

# 1 MINIMALLY INVASIVE BREAST BIOPSY: THE BREAST IMAGER’S PERSPECTIVE

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## INTRODUCTION

Since the initial implementation of film-screen mammography in the 1970s as a screening exam for breast cancer, breast imaging has evolved by leaps and bounds. Today’s breast imager utilizes multiple imaging modalities including full-field digital mammography (FFDM), ultrasound (US), and magnetic resonance imaging (MRI), and more recently, molecular imaging techniques including breast-specific gamma imaging (BSGI) and positron emission mammography (PEM) to aid in the evaluation of breast pathology. With these advances came the ability to diagnose smaller, non-palpable, and earlier-stage breast cancers. This carries with it the challenge of developing image-guided methods to provide a pathologic diagnosis in an accurate, cost-effective, and safe manner. The subsequent development of multi-modality techniques for minimally invasive, image-guided breast biopsy has largely occurred to help solve this diagnostic challenge.

The initial techniques for obtaining pathologic diagnoses of non-palpable, radiologic lesions included more invasive open surgical techniques, such as blind quadrantectomy or segmentomy. However, high rates of re-excision were reported. Therefore, the next development was preoperative internal needle and wire localization techniques, utilizing mammographic guidance. Wire-guided surgical breast biopsy was, until recently, the “gold standard” for the diagnosis of non-palpable radiographically detected breast lesions. However, this technique continued to be fraught with pitfalls, including inexact wire placement, dislodgement or fracture of placed wires, and a recovery rate of the radiographic abnormality anywhere from 2% to 20%.

However, one of the most consistent trends in medicine has been the steady strive to develop technology that allows

physicians to accurately and safely diagnose and treat patients via ever less invasive methods. Breast imaging and intervention has undergone great changes over the past several decades, due to the development of image-guided minimally invasive technologies. These techniques are now available utilizing all traditional forms of breast imaging, including mammographic (stereotactic), US, MRI and most recently, nuclear medicine guidance to include BSGI and PEM.

## BREAST IMAGING REPORTING AND DATA SYSTEM (BI-RADS)

The Breast Imaging Reporting and Data System (BI-RADS) is a standardized imaging lexicon developed to facilitate the communication of results and recommendations between radiologists and referring clinicians and therefore the appropriate management of patients. Various groups, including the American College of Radiology, developed BI-RADS as a collaborative effort with the American College of Surgeons and the College of American Pathologists. Standard terminology is used to first describe and characterize mammographic findings and then the exam is coded as one of six categories of patient management (see Table 1.1). BI-RADS was initially developed for mammography, but now is used for all breast imaging modalities.

BI-RADS 1 and 2 examinations are normal or benign and yearly mammographic surveillance is recommended. BI-RADS 3 lesions are likely benign, meaning they have a less than 2% chance of malignancy. The appropriate management for a probably benign finding is a short interval follow-up. This is usually conducted in six-month intervals, for up to five years, to establish stability of lesions having a less than 2% likelihood of malignancy. The

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Table 1.1: BI-RADS

Code	Assessment	Management
0	Incomplete	Additional work-up needed
1	Normal	Annual screening
2	Benign finding	Annual screening
3	Probably benign finding	Short interval follow-up
4	Suspicious abnormality	Biopsy recommended
5	Highly suggestive of malignancy	Appropriate action should be taken
6	Biopsy-proven cancer	Biopsy-proven, current cancer

rationale behind the BI-RADS 3 category is to reduce false positive biopsy rates while maintaining an acceptably high rate of diagnosing favorable, early-stage breast cancers. Inclusion criteria for a probably benign mammographic assessment are (1) a circumscribed mass (at least 75% circumscribed margins) less than 1 cm, (2) round, punctate, or oval microcalcifications or microcalcifications that are more diffusely distributed or loosely clustered, and (3) a focal asymmetry. A focal asymmetry is a space-occupying lesion, seen on at least two mammographic projections. BI-RADS 4 exams contain abnormalities with a probability of malignancy from 2% to 95%, and BI-RADS 5 exams greater than 95%. Biopsy is indicated for lesions in both these categories. Some BI-RADS 3 lesions do undergo biopsy, usually in patients who are high-risk or high-anxiety. A BI-RADS 6 designation is used to denote an exam demonstrating a biopsy-proven cancer. This is most commonly used for patients undergoing subsequent post-diagnosis imaging evaluation, such as for preoperative planning or re-assessment following neoadjuvant chemotherapy. BI-RADS 0 means the imaging evaluation is incomplete and either additional images, including other imaging modalities, or comparison with previous examinations, are needed. Of note, a BI-RADS 0 categorization is temporary and final assessment requires a designation of BIRADS 1–6.

