

Chapter 4

Breast Imaging

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Breast imaging is a clinical subspecialty within the larger field of radiology. One in eight American women will develop invasive breast cancer during their lifetime. According to the American Cancer Society's estimates, about 232,340 new cases of invasive breast cancer will be diagnosed in women in 2013, with approximately 40,000 deaths. There are projected to be additional 64,640 new cases of in situ (non-invasive) breast cancer [1]. Breast cancer is the second leading cause of cancer death in women behind only lung cancer. In recent years, increased publicity has made women acutely aware of the risk of developing this disease.

History of Breast Imaging

Efforts to use imaging to evaluate breast disease with radiography began shortly after Wilhelm Roentgen discovered X-rays. Despite all the efforts over the years, clinically effective use of mammography was not truly available until the 1960s. Besides radiography, many other modalities aimed at diagnosing breast cancer have been tried. Thermography was used in the 1950s purporting to measure heat emanating from breast tumors due to their neovascularity. This modality did not prove clinically effective, and although recent efforts have been made to reintroduce thermography, its effectiveness has not improved. Although some women still choose thermography because their breasts do not have to be compressed while performing a thermogram, it should not be used as a substitute for mammography [2]. Xeroradiography was introduced in the 1970s. In this technique, a plate coated with selenium rests on a thin layer of aluminum oxide. The X-ray beam passes through

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the breast and strikes the selenium plate, causing a charge distribution on the plate. Then, as with a paper copier, the image formed on the charged plate is transferred to paper for display. While xeroradiography produced usable images, it required too much radiation, and image storage and reproducibility were significant problems.

By 1960s, mammography was considered clinically safe although the radiation dose to the breast and shielding were not as good as they are today. The radiation dose currently delivered from a two view analogue mammogram has been reduced to approximately 2.37 mGY [3], about the equivalent amount of ambient radiation one receives from the atmosphere in 3 months. At the time the reproducibility, safety, and relative ease of performance also helped to make mammography a more viable option.

While mammograms became more available in the 1960s, it took time for its utility to be understood and utilized by the public. It was not until the mid-1980s that screening programs started to be promoted and until the 1990s that breast cancer awareness exploded with a marked increase in fundraising and cancer research. From the early 1960s when only 10–15 % of women took advantage of mammography, the number of women having yearly screening increased to a high of approximately 75 % in the early 2000s. As a result of strict adherence to a program of yearly mammographic screening after age 40, breast cancer deaths in women between 40 and 50 years of age who are screened have decreased by as much as 26–29 % [4].

The original technique of screen film mammography (analogue) while extremely useful does have limitations. Penetrating through breast parenchyma, particularly in dense breasts, is problematic. Dense parenchyma makes it more difficult to see masses and discern faint calcifications. Compressing the breasts during mammography helps improve penetration and makes lesions more conspicuous. Still, analogue mammography was not ideal.

The need for better techniques led to development of full field digital mammography (FFDM) which is now state of the art. Digital mammography has slightly worse spatial resolution than analogue mammography, but has much improved contrast resolution, allowing for better visualization of calcifications. With a digital display, post-processed magnification is easy and allows a much closer look at all areas of the breast. In addition, digital images permit computer-aided detection (CAD) techniques where a computer marks areas in the breast that it perceives as a mass or calcifications for closer examination after initial interpretation. The radiation dose with digital mammography has decreased to an average of approximately 1.86 mGy per study [3]. Digitized images are transported easily on disc, an aid in our highly mobile society to radiologists who need to compare all old studies to the current one to make an accurate assessment of the current study.

The FDA approved tomosynthesis, the next innovation in breast imaging, for clinical use in 2011. This is essentially a digital tomogram of the breast allowing review of the mammogram in 1 mm “slices.” Studies are being conducted currently to assess value of one-view tomosynthesis vs. two-view FFDM vs. one-view

tomosynthesis in combination with FFDM. One recent study showed that one-view tomosynthesis had better sensitivity and negative predictive value than FFDM in patients with fatty or very dense breasts [5].

In the process of attempting continually to improve and refine abilities to diagnose breast cancer earlier, an increased ability to diagnose benign conditions confidently was a significant by-product. Today, breast imaging is a vital component of overall management of breast health and disease, helping to diagnose benign as well as malignant conditions.

