Diagnostic evaluation of suspected breast cancer

AUTHORS: Laura J Esserman, MD, MBA, Bonnie N Joe, MD, PhD
SECTION EDITORS: Anees B Chagpar, MD, MSc, MA, MPH, MBA, FACS, FRCS(C), Daniel F Hayes, MD, Gary J Whitman, MD
DEPUTY EDITOR: Wenliang Chen, MD, PhD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Oct 31, 2023.**

INTRODUCTION

Diagnostic methods are those used for further evaluation after a potential breast cancer is suspected either by abnormal imaging or by physical findings.

The imaging modalities most commonly used to evaluate suspected breast cancers (ie, mammography, breast ultrasound, breast magnetic resonance imaging [MRI]) are described in detail in this topic. They are also discussed in other topics (eg, in the context of breast cancer screening for asymptomatic women). (See "Breast imaging for cancer screening: Mammography and ultrasonography" and "MRI of the breast and emerging technologies".)

Most breast cancers are diagnosed with a biopsy prior to treatment. Although breast biopsy is an integral part of the diagnostic evaluation of patients with suspected breast cancer, it is discussed in a dedicated topic separately. (See "Breast biopsy".)

Clinical evaluation of breast masses and the staging workup and management of patients with newly diagnosed breast cancer are discussed separately. (See "Clinical manifestations, differential diagnosis, and clinical evaluation of a palpable breast mass" and "Clinical features, diagnosis, and staging of newly diagnosed breast cancer" and "Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer".)

OUR APPROACHES

In general, recommended imaging options in the context of a suspected breast cancer include diagnostic mammography and breast ultrasound (US), the choice of which depends on patient age and the degree of clinical/radiologic suspicion. There is little role for advanced imaging modalities such as breast magnetic resonance imaging (MRI), positron emission mammography (PEM), or sestamibi scan (MBI) [1].

Nevertheless, there is significant variability in the diagnostic evaluation of patients with suspected breast cancer. Patterns of referral vary dramatically, as do rates of screening mammography recall. The workup and evaluation may differ depending upon which clinician is seen first. The following diagnostic algorithms are helpful as general guidelines, but they may be adapted to suit provider and patient preferences.

Mammographic abnormality — The majority of breast cancers are diagnosed as a result of an abnormal mammogram, but not all mammographic findings represent cancer. If an abnormality is found on a screening mammogram, diagnostic mammography and possibly targeted US are used for further evaluation. (See 'Diagnostic versus screening mammography' below.)

Following diagnostic mammography and possibly breast US, the lesion is assigned to one of the Breast Imaging-Reporting and Data System (BI-RADS) assessment categories (table 1), based on which further management can be formulated (algorithm 1):

- BI-RADS 1 or 2: Normal or benign findings. The patient can continue with routine annual screening mammography.
- BI-RADS 3: Probable benign findings. The patient should repeat diagnostic mammogram in six months.
- BI-RADS 4: Suspicious for malignancy. BI-RADS 4 lesions have a 3 to 94 percent risk of malignancy that could be either ductal carcinoma in situ (DCIS) or invasive cancer. Management may be affected by the patient's age, comorbidities, and the type of cancer.
- BI-RADS 5: Highly suggestive of malignancy. Such lesions have a ≥95 percent chance of being malignant. In addition to biopsy, BI-RADS 5 (and some BI-RADS 4C [50 to 94 percent risk of malignancy]) patients would benefit from early surgical consultation.

The current standard is for patients with BI-RADS 4 or 5 lesions to undergo percutaneous biopsy; the optimal biopsy method and post-biopsy management are discussed elsewhere. (See "Breast biopsy" and "Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer".)

Palpable breast mass — Approximately 85 percent of breast cancers are detectable with breast imaging. Regardless of imaging findings, a clinically suspicious mass should be biopsied, as approximately 10 to 15 percent of such lesions can be mammographically occult [1-3]. Even in the setting of palpable masses, image guidance for breast biopsy is preferred because it may improve diagnostic accuracy. Algorithms for diagnostic evaluation of palpable masses are stratified by the age of the patient:

Younger than 30 — The diagnostic approach to palpable masses in patients younger than 30 years of age differs among experts.

- The approach that is advocated by the National Comprehensive Cancer Network (NCCN) [4] and the American College of Radiology (ACR) appropriateness criteria expert panel [1] starts with a breast US (algorithm 2). US is the preferred initial imaging modality in younger patients because most benign lesions in young patients are not visualized on mammography, the incidence of breast cancer in young patients is low (<1 percent), and there is theoretically an increased radiation risk of mammography in young patients, although the overall radiation risk from mammography is minimal [1]. (See 'Breast ultrasound' below.)

  - If breast US identifies a simple cyst, then the lesion is assessed as BI-RADS 2 benign and no biopsy is needed. Although therapeutic aspiration of the cyst may be performed for symptomatic relief, surgical excision of a simple cyst is almost never done and generally not recommended. (See "Breast cysts: Clinical manifestations, diagnosis, and management", section on 'Simple cyst'.)

  - If breast US identifies a cystic lesion that is not a simple cyst (ie, a complex cyst or partially cystic mass), the lesion may be biopsied (if BI-RADS 4 suspicious; eg, there is a mass within the cyst), aspirated, or closely observed (if BI-RADS 3 probably benign) depending on the sonographic features and the patient's symptoms. (See "Breast cysts: Clinical manifestations, diagnosis, and management".)

  - If breast US identifies a solid lesion with sonographic features suggestive of a fibroadenoma (ie, oval circumscribed hypoechoic mass), this may be assessed as BI-RADS 3 probably benign, and six-month repeat US imaging is a reasonable option in lieu of biopsy, provided that the clinical examination also suggests a benign etiology. In some clinical scenarios for which it is impractical to perform imaging surveillance (eg, patients awaiting organ transplant, patients with known synchronous cancer, or patients trying to become pregnant), immediate biopsy to confirm benignity is warranted. Patients may also choose immediate biopsy over imaging surveillance as a management option for BI-RADS 3 probably benign lesions. Some authors recommend excision for particularly large, benign-appearing masses, although

there is no consensus as to a specific size above which excision is recommended. (See "Overview of benign breast diseases", section on 'Fibroadenomas'.)

- If breast US identifies a solid and indeterminate (ie, suspicious) lesion, mammography is often performed in addition to US, as mammography may find associated suspicious calcifications or additional masses. A biopsy is warranted for the suspicious mass seen at US even if the mass is not seen on the mammogram. If mammography identifies a benign lesion correlate to the US findings (eg, fat necrosis or calcified fibroadenoma), then biopsy may be avoided.

- If the mass cannot be visualized on US, mammography followed by biopsy should be pursued if the clinical suspicion for cancer is high, while a period of observation may be appropriate if the level of clinical suspicion is low and both US and mammography are negative. (See "Clinical manifestations, differential diagnosis, and clinical evaluation of a palpable breast mass".)

