Finding Early Invasive Breast Cancers: A Practical Approach¹

Detection of early invasive breast cancer is important, as patient survival is high when the cancer is 2 cm or smaller. Invasive breast cancers typically manifest mammographically as focal asymmetries or masses. Strategies for detecting focal asymmetries and masses on screening mammograms include side-by-side comparison, looking for parenchymal contour deformity, close inspection of the retromammary fat, identifying the presence of associated findings, and comparison with prior mammograms. Focal asymmetries are often normal but are concerning when there is distortion of the normal breast architecture. Masses and focal asymmetries are best evaluated in the diagnostic setting by using spot compression and true lateral views and, frequently, ultrasonography. Management of a lesion depends on the worst imaging feature. Indications for an assessment of probably benign findings are very specific but are often misapplied. This review for residents provides a practical approach to the detection and management of breast masses and focal asymmetries.

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Invasive breast cancer typically manifests as a mass at mammography. Before developing into a mass, a cancer may manifest as a focal asymmetry. Early detection of these masses and asymmetries that represent invasive carcinoma is important in reducing breast cancer mortality. Women with invasive cancers of 1 cm or smaller have a 95% chance of survival at 10 years, while those with invasive cancers 1–2 cm and 2–5 cm in size have, respectively, 85% and 60% survival at 10 years (1). For large invasive cancers, survival is dependent on tumor grade (1). However, survival is high for women with small invasive cancers, whether the cancer is low or high grade (2).

Thus, detection of small invasive cancers substantially affects breast cancer mortality.

The Breast Imaging Reporting and Data System (BI-RADS) (3) defines a mass as “a space occupying lesion seen in two different projections.” The BI-RADS lexicon states that a focal asymmetry “is visible as a confined asymmetry with a similar shape on two views, but completely lacking borders and the conspicuity of a true mass” (3). A potential mass is termed a focal asymmetry if it does not meet the three-dimensional criteria of a mass. Thus, if a lesion has definable borders but is only visualized in one projection, it is considered a focal asymmetry.

The detection of breast masses and focal asymmetries on screening mammograms is largely a challenge of perception. Once a lesion is detected, management is relatively straightforward. This is in contrast to breast calcifications, where perception of the finding is not as difficult, but disposition is more challenging. Diagnostic evaluation of breast masses and focal asymmetries includes additional mammographic views and often breast ultrasonography (US).

This Review for Residents is intended to provide a practical approach to the detection and management of breast masses and focal asymmetries. We will describe an approach to screening mammography with the goal of improving identification of breast masses and focal asymmetries, develop strategies for evaluating breast masses and focal asymmetries in the diagnostic setting, and describe proper application of the BI-RADS assessment and recommendation categories. The techniques and findings that we describe pertain primarily to invasive ductal carcinoma, which is the most common type of breast cancer. We have previously reviewed the findings of unusual breast cancers, which may provide clues to a diagnosis other than invasive ductal carcinoma (4).

An Approach to Detecting Masses and Focal Asymmetries at Screening Mammography

Screening mammograms may be interpreted “online” while the patient waits for results or may be batch interpreted, often on the next business day following the examination. Online interpretation of screening mammograms reduces patient stress for those women with abnormalities (5). Inefficiencies due to online interpretation of screening mammograms result in an increase in cost of nearly $30 per study that most women are not willing to pay (6). Batch interpretation is more efficient and results in improved specificity with equal cancer detection rates (7,8). The percentage of U.S. facilities using batch interpretation increased from 20% in 1992 (9) to 93% in 2002 (10).

A screening mammogram is two views of each breast: the craniocaudal (CC) view and the mediolateral oblique (MLO) view. Our protocol is to review the current CC views side-by-side (with the chest wall of the left breast next to that of the right breast) and the MLO views (also side-by-side, as for the CC views) on the lower panel of the rolle scope, with a comparison study obtained 2 or more years earlier hung in an identical fashion on the panel above. Your protocol may be different, but it should be consistent. Consistency aids in lesion detection as one becomes accustomed to reviewing studies with a particular visual pattern.

