Diagnostic intervention in breast disease

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Abstract Imaging-guided percutaneous biopsy techniques have been developed to diagnose the lesions detected in breast cancer screening programs based on mammography. Although traditional fine-needle aspiration cytology continues to be indicated in some cases, in many others it has been supplanted by more modern techniques such as core biopsy or vacuum-assisted biopsy guided by ultrasonography, stereotaxy, or magnetic resonance imaging. These highly reliable techniques have minimized the need for surgical biopsy.

Radiologists play a key role in the histological diagnosis of breast cancer in the early stages of disease and in the evaluation of its local and regional extensions through magnetic resonance imaging and sentinel node biopsy.

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PALABRAS CLAVE
Biopsia mama; Estereotaxia; Galactografía

Intervencionismo diagnóstico en patología de mama

Resumen Con el desarrollo de los programas de detección precoz de cáncer de mama basados en la mamografía se han ido desarrollando de forma paralela técnicas de biopsia percutánea guiadas por la imagen para el diagnóstico de las lesiones detectadas sospechosas de cáncer de mama.

Aunque la técnica tradicional de punción con aguja fina sigue teniendo indicaciones, se ha ido sustituyendo por las más modernas técnicas de biopsia con aguja gruesa o sistemas de biopsia asistidos por vacío, con guía ecográfica, estereotáxica o por resonancia magnética (RM). Los resultados de esta técnica son de una alta fiabilidad, por lo que se ha reducido al mínimo la biopsia quirúrgica.

El papel del radiólogo es determinante para el diagnóstico histológico del cáncer de mama en sus fases iniciales, la valoración de su extensión local y regional mediante la utilización de la RM y realización de la técnica del ganglio centinela.

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Mammography, ultrasonography, and magnetic resonance imaging (MRI) have proved to be very effective in the early detection, diagnosis, and evaluation of the extension of breast cancer, which have played a decisive role in reducing mortality caused by this disease.¹

Radiologists specialising in this field have recently assumed new responsibilities, including early detection of breast cancer, accurate diagnosis through percutaneous biopsy techniques, assessment of local extension using MRI, and use of radiotracers for a correct performance of the sentinel node technique.

Until recently, excisional surgical biopsy was the traditional technique for diagnostic confirmation. However, with the widespread implementation of population-based screening programs for early breast cancer detection and the definitive consolidation of ultrasonography and MRI as complementary imaging techniques, new interventional procedures guided by these techniques have been developed with the aim of achieving an accurate histologic diagnosis without the need of surgery.²

**Preoperative localization of non-palpable lesions**

Preoperative localization is the traditional technique and the most commonly used technique. Operative excision of non-palpable lesions requires prior localization of lesions that usually involves the placement of guide wires or marking the site of the biopsy by injecting a stable carbon solution or a radiotracer.³

**Technique and results**

Although the localization technique originally involved the placement of needles into the lesion site, guided by localization coordinates provided by mammography, overtime the use of needles has been replaced by wires as they allow for better anchorage into the breast.

**Wires (hookwires)**

Wires are radiopaque and their tips have been designed to avoid displacement once placed into the breast. Mammographic or ultrasonographic guidance can be used for placement, depending on which technique provides the best visualisation of the lesion.

Mammographic guidance is commonly performed with fenestrated compression plates with a radiopaque alphanumeric grid (Fig. 1). Some radiologists prefer to use the stereotactic device, but we need to keep in mind that unwanted displacement may occur due to the “accordion effect” that appears when the breast is decompressed.

![Figure 1](image-url)  
**Figure 1**  Preoperative localization for biopsy of a non-palpable lesion. (A) Fenestrated compression plate with radiopaque alphanumeric grid. (B) Types of needles with localizing guide wires (“hook wires”). (C) Harpoon insertion with fenestrated compression plate.
Whenever possible, ultrasonographic guidance should be used because the patient may lie down, the technique does not require breast compression and does not expose the patient to ionising radiation. Moreover, the mammography room is free and the procedure is monitored in real time.

Obviously, ultrasonographic guidance is not possible in those cases in which the lesion can only be visualised on MRI. In such cases, a non-ferromagnetic marker can be placed in the lesion site to facilitate subsequent mammographic or ultrasonographic localization.

Regardless of the guidance technique used, the access that provides the surgeon the shortest path to the lesion should always be chosen. In all cases, the localization of the hookwire must be confirmed using two views, lateral and craniocaudal that must be shown to the surgeon prior to operation so that he become aware of the spatial relationship between the wire and the lesion, the depth and the most appropriate surgical approach. Large lesions may require the placement of two or more hookwires.

