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# **FOLLOW UP OF ABNORMAL CLINICAL AND IMAGING FINDINGS OF THE BREAST: FIVE SELF-STUDY MODULES FOR PRIMARY CARE CLINICIANS**

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# Breast Cancer Module IV: Follow-up of Abnormal Imaging Findings – Biopsy Methods

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## Module IV Objectives

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Understanding breast imaging findings is essential for correlation with clinical findings and subsequent plan of action to prevent a delay of diagnosis of breast cancer. At the completion of this module, clinicians will be able to:

- Identify what they should expect from a quality imaging facility;
- Distinguish between screening and diagnostic mammography;
- Describe the 6 *BI-RADS* reporting categories and the respective recommendations for follow-up; and
- List the other standard imaging modalities commonly used to distinguish the degree of suspicion for a breast lesion.

# The Mammography Quality Standards Act

## Who regulates the quality of mammography facilities?

Wide variation in the quality of mammograms performed in the United States led to the development of the mammography accreditation program of the American College of Radiology (ACR) in 1986. Results from the voluntary program led to the passage of federal legislation in 1992, the Mammography Quality Standards Act (MQSA). Congress charged the US Food and Drug Administration (FDA) with developing and implementing MQSA regulations. In 1995, the FDA began to enforce MQSA by initiating a program whereby mammography facilities are inspected annually. The ACR serves as an accrediting body under MQSA for all states except Iowa and Arkansas, which serve as their own accrediting bodies under MQSA. Final MQSA regulations were made effective on April 28, 1999. As of March 2005, there were 8930 certified mammography facilities operating within the United States.

MQSA regulations affect breast imaging quality and the expected communication of results both to the primary care screening clinician and the patient. MQSA makes it easier to determine where best to refer patients for mammography screening. By law, MQSA ensures that facilities maintain baseline quality standards based on predetermined criteria for equipment, personnel, and quality control measures. Exception is made for facilities in the Veterans Health Administration, US Department of Veterans Affairs, and the Department of Defense. They have their own set of standards with similar surveillance.

The following list summarizes the MQSA requirements:

- MQSA mandates clear, concise transmission of a radiologist's interpretation of the mammography findings by utilizing a standardized overall assessment category.
- Notification of results is an MQSA requirement:
- A mammogram report of negative or benign findings must be provided to the referring clinician within 30 days of the exam.
- Results that are suspicious or highly suggestive of malignancy must be communicated within 24-48 hours to the primary care screening clinician.
- As of April 1999, a letter providing results of the mammogram must be provided to patients. See Module V for more information on tracking and follow-up to ensure patient follow-through with recommended procedures.

In order to meet the requirements for providing lay summaries and mammography reports, facilities can either demonstrate that:

- They have notified patients within 5 days and healthcare providers within 3 days of positive examinations. In the case of verbal communication, this may be done by

documenting such communication in the mammography report or in logs. In the case of written communication, see the next 2 bulleted items.

- They have a written mammography report/copies available within 30 days of the examination if negative and 3 business days if positive.
- They have written lay summaries/copies available within 30 days of the examination if negative and 5 business days if positive. If the facility does not keep copies of the patients' lay summaries, it may document such communication in the mammography report, or in logs, or by stating in the facility's Quality Assurance (QA) manual that the lay summary is provided within the appropriate time frames.

*Or* - they can furnish written documentation describing the procedure for:

- Providing (sending or giving) the written lay summary to patients within 30 days of the examination;
- Providing the mammography report to the healthcare provider (or the patient, if self referred) within 30 days of the examination; and
- Communicating the results of positive (suspicious or highly suggestive of malignancy) examinations to patients and healthcare providers as soon as possible (as guidance, within 5 and 3 business days respectively). This communication may be verbal or written. If verbal, it must be followed by a written lay summary and mammography report provided within 30 days of the examination.
- Mammogram films shall be maintained in a permanent medical record for a period of not less than 5 years (or 10 years if there are no additional mammograms at that facility), or for a longer period of time as mandated by state or local law.
- Upon request, a permanent or temporary transfer of original mammograms and copies of the patient's reports must be sent to a medical institution, healthcare provider, or the patient directly.
- MQSA requires that mammography facilities have a consumer complaint mechanism to provide patients with a process for addressing any concerns.

For a current list of FDA-certified imaging facilities and the consumer FAQ page of FDA/MQSA, go to: [www.fda.gov/cdrh/mammography](http://www.fda.gov/cdrh/mammography).

**The quality of the imaging facility is determined by which of the following organizations?**

- The American College of Radiology
- The Mammography Quality Standards Act (MQSA) of the FDA
- The medical director of the imaging facility
- The state radiology department that issues a license to the facility

# Breast Imaging Reporting and Data System (BI-RADS)

*BI-RADS* was created by the American College of Radiology (ACR) in collaboration with the National Cancer Institute (NCI), Centers for Disease Control and Prevention (CDC), the FDA, American Medical Association (AMA), American College of Surgeons, and the College of American Pathologists to provide a quality assurance tool to communicate mammographic findings clearly and accurately. Before the development of *BI-RADS*, medical organizations such as the AMA raised concerns that mammogram reports were often ambiguous and the interpretation indecisive. Much of the problem was caused by the lack of a universally accepted set of descriptive terms and a structured lexicon based on a decision-oriented reporting system. [1-3]

## Two Categories of Mammograms

**Screening mammography** consists of 2 standard views of each breast that are complementary -- the craniocaudal (CC projection) and mediolateral oblique (MLO projection) -- to image the entire breast. Women with diffuse breast pain, a history of benign breast biopsy, fibrocystic changes, and even high-risk women should have screening, not diagnostic mammograms, unless they have a specific symptom or suspicious finding on clinical examination or mammography. Asymptomatic women with breast implants should also be screened, although additional special views to image the breast tissue should be performed.

**Diagnostic mammography** is used for women presenting with a suspicious breast sign or symptom or abnormal screening mammogram. The diagnostic mammogram may include spot-compression views to evaluate symmetric densities or better define areas of clinical concern, and magnification views to delineate the morphology of calcifications or improve visibility of masses.

**How do I order mammography as clinically indicated?** The ordering clinician is obligated to provide adequate history to justify which type of mammogram is necessary. For example, ordering a diagnostic mammogram for a woman with fibrocystic breast changes or a high-risk family history is not appropriate. An asymmetric density describes a change seen in only 1 projection of a mammogram. A focal asymmetric density can be seen in 2 projections. It becomes a mass if seen in 2 different projections and has convex, outward borders. A round or oval mass *suggests* benignity, a lobular (multiple lobes) mass generates intermediate concern, and an irregular mass *suggests* malignancy. Circumscribed margins place a mass at the benign end of the spectrum whereas spiculated (with spikes or points on the surface) margins arouse a concern for malignancy. Ultrasound is often used by the breast imager to evaluate an abnormality detected by clinical examination or mammography, and the diagnostic mammogram and ultrasound reports may be dictated together. Many clinicians find this helpful and more straightforward.

## BI-RADS Reporting Structure

The *BI-RADS* framework includes a report structure, decision-oriented approach for film interpretation, coding (of outcomes) for database management and analysis, and standard reporting language (ACR reporting categories).<sup>[4]</sup>

The mammogram reports that you receive should include the following elements:

- Brief statement concerning the reason for the exam and a patient history;
- Description of the breast radiodensity on mammography (fatty replaced, scattered fibroglandular density, moderately radiodense, or markedly radiodense);
- Description of any significant findings;
- Assessment regarding any comparison with prior mammogram studies; and
- A final assessment category with overall recommendations for further action as illustrated below in Table IV-A.<sup>[5]</sup>

**Table IV-A: American College of Radiology *BI-RADS* Categories**

<b>ACR Category</b>	<b>Assessment</b>	<b>Probability of Cancer</b>	<b>% of Screening Mammograms</b>
<b>0</b>	<b>Assessment incomplete</b> - need additional imaging or comparison films (screening mammography only)	NA	≤ 10%
<b>1</b>	<b>Negative</b> – no further imaging suggested; routine follow-up	NA	> 90% of screening mammogram (exact number depends on population being screened by that facility)
<b>2</b>	<b>Benign findings</b> - negative; no further imaging suggested; routine follow-up (see specifications for use that follow)	NA	
<b>ACR Category</b>	<b>Assessment</b>	<b>Probability of Cancer</b>	<b>% of Diagnostic Imaging Evaluations</b>
<b>3</b>	<b>Probably benign</b> – short interval follow-up suggested	< 2%	4%
<b>4</b>	<b>Suspicious abnormality</b> – biopsy should be considered	3%-49%	2/1000 to 8/1000 (exact number depends on population being screened by that facility)
<b>5</b>	<b>Highly suggestive of malignancy</b> – appropriate action should be taken	≥ 95%	

6	Known biopsy-proven malignancy – appropriate action should be taken	NA	NA
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NA = not available

The referring clinician's understanding of the ACR reporting categories can help him or her to make the patient aware of whether an abnormal finding on a mammogram is likely to be benign or malignant. However, other tests that are diagnostic are always necessary to reach a definitive diagnosis for categories 0, 4, or 5.

**A diagnostic mammogram should be ordered for all but which one of the following clinical scenarios?**

- Palpation of an asymmetrical discrete mass
- Spontaneous asymmetrical nipple discharge
- Women with dense breasts
- Asymptomatic women with a personal history of breast cancer
- Women with breast implants

## Recommendation Summary

- As the primary care clinician, you can only offer the patient information if you know and understand the ACR reporting categories that the radiologist uses.
- As the primary care clinician, you must correlate the imaging result with the clinical finding and look for concordance. If discordant, more workup is necessary until there is concordance (see double/triple test later in this module).
- Although the radiologist recommends follow-up for your patient, you, the primary care clinician, are responsible for formulating a plan for your patient and for encouraging your patient to follow this plan. This is especially important in the case of the asymptomatic patient with imaging findings. This is equally important for patients who have a suspicious clinical finding, but a negative diagnostic imaging evaluation.

