An effective breast biopsy team requires detailed communication, particularly between radiologists and pathologists, to achieve the most accurate and useful diagnostic information from each minimally invasive breast biopsy procedure. A number of different biopsy devices are available and lend themselves to different imaging and clinical situations. The effect of biopsy size and number of biopsy fragments on diagnostic accuracy is discussed, with particular emphasis on biopsies directed at calcifications. In this context, differentiation of atypical hyperplasias from low-grade ductal carcinoma in situ depends not only on accurate targeting but also sufficient biopsy size. Some of the commonly used image-directed biopsy devices and site marking techniques are listed. Regular radiology–pathology correlation conferences foster collegial understanding of the strengths and limitations of each other's analytical techniques and can lead to better patient care.

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Proper care of patients undergoing breast biopsy requires complete cooperation by the entire breast care team. The team includes a variety of professionals, but centrally involved are radiologists, pathologists, surgeons, and medical oncologists. Continuous, free-flowing communication between team members through the various phases of the diagnostic and therapeutic process is essential to the success of the cooperative effort.

Understanding the value and limitations of various diagnostic biopsy maneuvers fosters efficiency in determining optimal patient management by the breast care team.

Currently in the US, most initial biopsy procedures are performed by radiologists or by surgeons using image-directed, minimally invasive technology.1 Biopsies thus acquired can allow optimal planning for definitive surgical treatment, which is, ideally, a single open surgical procedure yielding excision with adequate margins. An equally important role for minimally invasive biopsy is avoiding open biopsy for benign conditions that do not require further intervention or diagnostic efforts.

It is useful for those involved in biopsy performance and interpretation to be familiar with the strengths and limitations of each other’s procedures.

A variety of techniques and devices are employed for tissue acquisition and various methods are utilized to maintain identity of the biopsy site. The final common pathway of the tissue acquired for diagnosis is the pathology laboratory, from which diagnostic information is returned to other members of the breast care team. Within the laboratory, the basic analytic process is H&E histology, but a multiplicity of supplemental diagnostic methods are used to gain information needed for patient care, such as specimen radiography to further localize lesion(s). Immunohistochemistry, fluorescence in situ hybridization...
Figure 1 Example of a specimen submission form for core biopsy. Radiologist fills it out and telegraphically informs the pathologist of the reason for the biopsy, the biopsy site, the type of target, device used, the number of cores, and presence of calcifications, if any.
(FISH), and occasionally other gene testing studies may be used for prognostic information.

**Pathologist Role**

The pathologist’s role is to provide diagnostic information that is timely, accurate, and most importantly, in the form of a diagnostic report which addresses questions posed by imaging. For example, do the histopathologic findings from a minimally invasive breast biopsy (MIBB) explain a stellate mass? Is the fibroadenoma, which was predicted by imaging, actually present? Are calcifications identified and, more importantly, are they the ones targeted by the radiologist?

For the pathologist to be responsive to the questions posed by the imaging, communication of the nature of the lesion must be conveyed to the pathologist, preferably in written form, and provided with the specimen requisition. The form used by our group is shown in Figure 1. In addition to designating laterality and position within the breast, the size and nature of the lesion is noted along with size of needle employed. If calcifications are targeted, it is essential to provide the pathologist a specimen radiograph to correlate size, shape, and number of calcifications with histology (Fig. 2). The specimen radiograph is invaluable, but it is essential that the cores not dry out during specimen radiography, thereby compromising histological subtleties. In addition to providing specimen radiographs, inking cores with calcifications or submitting them in a separate container can assist the pathologist to more rapidly and economically identify and characterize the targeted lesion. Sometimes “benign” calcifications are identified in the initial slides but are not the calcifications of interest targeted by the radiologist for examination (Fig. 3). Deeper sections of the tissue block(s) should then be prepared. A radiograph of the tissue block (Fig. 4) can disclose the presence or absence of calcifications in the remaining tissue. The need for additional deeper histologic sections can be minimized if the histology laboratory carefully embeds the cores in a manner ensuring that the cores lie in the same plane and do not overlap each other. Additionally, placing too many cores in a single tissue cassette makes ideal embedding difficult.