STEREOTACTIC INTERVENTIONS

As mammography was the first examination used for the diagnosis of non-palpable breast cancers, it follows that this modality was the basis for image-guided biopsy of breast lesions. The minimally invasive biopsy of mammographic lesions employs stereotactic guidance, which today usually consists of microcalcifications. While masses can also be

targeted and biopsied via stereotaxis, a large multicenter trial performed in 2003 found that 70% of stereotactic vacuum-assisted biopsy (VAB) was performed for suspicious microcalcifications. Microcalcifications worrisome for malignancy are clustered (five or more particles per cubic centimeter), pleomorphic (varying in size and shape), or have a worrisome mammographic distribution, such as segmental or ductal (Figure 1.1). Nine percent of VAB were performed on masses with microcalcifications and 19% on masses without microcalcifications. Masses worrisome for malignancy demonstrate angular or spiculated margins and may distort the adjacent breast parenchyma. Two percent of biopsies were performed on architectural distortions alone, a mammographic finding where there is no visible mass, but the breast parenchyma is radiating from a central nidus, likely due to a scirrhous reaction.

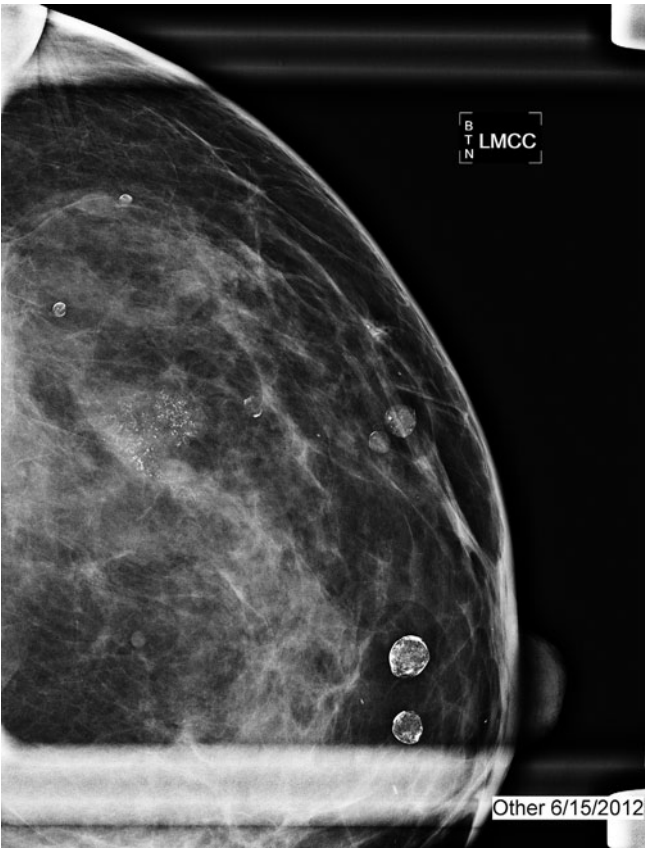


Figure 1.1. A craniocaudal spot magnification view demonstrates a large cluster of pleomorphic microcalcifications. Also seen are multiple coarse benign calcifications.

Commonly, stereotactic breast biopsies are performed on a dedicated prone table. However, when more efficient use of space is a priority, an attachment to an existing

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digital mammography unit with a special chair to allow for proper positioning of the patient is also an option. When utilizing a dedicated table, the patient is placed in a prone position with the breast positioned dependently through a large aperture in the table. Underneath the table is an attached mammography unit on an articulating arm sequentially angled at positive and negative 15 degrees and images are obtained. These angled images are then used by a computer to triangulate the target and generate *x*, *y*, and *z* coordinates to within 1 mm of accuracy.

Although the approach position is initially determined by reviewing the diagnostic mammograms and calculating the shortest distance from skin to lesion, the equipment allows for adjustments throughout the procedure, should they be necessary. Adjustments are most common, when, for example, it is noted that a large blood vessel is near the target, or in cases where the initial calculated depth coordinate (*z*) is either too superficial or too deep. Nicking a large blood vessel may cause undue bleeding and utilizing a different approach trajectory often avoids the vessel altogether. A generated *z*-coordinate that is too superficial or too deep runs the risk of either including skin within the biopsy or resulting in equipment damage by having the biopsy probe contact the image detector and cause misalignment. And though the stereotactic biopsy needle has undergone many permutations over the years, the standard biopsy device ranges in gauge from 8–11 and all are performed with vacuum assistance.

Steps in a stereotactic breast biopsy are as follows (Figure 1.2):

- Review of images to determine positioning of patient and biopsy trajectory
- Obtain scout image of lesion and subsequent  $\pm$  15 degree stereotactic images
- Generation of *x*, *y*, and *z* coordinates
- Mobilization of biopsy device to generated *x* and *y* coordinates
- Sterile prep of skin using a povidone-iodine topical antiseptic
- Administration of local anesthesia to overlying skin, subcutaneous and parenchymal tissues along anticipated biopsy tract
- Placement of a 3 mm skin nick with a scalpel at skin entry site
- Manual advancement of needle to *z* coordinate
- Review of pre- and post-fire stereotactic images
- Specimen retrieval (6–12 samples)
- Deposition of post-biopsy marker

- Achievement of hemostasis via manual or mammographic compression
- Placement of sterile dressing
- Post-procedure light-pressure mammogram

Once the specimens are obtained and following removal of the needle, a metallic biopsy marker is deposited in the post-biopsy pocket. This serves to mark the area of biopsy and is especially important in certain instances when the entire lesion is removed during the biopsy. This occurrence is reported in the literature ranging from 13% to 48% and in 59–93% of lesions smaller than 5 mm. However, multiple reports have demonstrated that despite complete removal of the mammographically visible lesion, the majority demonstrate residual histological abnormality at final surgical pathologic evaluation.

