

# Ultrasound-Guided Fine Needle Aspiration of Breast Lesions: Review of Technique and Imaging Findings

#### Almir GV Bitencourt\*, Luciana Graziano and Marcos D Guimarães

ACCamargo Cancer Center, R Prof Antonio Prudente, São Paulo, Brazil

\*Corresponding author: Almir GV Bitencourt, A C Camargo Cancer Center, R Prof Antonio Prudente, São Paulo-09015-010, Brazil, Tel: +5511985671045; E-mail: almirgyb@yahoo.com.br

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#### Abstract

Imaging methods are fundamental for the management of patients with breast cancer, especially in the early diagnosis of non-palpable breast lesions. Suspicious lesions identified in imaging studies of the breast should undergo percutaneous biopsy to confirm the diagnosis and plan appropriate treatment. Several procedures can be used, such as fine needle aspiration (FNA) and core needle or vaccum-assisted biopsy. The objective of this study is to review the main indications and limitations of each procedure to know what should be indicated for each type of lesion, with emphasis on ultrasound-guided FNAB, detailing its technique and imaging findings.

**Keywords:** Breast neoplasms; Breast cysts; Fine-needle biopsy; Image-guided biopsy; Ultrasound

#### Introduction

Imaging methods are fundamental for the management of patients with breast cancer, especially in the early diagnosis of non-palpable breast lesions. Mammography is still considered the method of choice for populational screening of breast cancer [1]. However, other imaging methods such as ultrasound (US) and magnetic resonance (MR) are useful in patients with dense breasts, in which mammography has insufficient sensitivity, and in patients with high risk for breast cancer [2,3].

Suspicious lesions identified in imaging studies of the breast should undergo percutaneous biopsy to confirm the diagnosis and plan appropriate treatment. Surgical biopsy should be reserved for cases in which percutaneous biopsy guided by palpation or imaging is not feasible. Performing invasive procedures guided by imaging methods is essential to ensure the adequate collection of material for analysis, especially in non-palpable lesions. Several procedures can be used, such as fine needle aspiration (FNA) and core needle or vaccumassisted biopsy [4-6]. The objective of this study is to review the main indications and limitations of each procedure to know what should be indicated for each type of lesion, with emphasis on US-guided FNAB, detailing its technique and imaging findings.

## **Imaging Methods for Evaluating Breast Lesions**

Mammography is still the primary imaging method for breast evaluation. It is inexpensive, widely available and is considered the only method that has proved to reduce mortality in breast cancer screening [1]. The main advantage of mammography is the ability to assess microcalcifications, which are often the only initial manifestation of cancer and are not well characterized in other methods. A mammogram may even show nodular lesions, asymmetries and areas of architectural distortion in breast parenchyma. The sensitivity of screening mammography depends on factors like patient age, breast tissue density and use of hormone

replacement therapy, as well as image quality technique and experience of the radiologist that interpret the exam. For example, sensitivity increases from 63% in patients with dense breasts to 87% in those with predominantly fatty breasts. In terms of age, sensitivity increases from 68% in women between 40 and 44 years to 83% in women between 80 and 89 years [7]. Other factors that may hinder the mammographic diagnosis of breast cancer include the presence of breast implants and post-therapeutic changes. Moreover, the specificity of mammography is low and most of the suspicious lesions found on this method presents as a benign diagnosis on histopathological study.

Breast US is usually indicated for further evaluation of suspected areas on mammography or physical examination, being able, for example, to differentiate between solid and cystic lesions [8]. It can also be used in cancer screening of young patients with dense breasts and high risk for breast cancer [9,10]. This method, although dependent on the equipment quality and examiner experience, has demonstrated good cost effectiveness and accuracy for diagnosis of breast lesions [11].

MR has become increasingly important in the management of patients with breast cancer. The main advantage of MR in relation to mammography and US is the ability to assess the vascularity of breast tissue after intravenous application of the paramagnetic contrast agent, e.g. Gadolinium-DTPA (Gd-DTPA). Due to neoangiogenesis and increased vascular permeability, most carcinomas show focal and early impregnation by intravenous contrast, unlike most benign lesions. In addition, MR has greater accuracy in evaluating the size and morphological characteristics of the tumor, as well as the detection of multifocal lesions [12]. Nonetheless, despite presenting a high sensitivity for the diagnosis of breast cancer (86 to 96%), specificity to breast MR is only moderate in most studies. On a meta-analysis of 44 studies, MRI combined specificity was 72% [13]. The false-positive results on MR usually represents high-risk lesions, such as lobular carcinoma in situ and atypical hyperplasia, fibrocystic changes and benign lesions, e.g. fibroadenomas, papillomas and lymph nodes [14]. Besides the low specificity, other limitations of MR include its

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availability, patient tolerance, team training, high cost and time of examination.