![Figure 2](image-url)

**Figure 2** Core specimen radiographs should be submitted to the pathology laboratory along with the specimen to guide histologic analysis by the pathologist. In these two illustrations, all cores contain calcifications. The pathologist should then visualize calcifications in size and number in each core corresponding to those seen in the specimen radiograph. In some instances, multiple additional sections must be prepared to achieve this goal.

![Figure 3](image-url)

**Figure 3** Core biopsy diagram illustrating that the plane of section shown in the initial slides may contain calcifications but may not contain the important calcifications targeted by the radiologist. (Color version of figure is available online.)

![Figure 4](image-url)

**Figure 4** Radiograph of tissue block containing calcification which was found to represent comedo DCIS. These calcifications, although extensive, were not present in initial shallow sections.
The pathologist’s analysis of the tissue is not complete until satisfactory correlation of histology and imaging has been accomplished and any discrepancies clearly addressed. If more than one lesion is biopsied, the precise location of each site within the breast should be specified should excision or additional biopsies be directed at that location.

For example, a specimen requisition form might read:

Specimen A: right breast, 11 o’clock, 4 cm from nipple, linear calcifications.
Specimen B: right breast, central, 2 cm deep to nipple, 1-cm oval mass.

Of course, depending on the findings of these biopsies, markedly different treatments might be contemplated.

Radiologist’s Role

The radiologist’s role, after obtaining the biopsy specimen, is to provide information to the pathologist that will optimize accurate evaluation and reporting. This information includes standardized written information regarding targeted lesion (Fig. 1) as well as a copy of specimen radiograph if the biopsy was for calcifications. The radiologist and pathologist should be readily available to each other by telephone to provide additional information as needed. The need for accurately labeled specimen containers and requisitions cannot be overemphasized. Additionally, the breast radiologist should have an understanding of the strengths and limitations of histopathologic evaluation of breast biopsies. Regularly held radiology–pathology correlation conferences not only serve to resolve imaging and pathology discrepancies, but also can be an effective means of developing mutual understanding of each other’s techniques.

Biopsy Techniques

A variety of techniques and medical devices are employed to obtain diagnostic information ranging from fine needle aspiration (FNA) to open excisional biopsy.

Figure 5  Examples of slides prepared from biopsies obtained using various percutaneous biopsy devices. (Color version of figure is available online.)

Figure 6  The number of cores retrieved can be almost limitless with directional vacuum-assisted large core biopsy devices. These were from a MRI-guided procedure. (Color version of figure is available online.)

Figure 7  Intact BLES® device. Photograph showing wand of BLES® device with 20-mm capture basket (arrow) containing simulated breast biopsy. After advancing wand to the target, the capture basket deploys using RF energy to encircle and retrieve a single ovoid segment of tissue. Inset shows bisected actual specimen. (Color version of figure is available online.)

Fine Needle Aspiration

A major advantage of FNA is that equipment and anesthesia requirements are minimal. There is limited patient preparation time, and there is a very low risk of complications such as hematoma. However, currently, the role of FNA as a primary diagnostic tool in breast biopsy is becoming progressively limited in the US. The nature of the FNA specimen, composed of disaggregated cells, can pose difficult interpretation problems for many pathologists. For example, high nuclear grade ductal car-
cinoma in situ (DCIS) can’t reliably be distinguished from invasive tumor. Because architectural features are not preserved in FNA specimens, cells from some low-grade invasive tumors may be difficult to differentiate from benign lesions with cytologic variability. As a consequence, most pathologists can more rapidly and confidently interpret biopsies than FNAs. The rate of insufficient samples in many centers compared with core biopsies is another limitation. However, despite its limitations for mammary parenchymal lesions, FNA in breast cancer diagnosis continues to be valuable in evaluating lymph node status before definitive therapy.

Core Needle Biopsy

Percutaneous minimally invasive breast biopsy (MIBB) is considered the optimal diagnostic technique for image-detected breast cancer.1

Rapidly evolving technology in this area has produced a myriad of percutaneous biopsy devices and techniques that can be suited to a variety of clinical situations. Most devices are intended to be image-guided, and produce tissue samples of various size and number. Depending on the device, image guidance can be through ultrasound, stereotactic, or magnetic resonance imaging (MRI).