## Workup: BI-RADS Categories

Accurate and reliable communication between the radiologist and the referring clinician is the basis for sound radiology consultation. Regardless of the finding, the primary care clinician must have an effective rapport with the radiologist so that important patient information can be exchanged. For example, providing specific and standard documentation of the clinical breast examination (CBE) (see Module II) or significant patient history to the radiologist is a critical element of a thorough mammogram evaluation.

### What is a Category 0 finding?

Incomplete - Need Additional Imaging Evaluation or Prior Mammograms for Comparison

**The finding** - In this case, additional imaging is needed. This is only to be used in a screening situation and cannot be used after a full imaging workup.

**The recommendation** - Spot compression magnification, ultrasound, magnetic resonance imaging (MRI), or special views are required to better assess a finding. There may be occasions where the image is less than optimal due to a processing issue or patient motion during the exam, and should be repeated for better assessment. If possible, comparison with prior studies should be done if recommended by the radiologist, as this may help to obviate the need for a patient recall or even biopsy of a lesion, if it can be demonstrated as unchanged from a prior examination. The radiologist should use judgment in how persistently to pursue previous studies if the films were done at a different facility.

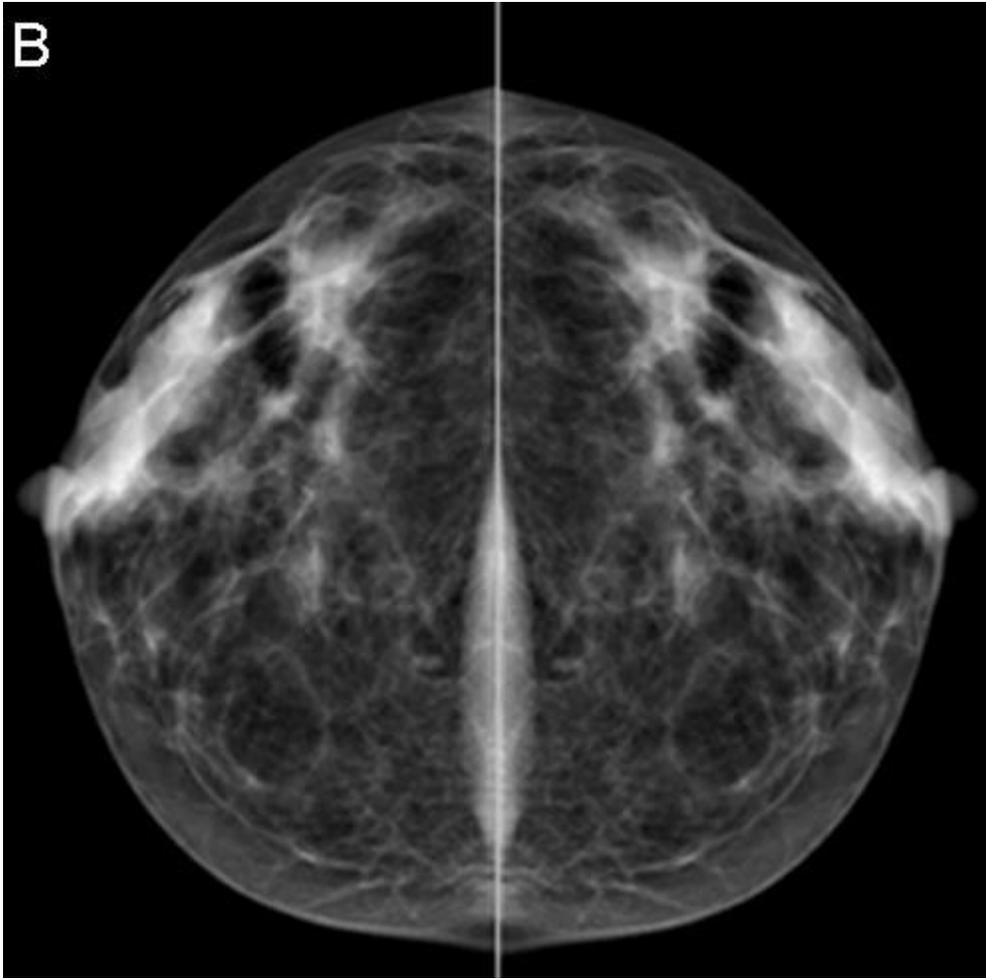
For women with dense breast tissue, ultrasound is a complementary tool to evaluate abnormalities not visualized by mammography. <sup>[6-10]</sup>

### **What is a Category 1 finding?**

Figures 1A and 1B demonstrate mammography views with Category 1 findings.



Figure 1A. Mammography MLO views: the breasts are symmetrical with no abnormal findings. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.



**Figure 1B.** Mammography CC views: the breasts are symmetrical with no abnormal findings. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

### **Negative**

**The finding** - The breasts are symmetrical and no masses, architectural disturbances, or suspicious calcifications are present.

**The recommendation** - Repeat the mammogram yearly or at age-appropriate screening intervals.

**Caution** - Even in the face of a Category 1 finding, any decision for further evaluation should be based on a suspicious CBE and will almost always warrant a biopsy of some sort.

### ***What is a Category 2 finding?***

Figures 2A through 2E show Category 2 findings on mammography and ultrasound.

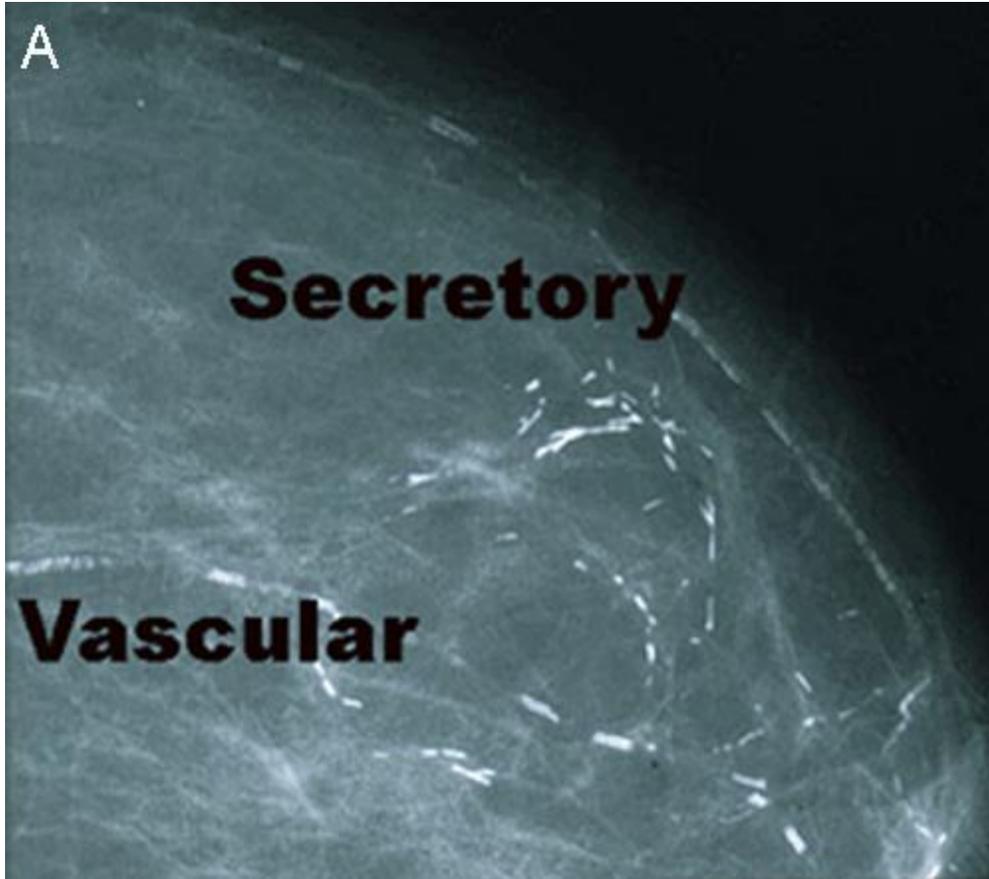


Figure 2A. Benign calcifications on mammogram, including secretory calcifications (ductal ectasia) and vascular calcifications. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