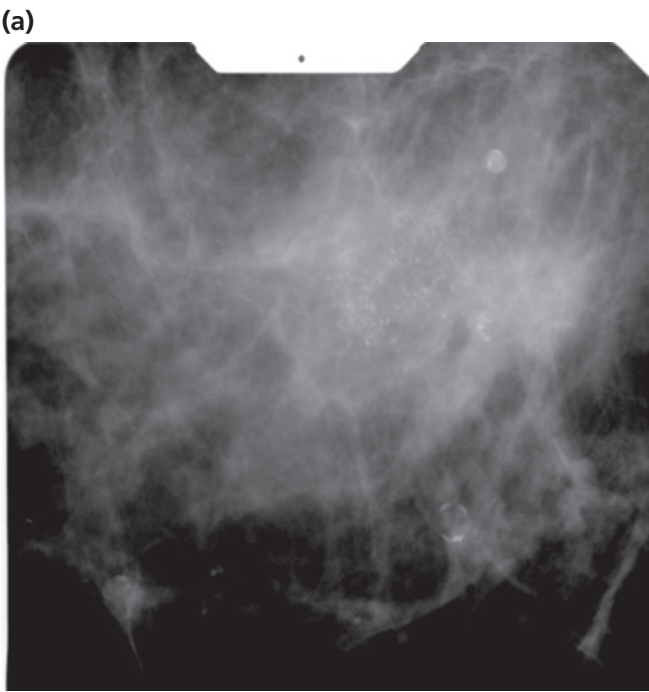


Figure 1.2. Images from several stages of a stereotactic biopsy.  
a. Scout image of cluster of pleomorphic microcalcifications during stereotactic biopsy.

Complications from stereotactic biopsy are noted in less than 1% of procedures, the most common including infections requiring antibiotics or drainage or hematoma necessitating surgical drainage, the latter occurring very rarely. The patient may be wrapped in a compression bandage for the next 24 hours, depending on the amount of bleeding and/or hematoma formation noted during the procedure.

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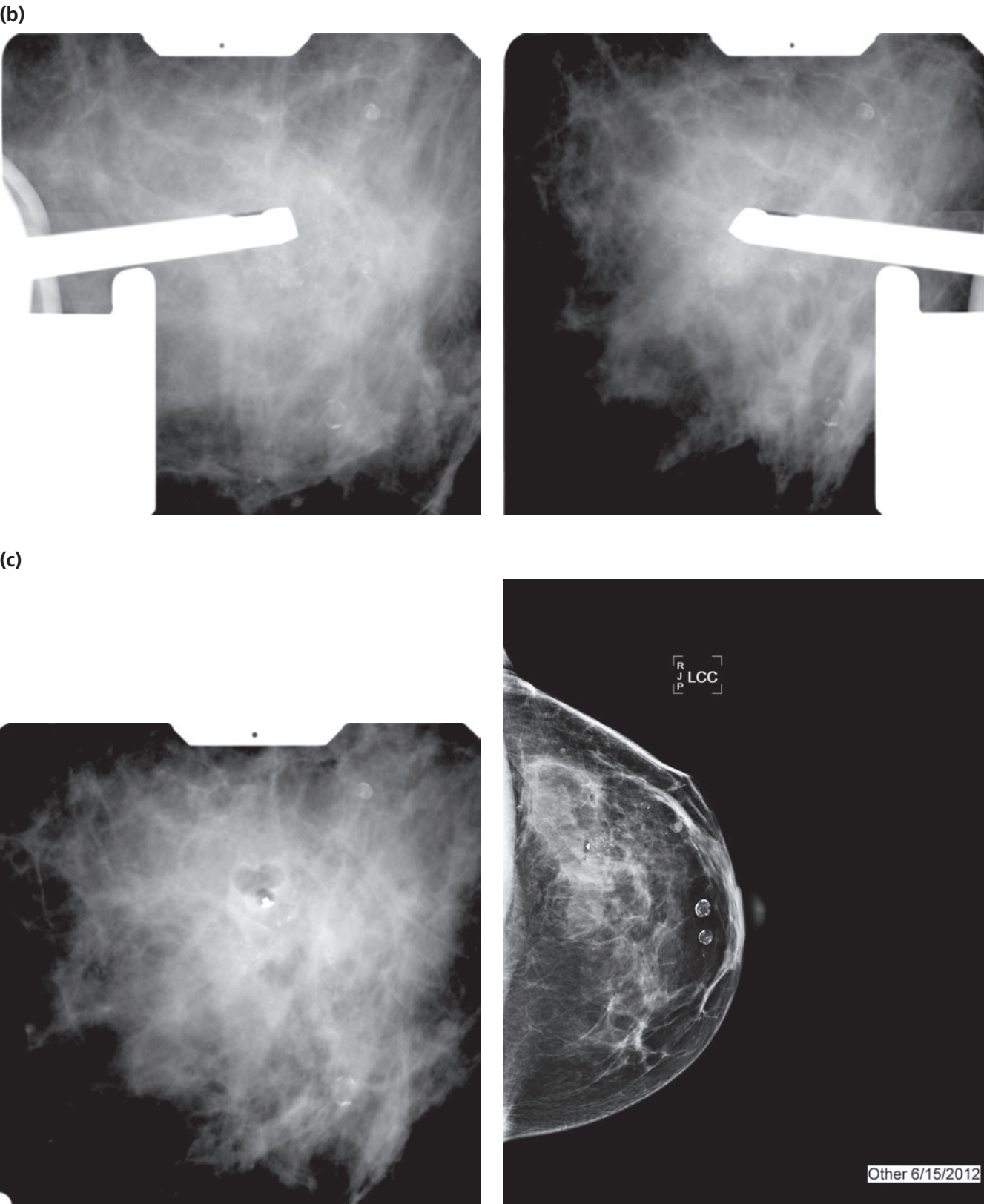