The findings of imaging studies should be characterized according to the Breast Imaging-Reporting and Data System (BI-RADS) lexicon developed by the American College of Radiology (ACR). The goal of this systematization is to standardize the nomenclature of the reports, which should have diagnostic conclusion and propose treatment course according to the probability of malignancy [15].

# **Image-Guided Procedures**

The collection of material from suspected breast lesions can be obtained by FNA or biopsy by large-core needles. The latter may be accomplished by cutting needle biopsy (core biopsy) or vacuum assisted biopsy (mammotomy). In cases where the patient will undergo the surgical procedure, for either diagnosis or definitive treatment, preoperative localization guided by imaging methods can be performed through the placement of a metal wire or radiopharmaceuticals within the lesion [4].

FNA is performed with a small caliber needle (23-27 gauge) for collecting material for cytological study. The main advantage of FNA is that it is easily accessible and can be quickly performed, being less painful and safer than biopsy by large-core needle, especially in patients with coagulation disorders [16]. The main disadvantages of FNA are the significant non-diagnostic sampling rates and false negative results [17]. For non-palpable lesions, the false-negative rate of FNA guided by imaging ranges from 0 to 32%, which can be caused by incorrect location of the lesion, small size, bleeding or a combination of these factors18. The correlation of the results of FNA with imaging findings is essential. Some benign lesions, such as fat necrosis and fibroadenomas, may show significant atypia on FNA. Additionally, in cases of highly suspicious lesions and negative in FNA, investigation should continue with large-core needle biopsy or surgery.

The cutting needle biopsy, or core biopsy, is performed with a largecaliber [14-20] gauge needle, allowing the collection of tissue fragments for a more definitive histologic diagnosis and avoiding inadequate samples [19]. This procedure is considered safe, even in patients receiving anticoagulant therapy or with platelet antiaggregants. Bleeding and infections that require treatment are much less common with biopsies with large-core needles than with surgical biopsy.

Mammotomy, or vacuum-assisted percutaneous biopsy, is usually performed with an 11 gauge needle, allowing the collection of more material than a cutting needle biopsy, reducing the number of falsenegative results. This method is ideally used to biopsy microcalcifications or small nodules of up to 1 cm, which can be totally resected during the procedure20. In the cases where the lesion is fully resected during this procedure, a metal clip should be put in place for future identification of the lesion 's location.

The choice of the procedure and imaging method for orientation depends on the characteristics of the lesion. All these procedures can be guided by any of the imaging methods cited (mammography, US or MR). The US-guided procedures should be preferred because they are less expensive and better tolerated than the procedures guided by mammography or MR. US guidance requires less preparation, avoids the need for ionizing radiation exposure and are usually performed in a confortable supine position, which results in shorter procedure times and less patient discomfort compared with prone stereotactic biopsy [21]. Unlike other methods, using US further permits to view the path of the needle in real time and confirm the location of where the material was removed and allows accessibility to all areas of the breast. However, the lesion in question should be identified accurately, having good correlation between sonographic findings and the findings of mammography or MR. If a non-palpable lesion is identified on mammography or MR does not show good correlation to US, it should be subjected to biopsy or pre-operative localization guided by the method that best characterizes the lesion. For patients with microcalcifications, asymmetries or distortions seen only on mammography, this method should be used to guide percutaneous biopsies. Likewise, for nodes or areas suspected for malignancy, as identified by MR and not characterized by other methods, they should be indicated for biopsy or pre-operative localization guided by MR [4-6,22].