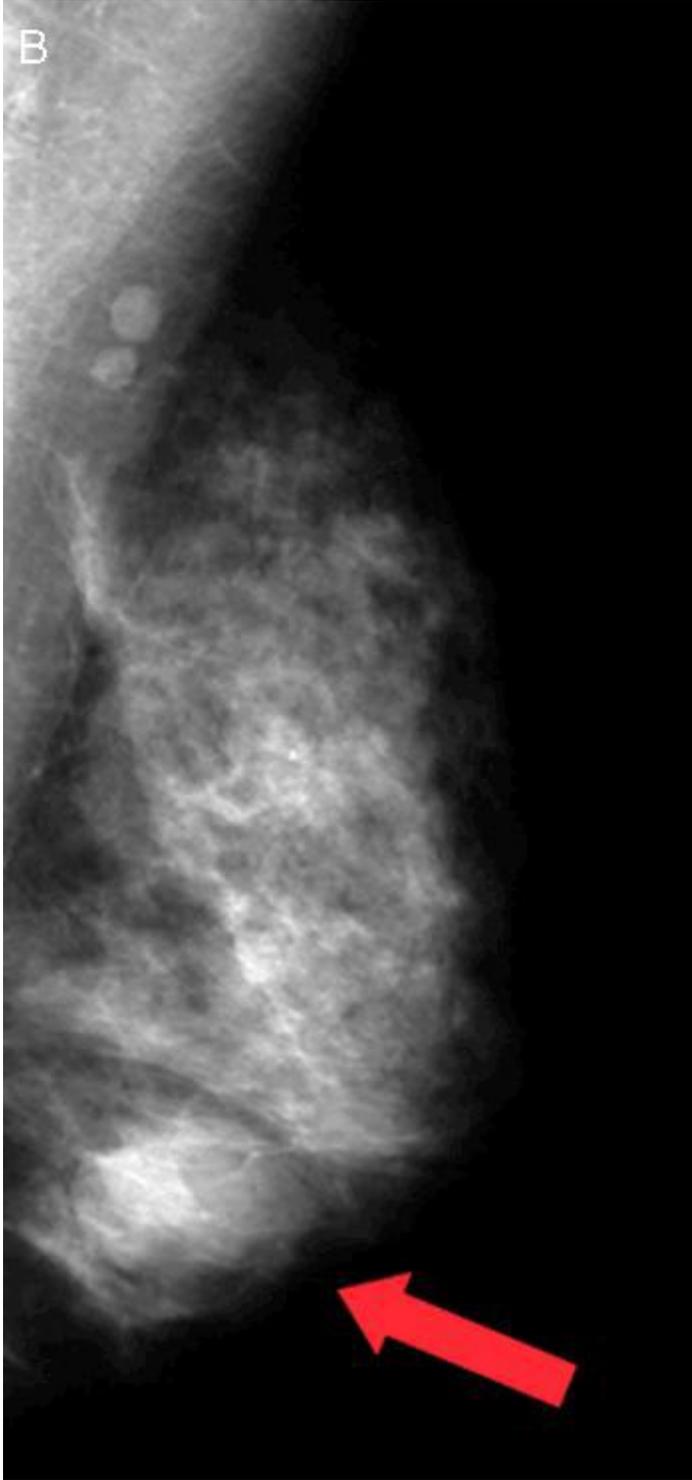


Figure 2B. Cyst. Mammography shows oval mass. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA

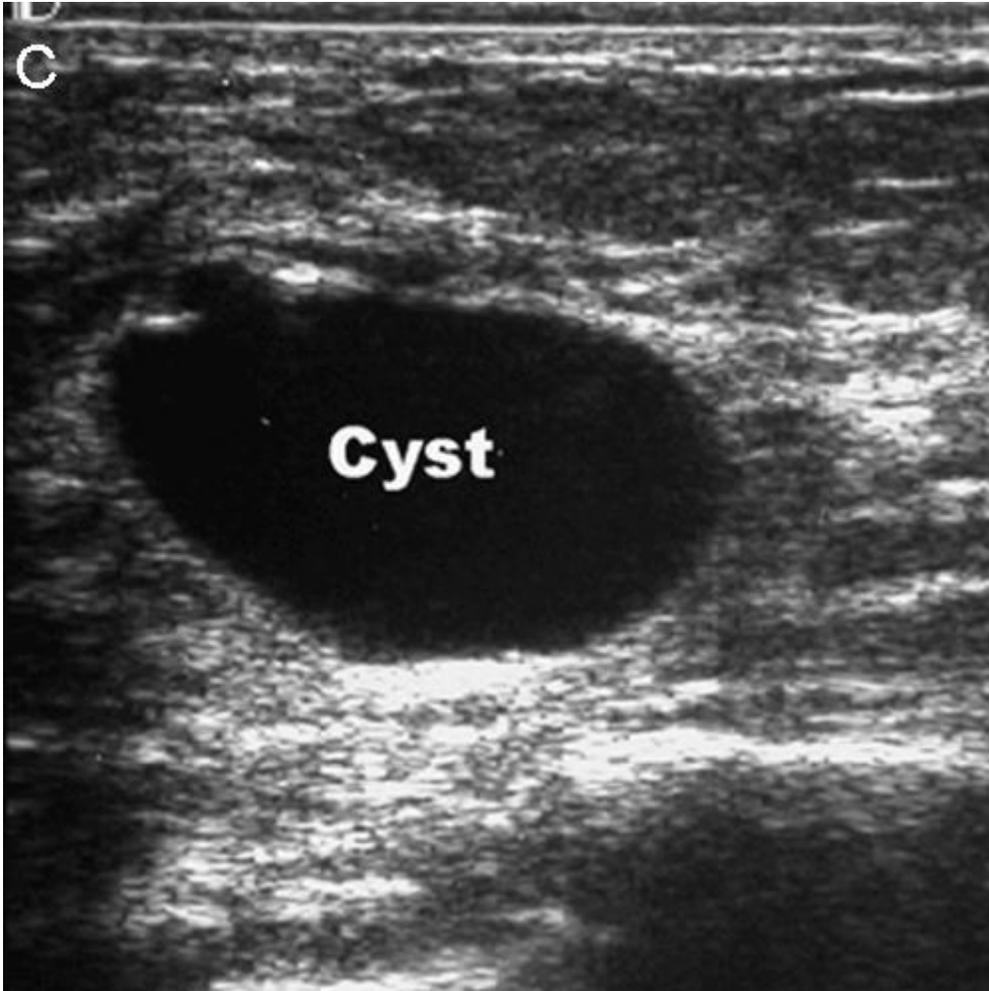


Figure 2C. Cyst. Ultrasound shows classic cyst with smooth margins, no internal echoes (anechoic) and enhanced through transmission of sound. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

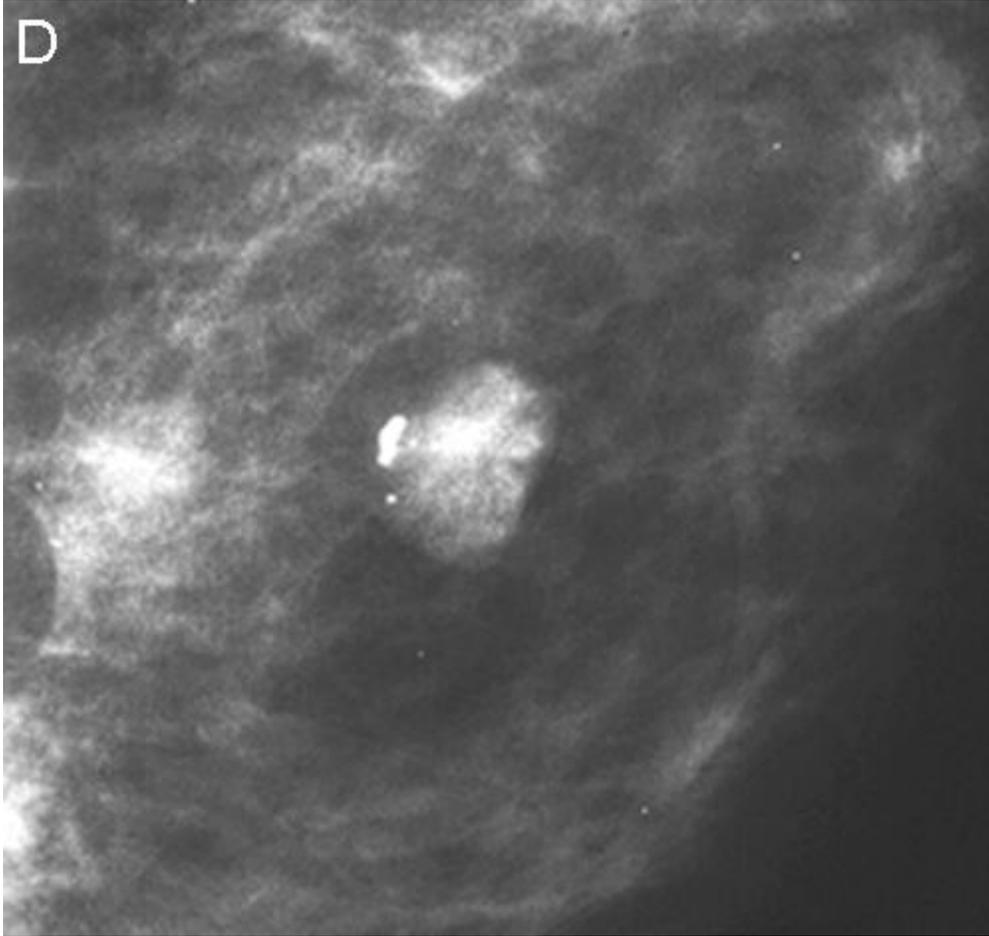
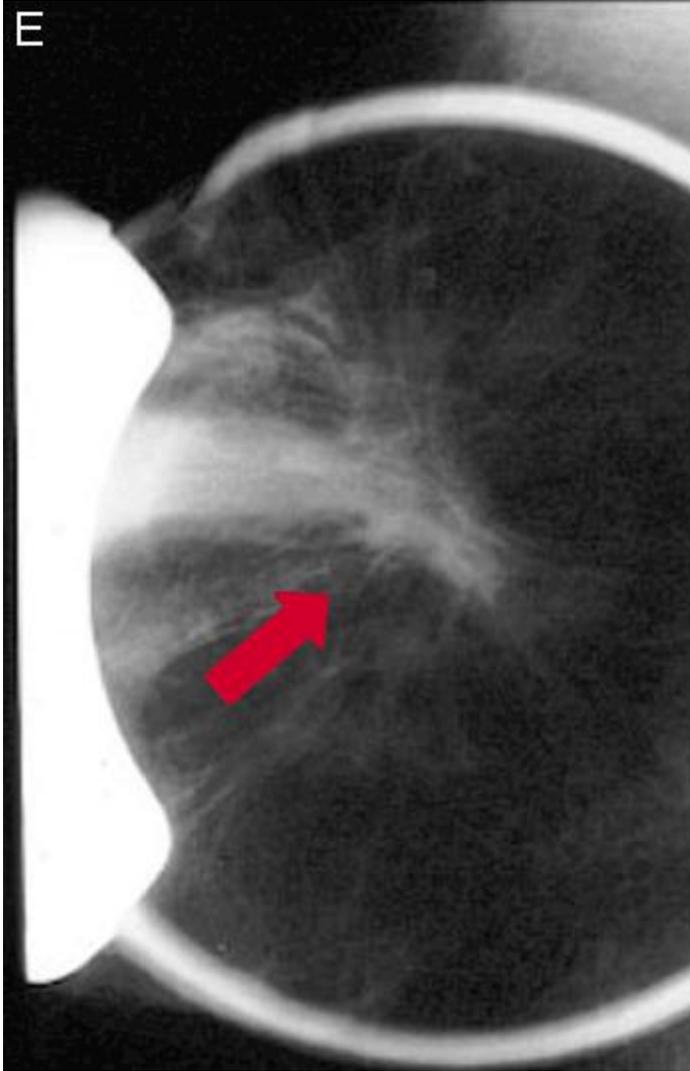