Figure 1.2. (cont.) b. (i) and (ii) Pre-fire stereo pairs obtained at +15 and −15 degree angles from scout image.  
c. (i) and (ii) Post-biopsy image with biopsy marker deployment.



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ULTRASOUND-GUIDED BIOPSY

US is the workhorse of the interventional breast imager, indispensable for both diagnostic evaluation and image-guided interventions. Supine positioning is well tolerated by most patients, there is no ionizing radiation or breast compression, and it provides quick and effective lesion visualization for the radiologist. US allows for lesions identified initially by mammography or palpation to be accurately characterized as solid or cystic. For a lesion to be characterized as a simple cyst it must be anechoic with no internal echoes, have a thin imperceptible wall, and demonstrate posterior acoustic enhancement. As long as these criteria are met, this particular lesion is labeled BI-RADS 2 and may be left alone. However, there are certain situations when interventions on simple cysts could be performed (Figure 1.3). Most commonly, if the cyst is causing symptoms for the patient, i.e. pain or burning. Second, if it is so large as to obstruct adequate visualization of a significant portion of breast tissue. Although cysts can be easily aspirated, a large portion of them may recur, and this should be explained to the patient. Cysts may be termed complicated, if they contain internal echoes, multiple thick septations, and/or debris. These complicated cysts may require fine needle sampling and cytology to clear them as benign.

Solid masses identified by US are divided into three categories based on imaging characteristics: BI-RADS 3, 4, or 5. These categories are meant to create a universal lexicon where the likelihood of malignancy of a mass and urgency for biopsy can be easily communicated. However, there can be overlap among these categories. The continuous development of sonographic technology has allowed radiologists to become more skilled at lesion characterization. For example, the development of high frequency, 7.5–13 MHz probes with improved lateral resolution, harmonic imaging, and real-time compound scanning for better contrast, panoramic views provide context of the lesion within the breast, and most recently, advances in elastography have been shown to improve the positive predictive value (PPV) of US.

The current sonographic guidelines utilized to separate benign from malignant lesions are called the Stavros Criteria, developed in 1995 in a landmark study by Stavros et al.

Benign sonographic lesion features and PPVs (Figure 1.4a):

- Well circumscribed, markedly hyperechoic 100%
- Orientation wider than tall 99%
- Gentle lobulations 99%
- Thin echogenic capsule 99%

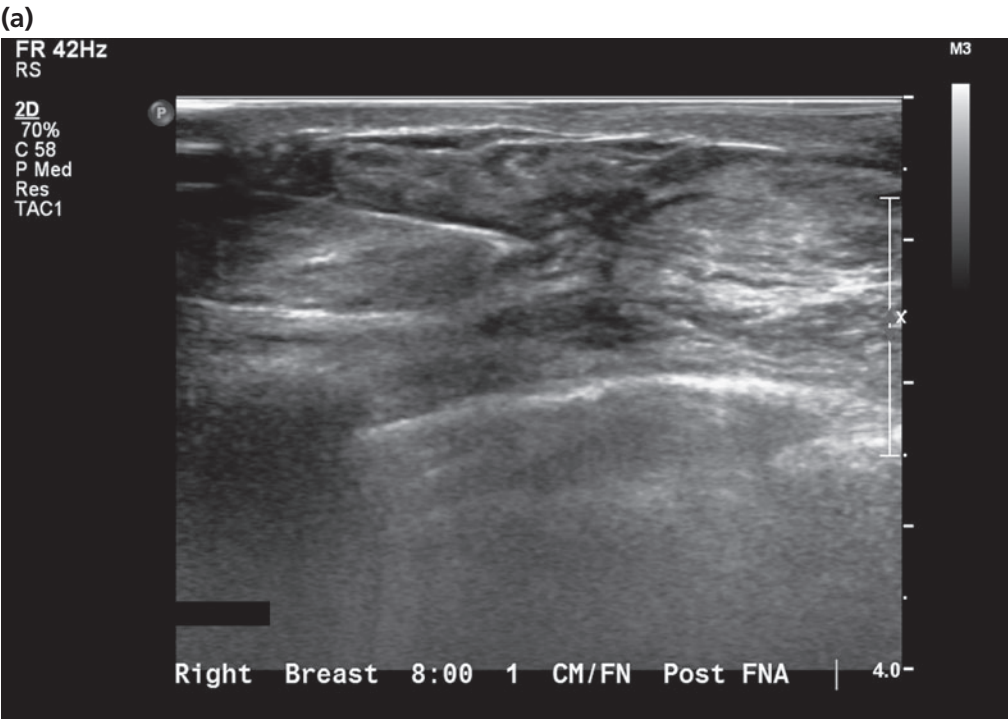


Figure 1.3. Images from US-guided cyst aspiration.  
A. Scout US image of a simple cyst.  
B. Post-aspiration US images demonstrating complete resolution of cyst.

