# Diagnosis and Management of Breast Tumors

## A Practical Handbook and Multidisciplinary Approach

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*This book is dedicated to my wife, Funmilola Ayodele (Aduke) and children, Michelle and Ethan - you all make the efforts worth it. I also wish to acknowledge Professor Bola O. Osifo, Dr. Celeste N. Powers, and Dr. David S. Wilkinson, for their invaluable and influential roles in my career.*

Michael O. Idowu

*I dedicate this book to my family, particularly my parents Anil and Varsha; my dear and ever supportive husband, Snehal; my mentor, colleague, and friend, Dr. Gilda Cardeñosa; my colleague and confidant, Dr. Tiffany Tucker; a team of skilled, compassionate, unwavering technologists and clerical staff; and the countless patients from whom I have learned so much.*

Priti A. Shah

*I wish to dedicate this to my wife Christine and my 3 sons, who have supported me from the start of my career. I also want to acknowledge the inspiration of my three most influential role models: my Father, S. Elmer Bear, DDS, who set an example of dedication to his profession and to his patients; Dr. Bernard Fisher, who demonstrated the joy of moving the field of breast cancer treatment forward through clinical research; and Dr. Walter Lawrence, Jr., who encouraged me to "get involved."*

Harry D. Bear

# Foreword

The sheer number of benign and malignant breast lesions and the options available for the management of breast cancer may appear daunting. Even in the setting of a unified, multidisciplinary team, there may be some disconnect among its members (namely, pathology, radiology, medical oncology, surgical oncology, and radiation oncology). For example, radiologists and pathologists may be unaware of specific surgical, chemotherapeutic, or radiotherapy approaches and management techniques (i.e., "what happens next"). Similarly, the oncologists (medical, surgical, and radiation) may be unfamiliar with the diagnostic challenges encountered by radiologists and pathologists. *The lack of clarity to the often asked question of "what next" or "what are they going to do next" may sometimes lead to ambiguous diagnosis and possibly suboptimal management of the patient*. The specialties involved in the initial diagnosis (radiology and pathology) may consider the rest of the management of patients "not their headaches," mostly due to limited awareness of "what happens next."

We believe that it would be ideal for all members of the multidisciplinary team, including the patient's primary care provider, to have a basic understanding of the entire process, from work-up to completion of treatment, including diagnostic and therapeutic options, approaches, and techniques.

With this in mind, this text aims to present a practical and concise handbook on the approach to diagnosis and management of breast diseases written by subspecialty experts for quick reference by trainees and general practitioners. There are comprehensive reference texts on the criteria for diagnosis and algorithm for management of breast diseases. This text aims to bridge the gap of "what next" and foster an understanding of the diagnosis and management of breast tumors.

The Editors

# Preface

This book focuses on the approach to the diagnosis and management of common breast lesions or tumors. There are generous illustrations and figures to enhance readers' appreciation of the lesions and processes being discussed. Medical students, trainees, and physicians involved in diagnosis and management of breast diseases will find relevant, practical points for their education and practice.

The book is divided into two parts. Part 1 is divided into five chapters. Each chapter is written by subspecialty experts. Chapters 1 and 2 discuss the radiologic and pathologic approach to diagnosis of breast lesions, respectively. Chapters 3, 4, and 5 address the surgical oncology, medical oncology, and radiation oncology approaches to management, respectively.

Part 2 focuses on the radiologic and pathologic diagnosis of selected breast lesions with emphasis on radiologic-pathologic correlation. Entities such as fibroepithelial lesions, papillary lesions, proliferative lesions, invasive carcinomas and miscellaneous lesions are highlighted. There are ample images to illustrate criteria used to assess and categorize each lesion presented. In addition to radiologic-pathologic correlation, Chap. 9 further highlights management approach and treatment options for invasive carcinomas.

It is our hope that this text will enhance appreciation for the multidisciplinary approach to the diagnosis and management of common breast lesions and provide some clarity for trainees and community/general practitioners on the question of "what next?".

The Editors

# Contents

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# Part I

# Overview of Evaluation and Management of Breast Diseases

# Overview of Radiologic Quality Assurance and the Imaging Evaluation of Breast Lesions

1

Priti A. Shah

## Quality Assurance in Breast Imaging

Although the field of radiology as a whole is subject to many levels of regulation and accreditation, breast imaging, and specifically mammography, is a subspecialty subject to rigorous standards of care that are legally mandated in the United States. Two major entities collaboratively regulate breast imaging in the interests of quality and safety. Responding to issues and inconsistencies in matters pertaining to patient care and image quality, the American College of Radiology (ACR) developed the Mammography Accreditation Program in the late 1980's as a means of periodic peer review and feedback from experts for improvement [1, 2]. Secondly, the Mammography Quality Standards Act (MQSA) was enacted by Congress in the 1990's to set national quality standards through specific regulatory requirements that were established by the Food and Drug Administration (FDA) for mammography [1, 3]. Under MQSA, all facilities that provide mammography services in the United States must be inspected by the FDA every year, earn accreditation by an FDA approved body (which includes the ACR, and the states of Arkansas, Iowa, and Texas) every 3 years, and be certified by Health and Human Services every 3 years. Mammography facilities under the Department of Veterans Affairs, while not included in MQSA, undergo accreditation by the ACR to maintain the same standards of care [2]. Through the interplay between these agencies' directives, every aspect of a mammography practice is overseen, including but not limited to technologist, radiologist, and physicist training, equipment quality control, radiation safety, image quality, result documentation and communication practices, and patient outcomes.