Figure 2D. Fibroadenoma. Mammography shows circumscribed mass with benign calcification. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.



**Figure 2E.** Postsurgical scar. Patient had a previous biopsy showing a fibroadenoma. This architectural distortion was caused by the previous surgery. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

***Benign Finding(s)***

**The finding** - In this case, again the mammogram is normal. The radiologist may wish to describe a benign finding. Involving calcified fibroadenomas, multiple secretory calcifications, postsurgical scars, and fat-containing lesions such as oil cysts, lipomas, and mixed-density hematomas all have characteristic appearances and may be labeled with confidence. The radiologist may also wish to describe inframammary lymph nodes, vascular calcifications, implants or architectural distortion clearly related to prior surgery while still concluding that there is no mammographic evidence of malignancy or need for further evaluation of an existing lesion.

**The recommendation** - Repeat the mammogram yearly or at age-appropriate screening intervals.

**Caution** - Any decision to biopsy should be based on a suspicious CBE finding that is not concordant with the imaging finding. If there is a palpable finding and an ultrasound was not performed as part of the imaging workup, ultrasound may be helpful, particularly if the breast tissue is dense.

### **What is a Category 3 finding?**

#### **Probably Benign - Initial Short-Interval Follow-up Suggested**

A Category 3 finding can only be issued with diagnostic mammography, so it cannot be issued for a screening mammogram (2 standard views). While this finding is not expected to change over the follow-up interval, the radiologist would prefer to establish its stability, so a short-term follow-up is suggested and a time frame should be specified (usually 6 months). Short-term follow-up should include a repeat unilateral mammogram (ultrasound included as indicated by the radiologist) to establish stability and then an interval bilateral mammography or ultrasound follow-up annually for the next 2 years, at which time the finding is considered benign.[11] For occult abnormalities *only*, the patient may be unwilling to accept the low, but possible, risk of a delayed diagnosis of cancer; hence, the primary care clinician may want to refer to a surgeon or to a radiologist who can perform a core needle biopsy (CNB), stereotactic needle biopsy, or fine needle aspiration (FNA) biopsy with cytology. This option may markedly decrease the number of excisional biopsies performed on benign lesions while not sacrificing the opportunity to detect early breast cancers. This should be the patient's choice; however, adherence to the recommended follow-up strategy is critical to the success of this management approach.

The primary care clinician's decision to plan a workup is based on the radiologist's recommendation and description in the report of the mammographic appearance and the patient's family history, history of breast cancer, and other significant risk factors.

#### **The Role of Ultrasound in Category 3 Findings**

- Breast ultrasound has evolved into the primary *adjunctive imaging* modality. The numbers of patients with palpable or nonpalpable lesions being referred for ultrasound have increased in recent years. Although it was frequently used as a tool to distinguish solid from cystic lesions in settings where trained radiologists or surgeons were available, ultrasound has been adapted to characterize lesions based on a strict set of criteria that allow lesions to be better selected for biopsy or follow-up approaches.

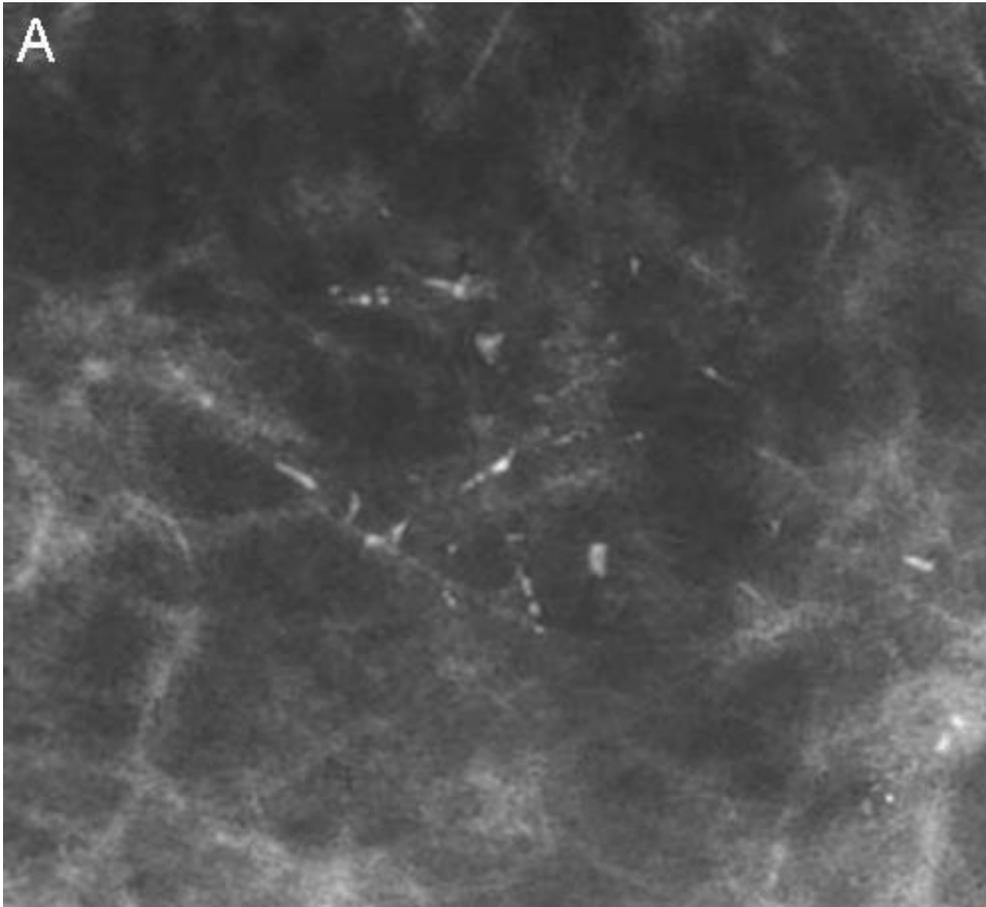
#### **Summary Recommendations for Category 3 Findings**

- Short-interval follow-up if expectation is that lesion is benign, followed by periodic imaging studies to assess biologic stability (surveillance over a 2-year period);

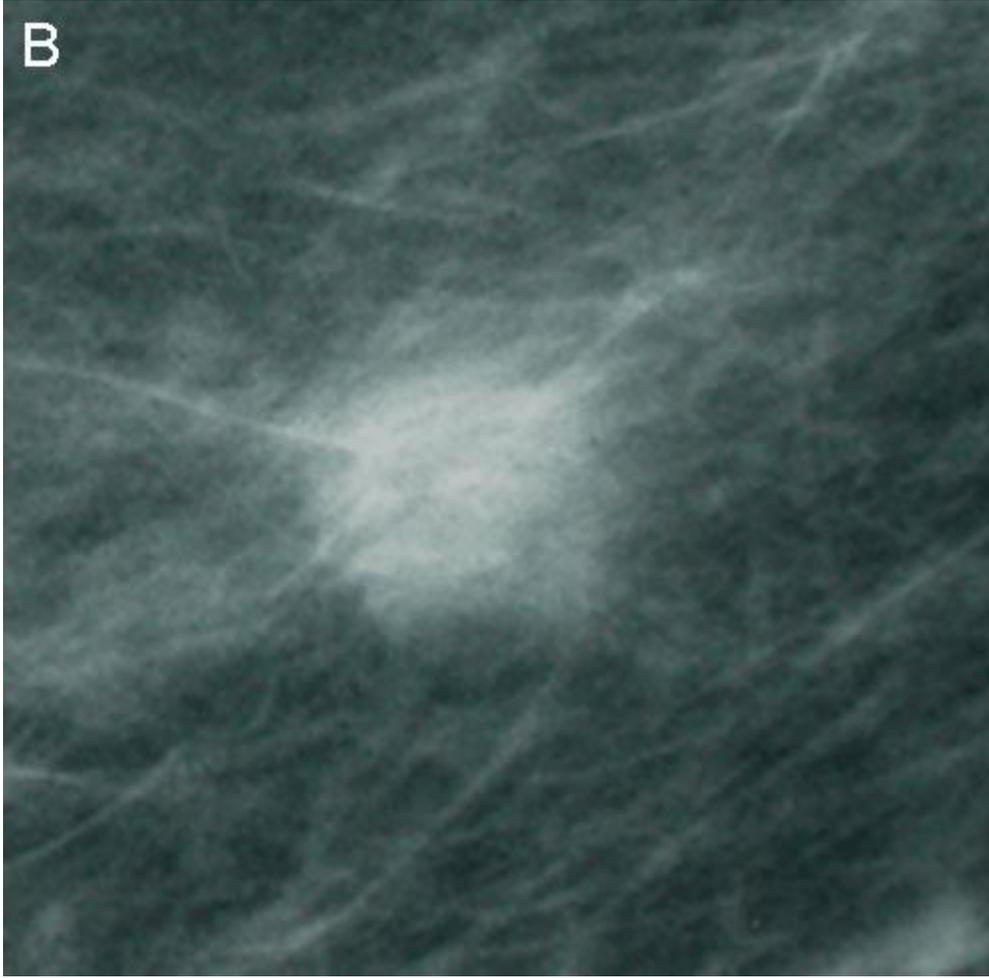
- Referral to surgeon or radiologist for second opinion or tissue diagnosis if elected by patient or clinician;
- Keep in mind the preference of the patient and the ability to adhere to a follow-up strategy; and
- Consider a 3-month follow-up CBE to detect any interval change; a new clinical finding should warrant immediate referral for biopsy.