Screening Recommendations

In 2009, the United States Preventive Services Task Force recommended that women begin having screening mammograms at age 50, with follow-up mammograms every 2 years thereafter. It also stated that breast self-examination should not be performed [5]. Although an authoritative body, the conclusions of this study were spurious, the result of a flawed meta-analysis of 20 years of retrospective data. As a result, the medical community has rejected the recommendations of this study.

Current breast screening guidelines and recommendations from the American College of Radiology and American Cancer Society are for women at average risk for developing breast cancer to have a baseline mammogram at age 40 with annual follow-up mammograms [1, 6]. Furthermore, these guidelines recommend that breast self-examination begin at age 20. No age has been specified at which to stop obtaining yearly mammograms. It had been suggested that yearly mammographic screening stop at age 85, but today longer life expectancy has made that recommendation obsolete.

There are specific indications to begin breast screening in women before age 40 [7]:

- Carriers of BRCA gene.
- Untested first-degree relatives (mother, sister, daughter) of known BRCA carrier.
- First-degree relative of a woman diagnosed before menopause with breast cancer. Screening should begin 10 years before the age at which the relative was diagnosed or between the ages of 25 and 30, whichever is later.
- Women who have received mantle radiation for Hodgkin's disease.
- Women with any previous biopsy showing atypical hyperplasia of any type (ductal, lobular, lobular carcinoma in situ).

Additional considerations that may prompt earlier commencement of breast screening:

- Family history of breast and epithelial ovarian cancer.
- Breast cancer in a male family member.
- At least two family members on the same side diagnosed with breast cancer.

The Radiologists' Role

Many women sent for mammograms are very anxious. A commonly held misconception is that having a mammogram is painful, and many women need encouragement to complete the procedure. The need for a breast biopsy magnifies a woman's anxiety.

Performing interventional procedures is a significant part of the specialty. These include stereotactic biopsy using mammograms as a guide, ultrasound-guided breast biopsies, MRI-guided biopsies, fine needle aspirations (FNAs), cyst and abscess drainage, needle localization of breast lesions as guide to the breast surgeon and occasional galactograms. This means that the radiologist works in close association with the patient's surgeon and is an active member of the clinical team. The radiologist should meet with the breast surgeon and the pathologist on a regular basis for "concordance conference." The breast images, pathologic slides, and clinical results of all patients who have had biopsies are reviewed. If pathological results are not concordant with expected results based on imaging and clinical picture, rebiopsy (preferably by a different modality) is recommended.

Breast Imaging Tools

Mammography is the gold standard of breast cancer diagnosis. Many other modalities play ancillary roles in the diagnosis of breast disease. These include ultrasound and magnetic resonance imaging (MRI), neither of which uses ionizing radiation, molecular breast imaging (MBI, BSGI, scintimammography), positron emission mammography (PEM), and PET scanning. With some exceptions, these modalities are rarely used as primary screening tools.

Mammography

Mammography is the primary test used for breast screening and diagnosis. Because of differences in the appearance of breast tissue from woman to woman and even side to side in each woman, there is no "normal" mammogram. Every woman's baseline mammogram is *her normal*, and all subsequent mammograms must be compared to her baseline and subsequent mammograms. Any significant changes from baseline or previous mammogram must be evaluated further.

Mammograms, whether analogue or digital (as with all radiographs), can only display five radiographic densities. From least dense to most dense these are air, fat, soft tissue including fluid, bone/calcium, and metal. Normal breast parenchyma is soft tissue density with abundant interlobular fat. Unfortunately, breast tumors, benign breast lesions, e.g., fibroadenomas, breast cysts, hematomas, and mesenchymal lesions (hamartoma, angiomyolipoma, phylloides tumors), and abscesses are all

basically soft tissue density and so similar in density to normal breast tissue. Subtle differences in the density as well as perceived morphology and significant asymmetries with remaining breast tissue allow masses to be visualized, some seen better than others. Masses usually require at least one additional modality for further characterization, most frequently ultrasound. This helps provide a more detailed analysis and ultimately either a diagnosis or a decision to biopsy.