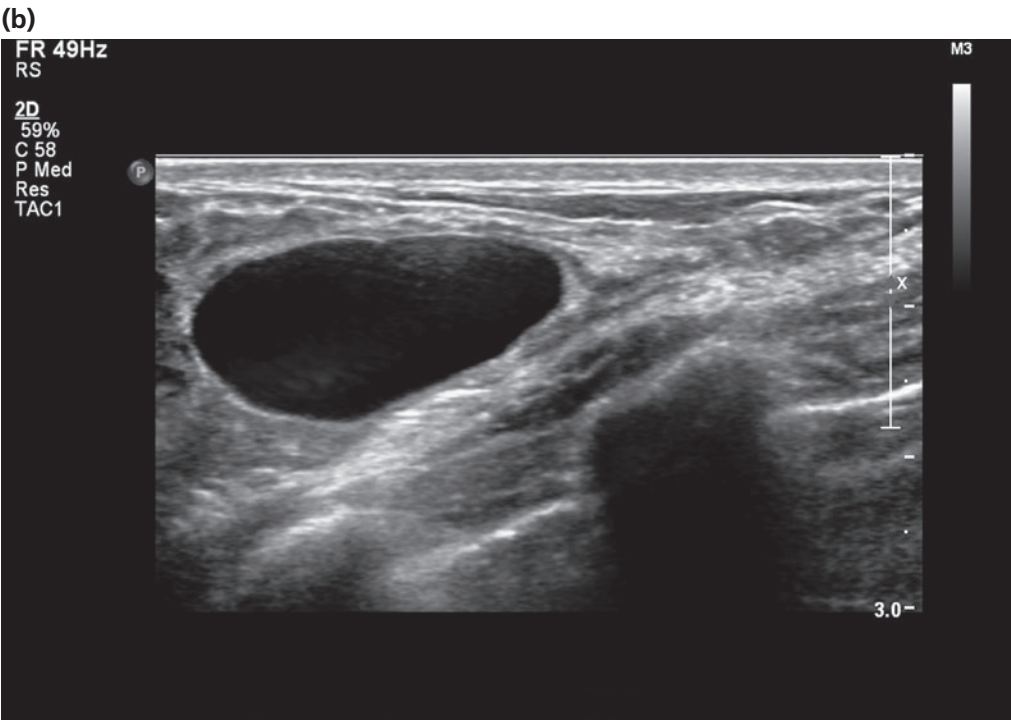


Figure 1.3. (cont.)

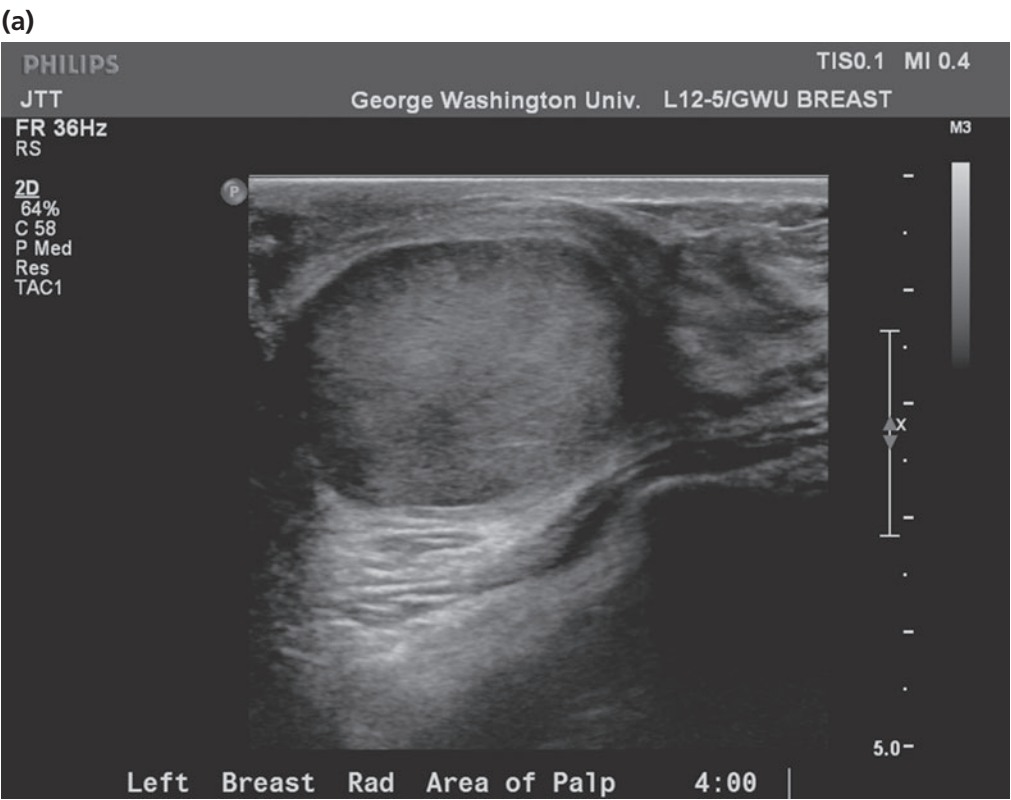


Figure 1.4. A. US image of a mass with typically benign characteristics (circumscribed, parallel).