- Alternatively, fine needle aspiration (FNA) can be selected as the initial approach to a suspicious breast mass in a younger patient [4]. This alternative approach requires that the facility has the capacity to perform and interpret FNA. However, there is no evidence to support the use of FNA as part of the initial workup in patients younger than 30 with a palpable lump, and it is preferable for imaging to occur before biopsy, as change related to the biopsy may alter image interpretation [1].

  - If nonbloody fluid is aspirated, and the mass resolves, the fluid is discarded and the patient can be seen in two to four months for reexamination. There is no need to send fluid for cytology. A recurrent mass requires breast US examination. Aspiration of bloody fluid or persistent mass after aspiration requires core biopsy or surgical excision of the mass. (See "Breast cysts: Clinical manifestations, diagnosis, and management", section on 'Simple'.)

  - If no fluid is aspirated and cytologic review of cell blocks from the needle washings is nondiagnostic, then breast US is performed. (See "Breast biopsy", section on 'Fine needle aspiration'.)

If the initial evaluation shows cancer, bilateral diagnostic mammography should be performed prior to any treatment to exclude unsuspected or more extensive disease. (See "Clinical features, diagnosis, and staging of newly diagnosed breast cancer", section on 'Staging'.)

40 years or older — Diagnostic mammography is the main initial modality for imaging a palpable breast mass in patients 40 years of age or older (algorithm 3). Even if the mass is clinically suspicious for cancer, it is still preferable to image before biopsy [4]. The goal of imaging in this setting is not to establish a diagnosis of cancer but rather to identify other

suspicious areas or calcifications in either breast, so that percutaneous biopsies of the most suspicious findings can be performed to establish a diagnosis of cancer and guide treatment. Further evaluation after the diagnostic mammogram depends on the lesion's BI-RADS category (table 1):

- BI-RADS 1 patients typically undergo a breast US to further characterize the lesion in a manner similar to that outlined above for patients under 30 years of age (algorithm 2):
  - Cystic lesions found on breast US may be aspirated, biopsied, excised, or observed, depending on the patient's symptoms and the sonographic features of the lesion. If US finds a benign correlate to the palpable mass (eg, simple cyst or benign lymph node), then clinical follow-up for the palpable mass is appropriate and the patient may return to routine screening mammography. (See "Breast cysts: Clinical manifestations, diagnosis, and management".)
  - Solid lesions that are likely fibroadenomas and meet sonographic criteria for a probably benign (BI-RADS category 3) mass have a ≤2 percent likelihood of malignancy and may undergo short-interval (six-month) sonographic follow-up provided that the clinical examination also suggests a benign etiology. However, biopsy is warranted if a mass is new on imaging or increasing in size by 20 percent in either volume or each dimension in a six-month period [1]. In addition, BI-RADS 3 lesions in high-risk patients, patients awaiting organ transplant, patients with known synchronous cancers, or patients trying to become pregnant should be biopsied.
  - Solid lesions that are sonographically indeterminate or suspicious should undergo biopsy or excision.
  - Lesions not visible on breast US may be biopsied or observed, depending on the clinical suspicion for malignancy. Specifically, when both mammography and US are negative or benign in the evaluation of a palpable mass, the negative predictive value is greater than 97 percent, which is reassuring when the clinical suspicion for cancer is low [5]. However, a clinically suspicious lesion should always be biopsied regardless of the imaging findings.
- BI-RADS 2 patients with a benign lesion that correlates to the palpable mass do not require further imaging with breast US and can return to annual screening mammography.
- BI-RADS 3 patients have a probably benign lesion. Mammograms should be repeated every 6 to 12 months for two to three years to document stability. Alternatively, if the lesion is visible on breast US, it can be followed with breast US every 6 to 12 months for

the same period of time. The lesion should be biopsied if it enlarges on either repeat mammogram or US.

- BI-RADS 4 or 5 lesions seen on mammography should be biopsied. In this setting, breast US would be performed to search for sonographic correlate of the lesion and to examine the axilla as warranted. Finding a sonographic correlate of the mammographic abnormality permits biopsy to be done with US guidance, which is better tolerated than stereotactic biopsy. If no sonographic correlate is found, stereotactic biopsy or mammographic-guided localization for excisional biopsy should be performed for BI-RADS 4 or 5 lesions seen only at mammography. (See "Breast biopsy", section on 'Image guidance'.)

30 to 39 years of age — Either breast US (algorithm 2) or mammography (algorithm 3) can be used as the initial imaging modality for evaluating a patient 30 to 39 years of age, although likely both US and mammography will be performed as the two studies are complementary.

Because the sensitivity of US is higher than mammography in this age group (96 versus 61 percent) and the specificities are similar (89 versus 94 percent) [6], it is reasonable to start with US as the initial modality, but with a low threshold for using mammography if clinical suspicion is high. If a suspicious mass is identified on the initial US in this cohort, bilateral mammography is indicated. In the setting of malignancy in this age group, breast MRI should be considered, especially for parenchymal lesions.

Imaging after breast surgery — Given that 20 to 40 percent of women who have percutaneous breast biopsy subsequently undergo breast surgery, it is also important to address how best to image women with a history of benign (including high-risk) breast disease or breast cancer [7]. For such patients, the surveillance recommendations are determined by their overall risk:

- Higher-than-average risk women with a history of benign surgery may require screening mammography starting at an earlier age before 40 and may benefit from screening MRI. (See 'Breast MRI' below.)

- For women with breast cancer who have undergone initial excision and have positive margins, imaging with diagnostic mammography or MRI can sometimes guide additional surgical planning. (See "Breast-conserving therapy".)

- Women who have completed breast conservation therapy for cancer should get annual mammography and may benefit from the addition of MRI or ultrasound to their surveillance regimen. (See "Approach to the patient following treatment for breast cancer", section on 'Breast imaging'.)

Importance of multidisciplinary care — A suspicion of breast cancer requires that care be coordinated among clinicians in several specialties. An integrated approach with breast radiologists and breast surgeons can minimize unnecessary biopsies and expedite diagnosis for the patient who receives a diagnosis of breast cancer. Similarly, once the diagnosis of cancer is made, multidisciplinary coordination among breast and reconstructive surgeons, radiation and medical oncologists, radiologists, and pathologists facilitates treatment planning and streamlines patient care [8].

For example, in settings where there is suspicion that the lesion may be ≥2 cm or greater, where there are neoadjuvant trials that require tissue for research, and where cytology is available and reliable, diagnosis using FNA may be performed first so that a conversation can be had with the patient and discussion of trial participation can be had prior to core biopsy, so that research cores and diagnostic cores can be taken at the same time, minimizing trauma and tumor disruption.