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Some practical aspects of patient care by breast radiologists are also regulated. For example, it is required by MQSA that patients are provided a written summary of their mammogram results in non-medical terminology. This is separate from the radiology report that is sent to the referring clinician. Because of MQSA, this direct communication with patients has been the standard of care before the days of web-based patient portals and widespread campaigns in medicine promoting patient-centered care.

*The breast radiologist is also responsible for establishing radiological – pathological concordance and directing patient management based on a biopsy result*, unlike for other image guided biopsies, or for other practitioners. In this way, breast imagers are uniquely subject to standards not legally required by non-radiologists. For example, a radiologist and a surgeon can both perform a core needle breast biopsy, however, the former must document and track the results, patient follow-up, and outcomes; and this data (among others) is then used to calculate individual and practice statistics that comprise a medical audit subject to review by the FDA. Recall rates, biopsy recommendations, true and false positives and negatives, re-biopsy rates, invasive cancer detection, positive predictive values, and so on are measured against established benchmarks, and routinely assessed. Part of this is because of the self-directed nature of the breast imaging work up that leads to procedures—there must be an internal system of checks and balances—but the main goal is to provide quality and consistency of patient care, with appropriate follow up.

Nearly contemporaneous to the inception of the MQSA was the creation of the Breast Imaging Reporting and Data System (BI-RADS) by the American College of Radiology [4, 5]. In the vein of creating guidelines for clear reporting and monitoring patient outcomes, BI-RADS is a quality assurance system most relevant to our referring clinicians with regard to the communication of findings and recommendations for management by the radiologist through, for example, standardized reports and categorization of follow-up. By using BI-RADS, the radiologist can generate specific, concise, consistent reports via a lexicon of approved terms, with clear, concise recommendations from defined assessment categories to allow for meaningful, clinically relevant consultation (Table 1.1).

**Table 1.1** Breast imaging lexicon: examples of finding descriptors (mammography) [5]

| | |
|---|---|
| Masses | Shape: round, oval, irregular<br>Margins: circumscribed, obscured, microlobulated, spiculated, indistinct<br>Density: high density, equal density, low density, fat containing |
| Calcifications | Morphology (suspicious): amorphous, coarse heterogeneous, fine pleomorphic, fine linear, branching<br>Distribution: grouped, regional, diffuse, linear, segmental |

Breast imaging lexicon - assessment categories, likelihood of malignancy, and management recommendation [5]:

0—Incomplete: need additional imaging evaluation or prior study for comparison
1—Negative: ~0% likelihood of malignancy, recommend routine screening
2—Benign finding (e.g.. cyst): ~0% likelihood of malignancy, recommend routine screening
3—Probably benign finding (e.g., probable fibroadenoma, focal parenchymal asymmetry): <2% likelihood of malignancy, recommend 6-, 12-, and 24-month follow-up; after which, if stable, finding is considered benign (BI-RADS 2)
4—Suspicious: 2–10% likelihood of malignancy (4a, low suspicion); 10–50% likelihood of malignancy (4b, moderate suspicion); 50–95% likelihood of malignancy (4c, high suspicion), biopsy recommended
5—Highly suggestive of malignancy: >95% likelihood of malignancy, biopsy recommended
6—Known biopsy-proven malignancy, treatment plan recommended

When used appropriately, each descriptor or combination thereof connotes a differential diagnosis and a level of suspicion. For example, a description of an oval low density mass with circumscribed margins suggests a specific differential diagnosis (perhaps a cyst, fibroadenoma, or papilloma), one that is vastly different from that implied by a description of an irregular dense mass with spiculated margins (such as an intermediate nuclear grade invasive ductal carcinoma or invasive lobular carcinoma). However, it is important to note that there is considerable inter-reader variability in choice of descriptors and terms even within the lexicon, possibly because of differences in perception and overlap in imaging features [6, 7].

There is some flexibility in these assessment categories to allow for the nuances of actual patient care. For example, a subareolar abscess is a benign finding, but short interval follow-up might be recommended to ensure resolution; a patient with a known malignancy may undergo imaging follow-up if she is not a surgical candidate. When used appropriately, the lexicon enables the radiologist to provide a meaningful report that guides patient care. Terms like "clinical correlation advised" are discouraged in favor of concrete recommendations and actions.

## Screening and Its Controversies

By definition, *a screening mammogram is for the routine surveillance of breast cancer in an asymptomatic patient*. It is comprised of two (nearly) perpendicular low-dose x-rays of each breast: a craniocaudal (CC or top-to-bottom) and a medial-lateral oblique (MLO or side-to-side) view. Two images of each breast are the standard of care to be able to include as much tissue in the image as possible; studies

have shown a 25–45% increase in cancer detection when two views are obtained compared with one [8]. This is because inherent in how the patient is positioned, each view has a "blind spot" that has the potential of excluding some tissue—even with superb technique, for example, a CC view may exclude some superior tissue, and an MLO view may miss far medial tissue.

The specifics of frequency and age of initiation of screening mammography are controversial. As with any screening program, the goal is early detection: to find early stage cancer that is more susceptible to less aggressive treatments and therefore has the best prognosis and survival. With breast cancer, the 5-year survival rate for localized disease at diagnosis can be up to 98.8%, and 12-year survival up to 95% with tumors smaller than 1cm at diagnosis [9, 10].