- Malignant sonographic lesion features and PPVs (Figure 1.4b):
- Sonographic spiculation 87–90%
  - Orientation taller than wide 74–80%
  - Microlobulations 75%
  - Thick echogenic halo 74%
  - Angular margins 70%
  - Marked hypoechogenicity 70%

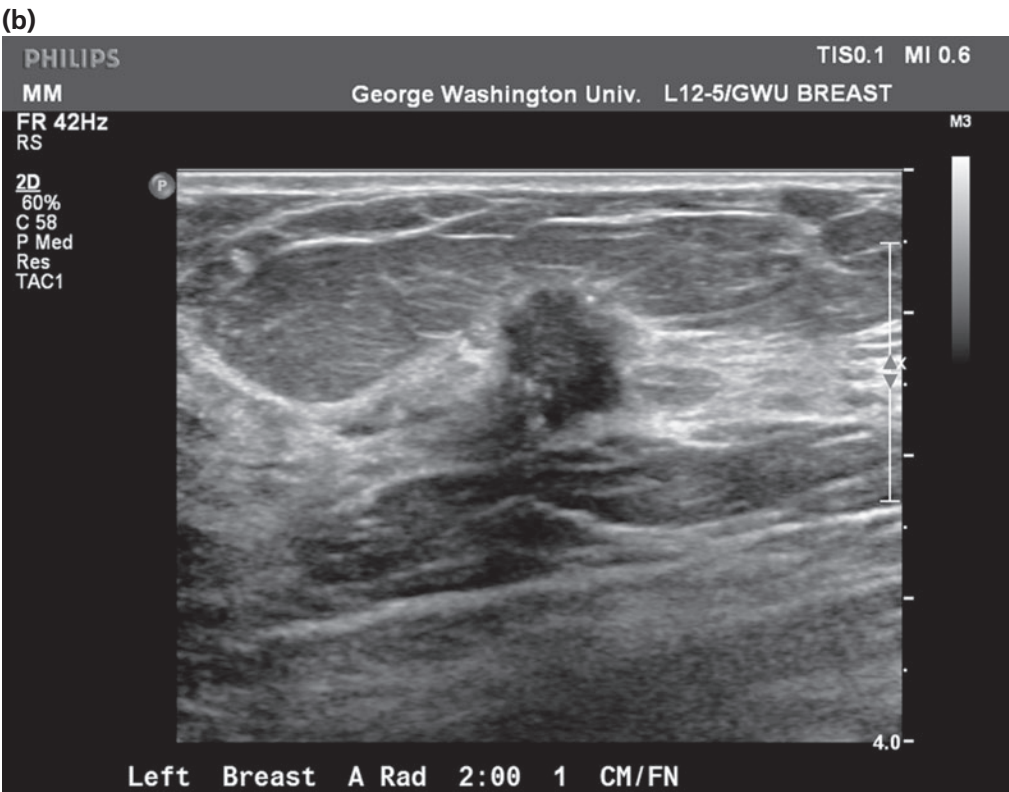


Figure 1.4. (cont.) B. US image of a suspicious, spiculated hypoechoic mass.