**Injection carbon solution**

Although less common, those who use this method argue that it is very accurate. It involves ”tattooing” the biopsy site by injecting a stable carbon solution. Although this technique is safe, less costly than wire localization and can be performed several days before the intervention, it is not free of adverse effects, such as potential histologic changes at the biopsy site.

**ROLL (radio-guided occult lesion localization) technique**

This method involves imaging-guided injection of a radionuclide into the biopsy site. The aim is the preoperative and postoperative localization of the lesion using a gamma probe. A main advantage of this technique is that, when used for localization in therapeutic procedures, it can be performed in conjunction with the sentinel node technique. Additionally, there seem to be evidence that the likelihood of obtaining tumor-free margins in the surgical specimen using ROLL.

Regardless of the technique and the imaging guidance modality used, the surgical specimen should be X-rayed to confirm lesion resection. On some occasions, ultrasonographic examination of the specimen is required to mark the site of the lesion by placing one or more needles to help the pathologist in the localization of the lesion.

The accuracy of these techniques for the localization of non-palpable lesions is variable. The failure rates range from 2% to 18%, but desirable values should be lower than 5%. Failure to resect the lesion is most frequently caused by incorrect placement of the localization device, displacement of the device, or poor communication between radiologist and surgeon.

**Figure 2** Fine needle aspiration (FNA). (A) Free-hands technique. Aspiration is performed by withdrawing the needle and pushing it back in a number of times, while maintaining aspiration in all planes. (B) Material spreading.
Figure 3 Fine needle aspiration (FNA) puncture. Pneumocystography. (A) Drainage of breast cyst. No cytologic examination is required. (B) Pneumocystography: after liquid aspiration, the cavity is visualised through air injection.

If the lesion is not visualised on the X-ray of the surgical piece, a new mammography will be necessary to check if the lesion is still in the breast.

Indications

Preoperative localization of non-palpable lesions has been the traditional biopsy method in patients with suspicious lesions in the BI-RADS categories 4 and 5, or with non-conclusive or high-risk findings after percutaneous biopsy.

Because of the increasing role that percutaneous biopsy techniques are currently playing, preoperative localization of these lesions is usually performed for therapeutic rather than diagnostic purposes in order to localize non-palpable malignant lesions which are to be treated with conservative surgery.

Fine-needle aspiration

Fine-needle aspiration (FNA) is a diagnostic technique that has been widely used for decades. This technique allows for sampling of cells for cytologic examination. Although initially used in the evaluation of non-palpable lesion through ultrasonographic and mammographic (stereotactic) guidance, this technique has currently been replaced by core needle biopsy (CNB), and thus, it is only used in those particular cases discussed in the Indications section.

Technique and results

Regardless of whether the lesion is palpable or not, FNA can be performed under ultrasonographic guidance, since this improves the diagnostic accuracy of the procedure. Usually the aspiration technique is used, applying vacuum with a syringe attached to a 20G–25G needle. To facilitate aspiration with only one hand, the needle protection cap can be tightly placed between the plunger and the syringe or a specific device can be used to secure the syringe.

After the skin is disinfected with alcohol, the procedure is performed without local anesthesia. Once ensured that the tip of the needle is inside the lesion, the needle is passed through the lesion a number of times, while maintaining aspiration in all planes to obtain the most representative sample. It is best to discontinue the aspiration before needle withdrawal to avoid contamination with material that might be aspirated as the needle is withdrawn and to avoid
aspiration of this material into the syringe. Once the needle is withdrawn, the material is transferred and smeared onto a slide and fixed according to the recommendations of the Pathologic Anatomy Laboratory (Fig. 2).

Although this technique has practically no complications, slight pressure on the site of puncture should be applied for some minutes to avoid hematomas. Significantly large hematomas rarely occur. The risk of more serious conditions, such as pneumothorax, is almost inexistent if an adequate puncture technique is performed with controlled needle advancement.

An expert cytopathologist is necessary to obtain conclusive findings. The cytopathologist report is based on the following categories: normal, benign, atypical, suspicious, malignant, and insufficient.

The sensitivity of FNA varies significantly (70–90%) because false negatives sometimes occur. Atypical or suspiciously malignant lesions always require histologic diagnosis by percutaneous or surgical biopsy. In spite of its high specificity, this technique also yields false positives (1–2%). For this reason, in case of malignant findings, most surgeons and gynecologists only take a surgical decision after performing an intraoperative biopsy. In addition, FNA does not discriminate between in situ and infiltrating carcinomas. A benign finding is only reliable in patients with BI-RADS category 3 lesions.