The national benchmark for overall sensitivity of mammography is 86.9%, and specificity 88.9% [11, 12]. Mammography is not a perfect test (is there a perfect test in medicine?); however, it is one of the most studied tests in medicine, resulting in a large volume of data, from but not limited to randomized control trials, that consistently shows a significant (at least 30%) decrease in mortality when done annually in average-risk women over 40, through early detection, with decades of follow-up [13–17]. Part of the advantage of mammography is its ability to detect microcalcifications associated with stage 0 disease (intraductal cancer or ductal carcinoma in situ) better than any other imaging modalities, even in women with dense breast tissue. This is because DCIS often manifests as microcalcifications, the detection of which is optimized by the radiographic technique used in mammography (low-dose, high-resolution imaging). Starting at age 40 is recommended because the incidence of breast cancer doubles in women ages 35–39 to ages 40–45 years old, and cancers grow more aggressively in these women than in postmenopausal patients [9, 18, 19]. Although cancers in postmenopausal women may be more indolent, causing some to favor less frequent screening in these patients, increasing age is a risk factor, and so earlier detection may allow for less aggressive treatment options that are better tolerated in the setting of other health problems that may come with age.

Recent changes in screening guidelines are not based on new or refuting data, but rather on a shift of attention away from the benefits of mammography to its potential harms (see below). Simply put, for women of average risk, the US Preventive Services Task Force (USPSTF) recommends biannual screening mammography for women ages 50–74, stating that the net benefit is moderate. For women younger than 50, the position of the USPSTF is that the decision to screen should be an individual one based on values of potential benefits versus potential harms and that the net benefit for women in this group is small. And for women older than 74, the current evidence is deemed "insufficient" to assess the balance of benefits and harms [20].

The American Cancer Society now advises that women should have the opportunity to begin screening at age 40 if they choose, and that mammography be done annually between 45 and 54; women over 54 can be screened every other year or annually, depending on personal preferences [21].

The changes in guidelines, and the controversies, stem from new attention on issues such as patient anxiety, radiation, false positives, and invasive procedures and their complications [22]. These are important topics; however, as discussed below, they do not outweigh the proven benefits of mammography when it comes to early detection and survival.

There is conflicting data regarding short term and long term effects of the anxiety related to mammography, however, there is evidence that women are still willing to return yearly even after a false positive; the apprehension is not incapacitating, nor does it outweigh the desire to "know" one's status regarding breast cancer [23, 24]. Direct, radiologist-led patient education about screening and breast cancer has also been shown to decrease anxiety through increased patient knowledge and feelings of empowerment [25]. Lastly, significant portion of this anxiety is attributed to waiting for results, and the fear of the unknown. But rather than discourage mammograms for this reason, there are ways to shorten the interval between screening, recall, diagnosis, and biopsy that serve to alleviate this component of anxiety [26]. As outlined above, radiologists are legally required to provide the patient with her imaging results, which is routinely done the same day in the case of a diagnostic workup. But practices may opt to do this even with screening studies, even if only at the specific request of the patient. Our practice routinely accepts add-ons and walk-in patients for screening and diagnostic studies and offers same-day ultrasounds and biopsies. We have an agreement with our pathologists to receive biopsy results the next day, and the radiologist provides those results directly to the patient at that time. If cancer is diagnosed, we immediately schedule the patient for a surgical consultation, and the patient is seen within the week. While this can make for unpredictable workflow, efforts by the entire team to streamline the process are seen as being in the best interest of the patients.

All x-rays use radiation. However, there is no data showing that the radiation from yearly mammograms is a cause of breast cancer. In the spectrum of medical tests, mammography is considered low dose [27, 28]. A standard four-view mammogram (two views of each breast) is approximately 1/7 of the radiation received from natural background sources annually, such as the air, water, and soil in our environment [29]. Moreover, as outlined above, all mammography facilities in the United States are required to undergo routine inspection and accreditation by entities such as the FDA and American College of Radiology: practices are regularly and systematically monitored with regard to equipment, safety, quality, radiation dose, and technologist and physician training. So even though mammography uses radiation, the vast, proven benefits of early detection outweigh the theoretical risks from the relatively small dose of radiation, a dose which is kept in check.

With regard to false positives in mammography, in addition to monitoring data such as equipment and dose, mammography facilities are also required to track measures such as patient outcomes and physician performance. Among many national benchmarks, the acceptable "abnormal interpretation rate" for *screening mammography* is 5–12% [12]. While this may seem high, the number of patients receiving a normal or benign result is, by definition, substantially higher: about 90 percent of screening patients get a clean bill of health. Of the 5–12% of patients recalled, the vast majority will also be "cleared" with additional mammographic views and/or ultrasound. Of the remaining, biopsy rates are less than 2 percent; benchmarks for acceptable PPV for biopsies performed are 20–45% for screening-detected abnormalities and 30–55% for palpable findings [12]. Many breast imagers work hard to minimize recalling patients, and even lower recall rates and higher positive predictive values can be acheived through better technologist and physician

training [30]. For example, for about a decade, the collective callback rate in our practice was less than 10% and our PPV for biopsies 50–60%. Double reading has also been shown to decrease call backs [31, 32]. In addition to better training and collaboration, advances in technology can contribute to lowering recall rates and false positives. 3-D mammography, or tomosynthesis, is an example of this. Instead of a single, "flat," 2-dimensional image, these 3-D studies provide the radiologist with multiple separate thin (1 mm) "slices" through the entire thickness of the breast that can be evaluated layer by layer. This can decrease the effect of summation or superimposition of normal structures encountered more frequently with the traditional (2-D) mammogram, thereby decreasing false positives, and allow for the increased detection of invasive cancers [33–35].