- Mammograms are done either for screening or for a diagnostic evaluation. Screening mammograms consist of two views of each breast. Diagnostic mammograms are reserved for women with known breast-related complaints or with suspected lesions not fully evaluated on the initial mammogram. Both examinations begin with an interview by the technologist about the patient's personal breast history.
- Screening mammograms are read later by the radiologist after which an official report is generated with recommendations for next necessary study.
- Diagnostic mammograms are reviewed by the radiologist while the patient is present in the mammography suite and as many additional views as required are obtained to evaluate the patient's problem. If the patient has a palpable lesion, typically an ultrasound is performed on the same day.
- Radiologists miss at least 10 % of breast cancers on mammography, particularly in women with dense breasts [8]. This means that all women with palpable lesions should have an ultrasound regardless of mammography findings.

Men who complain of swelling in one or both breasts also may require mammography, although it is usually better to begin evaluation with ultrasound. Most often male breast swelling is caused by gynecomastia, but breast cancer does occur in males and has the same mammographic findings as seen in female breast cancer.

Mammography reporting is standardized according to the Breast Imaging and Data Reporting System (BIRADS) system. This system was developed in an attempt to have uniform reporting throughout the country. It makes recommendations for additional evaluation and so also serves the purpose of guiding the ordering clinician in the patient's workup. There are seven BIRADS categories [9]:

0. Further study needed (additional views, ultrasound, MRI).
 1. Normal study. Recommend yearly follow-up mammogram.
 2. Benign finding. Recommend yearly follow-up mammogram.
 3. Probably benign finding. Recommend short-term (6 months) follow-up.
 4. Malignancy suspected. Biopsy recommended.

(May be subcategorized from A to C, according to increasing likelihood of malignancy.)
 5. Malignancy strongly suspected (95 % certainty). Biopsy recommended.

(Also may have A, B, and C subcategories.)
 6. Malignancy diagnosed but not fully treated. Often used for follow-up to neoadjuvant chemotherapy.

Tomosynthesis

Mammography is a projectional technique, depicting the entire three-dimensional (3D) breast volume in two dimensions. Tomosynthesis acquires 3D thin-section data. Images can be reconstructed in the conventional orientations of mammography. Adding tomosynthesis to mammography permits improved evaluation of the borders of a mass, architectural distortion within the breast parenchyma, and the extent of microcalcifications within the tissue. It also permits 3D localization for surgical planning [10].

Ultrasound

Because ultrasound (US) gives no ionizing radiation, it can be used more liberally than mammography and is preferred in younger patients. Ultrasound also can penetrate dense breast tissue. Not only is ultrasound able to penetrate the dense breast tissue better than mammography, but it images thin “slices” of tissues at different depths in the breast. This means that it shows detail in a limited volume of the breast. As such it is a problem solving technique that allows differentiation of solid and cystic lesions. Today, with improved gray scale imaging and better displays, some differential characteristics of solid masses also can be discerned.

Recently, an automated breast ultrasound screening machine (ABUS) has been approved by the FDA. Currently, ABUS is not reimbursed by insurance companies. The American College of Radiology Imaging Network (ACRIN) published a study in April, 2012 showing that adding annual screening ultrasound to mammography in women with high breast cancer risk and dense breast tissue gave an incremental cancer detection rate of 3.7 per 1,000 women screened [11]. The breast cancers detected only by ultrasound have been small invasive cancers with a high proportion of node negative cases. The addition of screening ultrasound also resulted in increased false-positive rates that resulted in further investigation and biopsy. Ultrasound does not replace mammography for routine screening since currently mammography is the only imaging modality that has been proven to reduce mortality from breast cancer. ABUS might be considered effective enough in the future to be used as a screening tool.

To avoid exposure to ionizing radiation in younger women, ultrasound should be used as the primary tool of breast diagnosis only in women under 30 years-of-age who present with a palpable mass. Mammography may be required after the ultrasound if further characterization of the lesion is needed. Ultrasound is safe to use in pregnant women who not infrequently complain of new masses in their breasts, which are radically changed by the elevated hormone levels of pregnancy.

Ultrasound often is used as a guide to perform percutaneous biopsies of mammographically or ultrasonically detected abnormalities. These can be performed safely on an outpatient basis.

