liver metastasis, with a reported incidence of 16–19%, in operable patient, and a not negligible impacting on survival [72, 73]. The risk of seeding is also substantial in primary pleural malignancy (approximately

4%) [74] and pancreatic carcinoma. Thus, in all these clinical conditions risks and benefits of PNB should be carefully evaluated, particularly in potentially resectable patients and when endoscopic biopsy can be performed as an alternative.

If the needle track metastasis is isolate, wide en bloc resection should be considered.

Conclusions

PNB is an established procedure, useful in numerous clinical conditions. Safety and technical efficacy is widely demonstrated. However, they are strongly dependent on several patient-related and team-related variables. Thus, qualified IRs should always perform PNB following clearly identified indications, in an appropriate environment and in the setting of a multidisciplinary pre- and post-procedural management [15]. In the precision medicine era with personalized cancer care, image-guided PNB has an evolving role to meet the future patients' needs [1].

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflicts of interest.

Appendix: SIR Classification of Complications by Outcome [3]

Minor Complications

- a. No therapy, no consequence.
- b. Nominal therapy, no consequence including overnight admission for observation only.

Major Complications

- c. Require therapy, minor hospitalization (<48 h).
- d. Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 h).
- e. Permanent adverse.
- f. Death.

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