With regard to the potential harm of invasive procedures, when a biopsy is necessary, there are opportunities to minimize local trauma and, therefore, associated discomfort and possible complications. Imaging-guided core needle biopsies are less invasive than surgical biopsies, can be done in the same exam room as the mammogram or ultrasound, and require no IV or general anesthesia, nor advanced preparation (such as fasting or stopping anticoagulation) by the patient. *The complication rate of imaging-guided needle biopsy is <1%, which includes bleeding, infection, and tissue damage* [36, 37]. Even then, there are opportunities for improvement. For example, smaller gauge, spring-loaded biopsy needles may be used instead of larger, vacuum-assisted ones in certain circumstances. Physician skill and more precise techniques can allow for taking fewer, "high-yield" samples (my mentor once said that theoretically, you only need one core to make the diagnosis—which drives me to make each pass count to this day). Using a patient-centered and specific approach to decide which patients may or may not benefit from placement of a marker clip, which is routinely placed at the biopsy site by almost all radiologists and requires a two-view post-procedure mammogram to confirm its location, may obviate the cost, extra time, and radiation associated with this part of the procedure.

In these ways, the potential harms of screening can be addressed and overcome, rather than being used as excuses to discourage annual mammography. To discourage or possibly limit access to this lifesaving test going forward may undo all of the gains in early detection and survival made previously.

It is important to reiterate here that the controversies in screening guidelines are with regard to the average-risk patient. Most organizations still agree that women who are high risk (see below) should start annual screening at 40 or earlier based on their risk factors such as age of onset of cancer in a first-degree relative.

## Diagnostic Imaging

As the name would imply, *diagnostic imaging is typically reserved for the workup or diagnosis of a specific sign or symptom of the breast or axilla or to evaluate an abnormality on a screening mammogram*. Common clinical examples include a "lump" felt on physical exam, skin changes, focal pain, and spontaneous nipple discharge. In most practices, diagnostic imaging involves a combination of

additional mammographic views and/or ultrasound, and the evaluation is tailored to the patient based on the findings at each step of the process. This "work-in-progress" approach keeps the radiologist alert, and, as he/she must (by MQSA) provide results directly to the patient in lay language, requires that the radiologist "own" his/her assessment and plan.

Without getting into the technical aspects of diagnostic workups, some of the additional mammographic images include *spot compression views* at the area of radiographic concern and full paddle views done at different angles than standard screening views. Altering the angle at which tissue is seen, and further compressing the breast in the specified area, can reduce the potential masking effect of normal overlapping tissue and allows for confirmation, improved visualization, and localization (for possible ultrasound or biopsy) of the finding in question. In the case of a mass, confirming it in two (perpendicular) planes is integral to the BI-RADS definition of a mass. If the suspected finding "disappears," it may be attributed to tissue overlap at the time of screening, and no further workup may be needed. As an analogy, for example, when we take our laundry out of the washer, it is often "balled up." When spread on the clothesline, we see that there was never really a "ball" in it. The radiologist may perceive a "mass" or "lump" at screening that "spreads out" as normal tissue once viewed from a different angle, and further, focal compression is applied. If a finding persists/is confirmed on spot compression views, ultrasound may be undertaken, particularly in the evaluation of a mass, architectural distortion, or focal asymmetry.

Calcifications are further evaluated with *magnification views* because of their size. These views use different patient positioning and technical factors than standard screening or spot compression views to optimize contrast and resolution and minimize the effect of superimposed tissue—all paramount when assessing structures smaller than a millimeter. Ultrasound is not usually useful in further characterization of microcalcifications. The detection and work up of breast calcifications is further outlined below.

## Breast Density

Breast tissue is composed of fatty, fibrous, and glandular tissue. These elements vary in proportion from person to person and sometimes between breasts in the same patient (see discussion on asymmetry below). The amount and combination of types of tissue are under genetic and hormonal influences, and though it can change somewhat during a lifetime, it is simply how an individual woman's breast is made.

Fatty tissue is radiolucent, translating to a higher sensitivity for mammography to detect small cancers, since invasive cancers (most often, masses) are typically equal or higher density than breast tissue. Fibrous and glandular tissue, sometimes termed together as fibroglandular tissue, is more opaque or "dense" radiographically. So it follows that the more fibrous and glandular the tissue, the denser the breast tissue appears, and the more challenging it is to detect a small cancer. It is the old polar bear in a snowstorm analogy, hence the decreased sensitivity of

mammography in dense breasts (Figs. 1.1 and 1.2). To add to this limitation in detection, studies also show a mild to moderate increase in cancer risk incurred by having predominantly dense tissue, the mechanism of which is still unclear [38].