### **What is a Category 4 finding?**

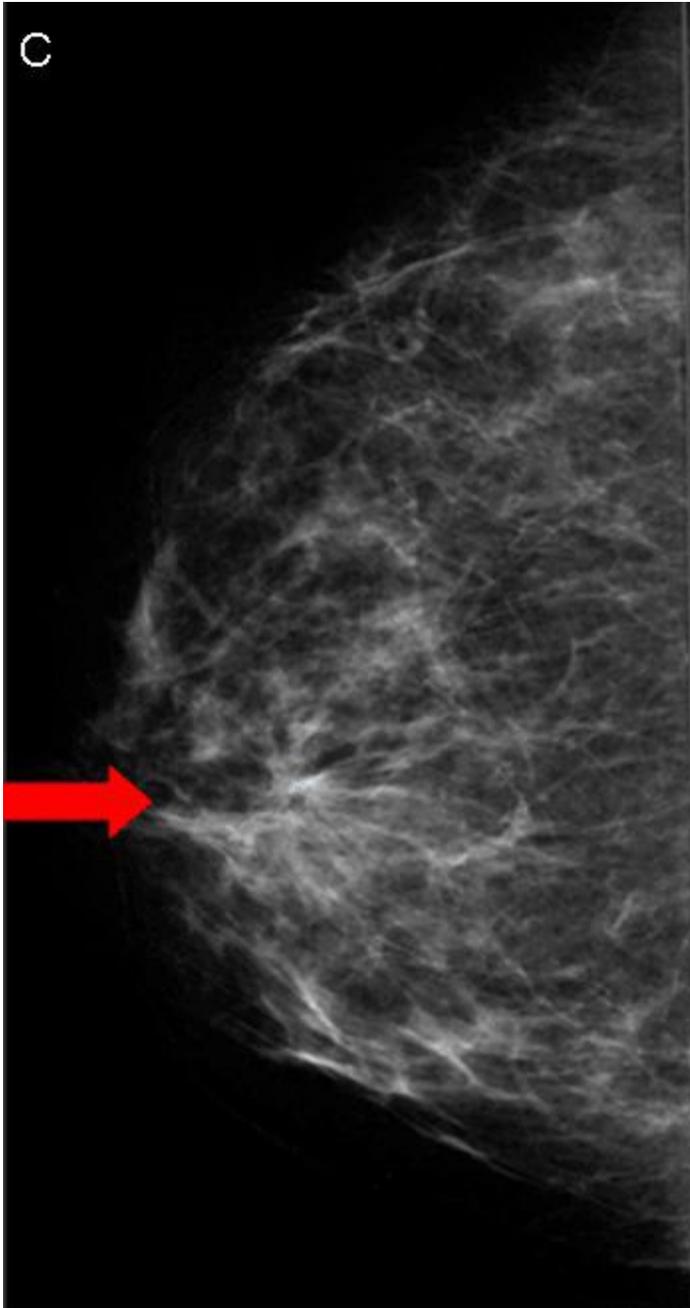
See Figures 3A through 3C, showing Category 4 findings on calcifications, a mass with ill-defined margins, and lobular carcinoma, as shown by mammography.



**Figure 3A.** Calcifications: Mammography shows suspicious calcifications which are heterogeneous (pleomorphic) and appear to be distributed in a linear branching distribution. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.



**Figure 3B.** Mass: Mammography shows a mass with ill-defined margins. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.



**Figure 3C.** Lobular carcinoma: Craniocaudal mammography shows a subtle architectural distortion which proved to be an invasive lobular carcinoma at biopsy. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

### **Suspicious Abnormality - Biopsy Should Be Considered**

If the mammogram finding is "suspicious," the radiologist should have a tracking system in place to ensure timely follow-up for both the referring clinician and the woman. To be effective, active communication between clinicians is necessary to ensure that communication with the woman is

coordinated as well as any follow-up procedure because of the greater chance of a breast cancer diagnosis.

**The finding** - Category 4 is reserved for findings that do not have the classic appearance of malignancy but have a range of probability of malignancy that is greater than those in Category 3. Thus, most recommendations of breast interventional procedures will be placed within this category. Category 4 can be subdivided into 4A, 4B, and 4C (moderate suspicion) to indicate relevant probabilities for malignancy so an informed decision on the ultimate course of action can be made.

**The recommendation** - Category 4 and 5 are usually a result of a diagnostic imaging evaluation that includes additional views and/or ultrasound. The diagnostic imaging is done with the interpreting radiologist in attendance so that the exam may be tailored to the woman's breast findings. Additional imaging studies should be completed before surgical referral. Most patients will require a CNB of a nonpalpable mammographically detected abnormality.

### What is a Category 5 finding?

Figures 4A and 4B show Category 5 findings on a palpable mass, as viewed on mammography and ultrasound.

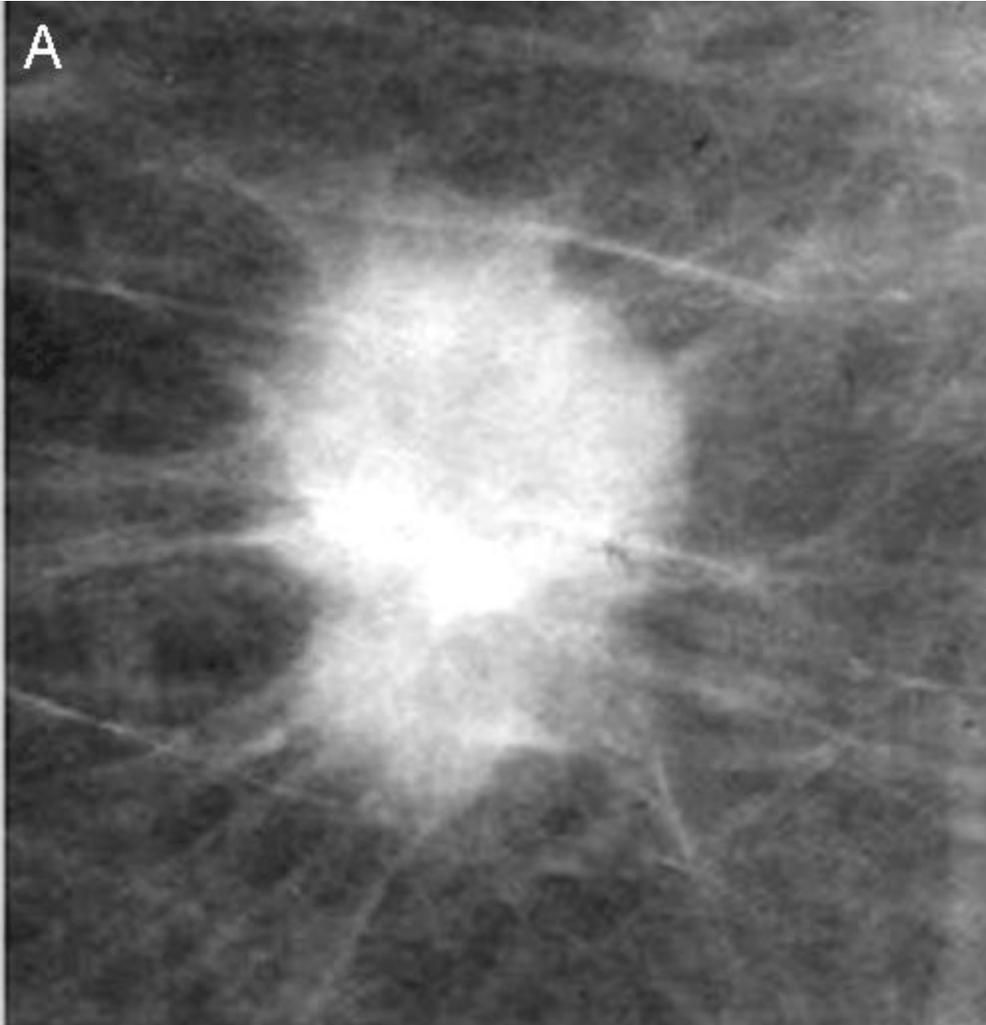
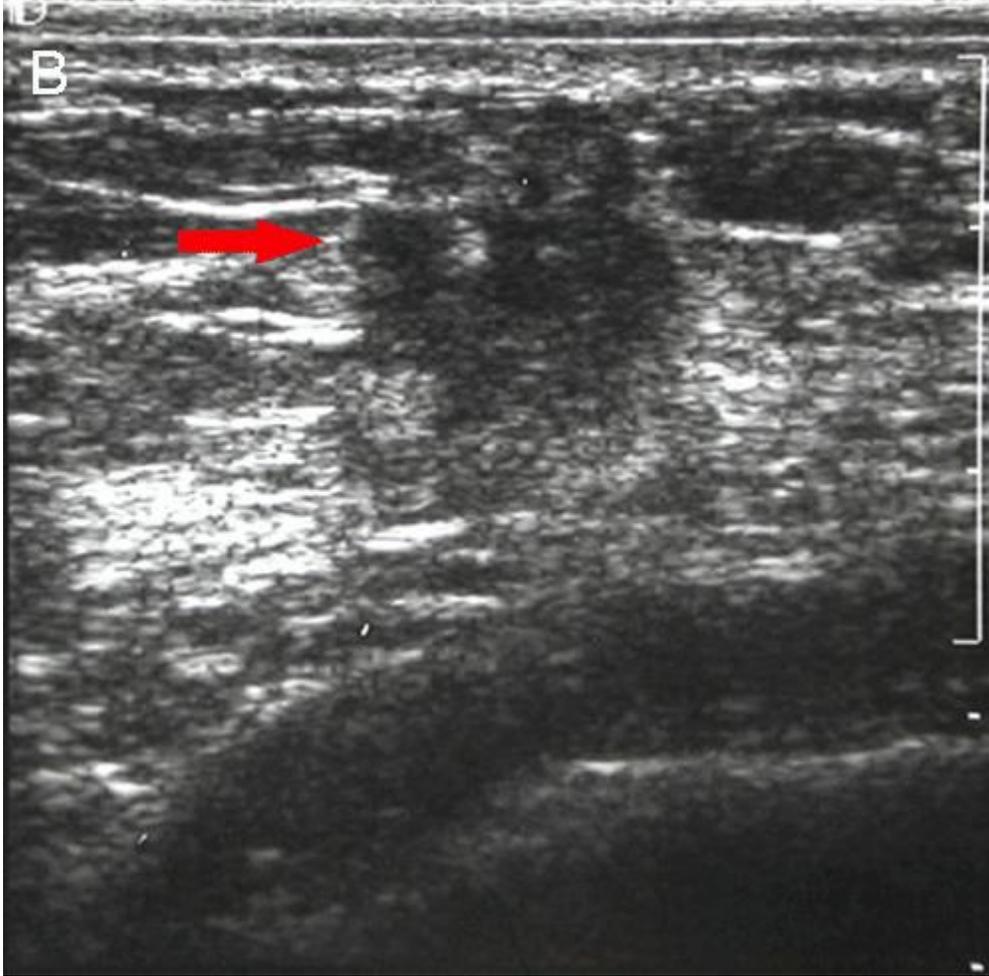