MAMMOGRAPHY AND DIGITAL BREAST TOMOSYNTHESIS

Over 90 percent of the breast cancers were identified mammographically, and fewer than 10 percent were detected solely by physical examination [9,10].

Mammography versus digital breast tomosynthesis — Digital breast tomosynthesis (DBT) can address some of the limitations of standard mammography by improving lesion localization and characterization in noncalcified lesions compared with conventional mammographic workup. Although it has been predominantly evaluated in the screening setting [11-13], DBT may be used in a diagnostic capacity as well and has demonstrated improvements in both screening and diagnostic outcomes compared with standard 2D mammography [14]. The performances of standard and digital mammography are considered equivalent in the diagnostic setting. (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'Digital mammography'.)

Diagnostic versus screening mammography — By definition, a screening mammogram is performed in a patient with no clinical symptoms or complaints. Abnormalities on screening mammography include masses, calcifications, architectural distortions, or asymmetries. Screening mammography is discussed in detail elsewhere. (See "Screening for breast cancer: Strategies and recommendations".)

If an abnormality is found at mammographic screening, supplemental mammographic views may be used for further characterization. A variety of mammographic techniques, including spot compression and magnification views (image 1 and image 2) and varied angled views, may characterize a lesion more precisely prior to making a final recommendation for management. These additional images are termed diagnostic mammographic views. (See

"Breast imaging for cancer screening: Mammography and ultrasonography", section on 'The mammographic examination'.)

Diagnostic mammography is associated with higher abnormal interpretation rate and higher cancer detection rate than screening mammography. Data on digital mammography from the Breast Cancer Surveillance Consortium (BCSC) showed an abnormal interpretation rate (AIR) of 12.6 percent for diagnostic mammography and cancer detection rate (CDR) of 34.7 per 1000 compared with AIR of 11.6 percent and CDR of 5.1 for screening mammography [15,16]. Such results are expected since diagnostic patients have signs or symptoms of breast cancer while screening patients are asymptomatic.

Some of the most aggressive cancers appear between screening mammograms and are therefore termed interval cancers [3], and younger patients may present with large tumors prior to the age at which screening is usually recommended. As such, when patients present with a suspicious new mass, diagnostic mammograms should be part of the initial workup, despite young age or the patient having had a negative routine screening mammogram. The only exception is that in patients younger than 30 years, initial evaluation with ultrasound is recommended. If ultrasound findings are suspicious, then mammography should be performed. (See 'Younger than 30' above.)

BI-RADS assessment categories — The radiologist summarizes the mammographic findings using the American College of Radiology (ACR) BI-RADS (Breast Imaging-Reporting and Data System) final diagnostic assessment categories, which indicate the relative likelihood of a malignant diagnosis [17].

The BI-RADS final assessment categories standardize both the reporting of mammographic and sonographic findings and the recommendations for further management (ie, routine screening, short-interval follow-up, or biopsy). Assessments are either incomplete (category 0) or one of the final assessment categories (categories 1 through 6) as described in the table (table 1) [17]. (See "Breast imaging for cancer screening: Mammography and ultrasonography", section on 'BI-RADS final assessment categories'.)

If a mammogram is assigned category 0, additional evaluation is required for further characterization, which may include additional mammographic views and/or ultrasound and, rarely, magnetic resonance imaging (MRI). Mammographic findings such as masses and calcifications can be stratified by suspicion for malignancy, and the BI-RADS 4A, 4B, and 4C categories are helpful in alerting the referring clinicians, pathologists, and surgeons to the underlying risk of malignancy [17,18].

Once pathology results become available, the radiologist issues a "statement of concordance" between imaging and pathology; any benign pathology discordant with the imaging findings should prompt further evaluation. A BI-RADS designation of 4C or 5 should

alert the pathologist that a malignant diagnosis is strongly suspected and that further evaluation of the specimen (and possible rebiopsy) is needed if the biopsy is initially interpreted as benign.

Mammographic features of breast cancer — There are two general categories of mammographic findings suggestive of a breast cancer: soft tissue mass or asymmetry and suspicious microcalcifications.

Soft tissue mass/asymmetry — The most specific mammographic feature of malignancy is a spiculated soft tissue mass (image 3); nearly 90 percent of these lesions represent invasive cancer.

Approximately one-third of noncalcified cancers appear as spiculated masses; 25 percent as irregularly outlined masses; 25 percent as less specific round, oval, or lobulated masses; fewer than 10 percent as well-defined round, oval, or lobulated masses; and 5 percent as areas of architectural distortion of dense tissue without an obvious mass [19].

Microcalcifications — Microcalcifications are seen in approximately 60 percent of cancers detected mammographically. Histologically, these represent necrotic cells in the center of a cluster of tumor cells (picture 1). Calcifications also are common in association with a mass, which usually signifies both invasive and in situ disease and can be present throughout the area of large, aggressive cancers.

It is relatively common for women to have tiny deposits of calcium that range from 0.1 to 1 mm, which are the footprints of cells that turn over. Scattered individual calcifications are benign, whereas the patterns in which calcifications group together may alert clinicians to the presence of an underlying ductal malignancy. As an example, segmental calcifications that align in a ductal distribution are particularly concerning for the presence of in situ carcinoma.

Specific patterns of calcifications are associated with different likelihoods of underlying malignancy:

- Linear branching microcalcifications (image 4A-B) are most commonly associated with the comedo histologic subtype and have a higher predictive probability for malignancy when compared with coarse, heterogeneous (ie, nonlinear irregular calcifications of varying size and shape) microcalcifications. This pattern is usually associated with high-grade ductal carcinoma in situ (DCIS).

- However, breast cancers, including DCIS, more often present with the small, clustered type of calcifications [10]. But these patterns are also associated with benign conditions (atypia, pseudoangiomatous stromal hyperplasia [PASH], proliferative fibrous hyperplasia, and others).

- Grouped coarse heterogeneous calcifications have a likelihood of malignancy of just under 15 percent, while amorphous calcifications have a likelihood of malignancy of 20 percent. Both would be assessed as BI-RADS 4B (table 1) [20].

- Grouped round and punctate calcifications at baseline have a probability of malignancy of less than 2 percent and can be safely placed in a short-interval (six-month) follow-up category as BI-RADS 3: probably benign. (See 'BI-RADS assessment categories' above.)

- Calcifications that are not suspicious for malignancy and considered benign include vascular and skin calcifications, rim calcifications, large and coarse calcifications (image 5), and smooth round or oval calcifications (image 6).