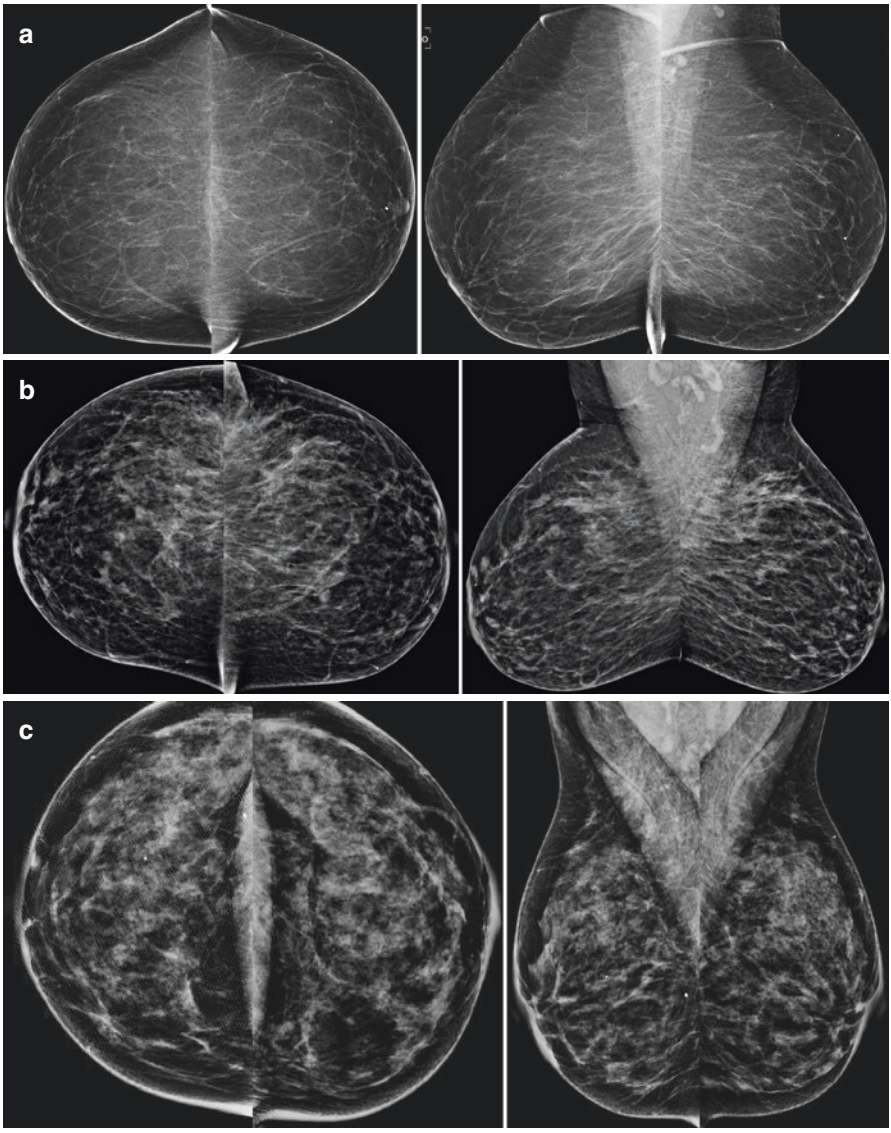



**Fig. 1.1** Breast composition as defined by the ACR BI-RADS mammography lexicon [36]. (**a**) Almost entirely fatty. (**b**) Scattered areas of fibroglandular density. (**c**) Heterogeneously dense. (**d**) Extremely dense

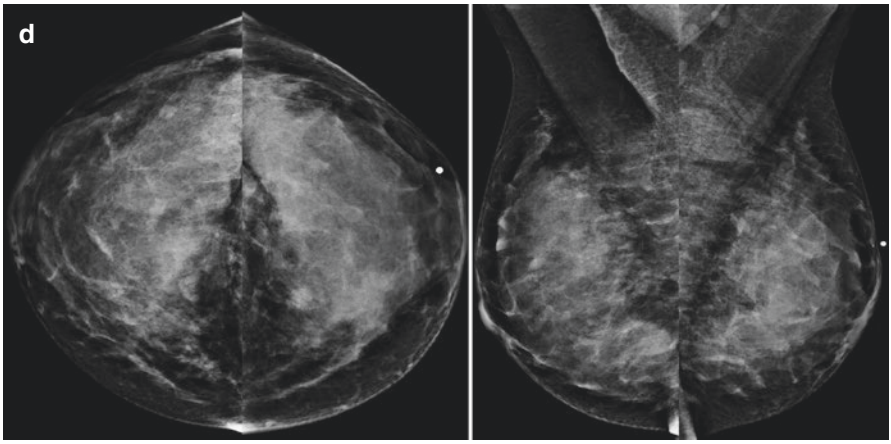



**Fig. 1.1** (continued)

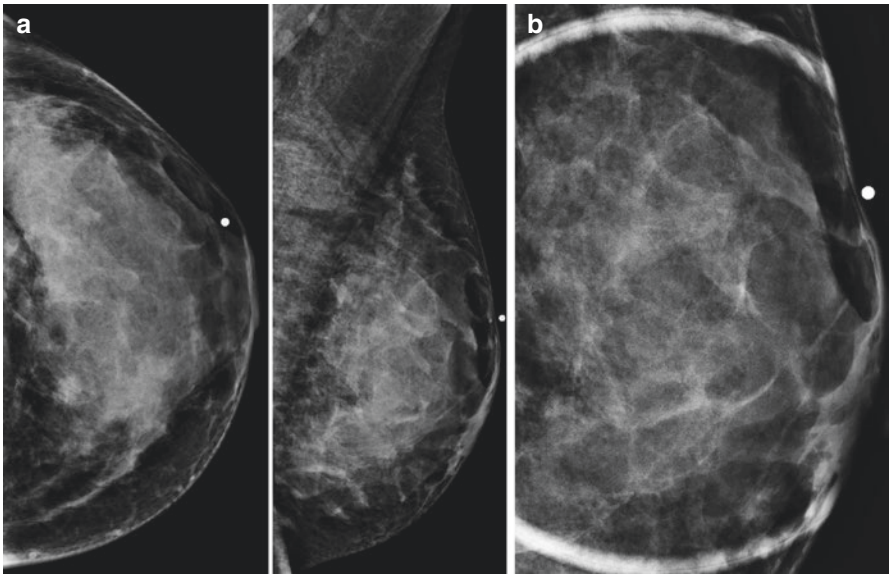
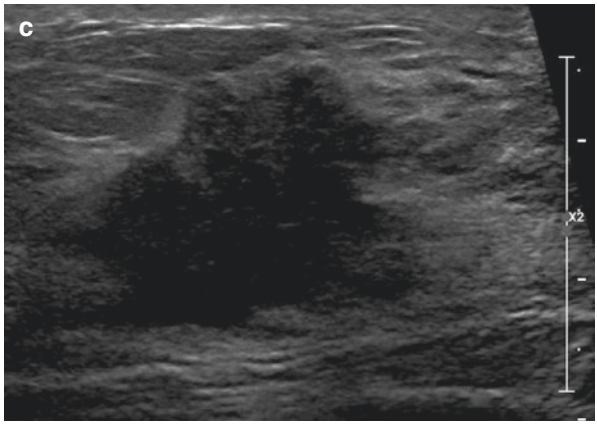