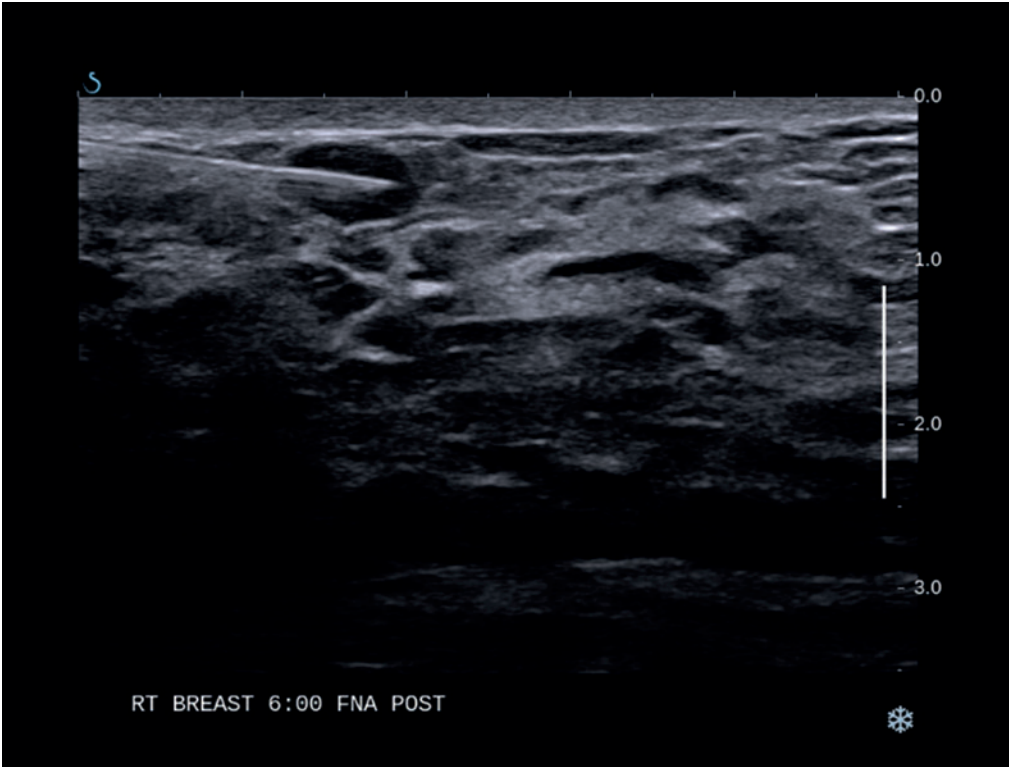


Figure 1.5. Fine needle aspiration of a solid mass.

Once one or a combination of the suspicious features are recognized, it is important to decide on the most optimal method of tissue sampling.

The first rung in the algorithm for US-guided procedures is choosing between fine needle aspiration (FNA) and large core

needle biopsy (CNB). FNA uses a small needle, typically 22–25 gauge, which involves making multiple passes through the lesion and capturing cells via a vacuum effect. FNA is inexpensive, quick, and there is a very low risk of bleeding compared to core and vacuum-assisted biopsies. However, one down side is

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the fact that the procedure is extremely operator-dependent and is prone to yielding insufficient samples. Additionally, since the process only isolates free-floating cells, there is no way to evaluate tissue architecture and determine if malignant cells represent ductal carcinoma in situ (DCIS) vs. invasive carcinoma. Typically FNA is preferred if the lesion is thought likely to represent a complicated cyst, have a very low likelihood of malignancy, or if the patient is anticoagulated (Figure 1.5).

The typical solid mass undergoes US-guided tissue sampling via CNB or VAB. CNB has been found to be comparable to excisional biopsy in terms of breast cancer diagnosis. Additionally, it can allow for more comprehensive patient counseling prior to treatment, as molecular markers can be determined from core tissue samples. More accurate staging is also achievable, as biopsy of any abnormal axillary lymph nodes can be performed at the same time, although this has now become controversial due to the findings in the ACO-SOG Z111 Trial. Studies have also found that knowledge of the pathology prior to lumpectomy yields a higher likelihood of negative margins and repeat trips to the operating room.

Steps in US-guided procedures (Figure 1.6):

- Lesion localization
- Prep skin with antiseptic solution

- Choose needle entry site based on lesion depth
- Administer subcutaneous, intradermal, and intraparenchymal local anesthesia, usually around 5 cc
- Advance the needle towards the lesion while constantly visualizing both the target and the needle in the same plane and remaining parallel to the chest wall
- Take average of 3 tissue samples
- Place marking clip (skip this step if FNA)
- Document needle or biopsy device position prior to and after sampling to prove adequate sampling and aid in radiologic–pathologic correlation.

US-guided VAB is a relatively new technique that is most helpful for proper sampling if the lesion appears to be intracystic (thought to be a papillary lesion), or if complete lesion removal is desired, as in the case of the excision of a fibroadenoma or papilloma. It utilizes larger 9- and 11-gauge needles and gentle suction to obtain larger cores. The procedure is similar to that for CNB, but most devices allow for continuous sampling, without the need to remove the needle to procure the specimen and re-insert to obtain subsequent samples.

With a few subtle alterations of the above steps, one can tailor the technique from FNA to VAB. One must take care at all times, particularly with the larger, vacuum-assisted



Figure 1.6. Images from US-guided core needle biopsy using a spring-loaded device.  
a. US image depicting pre-fire positioning proximal to lesion.



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Figure 1.6. (cont.) b. US image depicting post-fire positioning within lesion.

devices, that the needle is far enough away from both the skin, superficially, and the deep pectoralis muscle, as to avoid cosmetic scarring and undue pain/bleeding.