Despite the association of microcalcifications with DCIS, mammographic appearance alone cannot differentiate between purely intraductal and invasive ductal breast cancers; there is no mammographic correlate of basement membrane invasion [21]. Approximately 20 percent of invasive cancers diagnosed by mammography present only as microcalcifications [22]. One-third of invasive carcinomas are associated with microcalcifications, with or without a soft tissue mass, and 10 percent of intraductal cancers present as a soft tissue mass without microcalcifications [10]. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis", section on 'Mammography'.)

Assessing the extent of disease — Mammographic assessment of the extent of DCIS and early invasive carcinoma begins with diagnostic mammography and continues through the biopsy, specimen management, and postexcision mammogram [10].

- **Multicentric or multifocal disease** – Multifocal disease is usually defined as involvement of several areas within a breast quadrant, probably representing disease along an entire duct. Multicentric disease involves multiple areas within different quadrants, probably representing involvement of multiple ducts. Some authors define multifocal disease as multiple areas within 2 cm and multicentric as areas ≥2 cm apart.

  Mammography of both breasts is particularly important in the patient with DCIS or invasive cancer who is considering breast conservation. Preoperative diagnostic mammography can help to define the extent of disease and may identify multifocal or multicentric cancer that could signal a potential difficulty in achieving clear surgical margins. Multifocal or multicentric disease is not necessarily a contraindication to breast conservation but is one of the factors that should be taken into consideration along with breast size relative to the extent of disease on imaging. A larger extent of disease also warrants consideration of neoadjuvant therapy [23]. (See "Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer", section on 'Neoadjuvant systemic therapy'.)

Although the extent of mammographic nonlinear branching microcalcifications frequently underestimates the pathologic extent of the malignancy, the discrepancy is less than 2 cm in 80 to 85 percent of cases [24]. Several groups of microcalcifications separated by normal-appearing tissue should not be interpreted as multifocal or multicentric disease. Often, these represent areas of contiguous tumor that is only partially calcified within a ductal lobule [24,25]. Additionally, multiple groups of calcifications that are separated by normal breast tissue should be confirmed to be malignant before using the information as a basis for what to resect if it would change the surgical approach.

Mammographic assessment of tumor size for the staging of multifocal disease presents a unique dilemma. Most staging classifications require that the largest tumor mass be utilized for T staging, even in cases where multifocal disease is suspected. However, others suggest that the total surface area, volume, or aggregate measurements are a better indicator of prognosis [26-28]. Accurate delineation of the extent of odd-shaped, irregular, or multifocal tumors is important for treatment planning. (See "Tumor, node, metastasis (TNM) staging classification for breast cancer".)

- **Extensive intraductal component –** The combination of a mass and associated calcifications often indicates the presence of an extensive intraductal component (EIC). An EIC is defined pathologically as DCIS found adjacent to an invasive carcinoma, accounting for more than 25 percent of the volume of disease. This finding can be a predictor for a greater extent of disease than predicted by mammography and can be associated with residual tumor (usually DCIS) following gross excision of the lesion [29]. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis".)

- **Limitations of mammography –** A significant limitation of mammographic assessment of disease extent is the obscuring of the borders or extent of the primary tumor by dense overlying tissue. Dense breasts can limit the sensitivity of mammography both for detection of breast cancers and for delineating disease extent [30,31]. In this setting, contrast-enhanced breast magnetic resonance imaging (MRI) may complement mammographic staging. If the clinical extent of disease is larger than what can be appreciated by mammography, MRI may be considered, but its use remains controversial.

  For invasive cancers that are contiguous to the chest wall and not completely included on mammographic projections, ancillary imaging techniques such as MRI may be necessary to assess posterior tumor extension and pectoralis fascia or muscle involvement if that will determine a change in the surgical approach or the use of neoadjuvant therapy [32]. (See 'Breast MRI' below.)

- **Postoperative mammography** – Postoperative mammograms to look for residual calcifications after surgical resection should be performed routinely regardless of whether a specimen radiograph has been performed. The postoperative mammogram provides a new baseline for future screening mammography. It is especially important if the extent of calcifications removed is not documented on the specimen radiograph or when the margins are close or positive [4,33,34]. (See "Techniques to reduce positive margins in breast-conserving surgery", section on 'Specimen radiography'.)

Intramammary lymph nodes — Intramammary lymph nodes are detected in 1 to 28 percent of patients with breast cancer [35-39]. Benign nodes can often be distinguished from metastatic or infiltrated intramammary lymph nodes by their mammographic or sonographic appearance, but definitive assessment often requires histopathologic study [40]. Isolated intramammary lymph node metastases are considered to represent stage II disease, even if the axillary nodes are uninvolved. The presence of intramammary lymph node metastases appears to confer a worse prognosis, both in patients who otherwise have stage I breast cancer based upon tumor size and axillary nodal status and in those with stage II disease [35]. (See "Tumor, node, metastasis (TNM) staging classification for breast cancer".)

ULTRASONOGRAPHY

Breast ultrasound — Diagnostic or targeted ultrasound (US) examination of the breast is an important diagnostic adjunct to mammography. In patients suspected of having a breast cancer, breast US is most useful in the following circumstances:

- To further characterize a mammographically detected mass, focal asymmetry, or an area of architectural distortion. Breast US can help to characterize masses as either benign or malignant and localize them for the surgeon. In one report, the sensitivity of US for malignancy was 98.4 percent and the negative predictive value 99.5 percent [41]. Similar results have been reported in other studies [42-44].

  As an example, solid masses identified by ultrasound that are oval and circumscribed with benign imaging features have been shown to have a less than 2 percent likelihood of malignancy, and short-term (six month) follow-up and then periodic surveillance may be appropriate management in lieu of biopsy [42]. Note that this study was primarily in young patients (less than 50 years old).

  Breast US is often added to the initial diagnostic evaluation for patients with a suspected breast cancer if there is a palpable mass and/or an abnormality is seen on mammography. The benefit of this approach was suggested in a series of 2020 patients (470 with a palpable mass) who underwent clinical examination, mammography, and breast US [43]. The systematic addition of breast US detected eight additional

malignancies and correctly downgraded 332 cases of suspected malignancy to no suspected malignancy (predominantly cysts or fibroadenoma). Thus, the main benefit of breast US was improved specificity when used in a targeted manner. The sensitivity, specificity, and positive and negative predictive values for clinical examination plus mammography plus targeted US were 96.9, 94.8, 39.2, and 99.9 percent, while the corresponding values for clinical examination plus mammography were 91.5, 87, 19.7, and 99.7 percent, respectively.

However, US is highly operator dependent, and significant variability in the ability of radiologists to characterize solid breast lesions by US has been reported [45-47]. A benign solid appearance on US should not be used to avoid biopsy of a mammographically or clinically suspicious mass.

- To identify a cystic mass. Simple cysts need no further intervention because the risk of cancer is very low; one series found no malignancies in 223 cysts [48]. The management of cystic lesions of the breast is discussed elsewhere. (See 'Younger than 30' above and "Breast cysts: Clinical manifestations, diagnosis, and management".)