**Fig. 1.2** Lowered sensitivity of the detection of masses in extremely dense breast tissue. 40-year-old woman with family history of premenopausal breast cancer. (**a**) Standard and (**b**) spot compression views done for a "lump" in the left breast (marked with a metallic BB on the skin) do not clearly show a mass. (**c**) Targeted ultrasound demonstrates an irregular mass, biopsy of which yielded invasive ductal carcinoma, high nuclear grade

**Fig. 1.2** (continued)




The lowered sensitivity of mammography combined with increased cancer risk associated with dense tissue has driven patient advocates and politicians to establish state laws requiring radiologists to directly inform patients about their breast density in more than half of the United States—known as breast density notification legislation. The goal of this is to provide women information to allow them to make more informed decisions regarding screening and breast health. At our institution, the statement added to result letters reads:

> Your mammogram demonstrates you have dense breast tissue. Dense breast tissue is very common and is not abnormal. However, dense breast tissue can make it harder to find cancer on a mammogram and may also be associated with an increased risk of breast cancer. This information about the result of your mammogram is given to you to raise your awareness. Use this information to talk to your doctor about your own risks for breast cancer. At that time, ask your doctor if more screening tests might be useful, based on your risk.

Of note, by MQSA requirements, density information has always been included in the radiology report that is sent to the ordering clinician; it is only in recent years that individual states are mandating this information be included in the patient result letter as well.

However, the benefit of this information is not as clear cut as it seems and has given pause to radiologists and patients alike, especially amidst the controversies about screening guidelines. Some radiologists' threshold for classifying tissue as "dense" is when the mammogram is > 50% dense. This was further divided into categories of "heterogeneously dense" (51–75%) or "extremely dense" (>75%) by older editions of the BI-RADS lexicon; the current edition does not provide percentage guidelines, reflecting that the majority of radiologists make this assessment subjectively [39]. As would be expected, there is much (documented) inter- and intraobserver variability in breast density assessments [40]. Software programs exist to objectively quantify dense tissue; however, these are in large part investigational, and currently not in routine clinical practice. Secondly, density is also affected by radiographic technique. For example, if the image is undercompressed or underpenetrated, breast tissue can appear

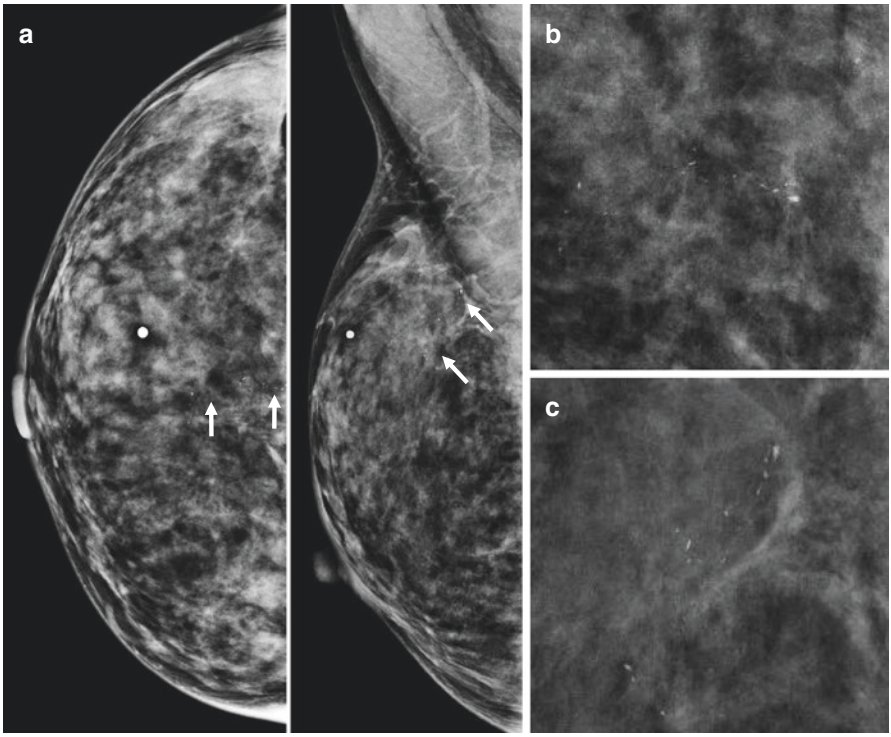



**Fig. 1.3** Microcalcifications superimposed on dense breast tissue. (**a**) Standard full paddle CC and MLO views in a 33-year-old patient presenting with a palpable "lump" (marked on the skin with a metallic BB) in the right breast. Calcifications can be seen in the upper central aspect of the breast posteriorly (*arrows*) even on routine views. (**b**) Spot compression magnification CC and (**c**) LM views confirm fine linear calcifications in linear orientation; biopsy showed ductal carcinoma in situ

artificially dense. Making a determination that tissue is dense has serious ramifications for the patient, not the least including anxiety and the possibility of additional tests, and therefore this assessment should be as accurate and reproducible as possible.