**Indications**

FNA is used both for palpable and non-palpable lesions. Below are the most common indications.

**Drainage of palpable cysts**

This is a very common clinical situation leading patients to a state of anxiety, although the use of FNA is very effective. Drainage is performed under ultrasonographic guidance, sometimes followed by a mammography after injection of a volume of air equal to two thirds of the extracted fluid (pneumocystography). This procedure is no longer diagnostically useful because of the high quality of current ultrasonographic imaging, and its therapeutic role in reducing the recurrence of cysts is being questioned (Fig. 3). Pneumocystography should not be performed on cysts with intracystic solid lesions given the possibility of failing to identify the solid lesions for subsequent biopsy. Although a cytoplastic analysis of the drained liquid is not necessary, it can be useful if a palpable lesion is still appreciable in the breast after drainage.

**Differentiation between solid and cystic lesions**

There may be nonconclusive diagnoses, as sometimes occur in complex cysts. These cysts are echogenic because they contain inflammatory fluid that can mimic a solid lesion on ultrasonography.

**Cytologic examination of palpable areas**

This analysis is particularly common when dealing with benign-looking lesions (BI-RADS category 3), which typically occur in young women, and are usually suggestive of a fibroadenoma.

Figure 4 Ultrasound-guided core needle biopsy (CNB). (A) Free-hands technique using an automated device with 14G trucut needle. (B) Devices for CNB: automated and semi-automated devices.

It can also be useful in patients with undefined palpable areas, having no clear radiologic correlation, or patients with dense breasts.

**FNA of axillary lymph nodes**

This is a common procedure that is performed in patients with breast cancer to assess the state of their axillas. Because of positivity of the FNA puncture, the sentinel node technique is not necessary. Puncture of supraclavicular, infraclavicular and laterocervical adenopathies is usual as well. All of these conditions are readily imaged by ultrasonography.

Further indications of the FNA technique are puncture of nodes of probable inflammatory or infectious nature, BI-RADS category 3 multiple nodes and other particular conditions.
Core needle biopsy

Core needle biopsy (CNB) puncture has gained wide acceptance as the technique of choice in the histologic diagnosis of palpable and non-palpable breast lesions, especially in those cases in which the lesion is visualised on ultrasonographic images. Being a safe, fast, complication-free and cost-efficient technique, CNB has been shown to have a high diagnostic accuracy to evaluate any breast lesions requiring histologic diagnosis.

Technique and results

CNB is performed with automated or semiautomated devices and 14G (2.1 mm in diameter) trucut needles used to

Figure 5  Core needle biopsy (CNB): types of samples. The higher flotability of the specimens means more concentration of fat tissue (less diagnostic value).

Figure 6  Vacuum-assisted biopsy (VAB): sequence featuring excision of a probably benign nodular lesion. Notice the 11G cannula below the lesion. Contiguous samples up to five times as big as those obtained with 14G needles.
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Figure 7  Stereotactic technique involving vacuum-assisted biopsy (VAB). (A) Patient on prone-table. For easier access to the breast tail, it is advisable to introduce the patient’s arm into the opening. (B) VAB with 11G cannula (lateral access). (C) VAB of breast calcifications performed with a 11G cannula. After resection, a clip is placed to mark the biopsy site.

removes a tissue sample from the lesion (Fig. 4). CNB is done with local anesthetic, normally taking three to five cores—although more cores are recommended in cases of biopsy of clustered calcifications.

The imaging techniques that are commonly used as guidance are stereotaxis, and particularly, ultrasonography.

Stereotactic guidance
This technique relies on the calculation of the localization coordinates of the lesion, based on evaluation of the apparent lesion displacements on two mammographic images obtained at a ±15–20° angulation on the lesion. Digital prone-table stereotactic units allow for shorter examination times and minimize the chance of the patient moving that improves the results.

Stereotactic biopsy provides highly reliable results, although false negatives may occur. Moreover, when dealing with calcifications, the lesion can be underestimated when biopsy findings reveal atypical hyperplasia or intraductal carcinoma (approximately 50% of the former are intraductal carcinomas, and 30% of the latter are found to be infiltrating carcinomas at surgery).10

Ultrasonographic guidance
This is the best technique for lesions that can be visualised on ultrasonography. The technique is similar to that
described for FNA, although the larger needle gauge requires the use of local anesthesia.