- To further characterize a lesion when a mass detected on clinical breast examination cannot be seen clearly on mammogram (often in patients with dense breasts).

- To determine whether a mammographically suspicious lesion can be visualized and therefore sampled by US-guided biopsy. US-guided breast biopsy is better tolerated than stereotactic biopsy and avoids radiation. (See "Breast biopsy".)

- To measure and clip a lesion prior to neoadjuvant chemotherapy. For patients who present with large or locally advanced tumors for which neoadjuvant chemotherapy is considered, careful anatomic localization is critical to ensure that the surgeon can localize the area of tumor after neoadjuvant therapy. Typically, the lesion is measured both clinically and ultrasonographically and reported in terms of size, the "o'clock" location on the breast surface, and the distance of the lesion from the nipple. The use of radiopaque clips placed at the time of biopsy to localize the primary tumor in case there is a complete clinical and radiographic response to induction therapy is discussed below. (See "Breast biopsy", section on 'Clip placement'.)

Axillary ultrasound — For patients with clinically suspicious lymph nodes, preoperative axillary US with fine needle aspiration or core biopsy of suspicious areas provides a means to identify patients who have positive nodes and place a marking clip [49]. This information may be used to guide future additional surgery, radiation, or systemic therapy. (See "Clinical features, diagnosis, and staging of newly diagnosed breast cancer", section on 'Lymph nodes' and "Overview of sentinel lymph node biopsy in breast cancer", section on 'Indications'.)

BREAST MRI

The use of breast magnetic resonance imaging (MRI) in the preoperative evaluation of a newly diagnosed breast cancer has increased significantly over the last two decades (image 7). However, there are no data from prospective randomized trials that demonstrate improved outcomes from the addition of breast MRI to the diagnostic evaluation of newly diagnosed breast cancer. Furthermore, the use of breast MRI increases unnecessary surgery, may delay definitive treatment, and may lead to overtreatment. (See "MRI of the breast and emerging technologies".)

Indications for preoperative breast MRI — Routine preoperative MRI is not indicated for the majority of patients with early-stage breast cancer. In keeping with consensus-based guidelines from major societies and the available data, we and others consider the role of breast MRI in the evaluation of patients with suspected or newly diagnosed breast cancer as follows [4,50-54]:

- For patients with axillary nodal metastases and a clinically occult primary tumor, breast MRI can facilitate the identification of occult breast cancer and help select patients most likely to benefit from surgery [55,56]. (See "Axillary node metastases with occult primary breast cancer", section on 'Breast MRI'.)

- For patients with Paget's disease of the breast who have a negative physical examination and negative mammography, breast MRI can define the extent of disease and aid in treatment planning [57,58]. (See "Paget disease of the breast (PDB)", section on 'Magnetic resonance imaging'.)

- For newly diagnosed breast cancers that are either indeterminant despite clinical and conventional imaging evaluation or clinically larger than that appreciated by mammography (particularly in the setting of dense breasts, which lower the sensitivity of mammography), breast MRI can help define the extent of disease and aid in treatment planning. (See 'Assessing the extent of disease' above.)

- For invasive cancers that are contiguous to the chest wall and not completely included on mammographic projections, MRI may be necessary to assess posterior tumor extension and pectoralis fascia or muscle involvement if that will determine a change in surgical approach or the use of neoadjuvant therapy [32]. (See 'Assessing the extent of disease' above.)

- For patients with locally advanced breast cancer, breast MRI may be used to determine eligibility and response to neoadjuvant endocrine or chemotherapy before, during, or after treatment. MRI can assess the extent of disease and the potential for breast-conserving therapy. However, it is not mandatory in patients undergoing neoadjuvant

therapy. (See "General principles of neoadjuvant management of breast cancer", section on 'Clinical assessment and indications for imaging'.)

- For patients at higher-than-average risk for breast cancer, breast MRI is also useful to screen the contralateral breast [59]. (See "MRI of the breast and emerging technologies", section on 'Screening high-risk women'.)

- For patients who are planning bilateral reconstructive surgery following breast cancer resection (eg, partial mastectomy with contralateral breast reduction or mastectomy with flap reconstruction), some surgeons prefer a preoperative MRI to assess the contralateral breast. An abdominal flap can only be raised once, and the reconstructive technique used might differ if bilateral reconstruction rather than unilateral reconstruction is planned. When a contralateral reduction is planned as part of the reconstructive process, MRI of the contralateral breast may avoid unexpected disease, particularly if there is a condition that will make mammographic screening less sensitive, such as dense breasts. MRI use for this indication is highly variable and not necessarily a standard recommendation. (See "Overview of breast reconstruction".)

Sensitivity and specificity — The sensitivity of breast MRI for breast carcinomas is between 88 and 100 percent in the diagnostic setting [60,61]. Breast MRI has been historically criticized for limited specificity due to enhancement of benign breast lesions. In a meta-analysis of 44 studies evaluating diagnostic breast MRI in patients with breast lesions, pooled specificity was 72 percent [62]. However, more contemporary studies have demonstrated specificity as high as 87 percent of breast MRI, albeit in the screening setting [61,63-66]. (See "MRI of the breast and emerging technologies".)

Impact of preoperative breast MRI — Because MRI is more sensitive than mammography, ultrasound, or physical examination and identifies additional ipsilateral disease in approximately 16 percent of patients with a known breast cancer [45,67,68], it was assumed that preoperative MRI would estimate the extent of disease more accurately than conventional imaging, thereby improving surgical planning (eg, prompting a change to mastectomy when breast-conserving therapy had been previously considered [69]) and enabling surgeons to better obtain clean margins in breast-conserving surgery.

However, use of preoperative breast MRI remains controversial because available data have shown that routine preoperative breast MRI has not improved overall survival outcomes, improved the rate of breast conservation surgery achievement, or lowered locoregional recurrence rates [70-83]. Additionally, preoperative MRI may lead to unnecessary surgery such as re-resection and mastectomy and case delay in treatment in some cases [52,69,84,85].

- **Positive margin and reoperation rate –** Evidence that routine use of breast MRI results in fewer positive margins at the time of partial mastectomy or a lower rate of reoperation to achieve clear margins is mixed [69,77]. Although some observational studies found lower re-excision rates in patients who underwent breast MRI compared with those who did not [86-88], two randomized trials (COMICE and MONET) showed no difference in positive margin rate or reoperation rate with or without preoperative MRI (table 2) [77,78,89]. In a meta-analysis that included the two trials and seven comparative cohort studies, the reexcision rate after breast-conserving surgery was similar with and without preoperative MRI (11.6 versus 11.4 percent).