Elastography

Elastography is a new tool in the ultrasound armamentarium. This technique compares signals of a tissue before and after displacement using compression strain imaging, vibration sonoelastography, acoustic radiation force generated by the ultrasound pulse, and real-time shear waves to characterize the hardness or stiffness of a lesion. Malignancies tend to be less deformable than benign lesions, and so elastography can provide additional clues as to the character of a mass [12].

Magnetic Resonance Imaging

A recent addition to the armamentarium of the breast imager is magnetic resonance imaging (MRI). This modality uses no ionizing radiation, but rather uses high strength magnetic fields to polarize protons. The imaging can be acquired and displayed in multiple planes and tissue thicknesses. This allows for thin cross-sectional examination of breast tissue with excellent soft tissue contrast. Sagittal images are performed both before and after gadolinium injection with five 1.5–2 min sequentially obtained acquisitions after the initial postinjection imaging. The pre-contrast images are then subtracted from the post-contrast images to highlight areas of true enhancement. Sequential images from identical locations within the breast are studied for their rapidity of enhancement and subsequent dissipation of contrast to generate enhancement curves. The pattern of enhancement can provide clues as to the nature of a lesion [13]. As with mammography, CAD is available with MRI.

MRI is highly sensitive for mass detection, but overlap of the appearance and enhancement behavior is high and so MRI is not very specific. Early experience with MRI and MRI biopsies in a selected patient population by breast imagers at Sloane-Kettering led to the conclusion that enhancing lesions 5 mm or less should be followed rather than biopsied [14].

The high sensitivity and low specificity of MRI mean that, in general, it should not be used as a screening tool. Currently accepted indications for screening with MRI are:

- A young woman with dense breasts and a 20–25 % increased risk of breast cancer.
- Strong family history—two first-degree relatives or a male family member with breast cancer.
- BRCA carrier.
- Relative of a BRCA carrier.
- A positive axillary lymph node without a known primary (and normal mammogram).

The American Cancer Society (ACS) and the Society of Breast Imagers (SBI) guidelines state that screening MRI is inappropriate for women with less than a 15 % increased risk of developing breast cancer. In high-risk patients MRI can be

alternated with mammography every 6 months or be performed yearly at the discretion of the radiologist and breast surgeon.

Otherwise, MRI is also employed to evaluate:

- The extent of disease preoperatively in a patient with known breast cancer.
- Tumor response to chemotherapy.
- For recurrence of tumor in an area of scarring.
- Breast implant leak or rupture.

Breast MRI should be performed between the third and fourteenth day of the woman's menstrual cycle to minimize background breast enhancement [12]. When abnormal areas of contrast enhancement are seen, breast ultrasound can be performed to see if the same lesion can be seen on US and therefore be biopsied with ultrasound guidance. Many MRI areas of enhancement are not mass-like and therefore cannot be seen on ultrasound. In these instances, MRI-guided biopsy is recommended.

It is not uncommon for the previously seen suspicious area of enhancement on MRI to have resolved when the patient returns for biopsy. This is a favorable finding since many physiologic changes can cause areas of MRI breast tissue enhancement. Enhancement from malignancies does not resolve, however. If suspicion persists despite disappearance of the enhancing region, a repeat MRI can be obtained in 6 months.

Molecular Breast Imaging (MBI, BSGI, Scintimammography)

Molecular breast imaging (MBI) was developed in the mid-1990s. Unlike other modalities that examine the breast anatomically, this modality measures cellular activity.

Breast-specific gamma imaging (BSGI) uses Tc^{99m} Sestamibi which accumulates in the mitochondria of the cells in direct correlation to the cellular energy conversion rate. Cancer cells produce more ATP from glucose than neighboring cells and so produce a hot spot on the BSGI image. When originally introduced, BSGI used a dose of 25 mCi of Tc^{99m} Sestamibi injected intravenously. This dose delivered too much radiation to the body and breast. Since then, improvements have been made including development of a dual headed scanner. This allowed the Sestamibi dose to be reduced to an acceptable 10 mCi and has the additional advantage of reducing examination time by half.