Figure 4A. Mammography of palpable mass that is BI-RADS 5. Irregular shape and spiculated margins. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.



**Figure 4B.** Ultrasound of the mass (arrow) that is BI-RADS 5. Irregular shape, not parallel to the surface of the breast (taller-than-wide), heterogeneous internal echoes, posterior acoustic shadowing, interrupts normal breast fascial planes. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

### **Highly Suggestive of Malignancy - Appropriate Action Should Be Taken**

Category 5 lesions have a high probability of cancer,  $\geq 95\%$ . Immediate action should be taken. Category 5 indicates classic findings of malignancy that could go on to definitive therapy without tissue diagnosis, although current oncologic management may require percutaneous tissue sampling as, for example, when sentinel node imaging is included in surgical treatment or when neoadjuvant chemotherapy is administered at the onset. For Categories 4 and 5, follow-up is considered timely if, from the time of the screening mammogram, follow-up procedures and documentation of follow-up results, including a final diagnosis in the patient's record, are completed within 60 days.<sup>[11]</sup> As with Category 4, timely and appropriate follow-up between the radiologist, primary care clinician, and the patient is critical to the likelihood of a breast cancer diagnosis with this category.

## Summary Recommendations

With rare exception, all mammograms with a Category 4 or 5 interpretation will lead to a tissue biopsy, such as:

- FNA;
- CNB (by stereotaxis, ultrasound, or palpation automated gun or vacuum-assisted device);
- Needle-directed surgical biopsy for nonpalpable lesions (done by a surgeon with a needle placed by the radiologist); or
- Excisional biopsy of a palpable finding (done by surgeon).

Developing a strong partnership with your radiologist is vital to you and your patients to ensure appropriate follow-up in a timely manner.

### What is a Category 6 finding?

#### Known Biopsy-Proven Malignancies - Appropriate Action Should be Taken

This category is reserved for lesions identified on the imaging study with biopsy proof of malignancy prior to definitive therapy. This is the appropriate category to utilize for second opinions on lesions previously biopsied and shown to be malignant or for the monitoring of responses to neoadjuvant chemotherapy prior to surgical excision.

**Recommendation** - There is no associated intervention required to confirm the malignancy for the finding.

## Other Imaging Modalities

### Full-Field Digital Mammography (FFDM)

Digital mammography allows x-ray images made from breast tissue to be recorded and processed on a computer to afford a closer look at variations within the breast tissue. The procedure for taking a digital mammogram is the same as for a conventional mammogram; however, the computer-generated image allows for online image magnification. Although this technology is probably the single biggest advance in mammography technology in 30 years, it has still not proven to be better than the gold standard of conventional film-screen mammography for women with average breast density. The overall diagnostic accuracy of digital and film mammography as a means of screening for breast cancer is similar, but digital mammography is more accurate in women under the age of 50 years, women with radiographically dense breasts, and premenopausal or perimenopausal women.<sup>[12]</sup>

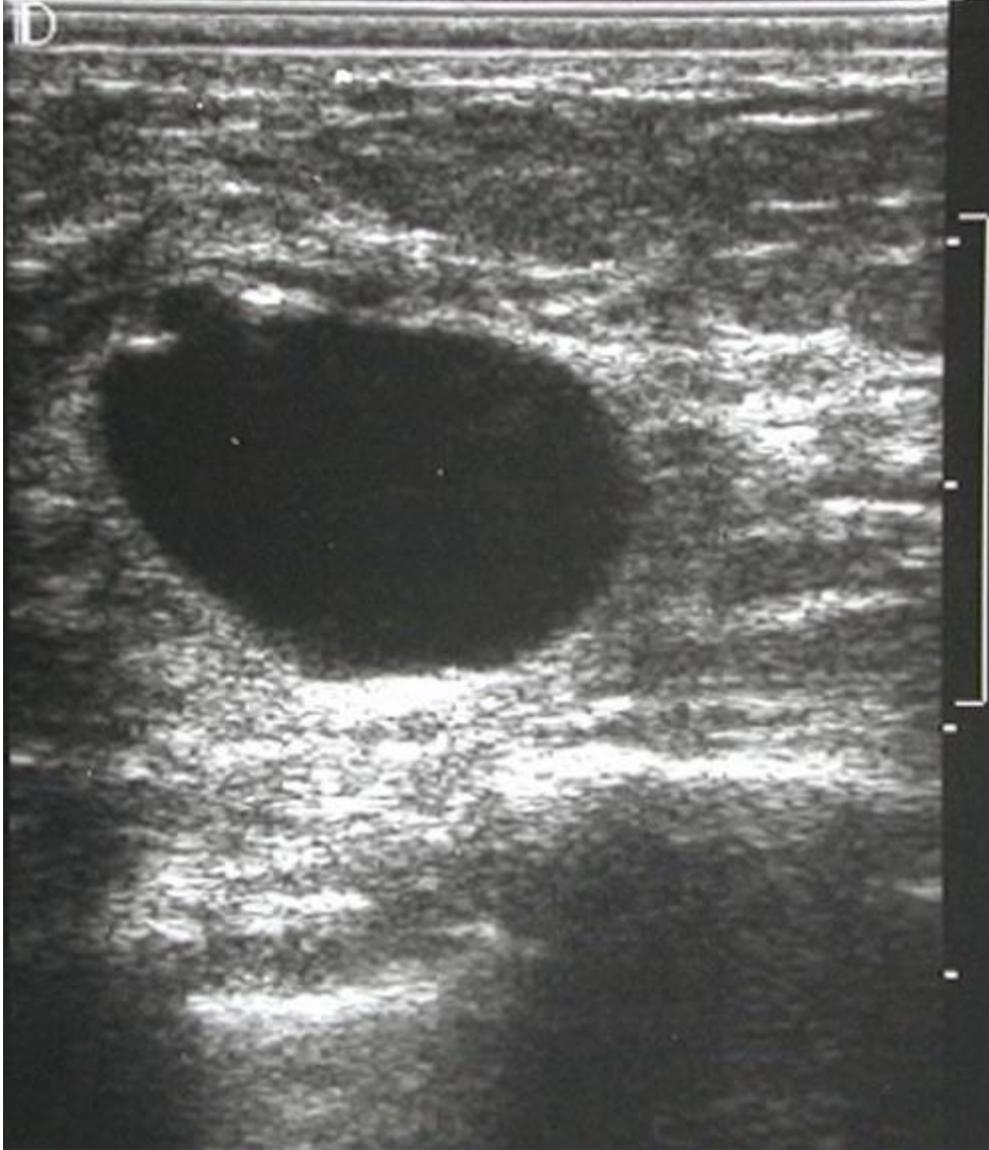
One of the biggest limitations of FFDM is the lack of a standard for reviewing the images. FFDM has recently gained FDA approval for screening and diagnosing breast cancer. Individual

insurance companies are still drafting policy for reimbursement for this procedure, although it has been a reimbursable procedure by selected payers since 2001.