  However, breast MRI-guided biopsy and MRI-guided localizations were not routinely used in these trials, thus minimizing or negating the potential impact of breast MRI. Breast MRI enhancement does not always represent malignancy and should be confirmed by biopsy before using MRI results to plan surgical management. The Preoperative Breast MRI in Clinical Practice: Multicenter International Prospective Meta-Analysis of Individual Data (MIPA) trial involves expert centers and is expected to provide more conclusive evidence regarding the impact of preoperative breast MRI. (See "Techniques to reduce positive margins in breast-conserving surgery", section on 'Role of MRI'.)

- **Mastectomy rate –** A number of studies have reported that MRI results in changes in surgical management and may be a factor in the increased use of mastectomy, bilateral mastectomy, and prophylactic mastectomy in patients with newly diagnosed breast cancers [90-94]. In the same meta-analysis of two trials and seven comparative cohort studies, MRI was associated with higher initial (16 versus 8 percent) and overall mastectomy rates (26 versus 18 percent) [90]. In another 3606 patients with newly diagnosed breast cancer, patients who underwent MRI were twice as likely to have contralateral prophylactic mastectomy performed [93].

- **Contralateral disease detection –** MRI imaging of the contralateral breast identifies a synchronous clinically and mammographically occult malignancy in 3 to 5 percent of cases, approximately one-half of which are invasive cancer and the remainder in situ cancer [93,95-98], and results in an approximately 12 percent chance of biopsy [93,95,96,99]. The clinical significance, especially the survival benefit, of detecting these cancers has not been extensively studied [100]. Thus, the role of MRI to assess the contralateral breast is controversial, and it is not routinely recommended for the majority of patients with a newly diagnosed breast cancer. There are some clinical scenarios where breast MRI might be beneficial prior to therapy to assess contralateral disease (eg, in high-risk patients or prior to major breast reconstruction). In the setting of dense breast tissue and elevated predisposition, MRI is clearly the more sensitive

modality. More abbreviated methods of conducting MRI have been shown to be more sensitive than 3D mammography [63].

- **Survival and recurrence rate –** In two trials [77,89] and one meta-analysis [90] that compared breast cancer surgery with or without preoperative MRI, there was no difference in overall survival or ipsilateral breast tumor recurrence rates. Similarly, preoperative MRI was not associated with improved recurrence or survival outcomes for ductal carcinoma in situ (DCIS) [101,102].

- **Specific tumors –** In general, tumor histology does not appear to be a predictor for the utility of breast MRI. However, in some studies, breast MRI has shown benefit for preoperative evaluation of invasive lobular carcinoma and DCIS [87,90,103-105].

  - Invasive lobular cancers are often associated with only subtle mammographic changes. Some studies have reported that MRI accurately determines disease extent for invasive lobular cancers, although this is not uniformly the case [24,40,43,45,106]. In a meta-analysis, the reexcision rate in patients with invasive lobular cancer was reduced after MRI (10.9 versus 18 percent) [90].

  - Although early studies reported difficulty in detecting DCIS on MRI, subsequent studies suggest that MRI can accurately determine the extent of high-grade DCIS, with sensitivities of 89 to 94 percent [45,103,107,108]. Preoperative MRI may have a role in evaluating patients with DCIS in terms of extent of disease, higher grades of DCIS, or occult invasion [63]. Preoperative MRI in patients with DCIS reduced positive surgical margins and repeat surgeries without resulting in a higher mastectomy rate in some studies [104], but the data are not yet conclusive.

BREAST BIOPSY

Patients with a suspicious mammographic abnormality (Breast Imaging-Reporting and Data System [BI-RADS] 4 or 5) or a clinically suspicious palpable breast mass typically undergo biopsy regardless of additional imaging findings. The goal of the initial biopsy is to obtain sufficient diagnostic material using the least invasive approach and to avoid surgical excision of benign lesions. (See "Breast biopsy".)

The only exceptions are those with a BI-RADS 4A lesion (low risk, <10 percent chance of malignancy), for whom a six-month follow-up rather than biopsy may be considered depending on whether the suspicion is for ductal carcinoma in situ (DCIS) or invasive cancer, prior biopsy, comorbidities, and patient preference.

Surgical biopsy should not be utilized as a diagnostic tool unless percutaneous palpation-guided or image-guided biopsy is not feasible. A preoperative histologic diagnosis of invasive

carcinoma permits better multidisciplinary treatment planning and patient decision making (eg, genetic testing, neoadjuvant therapy, breast conservation versus mastectomy). It also may allow the surgeon to plan a single operation to treat the cancer, including sentinel lymph node biopsy or full axillary dissection, depending upon the clinical circumstances. Excision of more extensive areas of DCIS may also be optimally planned if the diagnosis has been established by percutaneous core needle biopsy.

It is important to note that imaging should precede biopsy whenever possible as needle biopsy may cause hematomas and inflammation at the site of the mass and enlargement of the axillary nodes, which can make clinical and radiographic assessment and surgical planning more difficult. Although physical examination changes from needle biopsy often resolve by the time of surgery, if the palpable lesion is small or subtle, it is helpful to arrange image-guided localization of the clip placed at the time of biopsy to facilitate breast-conserving surgery. (See "Techniques to reduce positive margins in breast-conserving surgery", section on 'Localization of nonpalpable lesions'.)

Breast biopsy techniques are discussed in detail in a dedicated topic. (See "Breast biopsy".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Breast cancer".)

SUMMARY AND RECOMMENDATIONS

- **Mammographic abnormality –** The majority of breast cancers are diagnosed as a result of an abnormal mammogram, but not all mammographic findings represent cancer. Patients who have an abnormal screening mammogram need further diagnostic mammography and possibly breast ultrasound (US) evaluation to determine the need for tissue biopsy. The algorithm (algorithm 1) describes an approach to the evaluation of a mammographic abnormality, which integrates the Breast Imaging-Reporting and Data System (BI-RADS) assessment categories (table 1). (See 'Mammographic abnormality' above.)

- **Palpable breast mass –** A clinically suspicious mass should be biopsied, regardless of imaging findings, as 10 to 15 percent of such lesions can be mammographically occult. Approaches to diagnostic evaluation of palpable masses are stratified by the age of the patient (see 'Our approaches' above):

  - **Younger than 30 –** We prefer US for initial imaging of a palpable breast mass in patients younger than 30 years of age (algorithm 2). Further evaluation depends

upon whether US reveals no lesion, a cystic lesion, or a solid lesion. (See 'Younger than 30' above.)

- **Older than 40 –** We prefer bilateral diagnostic mammography for initial imaging of a palpable breast mass in patients 40 years of age or older (algorithm 3). Further evaluation depends upon the lesion's BI-RADS assessment category. (See '40 years or older' above.)