Ultrasoundographic guidance is a better approach than stereotactic guidance because it does not rely on ionising radiation, is more effective in multidirectional lesion localization, enables real-time visualisation and control of the needle, and offers greater patient comfort. Moreover, it costs less.

As with FNA, CNB under ultrasonographic guidance has virtually no complications. In fact, it can be performed in patients on anticoagulant therapy. The most common complications are hematomas, which are generally small, and do not require any treatment.

Needle-track seeding after is not unique to CNB since it can also occur in any other interventionional procedure, such as surgical biopsy, and is considered virtually irrelevant.11

Pneumothorax occurs very rarely if an appropriate technique is performed.

Advantages

The main advantage of CNB is that it provides a histologic diagnosis of all lesion types, with a rate of insufficient specimens significantly lower than that of cytology. The diagnostic value of ultrasound-guided CNB is very high (over 95%).12,13

Another advantage of this technique is that it can differentiate between intraductal and infiltrating carcinoma in most cases. This reduces the surgical decision-making process to one single stage. The costs of the biopsy process are also reduced because of the decreased need of diagnostic surgery.

Drawbacks

Below are the major drawbacks of this technique, which are generally associated with the biopsy of calcifications.

Sampling errors

CNB involves the removal of small tissue samples from the lesion, which may not be representative of the entire lesion. In highly suspicious lesions, a malignant finding is regarded as correct. However, if benign, it might prompt questions about the validity of the sample (particularly in cases of microcalcifications), thus, additional CNB or surgical biopsy is indicated. The sample is considered appropriate when the histologic findings are consistent with the imaging and clinical examination.

A good indication is the evaluation of the floatability of the cores in formalin (cores that sink in formalin are likely to be diagnostic) (Fig. 5).

Histologic underestimation

A CNB finding revealing atypical hyperplasia or intraductal carcinoma may significantly underestimate the presence of an intraductal or infiltrating carcinoma, respectively. This typically occurs with microcalcifications and requires an additional CNB or surgical biopsy in order to reach a confirmation of the diagnosis.14

In addition, there is a specific set of high-risk lesions that may also be misdiagnosed or underestimated at CNB: when biopsy reveals a benign papillary tumour, a radial scar, a benign phyllodes tumour or a lobular carcinoma in situ, it will be necessary to rely on surgery or on vacuum-assisted biopsy (VAB) (see next section) for a fully conclusive diagnosis.
Indications

CNB is indicated for all palpable and non-palpable lesions that are moderately or highly suspicious for malignancy (BI-RADS categories 4 and 5). CNB is also indicated for probable benign lesions (BI-RADS category 3) which require histologic diagnosis instead of radiologic follow-up.

As with FNA, some authors prefer CNB in axillary lymph nodes and other accessible lesions because CNB guarantees a more accurate diagnosis.

Vacuum-assisted biopsy

VAB techniques emerged to provide a larger volume of tissue, thus reducing the number of false negatives and underestimation errors caused by CNB.

Technique and results

VAB relies on the suction effect generated by a powerful vacuum-assisted pump connected to the device, the cutting effect provided by a rotational scalpel located in the needle lumen. The tissue is drawn into a sampling chamber by means of the vacuum effect (an aperture in the distal tip) and, once inside this chamber, the tissue is cut away from the breast. Usually 8G-14G needles are used in the procedure. Continuous and contiguous obtention of tissue allows for larger and higher quality samples than those obtained with CNB (Fig. 6).

VAB can be performed under stereotactic, ultrasonographic or MRI guidance.

Stereotactic guidance has become the most commonly used. In fact, it is currently regarded as the most suitable technique for percutaneous biopsy of suspicious calcifications, given the number of false negatives and histologic underestimation associated with CNB (Fig. 7).

Ultrasonography-guided VAB does not significantly differ from CNB (Fig. 8), and does not offer a better diagnostic performance in patients with lesions visible on ultrasonography. For these reasons, and because it is more aggressive and expensive, ultrasonography-guided VAB should not be considered an alternative to CNB. However, since VAB potentially allows for complete resection of lesions, this technique may offer an effective therapeutic treatment of BI-RADS category 3 lesions.15

MRI-guided localization is seldom performed because it is a complex and expensive technique, with little availability (Fig. 9). However, MRI guidance is undoubtedly the technique of choice when findings are only visible on MRI and mammography and ultrasonography cannot be used as guidance systems.