A consistent approach to reading will ensure that all aspects of the mammogram are reviewed. Ensure that you are reading in an optimal environment using high-luminance viewboxes (3500 nits) for screen-film mammography or high-resolution monitors for digital mammography, mask any extraneous light around the images, and reduce room light as much as possible. First, confirm that the name and other patient identifiers are correct (ie, you are reading the correct study) and that the images are of adequate quality. In mammography, the images must have good contrast, compression, positioning, and lack of blur or artifacts. In reviewing the mammogram, an overview is helpful to check for obvious abnormalities and changes from the previous study. Next, compare the MLO views side-to-side and then the CC views (or vice versa) to look for asymmetry in the breast paren...
chymal pattern, paying particular attention to the retromammary fatty regions. Evaluate the contour of the breast parenchyma where it interfaces with fat. Finally, with the magnifying glass, closely examine the breast parenchyma for architectural distortion and calcifications. If a finding is identified, compare with the prior mammograms to assess whether the finding is new, growing, or stable by using studies more than 2 years older if need be.

**Asymmetric Breast Tissue versus Focal Asymmetry**

Asymmetry in the breast may be global or focal. Asymmetric breast tissue, or global asymmetry, in which the parenchyma is overall greater in volume in one breast compared with the other, is common and usually normal. However, global asymmetry is of concern when there is associated architectural distortion, an apparent decrease in breast size at mammography, skin thickening, axillary adenopathy, or clinical findings. Breast cancers manifesting as global asymmetry are likely to be large.

Global asymmetry can be due to underlying invasive lobular carcinoma, particularly when associated with architectural distortion without a central mass or an apparent decrease in breast size (the “shrinking breast”) (11). Invasive lobular carcinoma accounts for 6%–9% of all breast cancers (12,13). Most breast cancers enlarge en mass, like a ball getting larger, whereas invasive lobular carcinoma spreads in single-layer sheets of tumor cells similar to a spider web. The breast density may increase and the breast tissue becomes less compliant. This may result in architectural distortion, manifested as straight lines, typically in a radial pattern in the breast. Use of the magnifying glass helps to identify subtle architectural distortion.

**Detecting Focal Asymmetries**

Focal asymmetry is also frequently a benign finding in the breast, representing summation of normal tissue. However, early breast cancer may manifest as a focal asymmetry on screening images. A mass may become apparent on diagnostic images. The goal is to find breast cancers at this early stage.

**Comparison.**—If you wanted to compare two different clothing items, you would put them next to each other to look at the differences. Look for early cancers by comparing the breasts from side to side in the manner mentioned previously (Fig 1). This can be done as the initial step in reading the mammogram after ensuring proper identification and quality.

**Contour deformity: look for the hook, slow down for the speed bump.**—Women with dense breast tissue typically have an outward convex margin to their breast parenchyma. Cancers may manifest with distortion to this outward margin, similar to taking a crochet hook and pulling in the tissue toward the cancer (Fig 2) (14). The subcutaneous fat is drawn into this space, creating straight lines (architectural distortion) with an angular fat density invagination into breast parenchyma. This may be the only sign of a cancer hidden within opaque breast tissue. When identified, additional imaging including spot views and US will usually unmask the hidden lesion.

In contrast, women with scattered...
fibroglandular densities or heterogeneously dense breast tissue typically have a scalloped or concave margin to the breast parenchyma. A breast mass may be detected by looking for an outward convex margin along the parenchymal margin (Fig 3). Think of this as a speed bump when you are following the edge of the parenchyma. Slow down and take a closer look at the area.

*Living in the wrong neighborhood (triangle).*—There are particular triangle-shaped zones of the breast that justify a higher level of suspicion when a focal asymmetry is identified (Fig 4). On the CC view, these zones are the retro-mammary fat between the breast tissue and the chest wall and the medial or inner triangle (Fig 4). On the MLO view, these are the central space between the breast tissue and the chest wall and the lower triangle (Fig 4). These are all typically fatty areas, so the presence of a focal asymmetry in these areas should raise suspicion. The retro-mammary fat area on the MLO view is often referred to as “the Milky Way,” because we are searching for white...
The retroareolar area of the breast is very difficult to evaluate because of the complex anatomy of the region. Mammography is less sensitive for breast cancer detection in this area (15). To improve detection of a subareolar cancer, having the nipple in profile on one of the two screening views (CC or MLO) may be helpful (Fig 5) (16). Once well-positioned images have been obtained, assess the retroareolar regions for asymmetry compared to the opposite side. Also be aware that not all round masses and densities in the retroareolar area represent nipples out of profile. True masses may look like nipples. Spot compression views of the subareolar region with a radiopaque marker on the nipple or with the nipple in profile will typically resolve whether a mass is present.