## **Ultrasound**

Ultrasound is an important adjunctive imaging modality for evaluation of detected abnormalities (Figure 5). Current uses for ultrasound include:

- Evaluation of palpable masses not seen or only vaguely seen on mammography in patients of all ages;
- Evaluation of palpable breast abnormalities in women 40 years of age or younger;
- Evaluation of a mammographically detected mass or distortion (not used to evaluate calcifications per se, but can be used to determine if there is an accompanying mass in women with dense breasts);
- Evaluation of an indeterminate palpable finding such as thickening or vague mass;
- Performance of image-guided tissue sampling procedures;
- Evaluation of extent of disease in newly diagnosed breast cancer diagnosis (detection of multifocality, especially in dense breasts where lesions may be missed on mammography) and evaluation of the size of the primary tumor;
- Evaluation of lymph node basins and biopsy as indicated to help in staging and surgical management of node-positive women;
- Evaluation of tumor response to neoadjuvant chemotherapy; and
- Second look after MRI reveals an enhancing lesion not previously anticipated.



**Figure 5.** Simple cyst on ultrasound, with smooth margins and absence of internal echoes. Republished with permission from Dr. Lawrence Basset, radiologist, UCLA.

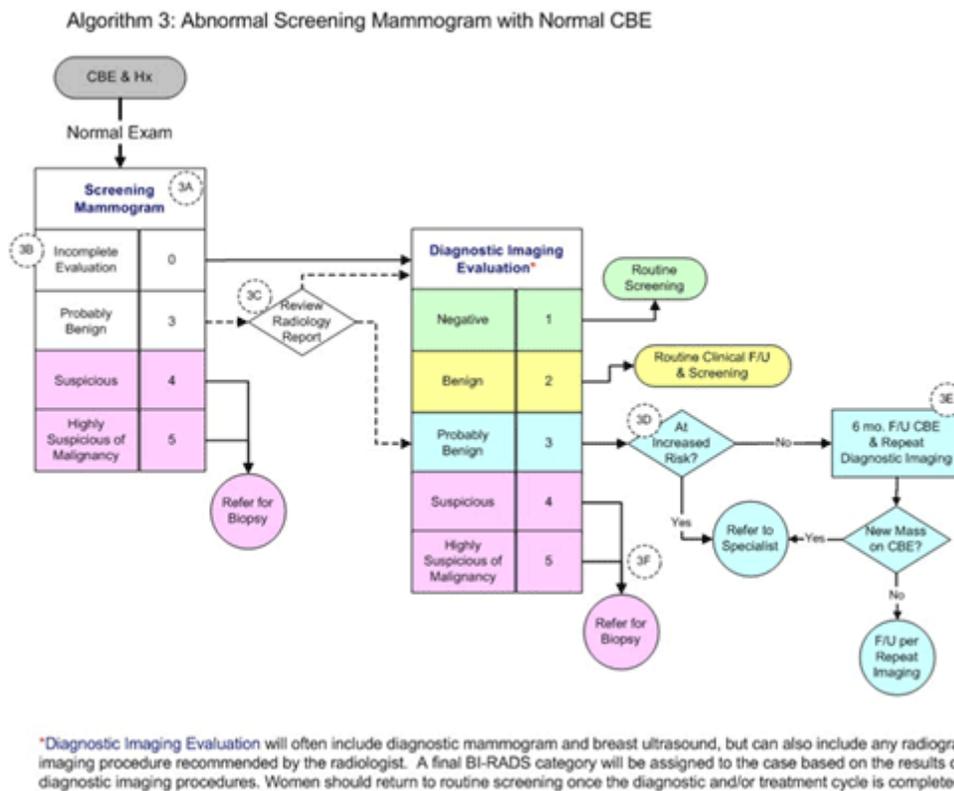
Benign simple cysts have the following characteristics:

- Round or oval;
- Sharply defined margins;
- Lack of internal echoes; and
- Posterior acoustic enhancement.

Suspicious characteristics include:

- Hypo echoic;
- Microlobulations;
- Oval shape or more tall than wide; and
- Posterior acoustic shadowing.

See Figure 6 (Algorithm #3) [13] for guidelines on the workup of an abnormal screening mammogram with normal CBE.



**Figure 6.** Algorithm for workup of abnormal screening mammogram with normal CBE.

Republished with permission from the professional education cancer detection section, California Department of Health Services.

## **Computer-Aided Detection (CAD)**

CAD is an adjunct to mammography and uses computer programs to mark suspicious areas in breast tissue. It does a "second read," putting signals on areas where the radiologist should focus attention. It is unclear whether CAD improves the accuracy of screening mammography. There remains controversy over the use of CAD, as cancer detection rates may be slightly enhanced by using this approach. Since 2001, reimbursement for this procedure is gaining greater acceptance, but remains a subject for further efficacy studies for the CDC and other public reimbursement programs. <sup>[9]</sup>

## **Magnetic Resonance Imaging**

This technology is quite sensitive and generates images from signals sent out by nuclear particles in a magnetic field. Many trials are under way to find its most useful purpose in the workup of breast abnormalities. MRI does not replace screening mammography, the standard for all women. MRI is often used in conjunction with mammography for the following cases:

- Presurgical evaluation for the extent of disease in newly diagnosed patients after a cancer diagnosis has been made (contralateral breast is particularly important in lobular cancer, which can be bilateral);
- Evaluation of women with extremely dense breast tissue where other modalities would not be as sensitive or specific;
- Evaluation of extent of disease post surgery if margins suggest residual cancer;
- Ascertaining the possibility of a ruptured breast implant using contrast MRI;
- Deciding on the response to chemotherapy during neoadjuvant use;
- Searching for an occult primary breast cancer in a patient with positive lymph nodes;
- Detecting recurrences in women who have been treated conservatively for breast cancer; and
- As a screening test for breast cancer in women at high risk for the disease (e.g., BRCA1/2 carriers).

## **Positron Emission Tomography (PET)**

A diagnostic imaging procedure, PET uses radioactive substances that are intravenously administered to the patient. Often, PET scans are used as an adjunct or complement to x-ray technology for restaging patients with local, regional, or distant metastasis; changing therapies from one chemotherapeutic agent to another; changing the type of treatment; and detecting recurrences.

## **Biopsy Methods**

The majority of both palpable and nonpalpable lesions are not malignant, but for most cases, it is not possible to make that determination definitively without microscopic tissue examination

(cyst and calcified Category II fibroadenoma are exceptions). Historically, surgical excision biopsy was considered the gold standard for tissue diagnosis, but this is no longer desirable, due to cost, morbidity, and the frequent multifocal nature of breast masses requiring multiple surgical procedures. Therefore, other, less invasive biopsy procedures, such as FNA biopsy (for cytology) or CNB, are employed. Choice of biopsy method should be based on the availability of expertise to perform the biopsy and interpret the pathologic findings. CNB and FNA are more cost effective and results in fewer operative procedures, for patients with both benign and malignant lesions (palpable and nonpalpable). Other factors to consider include location of the lesion within the breast and, in the case of nonpalpable lesions detected on mammography, mammographic appearance. FNA and CNB can be performed on palpable lesions using palpation guidance or non-palpable lesions using imaging guidance.

### ***FNA Cytology***

***For specialists with expertise***, FNA is useful for the evaluation of palpable lesions, since the frequency of palpable lesions requiring evaluation is high, the incidence of cancer is very low, and the procedure is more easily tolerated due to the 22- or 25-gauge needle employed. The procedure is not commonly done in primary care settings because of the skill necessary to aspirate effectively and the cytology expertise necessary to interpret the results. All clinicians who perform FNA biopsy must wait 2-6 weeks (depending on the effectiveness of the procedure) to perform imaging as the blood shadow on mammography and ultrasound is compromised.

**Key Message:** For nonpalpable lesions, CNB is preferred due to the ability to distinguish in-situ carcinomas from invasive carcinoma, or well-differentiated carcinoma like tubular carcinoma from fibrocystic change.

### **Benefits:**

- Diagnosis can be obtained more rapidly than by CNB or excisional biopsy since overnight histologic processing is not required.
- Sample adequacy can be evaluated at the time of the procedure if a cytologist is present.
- Lower cost than either CNB or excisional biopsy since processing cost is lower.
- Palpable lesions can be sampled in the office or clinic setting as an extension of the physical exam.
- Lower morbidity than either surgical biopsy or CNB, chiefly consisting of an occasional small hematoma, and minimal to no discomfort during the procedure due to the use of a 22- or 25-gauge needle.
- Specialized equipment is not required.
- Diagnostic accuracy is 98% if employed as part of the "triple test"<sup>[14]</sup> (see section on diagnostic concordance below).
- Useful in resectable and unresectable tumors.
- Allows preoperative counseling and can help select, guide, and modify surgery.

### **Limitations and Diagnostic Pitfalls:**

- Common causes of false-negative diagnoses are sampling errors due to errors in needle placement, highly sclerotic cancers, such as infiltrating lobular carcinoma, and uncommon well differentiated ductal carcinoma subtypes, such as tubular or papillary carcinomas.<sup>[15-17]</sup>
- False-positive diagnoses are extraordinarily rare when they are interpreted by experienced cytopathologists. Slightly more common are false diagnoses<sup>[11]</sup> among suspicious lesions (which can occur in fibrocystic change with moderate to florid epithelial hyperplasia, complex fibroadenomas, or hyperplasia due to pregnancy or lactation<sup>[15-17]</sup>). Adequate sampling is highly operator dependent and requires special training. An individual's false-negative rate should not exceed the threshold established by the laboratory<sup>[18]</sup>
- Pathologic interpretation requires special expertise, possibly requiring a subspecialist (cytopathologist). Primary care clinicians should be aware of who has this special expertise in their communities, and request overread of slides by an experienced cytopathologist if there is any question about the diagnosis.
- Usually not appropriate for lesions composed of clustered microcalcifications.
- In situ carcinoma cannot be distinguished from invasive carcinoma, nor can ER/PR and Her-2 neu status be determined

### **Core Needle Biopsy**

CNB is usually the preferred biopsy method for nonpalpable lesions, since it can more readily distinguish in situ carcinomas from invasive carcinoma, or well-differentiated carcinoma (such as tubular carcinoma) from fibrocystic change. These lesions occur with greater frequency in nonpalpable lesions, and FNA would not be able to make these distinctions.