- **Between 30 and 40 –** Either breast US or mammography can be used as the initial imaging modality for evaluating a patient 30 to 39 years of age with a palpable breast mass. US may be preferred given its higher sensitivity. If US is negative, mammography should still be performed.

- **Mammography –** Over 90 percent of breast cancers are visible on mammography. Screening mammography is performed in asymptomatic patients. Diagnostic mammography is performed in symptomatic patients or for further evaluation after a recent abnormal (BI-RADS 0: incomplete (table 1)) screening mammogram. Diagnostic mammography is associated with higher abnormal interpretation rate and higher cancer detection rate than screening mammography. (See 'Mammography and digital breast tomosynthesis' above.)

- **Ultrasonography –** US examination of the breast and axilla can differentiate between solid and cystic masses, assess axillary lymph nodes, and provide guidance for interventional procedures. (See 'Breast ultrasound' above.)

- **Breast MRI –** For most patients, breast MRI is not a routine component of the diagnostic evaluation of breast cancer. Breast MRI may be used in the evaluation of patients with newly diagnosed breast cancer in special circumstances (see 'Indications for preoperative breast MRI' above and "MRI of the breast and emerging technologies"):

  Breast MRI is more sensitive than mammography, ultrasound, or physical examination and thus can identify additional ipsilateral disease and/or contralateral disease. However, use of preoperative breast MRI has not improved survival outcomes, breast conservation rates, or locoregional recurrence rates. Additionally, preoperative MRI may increase mastectomy rate and cause delay in treatment. (See 'Impact of preoperative breast MRI' above.)

- **Breast biopsy –** In the patient with a suspicious mammographic abnormality or a palpable breast mass, the obligatory diagnostic technique is biopsy. Surgical biopsy should not be utilized as a diagnostic tool unless percutaneous palpation-guided or image-guided biopsy is not feasible; imaging should precede biopsy whenever possible. (See "Breast biopsy".)

REFERENCES

1. Expert Panel on Breast Imaging, Klein KA, Kocher M, et al. ACR Appropriateness Criteria® Palpable Breast Masses: 2022 Update. J Am Coll Radiol 2023; 20:S146.
2. Barlow WE, Lehman CD, Zheng Y, et al. Performance of diagnostic mammography for women with signs or symptoms of breast cancer. J Natl Cancer Inst 2002; 94:1151.
3. Lin C, Moore D, DeMichele A, et al. Detection of locally advanced breast cancer in the I-SPY TRIAL (CALGB 150007/150012, ACRIN 6657) in the interval between routine screening (abstract 1503). (Abstract available online at www.abstract.asco.org/AbstView_65_31279.html, accessed February 11, 2010). J Clin Oncol 2009; 27:1503s.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Breast Cancer. Version 3.2020 - March 6, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf (Accessed on April 29, 2020).
5. Gumus H, Gumus M, Mills P, et al. Clinically palpable breast abnormalities with normal imaging: is clinically guided biopsy still required? Clin Radiol 2012; 67:437.
6. Lehman CD, Lee CI, Loving VA, et al. Accuracy and value of breast ultrasound for primary imaging evaluation of symptomatic women 30-39 years of age. AJR Am J Roentgenol 2012; 199:1169.
7. Expert Panel on Breast Imaging, Mehta TS, Lourenco AP, et al. ACR Appropriateness Criteria® Imaging After Breast Surgery. J Am Coll Radiol 2022; 19:S341.
8. Chang JH, Vines E, Bertsch H, et al. The impact of a multidisciplinary breast cancer center on recommendations for patient management: the University of Pennsylvania experience. Cancer 2001; 91:1231.
9. Smart CR, Hartmann WH, Beahrs OH, Garfinkel L. Insights into breast cancer screening of younger women. Evidence from the 14-year follow-up of the Breast Cancer Detection Demonstration Project. Cancer 1993; 72:1449.
10. Stomper PC, Winston PS, Proulx GM, et al. Mammographic detection and staging of ductal carcinoma in situ: mammographic-pathologic correlation. Semin Breast Dis 2000; 3:1.
11. Skaane P, Bandos AI, Niklason LT, et al. Digital Mammography versus Digital Mammography Plus Tomosynthesis in Breast Cancer Screening: The Oslo Tomosynthesis Screening Trial. Radiology 2019; 291:23.
12. Conant EF, Barlow WE, Herschorn SD, et al. Association of Digital Breast Tomosynthesis vs Digital Mammography With Cancer Detection and Recall Rates by Age and Breast Density. JAMA Oncol 2019; 5:635.

13. Durand MA, Friedewald SM, Plecha DM, et al. False-Negative Rates of Breast Cancer Screening with and without Digital Breast Tomosynthesis. Radiology 2021; 298:296.
14. Chong A, Weinstein SP, McDonald ES, Conant EF. Digital Breast Tomosynthesis: Concepts and Clinical Practice. Radiology 2019; 292:1.
15. Sprague BL, Arao RF, Miglioretti DL, et al. National Performance Benchmarks for Modern Diagnostic Digital Mammography: Update from the Breast Cancer Surveillance Consortium. Radiology 2017; 283:59.
16. Lehman CD, Arao RF, Sprague BL, et al. National Performance Benchmarks for Modern Screening Digital Mammography: Update from the Breast Cancer Surveillance Consortium. Radiology 2017; 283:49.
17. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System, 5th ed, D'Orsi CJ, Sickles EA, Mendelson EB, et al (Eds), American College of Radiology, Reston, VA 2013.
18. Esserman LJ, Thompson IM, Reid B, et al. Addressing overdiagnosis and overtreatment in cancer: a prescription for change. Lancet Oncol 2014; 15:e234.
19. Stomper PC. Breast imaging. In: Atlas of Breast Cancer, Hayes DF (Ed), Mosby, Philadelph ia 2000. p.54.
20. Sickles EA, D'Orsi CJ, Bassett LW, et al. ACR BI-RADS Mammography. In: ACR BI-RADS® At las, Breast Imaging Reporting and Data System, 5th ed, D'Orsi CJ, Sickles EA, Mendelson EB, et al (Eds), American College of Radiology, Reston, VA 2013.
21. Stomper PC, Geradts J, Edge SB, Levine EG. Mammographic predictors of the presence and size of invasive carcinomas associated with malignant microcalcification lesions without a mass. AJR Am J Roentgenol 2003; 181:1679.
22. Venkatesan A, Chu P, Kerlikowske K, et al. Positive predictive value of specific mammographic findings according to reader and patient variables. Radiology 2009; 250:648.
23. Hurvitz SA, Martin M, Symmans WF, et al. Neoadjuvant trastuzumab, pertuzumab, and chemotherapy versus trastuzumab emtansine plus pertuzumab in patients with HER2-positive breast cancer (KRISTINE): a randomised, open-label, multicentre, phase 3 trial. Lancet Oncol 2018; 19:115.
24. Holland R, Hendriks JH, Vebeek AL, et al. Extent, distribution, and mammographic/histological correlations of breast ductal carcinoma in situ. Lancet 1990; 335:519.
25. Kopans DB, Lindfors K, McCarthy KA, Meyer JE. Spring hookwire breast lesion localizer: use with rigid-compression mammographic systems. Radiology 1985; 157:537.
26. Fish EB, Chapman JA, Link MA. Assessment of tumor size for multifocal primary breast cancer. Ann Surg Oncol 1998; 5:442.