Another issue is that breast density does not tend to affect the ability to detect microcalcifications associated with early breast cancer, DCIS, to the same degree as it does for small masses. Calcifications are denser, or "whiter," than dense breast tissue and can therefore still be seen in a background of dense tissue. Therefore, discouraging women from mammography because of dense breast tissue may result in missing the opportunity to find an early-stage intraductal cancer, before it has a chance to progress to invasive disease and form a mass obscured by overlying tissue (Fig. 1.3).

In a similar vein, one of the myths amidst the screening controversies is that mammograms are ineffective in young women because they mostly have dense breast tissue. This is untrue for two reasons. That all young women have dense tissue is a myth; and as indicated above, microcalcifications of DCIS are still apparent in dense tissue.

Women with dense breasts may undergo supplemental screening; however, the trade-off for the increased cancer detection may be increase in false positives, particularly with ultrasound. Perhaps even more of an obstacle is that while breast

density notification legislation obligates radiologists to inform patients of their density, in most states, the legislation does not mandate insurance companies to cover supplemental screening tests such as whole-breast ultrasound or MRI, which cost significantly more than screening mammograms. So while we empower patients with information, their ability to act on it may be limited.

## Ultrasound

Ultrasound can be used as first line for diagnostic purposes when the risk of even low-dose radiation to the breast tissue outweighs its benefits, mostly when breast tissue is more "active" under strong hormonal influences. This is the case for women under 30, given the continued growth of breast tissue into the 20s, versus the low likelihood of cancer in this age group. Ultrasound is also used preferentially in patients who are or were recently pregnant or breast feeding. Patients who have undergone a mastectomy can also be imaged with ultrasound if presenting with a symptom that requires imaging evaluation.

Otherwise, sonography (ultrasound) should be used as an adjunct to mammography, to further characterize a palpable or radiographic finding and to provide biopsy guidance. Although the utilization of screening ultrasound is increasing with recent breast density notification legislation, even when these are recommended, it is in the setting of concomitant mammography, as the sensitivity and specificity of ultrasound for cancer detection are higher when combined with mammography than when used alone [41, 42]. As mentioned earlier, mammography is not a perfect test; however, we know that some cancers—e.g., intraductal and even some invasive lobular carcinomas—may be occult or at best subtle sonographically. *Mammography is the gold standard for cancer detection, and we would be remiss if we start substituting ultrasound for patients who simply don't want to undergo a mammogram.*

Quality assurance programs similar to those established for mammography are also in place for ultrasound. Though not required by law as for mammography, facilities may participate in the voluntary peer-reviewed ultrasound accreditation process by the ACR, comparable to that required for mammography. This accreditation for ultrasound is mandated by some insurance companies for reimbursement. Similar to mammography, the ultrasound accreditation program, which separates diagnostic ultrasound and ultrasound-guided interventions, assesses issues such as radiologist and technologist qualifications and experience, equipment, image quality, documentation, needle positioning, and radiologic-pathologic concordance and patient outcomes with regard to biopsies and fine needle aspirations.

With regard to day-to-day practice of ultrasound, the ACR has also set practice parameters for image acquisition and annotation. These are not merely boxes to be checked for accreditation, but, when followed, allow for optimum image quality and therefore the best possible visualization and categorization of the finding and subsequent management of the patient. Being mindful of and adjusting technical parameters (such as field of view, focal zone, depth) appropriately must be a part of every

patient's scan to obtain accurate diagnostic information. Ensuring that ultrasound findings (with regard to lesion location and imaging characteristics) are concordant with the mammogram is also paramount and is the responsibility of the radiologist even if a sonographer acquires the images. For example, if working up a mammographic finding of a spiculated, solid mass in the upper inner quadrant, a cyst (which is characterized by circumscribed margins and absence of internal echoes) found in the upper outer quadrant would be considered incidental and incongruent with the mammographic finding, which would still need to be identified. Confirmation of findings in perpendicular planes, similar to mammography, is also necessary.

## MRI (Magnetic Resonance Imaging)

For breast MRI to be useful in the diagnosis of breast cancer, it must be done with the administration of intravenous gadolinium-based contrast, following which multiple "runs" of repeat imaging are done to provide a dynamic set of images over time. This is because most cancers have avid, rapid influx and outflux of contrast due to increased vascularity and vascular permeability compared with normal tissue, related to tumor angiogenesis [43, 44]. In addition to the visual assessment of lesion morphology and contrast uptake, special software is used to process the kinetic curves of this enhancement. For example, lesions that demonstrate "fast" initial enhancement (>100% signal intensity in the first 2 minutes after contrast injection) and "washout" on delayed images (decrease in signal intensity by >10% from peak enhancement) have the highest likelihood of malignancy.

That being said, hormonal influences can cause (sometimes marked) normal background parenchymal enhancement from which the radiologist must tease out possible lesions (Fig. 1.4). Abnormal findings at MRI may be further worked up with targeted ultrasound and/or biopsy (either sonographically or MRI guided).