There are no universal indications for each type of procedure and this depends on the methods available in each institution, the conduct to be adopted by patient's mastologist and the radiologist expertise. In the authors daily practice, US-guided FNA is indicated for symptomatic or complicated cysts, small and probably benign mass, suspected lymph nodes and suspicious mass lesions when an immediate diagnosis is needed. US-guided core-needle biopsy is indicated for most suspicious mass lesions on the breast and some architectural distortions that are well characterized on US. The most common indication for US-guided vacuum-assisted biopsy is for a smaller probably benign mass, that could be fully resected with this procedure. Mammography-guided vacuum-assisted biopsy is usually indicated for suspicious microcalcifications, asymmetries and architectural distortions only seen at mammography. MR-guided vacuum-assisted biopsy is indicated for lesions not seen on secondlook US and mammography, especially for non-mass enhancements. Mammography and MR-guided FNA or core-needle biopsies are not usually indicated, unless it is not possible to perform a vacuumassisted biopsy in these cases.

# **US-Guided** FNA

Currently, almost all image-guided FNA biopsies are guided by US. Beyond allowing real-time monitoring of the trajectory of the needle, this method allows greater mobility of the needle within the lesion, increasing the amount of collected material and reducing the number of insufficient samples when compared with FNA biopsy guided by mammography or MR [5].

The advantages of FNA are low cost and efficiency. However, some limitations are inherent to the method. Inconclusive or false-negative results can be caused by: acellular or paucicelular material; problems in the smear, fixation or staining of slides; hemorrhagic or necrotic material, and; experience of the examiner, among others. Cytologic analysis does not provide the histologic type of tumor and may not allow the differentiation between invasive or in situ carcinomas. Moreover, lesions that have a large amount of fibrous tissue, nonpalpable spiculated lesions which exfoliate little material and lesions represented only by microcalcifications may not be well sampled, especially when a cytopathologist is not available in the puncture room [17,23].

Additionally, the existence of a well-trained staff, whether at the time of collection or cytological analysis, significantly improves the performance of this procedure.

## **Pre-Biopsy Care Procedures**

It is important prior to any interventional procedure to carefully analyze the exams that led to biopsy. This control is useful to ensure greater trust between the clinician, the radiologist and the patient. Explanation of the purpose, benefits and risks of procedures are mandatory, facilitating their realization. Informed consent is recommended and should be obtained in all procedures guided by imaging methods. It should contain relevant information related to the procedure, including the risks and the need for surgical biopsy if the result is not what is expected.

Before the procedure, it is also important to obtain information about the state of blood coagulation, on the use of anticoagulants or platelet antiaggregants and on the presence of valvular disease. Nevertheless, it is not necessary to suspend the use of these medications or take antibiotic prophylaxis for FNA. There is more precaution taken when performing a biopsy with a large-core needle than for punctures with a fine needle, as in these cases the risk of complications are minimal. The potential risks of the procedure include bleeding and infection, which fortunately, are rare [24].

## Technique

The physician who will perform the procedure should check the needed materials to avoid delays or interruptions. The procedure table should contain an aspiration gun, disposable fine needles (20-25 gauge), disposable syringes (10-20 ml), liquid anesthetic and gel, topical antiseptics and gauze bandaging along with a CytoLyte solution (Cytyc Corporation, Marlborough, MA), or slides and dry vials, tubes with alcohol or liquid fixator, or spray fixator, depending on the routine of each service (Figure 1).



**Figure 1:** Table with material for FNA, including: **(A)** aspiration gun; **(B)** 20-25 gauge disposable needles; **(C)** 10-20 ml disposable syringes; **(D)** liquid anesthetic; **(E)** gel anesthetic; **(F)** topical antiseptics; **(G)** gauze bandaging; and **(H)** CytoLyte solution.

US-guided FNA is usually performed with the patient supine, oblique or lateral, with their arms raised and hands positioned behind or over the head. Depending on the physician who will perform the procedure, this can be handled with only a trained operator holding the transducer with one hand and puncture needle with the other, or with two operators: one to guide and the other to collect the material.

After aseptic preparation of the probe with placement of a sterile sheath, and local skin asepsis, the lesion should be identified on US to choose the needle to be used, planning of best needle trajectory and positioning of the patient. The puncture needle should be attached to a 10 to 20 ml disposable syringe that is then introduced transfixed to the cutaneous and subcutaneous planes parallel to the transducer to allow complete visualization of the path from the entrance of the skin to the interior of the lesion (Figure 2).



**Figure 2:** Procedure for fine needle aspiration (FNA) guided by ultrasound (US): **(A)** Needle inserted into the skin parallel to transducer; **(B)** US showing the needle tip inside a complicated cyst.