Biopsy Size

Increased size of individual biopsy fragment fosters accuracy of histopathologic assessment and can reduce number of procedures required for diagnosis and definitive treatment.4,5 Biopsy size considerations are particularly important in the reliable differentiation of atypical ductal hyperplasia (ADH) from low nuclear grade DCIS.6 To make this important diagnostic distinction, the pathologist must be able to evaluate the complex interplay of cytological, architectural, and extent criteria to establish accurate diagnoses.7,8 In this context, the histology of abnormal cellular proliferations in contiguous terminal duct lobular units visualized in a single large core often provides more definitive diagnostic information than can be derived from multiple small cores derived from the same tissue. Even though numerous small cores may be re-

Figure 8  (A) Radiograph of BLES® specimen targeting clustered calcifications. Entire cluster is captured (arrows). (B) Lesion is enlarged lobular unit with columnar alteration. (C) Single focus of atypical ductal hyperplasia (arrow) is present. (D) High-power view of ADH. Because architecture was preserved, this lesion is definitively not DCIS. (Color version of figure is available online.)
moved encompassing a wide area of tissue, the effect on some low-grade lesions can be likened to that of a disassembled jigsaw puzzle, often precluding any diagnosis other than “atypia.” Other benefits of larger tissue samples are conservation of time and technical resources. Having a few large cores rather than numerous small ones generally requires processing fewer slides. In addition, calcifications may be less easily displaced from the larger cores during processing. Moreover, the histologic patterns, being more intact, require less mental reassembly of the histologic jigsaw puzzle, thus facilitating a more rapid specific diagnosis. Similarly, papillomas and radial scars may be more precisely evaluated with increased biopsy size that preserves spatial orientation of these complex proliferative lesions.

Where the patient is found to have a single mass, generally only a few cores are needed to obtain diagnostic tissue.

Core biopsy devices appear to produce cores of variable diameter depending on the tissue type being biopsied. For example, fatty tissues tend to yield smaller cores or cores with irregular, beaded contours than cores from the same device targeting fibrous breast tissue. Biopsy devices employing suction tend to produce larger cores than devices of equivalent inner diameter, which are not vacuum-assisted.9-11

Even though extensive sampling of breast tissue is possible with many of the MIBB devices, tissue removed with these procedures should be considered to be of diagnostic value, and not therapeutic.

Although different technology and device designs are employed, choice of biopsy device largely reflects imaging modality to be utilized, the ease of use of the biopsy device in that particular context, and possibly the experience and skill of the operator. With the currently available biopsy equipment, histologic quality is, in our experience, less dependant on the device used than the type of tissue sampled, the size of the individual biopsy fragments, the proper fixation of the biopsy and, of course, the quality of slide preparation within the laboratory. Histologic sections from various commonly used core devices are shown in Figure 5.

Biopsy Acquisition
Devices for MIBB

Spring-loaded (automated) needle biopsy guns are available in 18-, 16-, and 14-gauge, and are generally utilized for diagnosis of larger BI-RADS 4-5 lesions or fibroadenomas. These automated guns are generally ultrasound-guided and, of course, can be used for palpable masses. Generally, there is no return other than blood after 5 to 6 repeat passes.5,12 These devices return better cores when tissue has a fibrous quality and do not tend to perform well in fatty tissue. Another potential limitation of these devices is that localizing markers are not readily placed postbiopsy. Increased diagnostic accuracy is generally conferred by the use of larger gauge needles.2,13

Directional vacuum-assisted biopsy may provide almost limitless number of cores (Fig. 6). They have been shown to provide superior diagnostic accuracy compared with spring-loaded guns for lesions with suspicious calcifications and, additionally, allow placement of radio-opaque localizing clips.3,14-16 However, spring loaded guns may be more cost-effective than vacuum-assisted core biopsies for noncalcified mass lesions.17

Three vacuum-assisted biopsy systems are in common use in our area. Perhaps the most extensively employed is Mammotome® Breast Biopsy System from Ethicon Endo-Surgery. Via a single insertion of available 8-, 11-, and 14-gauge needles, multiple vacuum-assisted cores can be obtained using stereotactic or, less commonly, ultrasound guidance.