Stereotactic needles

Stereotactic biopsy needles have evolved since the inception of this procedure. Initially, 14-gauge spring-loaded needles were used, but due to the relatively high false negative rate for sampling microcalcifications, the needle caliber has become progressively larger. At our institution, a 9-gauge needle is standard. Additionally, vacuum assistance has been employed to draw tissue into the chamber prior to cutting, which yields samples that are larger in size and greater in weight, thereby decreasing sample error. The vacuum suction is constant throughout the entire sampling procedure so the needle does not need to be repeatedly removed and re-inserted during the process. Then the samples are transported through tubing into a collection chamber that can be easily removed and radiographed en bloc. All of these developments help to decrease trauma to the breast while yielding more accurate pathologic diagnoses. This had been particularly important in the diagnosis of atypical ductal hyperplasia (ADH) vs. DCIS. The reported upgrades from ADH to DCIS are as follows:

- 14-gauge spring-loaded CNB 44%
- 14-gauge directional VAB 24%
- 11-gauge directional VAB 19% (range 0–58%)

Lesion confirmation

Radiologic–pathologic correlation is an essential component of minimally invasive breast biopsy. The two basic questions that need to be answered are (1) Was the correct lesion sampled? and (2) Are my samples representative of the lesion? Adequate sampling confirmation can occur in a number of ways depending on the biopsy modality. For both palpable and non-palpable lesions, placement of marking clips at the biopsy site, post-biopsy imaging, specimen radiographs, and radiologic–pathologic correlation all play a role in limiting false negative results. To answer the first question, in all modalities, the comparison of pre- and post-biopsy imaging is paramount, and highlights the importance of post-biopsy marker placement. In the case of stereotactic interventions, a radiograph of the sample demonstrating microcalcifications is needed. The retrieval rates of microcalcifications in the literature range from 95% to 100%. If no microcalcifications are identified, the next step is to ask for x-ray of the paraffin block to see if the calcification was left behind during processing. If no calcifications

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are identified, the sample is considered insufficient and re-biopsy is indicated. In all cases, it is important that the pathologic result provides a logical explanation for the imaging appearance of the target lesion. For example, if the lesion biopsied was clearly a mass, a pathology result of fibrofatty tissue is considered discordant. Overall, the reported incidence of radiologic–pathologic discordance ranges from 0.9% to 6.2% in the current literature. And it is vital that any lesion deemed a BI-RADS 5, with greater than 95% chance of malignancy, be excised if minimally invasive biopsy yields a benign result.

As image-guided, minimally invasive biopsies have become the standard of care, the false negative rate is decreasing. Current literature quotes a false negative rate for core needle biopsy of 2.9% to 10.0%, but it is much lower than 10.0% in our experience. This relatively high false negative rate may have been due to the previous practice of sampling microcalcifications with core biopsy, which is no longer performed. Currently, vacuum-assisted core biopsy of calcifications with an 8–11 gauge needle is the standard of care. It is also the standard when sampling intraluminal masses (mass within a cyst or duct) or a mass thought to be papillary in origin. One recent study showed a sensitivity of 28% and a specificity of 100% for core sampling alone, while both sensitivity and specificity jumped to 100% with the use of vacuum assistance. Sampling error is not usually an issue with masses, as it can be with microcalcifications. The specimens are easily obtained with a 12–14 gauge spring-loaded device.

MRI

In recent years, breast MRI has emerged as an important physiologic adjunct to the traditional, anatomic methods of screening, mammography, and high-frequency US. The American Cancer Society now recommends breast MRI as a screening tool for women at a  $\geq 20$ –25% increased lifetime risk for breast cancer. In addition to screening high-risk women, MRI is indicated for evaluating the extent of disease in patients diagnosed with breast cancer, particularly for detecting additional foci of mammographically or sonographically occult malignancy. However, while MRI has demonstrated very high sensitivity for breast cancer detection, its specificity varies widely. Most experts thus suggest careful consideration when recommending patients undergo MRI in order to minimize false positives.

BI-RADS lexicon for MRI has been developed for the purpose of improving reporting. As with mammography,

BI-RADS reporting may facilitate appropriate follow-up, improve communication of results with referring clinicians, and standardize dictations. As with mammography and sonography, lesions given a BI-RADS score of 4 or 5 on MRI are recommended to undergo biopsy.

BI-RADS MRI descriptors

- Morphology
  - Masses: irregular or spiculated borders are worrisome for malignancy (PPV 80–100%) (Figure 1.7)
  - Nonmass-like enhancement: enhancement of an area of breast parenchyma without a space-occupying effect, but distinct from surrounding tissues; further characterized by distribution and pattern of enhancement
    - Ductal enhancement: worrisome distribution pattern, with PPV 26–58.5%
    - Segmental enhancement – triangular or cone-shaped with apex directed at the nipple – represents involvement of a single ductal system, with a PPV ranging from 67% to 100%
  - Foci: enhancing lesion smaller than 5 mm whose margins cannot be well described due to size; lesions measuring less than 5 mm exhibit a very low (3%) PPV
- Enhancement kinetics
  - The enhancement kinetic curve is evaluated in two phases: initial (0–2 minutes) and delayed (typically 5–7 minutes)
  - Initial phase descriptors:
    - -slow
    - -medium
    - -fast
  - Delayed phase descriptors:
    - -persistent
    - -plateau
    - -wash-out

Carcinoma commonly exhibits a kinetic curve demonstrating a fast washout or plateau reaching maximum enhancement in the first 2–3 minutes. Persistent enhancement typically indicates benign findings. A study by Bluemke et al. using plateau vs. washout curve as indicators of malignancy found a sensitivity of 63.2% and a specificity of 65.4%. The persistent enhancement curve demonstrated 71% specificity for benign lesions. The maximum percentage of enhancement over baseline on the kinetic enhancement curve is not well defined and warrants further investigation.