**Associated findings: looking for more clues.**—When a potential lesion is identified, the level of suspicion is increased when associated findings are also identified. Architectural distortion that is present with a focal asymmetry is suspicious (Fig 6). Calcifications associated with a focal asymmetry may represent ductal carcinoma in situ (calcifications) associated with invasive carcinoma (focal asymmetry) (Fig 7). The presence of ipsilateral adenopathy likewise increases suspicion, as the focal asymmetry may represent an invasive cancer with metastasis to axillary lymph nodes (Fig 8). Occasionally, axillary or intramammary adenopathy may be mistaken for a primary breast carcinoma (Fig 9).

**Use of prior studies: beware of stability!**—Breast cancers may grow slowly. Therefore absence of substantial growth or change on a mammogram when compared to the previous year’s mammogram may mislead one to a false assumption that the lesion is benign (Fig 10). Our standard practice is to compare the current mammogram to studies that are 2 or more years old. If there is a finding for which change is difficult to assess by using that previous mammogram, older studies are reviewed. It is typical that comparison
**Figure 5:** Subareolar region. Bilateral mammogram obtained in a 67-year-old woman with new right nipple retraction. Left: A small mass (arrow) with architectural distortion is seen in the right subareolar region of the CC view. Right: The lesion is difficult to perceive on the MLO view because the nipple (arrow) is not in profile.

**Figure 6:** Architectural distortion. Left breast mammogram in a 68-year-old woman after remote right breast mastectomy with no current breast complaints. (a) Left mammogram shows a focal asymmetry (arrows) in the central left breast. (b) Spot compression view in MLO projection shows numerous straight lines (arrows) associated with the focal asymmetry consistent with architectural distortion. The lesion was assigned BI-RADS category 5 (highly suggestive of malignancy). Core-needle biopsy specimen showed an invasive ductal carcinoma, which measured 7 mm at excision.
Figure 7: Mass with calcifications. Close up of a left CC view from a screening mammogram in a 53-year-old woman shows a 6-mm oval, spiculated, equal-density mass (straight arrows), with associated amorphous microcalcifications (curved arrow). Stereotactic-guided core-needle biopsy specimen showed invasive ductal carcinoma with associated ductal carcinoma in situ.

Figure 8: Abnormal lymph node. (a) Right MLO view from a screening mammogram in a 67-year-old woman shows a 20-mm round ill-defined mass (straight arrow). An abnormally dense axillary lymph node is also noted (curved arrow). (b) US image of the right axilla confirms focal areas of thickening (outward contour) of the lymph node cortex (arrows). Findings at US-guided core-needle biopsy of the right breast mass showed invasive ductal carcinoma. Findings at US-guided core-needle biopsy with an 18-gauge Temno needle (Alleghiance HealthCare, McGaw Park, Ill) showed metastatic adenocarcinoma.

Figure 9: Bilateral mammogram in a 29-year-old woman with palpable lump in the right breast at 10 o’clock position. The obvious axillary mass represents metastatic adenopathy (straight arrows). Side-to-side comparison (rectangles) reveals focal asymmetry in the right upper outer quadrant (curved arrows), corresponding to the palpable lump. Biopsy specimen of the focal asymmetry showed invasive ductal carcinoma, grade III.
with studies that are 4 or 5 years older makes clear that a finding has been present for some time and is unchanged, and thus likely benign, or that the finding is indeed developing and recall is indicated. The exception is that when a round or oval mass is identified and a cyst is suspected, comparison with studies from the previous year is helpful if the mass was shown at US to be a simple cyst at that time and has not changed in size since then. Note, however, that a finding that looks suspicious should not be discounted just because someone worked it up last year and said it was benign. In all cases, lesion morphology takes precedence over stability. If the morphology is suspicious, work up

Figure 10: Comparison mammograms. MLO views of the left breast demonstrate a slow-growing mass (arrows). The current mammogram (left) was not substantially different from that of the previous year (middle) but was considerably different from that of 3 years earlier (right). Biopsy specimen showed invasive lobular carcinoma, grade I.