Mammotome MR® is an 11-gauge, MRI-compatible device which was recently released in the US. Another automated vacuum assisted device is Suros Surgical’s, ATEC® Saphire system. It is completely compatible with ultrasound, stereotactic, and magnetic resonance imaging guidance and reportedly can produce 6 to 12 cores in 60 seconds.

A third vacuum-assisted device is the Vacora® from Bard. Its unique feature is its compact design. Unlike the other devices that employ floor-mounted consoles connected to the probe with wires and tubing, the entire mechanism of the Vacora®, including vacuum source, is contained within the handle, allowing easy maneuverability. It may be used with stereotactic, ultrasound, or MRI guidance and retrieves a single 10-gauge core. An introducer is used, allowing multiple repeat biopsies in contiguous breast tissue.

There are two unique percutaneous biopsy devices.
The Intact™ Breast Lesion Excision System (Intact BLES, Intact Medical Corporation), was formerly known as en-bloc® (Neothermia, Inc.). It uses a percutaneous wand-mounted capture basket employing RF energy to encircle and remove a relatively large ovoid segment of tissue in a single pass. Four basket sizes are available (10, 12, 15, and 20 mm). The device is compatible with standard stereotactic tables, and can be used for ultrasound-guided procedures (Figs. 7 and 8a–d).

Because RF energy is used to circumscribe the biopsy, thermal damage may be present at the edges. However, in experienced hands, thermal artifact is minimal, generally involving less than 0.2 mm at edge of a fibrous specimen. If tissue is fatty, however, almost no artifact is evident. Preliminary studies suggest that the large sample size more than offsets problems that may be attributed to artifact.24

The Sanaurus CASSI® rotational core biopsy device uses ultrasound-guided, 19-gauge securing needle and a 10-gauge serrated cutting cannula. A CO₂ quick “stick freeze” localizes the target tissue around the securing needle, followed by advancement of cutting cannula (Fig. 9). An 8-gauge introducing stylet allows multiple passes through the original incision.

On histologic examination of the “stick-freeze” specimens, freezing artifact appears minimal, but a faint irregular central needle track (from the securing needle) is sometimes detectable (Fig. 10a–c). In our experience, so far, neither artifact has compromised interpretation.

Artifacts Associated with MIBB Specimens

All biopsy procedures introduce artifacts. Some are less apparent than others. Calcifications tend to be more easily displaced from thinner cores during postbiopsy handling and processing. There may be subtle shredding of ductal proliferative lesions along the edges of cores obtained by vacuum-assisted devices (Fig. 11a and b). CASSI® freezing does not seem to adversely affect histology or prognostic marker studies by immunohistochemistry. The central securing/freezing needle produces minimal disruption of architecture that is

Figure 10 CASSI® “stick freeze” core biopsies show faint tracks of the “securing needle” in some planes of section appearing as a fracture (arrows, A and B) or as minute focus of blood in track (C). These artifacts have not, as yet, compromised interpretation in our experience. (Color version of figure is available online.)
not significant for interpretation of mass lesions. The BLES® device does, in some circumstances, particularly in dense fibrous tissue, produce the most readily apparent artifact in the form of thermal damage. Generally this artifact is less than 0.2 mm in thickness in a specimen that is up to 1 to 2 cm in size.

**Markers Used to Indicate MIBB Site**

Metallic markers or clips are deployed after MIBB, especially when the biopsy process removes all, or substantially all, of a lesion. These markers facilitate subsequent localization of biopsy site for open excision, if necessary. Additionally, after neoadjuvant chemotherapy, the tumor may have regressed completely, or be unapparent to imaging. At that point, accurate excision of the original tumor site is facilitated by the presence of a marker that can be readily imaged and localized. One limitation of metallic clip markers is that substantial clip migration may occur following placement at the biopsy site. Although the vast majority of the markers remain within 10 to 12 mm of the target, at least 10% to 20% of cases may exhibit migration distances of more than 20 mm from the intended site of deployment. Immediate postbiopsy, two-view mammography has been recommended to identify situations of excess clip migration. Ultrasound localization of the post biopsy hematoma, if present, can assist in

**Figure 11** (A) An 11-gauge vacuum-assisted core biopsy showing artifactual fragmentation and fraying of a cellular intraductal lesion. (B) Histology suggests low-grade DCIS, but lacking sufficient architectural and extent criteria, findings are not diagnostic in this specimen. (Color version of figure is available online.)