Also recommended is the use of an aspiration gun coupled to a syringe-needle system (Figure 3), because it makes the procedure easier to perform. Alternatively, the needle may be inserted perpendicular to the transducer, depending on the experience of the US imaging specialist, although with this technique it is only possible to view the tip of the needle in the lesion. After confirmation of needle location within the lesion, negative pressure should be retained on the syringe and small frictional movements performed with the needle within the lesion in order to collect material suitable for analysis.



Figure 3: Aspiration gun coupled to a syringe for FNA.

Some operators prefer a non-suction or capillary technique, which avoids aspiration and relies on the physical property of capillary pressure to suck cells inside the needle bore. This technique is less traumatic, allowing for much better control of the needle while in the lesion and reducing the risk of blood contamination. It is equally cost

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effective than fine needle aspiration and commonly used in thyroid nodules and lymph nodes, however it is less effective in fibrotic and cystic lesions [25].

Cytology specimens may be prepared as direct smears (air-dried or alcohol-fixed) or as liquid-based thin-layer slides (ThinPrep or SurePath). In addition, aspirated material from FNA can be rinsed in RPMI or Cytolyte solution to prepare tissue blocks that are fixed in formalin, processed routinely similar to surgical tissues. The Cytolyte solution consists of a buffer solution for water-based cell washing designed for the lysis of red blood cells, preventing protein precipitation, dissolving mucus and preservation of the morphology of general samples of cytologic cells before slide preparation with the ThinPrep 2000 Processor (Cytyc Corporation, Marlborough, MA). The use of liquid-based cytology in breast FNA shows a good correlation with conventional preparation, being easier and less time consuming and allows the possibility of adjunctive investigations (e.g. immunocytology, flow cytometry) on the same material [26].

The number of punctures depends on the characteristics of the lesion. In the case of simple cysts, only one puncture for aspiration of the liquid is usually performed. In cases of complex cysts or solid lumps, usually more than one puncture is necessary to increase the chances of suitable collection material for analysis. If a cytopathologist is in the exam room, they can assess the suitability of the material collected at the time of puncture, optimizing the collection. Otherwise stated, it is possible to reduce the number of punctures, and consequently, procedure-related complications without compromising the quality of the material collected.

The procedure can be performed with or without local anesthesia, depending on the protocol for each service. It is a quick procedure and with a fine needle, usually well tolerated, even without the use of anesthetic. For example, when in the planning phase, only one puncture is observed to be enough to collect all the material (i.e. aspiration of a simple cyst), it does not requires local anesthesia. However, when multiple punctures should be performed, the use of local anesthesia with 2% lidocaine without vasoconstrictor can cause greater comfort and less anxiety to patients.

FNA biopsy can be used for any lesion identified by US, even those very small, lesions superficial or proximate the chest wall, or those difficult to access for large-core needle biopsies. A larger amount of material may be aspirated from cell lesions such as invasive ductal carcinomas and metastatic lymph nodes in comparison to lesions less cellular, such as fibroadenomas with hyalinization, fibrotic lesions or invasive lobular carcinomas. Thus, large-core needle biopsy can provide a definitive diagnosis of these less cellular lesions in which the result of FNA is inconclusive.

# **Characteristics of Breast Lesions in US**

Several types of breast lesions identified in US may undergo FNA. The pathologist should know the main imaging findings of lesions subjected to pathological study. The correlation between imaging findings and the cited or histopathology outcome is essential for proper diagnosis and choice of the most appropriate course of treatment for each patient [27].

Cystic lesions can be divided into simple or complex cysts. Simple cysts are typically benign lesions that have thin and regular walls, with homogeneous anechoic content (Figure 4). In these cases, biopsy will only be indicated when lesions have greatly increased dimensions,

causing pain or discomfort to the patient. For the most part, puncture of the cyst will demonstrate the disappearance or immediate reduction of the same. Completely punctured cysts recur less frequently than cysts punctured with residual liquid. The liquid inside a simple cyst can be clear, yellow-citrine, dark, milky or bloody. The liquid collected from a simple cyst should be sent for analysis if there is clinical suspicion, radiological characteristics suggestive of malignancy or is bloody, except in cases of bleeding secondary to trauma by puncture.