Figure 11: Normal focal asymmetry. (a) Bilateral digital mammogram obtained in a 42-year-old woman for baseline screening. A focal asymmetry is present in the left breast at 12 o’clock position, posterior third (arrows). The asymmetry respects normal architecture of the breast, with no straight lines or outward convex margins. (b) Looking at the black fat lobules (circles) rather than the white breast parenchyma can be helpful in assessing whether a focal asymmetry is respecting normal breast structures. This was assigned BI-RADS assessment category 2 (benign finding) and has remained stable for 2 years of follow-up.
When to ignore a focal asymmetry: respect for normal breast architecture.—When a focal asymmetry represents summation of normal tissue, there will be no distortion of Cooper ligaments or the regular, symmetric, undulating interface between glandular tissue and subcutaneous fat (Fig 11). In other words, normal tissue will respect normal boundaries. One approach is to look at the black on the image instead of the white. You should see oval fat lobules, with soft curved Cooper ligaments separated by strands of white breast tissue. Invasive breast cancer grows through normal structures and may result in abnormal outward convex margins and straightening of Cooper ligaments. A focal asymmetry should be recalled for evaluation, even if it appears to be respecting normal breast structures, if it is new in comparison to prior mammograms, since early breast cancers may cause little distortion. Spot compression views will help define if a focal asymmetry is behaving respectfully.

A focal asymmetry that has outward convex margins or is associated with straight lines is not respecting the normal architecture of the breast and should increase suspicion (Fig 12). Breast cancer does not respect normal breast structures but grows through them instead creating abnormal lines. These straight lines represent early spiculation around a mass or focal asymmetry (Fig 12).

Leave-alone masses.—Fat-containing masses in the breast are benign with rare exception if circumscribed and round or oval in shape (17,18). These masses include: lymph node, lipoma, oil cyst, hamartoma, and galactoceole. If a mass identified at screening clearly represents one of these five, no additional work-up is needed. However, fat-containing masses are not necessarily benign if the margins are irregular or spiculated, since cancers can engulf fat as they grow.

Volume counts.—As with any task, practice increases skill. Read as many mammograms as possible during your residency. At our institution, residents
spend their first month of breast imaging seeing diagnostic imaging patients so they will see many breast cancers. The second month focuses on screening mammography and breast procedures. The third month focuses on managing difficult diagnostic cases, as well as further experience in screening and procedures. We expect our residents to read at least 500 screening mammograms during each of their second and third months. Even those who are planning to perform a fellowship in another area of radiology are likely to read mammograms if they are in private practice. You will be much more confident if you have first read at least 1000 mammograms with a mentor.

**Double reading and computer-aided detection.**—Both double reading of mammograms and computer-aided detection, or CAD, improve sensitivity (19,20). A CAD system places marks on potentially suspicious calcifications and possible masses. Freer and Ulissey (20) found a 19.5% increase in cancer detection with the use of CAD in a community breast center, with an increase in screening recall rate from 6.5% to 7.7%. However, the benefit can differ (21). If you are a resident at an institution that uses CAD, gain experience using the tool so that you will be accustomed to its potential benefits and pitfalls before entering practice.

**Evaluating a Mass or Focal Asymmetry Identified at Screening**

The next step after identifying a mass or focal asymmetry is diagnostic evaluation. Biopsy should not be recommended based on the findings of screening mammography. Additional imaging in the diagnostic setting allows characterization of the mass or focal asymmetry to evaluate if the finding is real and to permit the imager to develop a level of suspicion. If a lesion is highly suspicious for breast cancer on the screening images, recall for diagnostic evaluation is still useful to evaluate for the extent of disease, multifocality, and staging of the axilla with US. In addition, diagnostic evaluation allows the radiologist to discuss the findings with the patient, an-
swer questions, and arrange for biopsy. An important advantage to this approach is that scheduling of procedures is very efficient, since biopsies will rarely be cancelled if the lesion has been characterized at imaging prior to the procedure. If a lesion is highly suspicious on the screening mammogram, recall of the patient should be prioritized, however, so that minimal delay occurs between screening and diagnostic evaluation.