Another isotope currently available for nuclear breast scanning is fludeoxyglucose (FDG) which is also used in traditional PET scans. FDG is less available than Sestamibi, requires the patient to fast overnight, and also must have a 1 h delay between injection and scanning. Care must also be used in diabetic patients. As a result Sestamibi is often the preferred radionuclide. Similar to MRI scanning, BSGI is ideally performed between the 2nd and 12th day of the menstrual cycle. Because the projections are the same as those performed in a routine mammogram, the two studies can and should be directly correlated, view by view.

The majority of breast cancers 5 mm or greater will accumulate isotope [15]. Tumors as small as 3 mm have been diagnosed using this technique. MBI is particularly good at detecting infiltrating lobular cancers. Multifocal and multicentric cancers may be detected as well.

As with MRI, BSGI is extremely sensitive, but has greater specificity than MRI. A recent study showed that BSGI can detect cancers missed by both mammography and ultrasound. In this study BSGI had the overall highest sensitivity (91 %) for breast cancer detection, much higher than mammography and ultrasound, 74 % and 84 %, respectively [16].

Entities beside breast cancer that show increased isotope uptake on BSGI include atypical ductal hyperplasia (ADH), papillomas, breast abscesses, and sclerosing adenosis. The negative predictive value of BSGI is 95–99 %, making it a valuable tool in breast cancer detection.

The indications for BSGI are similar to those for MRI and include evaluating the extent of disease in a patient with known breast cancer, monitoring response to chemotherapy, bloody nipple discharge, palpable abnormality with negative mammogram and ultrasound, positive axillary lymph node with no known primary tumor, patients with implants, patients with strong family history, and patients for whom MRI is contraindicated.

MBI has some limitations. Surgery may cause abnormal activity for up to a year. Lesions close to the chest wall or deep in the axilla may not be detected. One cannot adequately assess lesions adjacent to the chest wall or involving the chest wall. At least one company has developed a device capable of MBI directed biopsy.

Interventional Procedures

A number of diagnostic and therapeutic procedures, developed specifically for breast disease and all of which can be performed on an outpatient basis, have been developed. For biopsies, patient should be off all blood thinners and NSAIDs for 5–7 days.

Stereotactic Core Biopsy

This procedure uses a stereotactic pair of radiographs from which the location of the lesion within the breast can be calculated to within 0.1 mm in a single plane. This procedure is used primarily to biopsy suspicious calcifications and occasionally masses that are unreachable or not well-defined using US [17, 18].

The patient often lays prone on the biopsy table for stereotactic biopsy which may not be possible in patients with significant respiratory problems, scoliosis or arthritis, occasionally patients with pacemakers, or patients who have had recent surgery. For these people there are institutions that have erect stereotactic biopsy machines.

Ultrasound-Guided Breast Biopsy

Ultrasound can guide sterile biopsy of any lesion that cannot be called definitively benign, abnormal appearing lymph nodes and cysts that have mural nodules, thick walls, or internal solid components.

MRI-Guided Biopsy

This technique is used less commonly than US-guided biopsy because of the awkwardness of using an MR scanner, the time required to do the biopsy, the cost, and the inability to use in patients with internal ferromagnetic materials. It is used for lesions deemed suspicious on diagnostic MRI that cannot be seen on ultrasound.

Patients scheduled for any of the stereotactic, ultrasound, or MRI biopsy must have bleeding profiles as close to normal as possible. Warfarin and Plavix must be stopped for at least 5 days prior to biopsy. It is preferred that Aspirin and NSAIDs not be used for at least 1 week prior to biopsy.

Cyst and Abscess Aspiration

Simple cysts, i.e., smooth, thin wall; no mural thickening or nodules, are left alone unless the patient requests that they be aspirated. In 40 % of aspirated cysts the fluid will reaccumulate. Abscesses and cysts are drained under US guidance.

Fine Needle Aspiration

FNA is used primarily to biopsy abnormal appearing lymph nodes in a “tight” axilla (one with little fat where stereotactic core biopsy is not chosen because of close proximity of the axillary neurovascular bundle). The advantage of FNA is that it is quick and easy to perform. The drawback is that while differentiation between benignancy and malignancy often can be made, the amount of the tissue obtained using this technique is not enough to evaluate the hormonal status of malignant cells. Hence, another biopsy with a larger bore vacuum needle may be necessary [19].