Figure 4: Examples of simple cysts (A and B).

Complex cystic lesions include minimally complicated cysts and cystic lesions suspected of malignancy. Minimally complicated cystic lesions include cysts with thin septa, clustered, and with parietal calcifications in its interior (milk of calcium), with thick content/ debris or cutaneous/subcutaneous cysts (Figure 5).



**Figure 5:** Examples of minimally complicated cysts: **(A)** cyst with echogenic content; **(B)** cyst with thin septa; **(C)** cyst with echogenic content deposited in the interior.

Such lesions should be monitored and puncture or biopsy should be indicated if there is increase in size or change its characteristics in control examinations. Complex cystic lesions suspected of malignancy include cysts with thick walls, thick septa (> 0.5 mm thickness) or solid component (Figure 6).



**Figure 6:** Examples of complicated cysts suspected of malignancy: **(A)** cyst with thick irregular walls; **(B)** cyst with solid nodule; **(C)** cyst with solid nodule with high-resistance blood flow on Doppler US.

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These lesions are usually subjected to puncture or percutaneous biopsy to exclude the possibility of malignancy. In the case of FNA, it is important to collect material from the suspected area (i.e. solid component) and not just the cystic portion.

The solid nodules should be characterized by US in relation to its shape, orientation, echogenicity, contours, dimensions, location and presence of posterior enhancement or acoustic shadowing, as well as the presence of vascularization on Doppler US28. Benign solid nodules usually are rounded or oval, parallel to the skin, have regular contours and can be hyperechoic or slightly hypoechoic (Figure 7). Some of these nodules exhibit posterior acoustic enhancement and others may have slight acoustic shadowing (i.e. fibroadenomas with hyalinization). Usually Doppler US presents little or no vascularity within these nodules.



**Figure 7:** Examples of nodules with benign characteristics: (A) isoechoic oval nodule with circumscribed margins; (B) heterogeneous oval nodule with circumscribed margins; (C) hypoechoic oval nodule with macrolobulated margins; (D) hyperechoic round nodule with circumscribed margins; (E) isoechoic round nodule with circumscribed margins.

Malignant solid nodules usually present irregularly, perpendicular to the skin, imprecise boundaries, irregular or spiculated contours, enhanced hypoechogenicity, presence of hyperechogenicity in the adjacent fatty tissue (suggesting inflammation/surrounding desmoplasia) and enhanced posterior acoustic shadowing (Figure 8). Usually these nodules have some degree of vascularization on Doppler US.

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**Figure 8:** Examples of nodules with characteristics suggestive of malignancy: **(A)** heterogeneous irregular nodule with spiculated margins; **(B)** hypoechoic irregular nodule with vertical orientation and angular margins; **(D)** hypoechoic irregular nodule with indistinct margins; **(E)** hypoechoic irregular nodule with microlobulated margins; **(F)** hypoechoic irregular nodule with posterior acoustic shadowing.

Other breast lesions that may be subjected to FNA include focal duct ectasia with thick content or intraductal nodule and intramammary lymph nodes, axillary or internal thoracic chain with increased dimensions, thickness or cortical hypoechogenicity (Figure 9).



**Figure 9:** Examples of other lesions: **(A)** intra-mammary lymph node; **(B)** focal duct ectasia with intraductal nodule (arrow).

# **Post-Biopsy Complications and Care Procedures**

FNA is not associated with any serious complications or adverse effects and is well tolerated by most patients. Patients who undergo FNA usually are released after the end of the procedure and not requiring further care, as it is considered a minimally invasive method. Possible complications related to FNA include pain, bleeding and infection. If any bruising or pain at the puncture site should occur, an ice bag, analgesic and local anti-inflammatory ointment should be indicated.

## Conclusion

Breast lesions are very frequent in the clinical practice and USguided procedures are the preferred method for histological and cytological diagnosis because it is easy to perform, faster, more comfortable, less expensive, allowing real time control of the needle path and a multidirectional sampling, when compared to procedures guided by mammography or MR. Among US-guided biopsies, FNA is the fastest procedure, with low cost and high efficiency in the diagnosis of invasive breast carcinomas, when it is performed by a well-trained medical professional; however, some limitations are well known, e.g. some cancers may not be possible to be diagnosed with cytology only, requiring core-needle or vacuum-assisted biopsies.

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