CNB of the breast provides a core of tissue for histologic evaluation, and when properly done in appropriately selected patients, is a safe, well tolerated, and cost-effective alternative to surgical biopsy. Any pathologist can interpret large-CNB specimens, and they can provide a specific histologic diagnosis. When a mass is palpable, a surgeon sometimes does this type of biopsy. A nonpalpable mass detected at screening mammography can be biopsied by a radiologist using ultrasound or mammographic (stereotactic) guidance. Core biopsy is a sampling technique and is not intended to remove the lesion. For this reason, the histologic result must be consistent with the imaging findings. If it is not, repeat biopsy is mandatory. Patients with histologically benign findings that are concordant with the imaging findings may be followed with imaging for 2 years after biopsy to exclude the 1% to 2% sampling error rate (or missed malignant lesion) of this type of biopsy.<sup>[19-22]</sup> The radiologist or surgeon who performs the biopsy is responsible for

comparing the histology results with the imaging findings and for making follow-up recommendations.<sup>[23,24]</sup> The follow-up interval will usually be the same as for Category 3 lesions (i.e., 6, 12, and 24 months). When a fibroadenoma is diagnosed by core biopsy, the 6-month follow-up may be omitted. If histologic results from a core biopsy include atypical hyperplasia or radial scar, follow-up with excisional biopsy is necessary.<sup>[22, 25, 26]</sup>

### **Benefits:**

- CNB is less expensive than surgical biopsy.
- Palpable lesions can be sampled in the office or clinic setting as an extension of the physical exam.
- Morbidity is lower than that of surgical biopsy.
- Subspecialist expertise for pathologic interpretation is not required.
- It is appropriate for most palpable and nonpalpable lesions, including suspicious clusters of microcalcifications.[16]
- In situ carcinoma can be distinguished from invasive carcinoma.
- It is useful in resectable and unresectable tumors.
- In cases of carcinoma, it aids in patient decision making as sentinel node biopsy can be done at the same time, and it allows preoperative counseling and can help select, guide, and modify surgery.
- It is associated with a "cancer-miss" rate of 2%.[27]
- For women with a cancer diagnosis, it reduces the number of total surgical procedures.
- Morbidity is greater than that associated with FNA biopsy, with more bruising and tenderness that may limit activities for approximately 1 day, and more discomfort during the procedure due to use of an 11- or 14-gauge needle.
- Special equipment is required.
- Adequate sampling is operator dependent and requires special training.
- Overnight specimen processing is required, leading to greater expense and longer turnaround time for diagnosis, as compared with FNA.

### **Open Surgical Excision Biopsy**

Surgical removal of breast tissue was the gold standard against which newer diagnostic techniques have been compared. It is now used for highly suspicious palpable masses or nonpalpable screening-detected lesions; however, large-CNB is now being used more frequently in the evaluation of these lesions. Needle-localized surgical biopsy for nonpalpable breast lesions has a 2% to 3% error rate, which is similar to the sampling error of large-CNB.<sup>[19-22, 28-31]</sup>

### **Indications for Surgical Biopsy:**

- Patient preference for surgical excision;

- A nonpalpable mammographic lesion, which is not amenable to image-guided core biopsy, as determined by the radiologist;
- Nonpalpable lesion that mammographically is highly suspicious for cancer (*BI-RAD* Category 5), and surgeon or patient do not desire preoperative tissue diagnosis;
- Core biopsy is unavailable; and
- Lesion previously biopsied by core needle technique where histology shows atypical hyperplasia or radial scar, or where the imaging findings are not concordant with the histology results.

#### **Benefits:**

- Examines entire abnormal area so there are no sampling errors;
- Removes the entire lesion;
- Serves as adequate treatment for benign lesions; and
- Provides adequate tissue for all pathologic tests when the mass is small.

#### **Limitations:**

- Requires a sterile operating room setting and anesthesia;
- Leaves a small 2- to 4-cm scar;
- May require 2 surgeries if patient wants lumpectomy and the margin is positive or patient selects mastectomy;
- For benign lesions that do not require excision, it is an unnecessarily invasive procedure given the associated morbidity, risks, and expense;
- Diminishes the accuracy of sentinel node identification if not performed simultaneously with sentinel node identification; and
- More expensive than CNB or FNA biopsy.

## **Diagnosis and Clinical Decision Making**

**How will I know when my diagnostic workup is complete?** Correlation with imaging findings with CBE (for palpable lesions) and biopsy is required for accurate diagnosis and clinical decision making. Discordant imaging, clinical and biopsy findings suggest that the lesion was not adequately sampled, and removing the lesions with surgical excision and/or reevaluation of cytology/pathology is recommended. In addition, a CNB diagnosis of atypical ductal hyperplasia requires surgical excision since as many as 20% to 35% (10% if using vacuum-assisted device) of patients will subsequently demonstrate carcinoma at or near the CNB site. [32-34] Surgical excision is not required for a CNB diagnosis of lobular neoplasia (LCIS/ALH), since the incidence of carcinoma associated with this finding is low. [35, 36]

Diagnosis and clinical decision making are often based on the "triple test," a breast cancer diagnostic work-up. [37-40] "Triple test" (for palpable lesions) components include:

1. High quality and thorough clinical breast examination;
2. Breast imaging, to validate and analyze a palpable mass and to evaluate for multicentricity or extensive ductal carcinoma in situ; and
3. FNA or CNB (with or without image guidance).

Note: All 3 components of the "triple test" must be done within 3 months of each other!

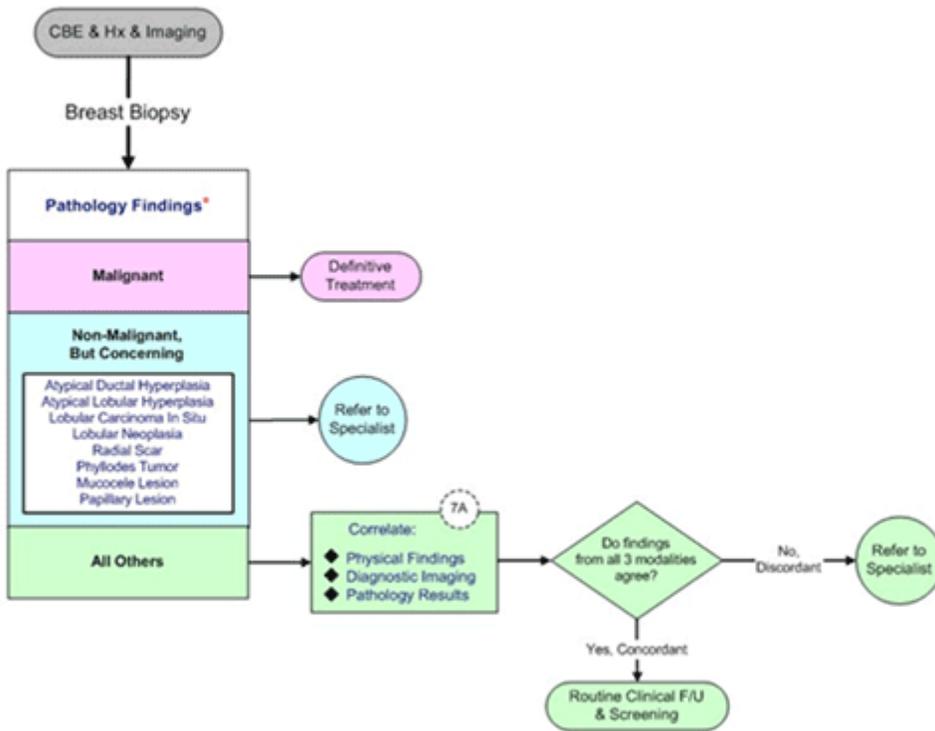
Larry Wagman, MD  
Breast Surgeon  
City of Hope, Louisiana

The cytologic findings should be correlated with the clinical and imaging characteristics to formulate a final conclusion on which patient management is based. Combining information from all 3 components of the triple test for clinical decision making and diagnosis has an accuracy of almost 98%.

- Triplet Test" - Benign triplets (all 3 components appear benign) - follow clinically with return visit within 6 months;
- "Triple Test" - Malignant - refer for definitive therapy;
- Malignant cytologic diagnosis with benign CBE and/or mammography - refer for surgical excision for confirmation of the diagnosis; and
- Mixed or inconclusive triplets - review everything for reason and consider surgical excision if unresolved.

See Figure 7 (Algorithm #7) [13] for guidelines on the work-up of a breast pain in a nonlactating woman.

Algorithm 7: Management of Breast Biopsy Results



\*Definitions of pathologic terms can be found in *italics* in Appendix A-4: Glossary of Terms.

Figure 7. Algorithm 7: Management of Breast Biopsy Results.

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**When can a breast diagnostic workup be considered complete?**

- When the clinical finding is imaged and the results are negative
- When a BI-RADS 2 result is issued, without correlation to the CBE documentation
- When the CBE finding, imaging finding, and pathology finding are all concordant
- When the woman refuses to have the biopsy done as scheduled

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