Diagnostic Evaluation of Masses and Focal Asymmetries

Spot compression views.—All screening recall examinations with a mass or focal asymmetry should include spot compression views as well as a true lateral view. Spot compression views should be obtained in both CC and MLO projections without coning. Obtaining spot compression views in both projections is important because some cancers may not appear masslike on a spot compression view in one projection but may appear spiculated in the other projection. If a focal asymmetry is seen on only one view, a “best guess” at location may be approximated by using the distance of the lesion from the nipple (Fig 13). Many breast imagers prefer to obtain spot compression views with magnification, although this is not routine at our institution.

Go to the lateral view for more information.—The true lateral view may be either a mediolateral or lateromedial view. Our standard protocol is to obtain a mediolateral view in all patients recalled for an abnormal screening examination. However, if the lesion is located in the medial breast, then a lateromedial view may provide better visualization of the lesion, since it will be closer to the film or digital receptor. Other mammographic views such as rolled, exaggerated CC lateral, and cleavage views may also be useful in localizing a lesion and to evaluate if a finding represents summation of normal tissue or a suspicious lesion. US is frequently useful for confirming that a focal asymmetry represents normal tissue or characterizing a mass as benign or malignant.

Lesions seen on only one view.—If a lesion is seen only on the CC view, it may be obscured on the MLO view or may be medial and superior, since this is where the MLO view is most likely to miss tissue. Obtaining a true lateral view may reveal the finding. Rolled views, in which the breast is rolled either medial or lateral in the CC projection, may be helpful in localizing the lesion. The direction in which the lesion moves on each rolled CC view provides a clue to the true lesion location.

If a lesion is seen only on the MLO view, it may be obscured on the CC view or may be far lateral, since this area may not be visualized on the CC view. An exaggerated CC lateral view is frequently helpful because most breast cancers are located in the lateral breast. A true lateral view (mediolateral or lateromedial) is very useful for localizing the lesion if not seen on the CC or exag-
Lesions in the lateral breast project higher on the MLO view than they are actually located in the breast, because the MLO view is obtained at an oblique angle. Likewise, lesions in the medial breast project lower on the MLO view than they are actually located in the breast. Thus, lesions that shift lower in position on the mediolateral view are located in the lateral breast while lesions that shift higher in position on the mediolateral view are located in the medial breast (Fig 15). This leads to the well-used adage, “Lead (lateral) sinks, muffins (medial) rise.” Note, however, that lesions that are more central in the breast (slightly lateral or slightly medial to the nipple) will shift little or not at all between the MLO and mediolateral views. The best approach is to think about the geometry of the views rather than by relying on a saying. Lesions seen in only one projection can also be localized by using step-oblique mammographic views, where mammographic views are obtained at 15° intervals between the true lateral and CC views. Pearson et al (22) successfully localized 50 of 50 true masses in three dimensions by using this technique.

Occasionally a lesion may be seen well only in one projection, despite obtaining additional mammographic views. If a lesion is suspicious at mammography, biopsy can often still be performed in most cases by using stereotactic guidance. If the lesion is too far posterior, US or magnetic resonance (MR) imag-
ing may be useful for localization. Placement of a marking clip at the time of biopsy and a subsequent mammogram documenting clip location can confirm that the lesion identified at US or MR imaging represented the mammographic finding.

Using US in the diagnostic setting.—Early use of US in the diagnostic breast evaluation setting was to differentiate benign simple cysts from solid masses. The work of Stavros et al (23) defined benign and malignant characteristics of breast masses, allowing more appropriate disposition of breast findings. At our institution, we frequently use US as a second check of a focal asymmetry identified at screening mammography when the spot compression views do not show an underlying mass, especially with dense tissue (Fig 16). If a mass is not identified at US, focal areas of shadowing or hypoechogenicity may be identified that would increase suspicion or, alternatively, a corresponding island of normal breast tissue (arrows) is identified that corresponds to the focal asymmetry in location. Biopsy was cancelled.

**Management of Breast Masses and Focal Asymmetries**

**The Worst Feature Wins**

Lesions in the breast should be managed based on their worst features. If the mammogram finding is suspicious but the US examination is normal, or vice versa, biopsy should still be considered.