Needle Localization for Breast Biopsy or Definitive Treatment of a Known Malignancy

Some suspicious microcalcifications cannot be assessed by stereotactic biopsy for technical reasons. In some cases a prior stereotactic biopsy failed, and a repeat

biopsy is needed. Other patients who have had a positive biopsy return for definitive surgery. In these cases the target tissue will be difficult for a surgeon to find in operating room. A percutaneous localization is therefore performed. The radiologist, using imaging as guide, can put a needle with a hooked wire into the breast leaving its tip in the target area as a marker for the surgeon. The surgical specimen is sent for radiography to confirm that the target has been removed.

Galactography

Galactography is done to evaluate the intramammary ducts. Most often, this is done for patients with complaints of nipple discharge. Galactography requires cannulation of the duct orifice whence the discharge arises. Contrast is injected into the duct and radiographs of the opacified ducts are obtained and evaluated for intraductal lesions.

Clinical Scenarios

1. Palpable lump:
 - (a) Patients under 35 years-of-age: Order ultrasound. You may also order mammogram if indicated allowing the radiologist the ability to order mammogram immediately if deemed necessary.
 - (b) Patients over 35 years-of-age: Mammogram and ultrasound. Any woman complaining of a mass should have both a mammogram and ultrasound.
2. Inflamed, swollen breast with or without a palpable mass:
 - (a) Start the patient on a 2-week course antibiotics when seen and obtain mammogram and ultrasound after the antibiotics course has been completed.
 - (b) Both mastitis and inflammatory breast carcinoma will improve on antibiotics, but only mastitis will completely clear.
 - (c) A punch biopsy of the skin is a quick and efficient way to biopsy since dermal lymphatics are involved in inflammatory carcinoma.
3. Breast pain:
 - (a) Breast pain is a common complaint, but one that is unlikely to be related to cancer (other than inflammatory carcinoma).
 - (b) Most women complain of breast pain at some time during her cycle—usually before menses.
 - (c) If needed, obtain ultrasound in young women, ultrasound and/or mammogram in older women.

4. Mammogram shows indeterminate microcalcifications, asymmetric density(ies) or partially imaged lesion:
 - (a) Obtain further views of that breast as recommended by the radiologist to better evaluate morphology. Any of these findings can arise from a malignancy.
 - (b) If magnification views show calcifications to be suspicious, obtain stereotactic biopsy.
5. Palpable mass in a pregnant woman:
 - (a) Obtain breast ultrasound.
 - (b) Request mammogram per radiologist as necessary for further diagnosis. (All attempts are made to avoid mammography in pregnant patients.)
6. Male with palpable breast mass or swelling:
 - (a) Obtain breast ultrasound and if necessary mammogram.
7. Patients who have had a breast biopsy, local excision, or partial mastectomy require a 6-month follow-up unilateral mammogram.
8. Patient complains of nipple inverting or a new skin dimple:
 - (a) Obtain mammogram to study area beneath finding.
9. Patient with bloody or clear nipple discharge:
 - (a) Obtain breast ultrasound in periareolar area, with possible mammogram at discretion of radiologist.
 - (b) MRI might become necessary.
 - (c) If these examinations fail to show the etiology of the discharge, a galactogram may be needed.
10. Breast reduction surgery planned:
 - (a) Obtain mammogram as appropriate to the patient's age for surgical planning and to exclude cryptogenic disease.
11. Biopsy proven lobular carcinoma in situ (LCIS) (30 % lifetime increased breast cancer risk):
 - (a) Patient needs wide excision of area.
 - (b) More rigorous screening required either mammogram every 6 months, or mammogram alternating with MRI or BSGI every 6 months.
12. Ultrasound suggests fibroadenomas, *not* biopsied:
 - (a) In younger woman (<30–35) biopsy or obtain 6-month follow-up ultrasounds for 2 years to assess lesion stability.
 - (b) If first seen in woman over 35 or if growing in woman over 35, biopsy
13. Patient with 20 % increased risk of breast cancer
 - (a) Start early breast screening with mammography (10 years before age at which first-degree relative was diagnosed.)

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