Since VAB techniques allow for complete resection of lesions, it is sometimes necessary to use non-ferromagnetic
markers to identify the lesion site in prevision so that subsequent surgical resection is required (patients diagnosed with carcinoma, high-risk lesions or suspicion of underestimated lesion). These markers are particularly indicated after complete excision of small lesions of categories 4 and 5 since subsequent surgical resection of the biopsy site is most likely necessary. The markers can be placed immediately after the procedure (through the needle) or at a later stage under ultrasonographic guidance, taking the hematoma at the biopsy site as a reference.

Although VAB is as accurate as surgery, false-negative results may also occur. Furthermore, although VAB devices significantly reduce the rate of histologic underestimations (findings of atypical epithelial hyperplasia and intraductal carcinoma), they cannot be totally eliminated. As a matter of fact, about 20% of atypical hyperplasias and 10% of intraductal carcinomas diagnosed by VAB turn out to be intraductal and infiltrating carcinomas at surgery, respectively. Histologic underestimation may also occur in cases of papillary tumour, even with complete resection of the lesion.

A major complication is the significant rate of hematomas, higher than in CNB, which is especially common in ultrasonography- and MRI-guided VAB because breast is less compressed during these procedures. Nevertheless, these hematomas usually disappear without treatment. Additionally, VAB may be more painful, so a higher dose of local anesthetic is normally required.

**Indications**

There are a variety of indications that affect the guidance modality of choice. For the majority of radiologists, stereotactic guidance is the most common technique. The most relevant indication to perform stereotactic guidance is the biopsy of suspicious microcalcifications and architectural distortions. The larger number of samples results in a reduction of underestimation of lesions.

The most relevant indications for ultrasonographic guidance are: repeat biopsy based on a high-risk histologic finding or a result that is inconsistent with CNB findings;
excision of probably benign nodes as an alternative to surgery; and excision of intracystic and intraductal papillary lesions.

The only indication for MRI guidance is biopsy of suspicious lesions that are exclusively visible with this imaging technique.

**Galactography**

Nipple discharge is a common symptom in breast disease. It is usually secondary to medication or to processes that are not associated with local breast conditions. Only unilateral and spontaneous (i.e. without breast expression) discharge is normally described as pathologic. This discharge is usually serous, serosanguinous, and bloody, and is most commonly caused by intraductal papilloma. Breast cancer is a relatively rare cause, ranging from 1% to 15% of the cases reported.17

The management of nipple discharge is a controversial issue. Although some surgeons opt for excision of the retroareolar tissue, with no previous imaging evaluation, in order to include the discharging duct, as a general rule, the recommended procedure involves a galactogra-
phy before surgical decision-making since this technique is accurate in indicating absence or presence of an intraductal lesion and its localization within the abnormal duct.\textsuperscript{18}

**Technique and findings**

Galactography is commonly performed with the patient lying supine. The breast is first tenderly expressed for identification of the discharging galactophorous duct and cannulation of the duct is then done with dedicated cannulas or sialography catheters.

Disinfecting the nipple and removing any air bubbles from the catheter are initial steps of the procedure. The catheter is then introduced about 5 to 10 mm into the duct. A small dose of water-soluble iodinated contrast (0.5–1 ml) is next injected until the patient has a stinging feeling or pain. After injecting the contrast, the catheter can be extracted or left in place in case further injections are required. Subsequently, two orthogonal mammographic projections (craniocaudal and mediolateral) are performed, and preferably magnified.

Intraductal lesions manifest as filling defects or stop in the contrast column (Fig. 10). The majority of lesions causing discharge are benign, mostly papillomas.

Resection of the intraductal lesion identified at galactography can be performed by percutaneous VAB, generally under ultrasonographic guidance,\textsuperscript{19} in institution where this technique is available (Fig. 11).

Localization of these lesions for surgical biopsy commonly relies on the coordinates provided by the galactogram ("galacto-hook"). Other techniques for localization of the affected duct involve injecting methylene blue or inserting metal guides (Fig. 12). Preoperative localization of the discharging duct is essential and failure to do so may result in missed identification of the lesion in the surgical specimen.\textsuperscript{20}

**Indications**

Galactography is indicated in cases of abnormal nipple discharge because it is commonly associated with intraductal lesion, mostly papillomas.

Galactography is not indicated for bilateral or multifocal discharge because this type of discharge is not suggestive of breast disease, except for ductal ectasia.

**Conflict of interests**

The authors declare not having any conflict of interests.

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