**Malignant Features**

Biopsy should be performed if malignant features are present at mammography or US. On mammograms, these features include irregular shape, spiculated or irregular margins, or high density. On US images these include spiculation, angular margins, marked hypoechogenicity, posterior acoustic shadowing, calcifications, duct extension, branch pattern, or microlobulation (23). For lesions with these characteristics, assessment of stability has no role—for example, “stable” and “spiculated” do not belong in the same sentence in a report. Lesions should be considered suspicious when the margins are ill defined or microlobulated with any shape or density of lesion; biopsy should be considered.

For highly suspicious lesions (BI-RADS category 5), US may be useful for evaluating for additional masses.

**MR imaging for problem solving.**—Current indications for breast MR imaging may include evaluation of extent of a known breast cancer, detection of an unknown primary breast carcinoma in patients manifesting malignant adenopathy with a normal mammogram, or screening in high-risk women (24,25). Breast MR imaging is not ordinarily indicated for routine evaluation of masses or focal asymmetries on mammograms, and it should never replace a thorough diagnostic evaluation including additional mammographic views and US images. However, breast MR imaging can be useful in some circumstances, particularly when a lesion is quite suspicious on one view but cannot be localized despite appropriate and complete additional imaging (Fig 18).
that may represent multifocal invasion and for abnormal lymph nodes in the axilla. Remember that lymph enters the node on the capsule, not the hilum, so an abnormal outward contour of the lymph node should be considered with suspicion (Fig 8). The most predictive signs of axillary metastasis in lymph nodes are maximum cortex thickness greater than 2 mm and appearance of the cortex (26).

**Benign Features**
Masses have benign features if round, oval, or lobular in shape with circumscribed margins. A focal asymmetry has benign features when there are no outward convex margins or associated straightening of Cooper ligaments. Having prior mammograms for comparison is key in the disposition of lesions with benign features. Routine follow-up can be performed if the lesion is stable for 2 or more years (BI-RADS 2: benign finding). However, when a lesion with benign features is new, biopsy should be considered (BI-
RADS 4: suspicious) unless shown to be a simple cyst at US examination (BI-RADS 2). If this was the patient’s first mammogram (baseline) or it is not possible to obtain earlier studies, short-term follow-up imaging in 6 months (BI-RADS 3: probably benign) is reasonable since the risk of malignancy is less than 2% (27).

**Probably Benign**
The BI-RADS 3 (probably benign) category is a frequently misapplied category (28). Probably benign does not equate to “I am not sure what to do with this lesion.” If you are not sure, get more information by obtaining more mammographic views or US images or get input from someone else. The two primary indications for a probably benign assessment are a round or oval mass or grouped round calcifications on a baseline mammogram. It is also okay to consider a lesion probably benign if it is far posterior and that portion of the breast was not visualized previously. A round or oval mass that is new is not “probably benign” unless it represents a specific benign diagnosis such as a simple cyst or lymph node.

The key to successful application of the BI-RADS 3 category is rigorous evaluation of the lesion characteristics and strict adherence to the criteria differentiating benign from possibly malignant. Many lesions that are assigned a BI-RADS 3 classification and are ultimately determined to be malignant at follow-up examination were, in retrospect, misclassified as BI-RADS 3 initially (29). Findings recalled from screening for diagnostic evaluation should be assigned a category of BI-RADS 0 (needs additional evaluation), not BI-RADS 3, even if the level of suspicion is low that the finding represents a cancer.

**Summary**
Asymmetric breast tissue is usually normal but is worrisome when new or when there are associated findings, including architectural distortion, a palpable lump, or thickening at clinical examination, or when the breast appears to be smaller at mammography (“the shrinking breast”).

Look for asymmetry (side-by-side comparison), contour deformities (look for the hook, slow down for the speed bump), lesions in the retromammary fat (living in the wrong triangle), and associated findings to identify early breast cancer.

Use studies that are 2 or more years old for comparison when available, but beware of stability. Suspicious morphology outweighs stability (”stable” and “spiculated” do not belong in the same sentence).

Diagnostic evaluation should be performed when a concerning mass or focal asymmetry is identified at screening mammography and should include a true lateral view, spot compression views in both CC and MLO projections, and often US.

If in doubt about the finding after obtaining additional mammographic views, consider performing US. This will often lower or raise the level of suspicion. If still in doubt, biopsy can often be performed with stereotactic guidance, even if the lesion is seen only on one view.

**References**
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