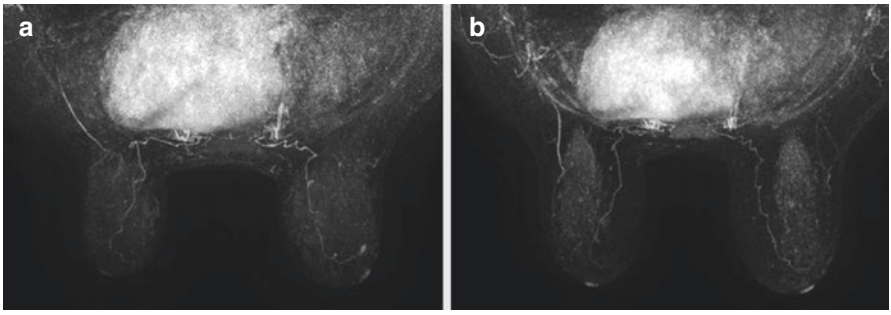



**Fig. 1.4** Variations in background parenchymal enhancement related to hormonal changes. These 2 images are from a screening MRI done one year apart in the same patient, at different times in her menstrual cycle. Typically there is less physiologic enhancement during days 7-14, the follicular / proliferative phase, as in (**a**), compared with the luteal/secretory phase as in (**b**)

Although more sensitive than mammography for invasive cancers (88–100%), MRI can be less specific [43, 45, 46]. In addition, *some radiographically apparent low-grade intraductal cancers, and some invasive lobular cancers, may not enhance*. This is why we interpret MRI in conjunction with a recent mammogram; we do not supplant mammography with MRI.

Other "downsides" to MRI include the cost and length of the exam (some protocols are about 35 minutes, although abbreviated protocols are on the horizon) and some of its contraindications that exclude certain patients—e.g., those with pacemakers or other implanted metal and those with renal failure (due to the risk of nephrogenic systemic fibrosis with gadolinium-based contrast, not impairment of renal excretion per se). Claustrophobia is also an issue for many patients.

With regard to quality, facilities that perform and interpret breast MRI may also choose to earn accreditation analogous to that for mammography and ultrasound. Sites that achieve accreditation by the ACR for four breast imaging modalities (mammography, ultrasound, MRI and stereotactic biopsy) are given the designation as a Breast Imaging Center of Excellence.

## Screening MRI

The American Cancer Society recommends annual MRI as an adjunct to mammography in women with a >20–25% lifetime risk of breast cancer [21]. This risk may be calculated by one or more of several risk models such as Claus, Tyrer-Cuzick, BRCAPRO, and BOADICEA, the results of which can be discussed with the patient in a larger context of genetic counseling with regard to overall risk assessment and prevention. Patients who are assigned a lifetime risk of >20% include those with a known genetic predisposition; a mutation in one of the many identified genes implicated in breast cancer, such as BRCA1 or BRCA2; those with a first-degree relative with such a mutation but are untested themselves; those who have had mantle (chest) radiation between the ages of 10 and 30 (usually for lymphoma); and those with (or a first-degree relative with) Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome. With the advancement of genetic testing, more and more mutations are being discovered that may also have a role in increasing risk. For women at high risk, the consensus is to start yearly screening with mammograms and MRIs at 30, but depending on certain risk factors, some may start as early as 25 after discussion with their primary doctors and/or genetic counselors.

In light of the discussion on dense breast tissue above, it is important to note that dense breast tissue alone is currently *not* an indication for screening MRI; nor is a prior history of breast cancer or high-risk lesion. Unless a combination of these and other factors adds up to a >20% lifetime risk, insurance companies may not provide coverage in the United States.

Diagnostic MRI can be used to evaluate the extent of a newly diagnosed breast cancer (including multifocal and multicentric disease, chest wall involvement and

axillary lymph nodes), the response to neoadjuvant chemotherapy, and in the setting of axillary node metastatic disease with an unknown primary. Less often, it is used for problem-solving—e.g., to help distinguish between scar versus recurrence—at the discretion of the radiologist. MRI is also helpful in the evaluation of silicone implant integrity, specifically for intracapsular ("internal") rupture.

## Imaging Evaluation of the Patient

What is a breast radiologist looking for? Generally speaking, masses, architectural distortion, asymmetries, diffuse changes and calcifications. But, as with everything in medicine, each of these has a differential diagnosis—not everything reported will be a cancer. Actually, the vast majority of findings are benign, and depending on practice variations, some radiologists may not include them in a dictation to prevent cluttering their reports, or confusion or worry on the part of the patient and clinician. For example, normal intramammary and axillary lymph nodes, or skin and vascular calcifications, may not even be mentioned, with preference given to a more general statement such as "no suspicious masses or malignant type calcifications are identified."

So how does the radiologist decide what constitutes a benign finding and what warrants further workup? Therein lies the BI-RADS lexicon (…and experience). Not only does the lexicon allow for clear, consistent reporting, but its focus on feature analysis through specific terminology allows for "triage." When, as an example, through actively looking and engaging in an internal dialogue, the radiologist could describe a mass as oval and fat containing with circumscribed margins in the upper outer quadrant, he/she knows that is defining a normal intramammary lymph node and may decide not to report it at all. If one could report oval, lucent-centered calcifications at the inframammary fold, these are congruent with skin calcifications and can be left alone, even if they are new.

A *mass*, by definition, must occupy space in three dimensions, or on two orthogonal imaging projections. It has convex borders and mammographically is denser centrally than peripherally. Radiologists evaluate masses with regard to shape, margins, radiographic density, internal composition, and other imaging characteristics depending on the modality, such as the effects on surrounding tissue.

*Architectural distortion* is the disruption of normal tissue planes. Mammographically and on MRI, it appears as straightening of parenchymal lines (Fig. 1.5); normally, the interfaces of intermingled fatty and fibroglandular tissues are gently undulating. Sonographically, the disruption of tissue planes may be more apparent as ligaments seem to stop and start, with interspersed ill-defined, "hazy" parenchyma. While distortion can reflect underlying invasive lobular cancer (Fig. 1.5) or DCIS, benign etiologies such as postsurgical change or trauma need to be considered if consistent with the patient's history and physical exam (i.e., a scar on the skin directly over the area in question on imaging).