**Figure 12** (A) One brand of marker (gelmark® and gelmark ultra®) uses gas-impregnated pellets of bioabsorbable material, one of which contains a metallic clip of variable shape. The pellets completely dissolve over time depending on the composition of the plug. (B) In the case of the polymer in this example, the material almost totally dissolved during tissue processing, leaving a cavity adjacent to the DCIS. Note the absence of tissue reaction to this material. (Color version of figure is available online.)
correcting for clip migration at the time of open excision. Naturally, hematomas regress with time and some biopsies produce little or no hematoma.

When examining a specimen, it is important for the pathologist to be cognizant of the potential problem posed by clip migration. Although the location of the clip is easily identified on radiographs of the sliced specimen, the true location of the original target may be some distance from the metallic marker. The radiologist can be helpful in this regard since the post biopsy radiograph may have indicated the extent and direction of the clip’s migration. In most situations, the biopsy site is either grossly or microscopically evident in the form of hematoma or scar, often with hemosiderin deposition. Nonetheless, if the postbiopsy interval is prolonged, as in the case of neoadjuvant chemotherapy, none of these clues may be evident. In that circumstance, tissue sampling should not be concentrated to the immediate area of the clip, but extended in all directions to give the most accurate histopathologic assessment. As indicated above, if the radiologist has recognized that substantial clip migration has occurred, the pathologist should be so notified at the time of excision.

A variety of clips are available, composed of different metals with a number of shapes. Clips may be surrounded by cylindrical plugs of material that inhibit migration and facilitate subsequent ultrasound localization (Fig. 12a and b). Depending on whether the material is porcine gelatin, artifi-

**Figure 13** (A) Tissue slice with easily identified BLES® biopsy site marked with metallic clip and collagen plug. (B) Collagen plug histology is characterized by a sponge-like aggregate of hyaline angulated red–purple acellular material. (Color version of figure is available online.)

**Figure 14** (A) Specimen radiograph of excision specimen and of sliced excision specimen showing wire clip (arrow). Note the marker clip is eccentrically placed within the specimen. (B) Specimen tissue slice from a wire clip (arrow) partially embedded in tissue. Polymer plug originally surrounding clip is completely unapparent grossly and microscopically. The plane of section was fortuitous in disclosing location of clip. Radiograph of specimen slices is usually necessary to determine exact location of marker clips, particularly after a prolonged postbiopsy interval. (Color version of figure is available online.)
cial polymers, or bovine collagen (Fig. 13a and b), the plug surrounding the wires may be reabsorbed at different rates maintaining ultrasound visibility from 2 to 6 weeks, leaving the metallic clips for long-term radiographic marking (Fig. 14a and b). These marker-associated plugs have different gross and histological appearances, depending on length of time since deployment.

Open Excision

Wire-guided open excisional biopsy is rarely used as primary diagnostic procedure, but if imaging is difficult or in that rare circumstance where anatomic considerations limit needle biopsy techniques, needle localized excision (NLE) may be used. More commonly, NLE is employed after core biopsy to fully excise an in situ or invasive tumor or to obtain supplemental diagnostic information where “high-risk” lesions such as atypical hyperplasias are identified on core biopsy. Of course, when core biopsy findings do not fully correlate with imaging or clinical impressions, NLE is frequently contemplated rather than repeating the core biopsy. Bracketing wires (Figs. 15 and 16) can be placed with a variety of techniques and have recently been described using MRI guidance.

In conclusion, proper care of patients undergoing breast biopsy is enhanced by close communication among members of the breast care team. Familiarity with the strengths and limitations each other’s techniques and procedures is essential to achieve the goal of gaining maximum diagnostic information while minimizing number of procedures, patient expense, and discomfort.

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