27. Coombs NJ, Boyages J. Multifocal and multicentric breast cancer: does each focus matter? J Clin Oncol 2005; 23:7497.
28. Andea AA, Wallis T, Newman LA, et al. Pathologic analysis of tumor size and lymph node status in multifocal/multicentric breast carcinoma. Cancer 2002; 94:1383.
29. Healey EA, Osteen RT, Schnitt SJ, et al. Can the clinical and mammographic findings at presentation predict the presence of an extensive intraductal component in early stage breast cancer? Int J Radiat Oncol Biol Phys 1989; 17:1217.
30. Baines CJ, Dayan R. A tangled web: factors likely to affect the efficacy of screening mammography. J Natl Cancer Inst 1999; 91:833.
31. Mandelson MT, Oestreicher N, Porter PL, et al. Breast density as a predictor of mammographic detection: comparison of interval- and screen-detected cancers. J Natl Cancer Inst 2000; 92:1081.
32. Morris EA, Schwartz LH, Drotman MB, et al. Evaluation of pectoralis major muscle in patients with posterior breast tumors on breast MR images: early experience. Radiology 2000; 214:67.
33. Gluck BS, Dershaw DD, Liberman L, Deutch BM. Microcalcifications on postoperative mammograms as an indicator of adequacy of tumor excision. Radiology 1993; 188:469.
34. Waddell BE, Stomper PC, DeFazio JL, et al. Postexcision mammography is indicated after resection of ductal carcinoma-in-situ of the breast. Ann Surg Oncol 2000; 7:665.
35. Shen J, Hunt KK, Mirza NQ, et al. Intramammary lymph node metastases are an independent predictor of poor outcome in patients with breast carcinoma. Cancer 2004; 101:1330.
36. Egan RL, McSweeney MB. Intramammary lymph nodes. Cancer 1983; 51:1838.
37. Jadusingh IH. Intramammary lymph nodes. J Clin Pathol 1992; 45:1023.
38. Stomper PC, Leibowich S, Meyer JE. The prevalence and distribution of well circumscribed nodules on screening mammography: Analysis of 1500 mammograms. Breast Dis 1991; 4:197.
39. Upponi S, Kalra S, Poultsidis A, et al. The significance of intramammary nodes in primary breast cancer. Eur J Surg Oncol 2001; 27:707.
40. Günhan-Bilgen I, Memiş A, Ustün EE. Metastatic intramammary lymph nodes: mammographic and ultrasonographic features. Eur J Radiol 2001; 40:24.
41. Stavros AT, Thickman D, Rapp CL, et al. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. Radiology 1995; 196:123.
42. Harvey JA, Nicholson BT, Lorusso AP, et al. Short-term follow-up of palpable breast lesions with benign imaging features: evaluation of 375 lesions in 320 women. AJR Am J Roentgenol 2009; 193:1723.

43. Flobbe K, Bosch AM, Kessels AG, et al. The additional diagnostic value of ultrasonography in the diagnosis of breast cancer. Arch Intern Med 2003; 163:1194.
44. Soo MS, Rosen EL, Baker JA, et al. Negative predictive value of sonography with mammography in patients with palpable breast lesions. AJR Am J Roentgenol 2001; 177:1167.
45. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004; 233:830.
46. Baker JA, Kornguth PJ, Soo MS, et al. Sonography of solid breast lesions: observer variability of lesion description and assessment. AJR Am J Roentgenol 1999; 172:1621.
47. Rahbar G, Sie AC, Hansen GC, et al. Benign versus malignant solid breast masses: US differentiation. Radiology 1999; 213:889.
48. Sickles EA, Filly RA, Callen PW. Benign breast lesions: ultrasound detection and diagnosis. Radiology 1984; 151:467.
49. Marino MA, Avendano D, Zapata P, et al. Lymph Node Imaging in Patients with Primary Breast Cancer: Concurrent Diagnostic Tools. Oncologist 2020; 25:e231.
50. Lehman CD, DeMartini W, Anderson BO, Edge SB. Indications for breast MRI in the patient with newly diagnosed breast cancer. J Natl Compr Canc Netw 2009; 7:193.
51. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA Cancer J Clin 2007; 57:75.
52. Sardanelli F, Boetes C, Borisch B, et al. Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group. Eur J Cancer 2010; 46:1296.
53. The American Society of Breast Surgeons. Consensus guideline on diagnostic and screening magnetic resonance imaging of the breast. Available at: https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Diagnostic-and-Screening-Magnetic-Resonance-Imaging-of-the-Breast.pdf (Accessed on May 28, 2019).
54. Canadian Association of Radiologists (CAR). Practice guidelines and technical standards for breast imaging and intervention. Approved 2012, modified 2016. Available at: https://car.ca/wp-content/uploads/Breast-Imaging-and-Intervention-2016.pdf (Accessed on May 28, 2019).
55. de Bresser J, de Vos B, van der Ent F, Hulsewé K. Breast MRI in clinically and mammographically occult breast cancer presenting with an axillary metastasis: a systematic review. Eur J Surg Oncol 2010; 36:114.
56. Fayanju OM, Stoll CR, Fowler S, et al. Geographic and temporal trends in the management of occult primary breast cancer: a systematic review and meta-analysis. Ann Surg Oncol 2013; 20:3308.

57. Morrogh M, Morris EA, Liberman L, et al. MRI identifies otherwise occult disease in select patients with Paget disease of the nipple. J Am Coll Surg 2008; 206:316.
58. Frei KA, Bonel HM, Pelte MF, et al. Paget disease of the breast: findings at magnetic resonance imaging and histopathologic correlation. Invest Radiol 2005; 40:363.
59. Monticciolo DL, Newell MS, Moy L, et al. Breast Cancer Screening in Women at Higher-Than-Average Risk: Recommendations From the ACR. J Am Coll Radiol 2018; 15:408.
60. Bluemke DA, Gatsonis CA, Chen MH, et al. Magnetic resonance imaging of the breast prior to biopsy. JAMA 2004; 292:2735.
61. Plana MN, Carreira C, Muriel A, et al. Magnetic resonance imaging in the preoperative assessment of patients with primary breast cancer: systematic review of diagnostic accuracy and meta-analysis. Eur Radiol 2012; 22:26.
62. Peters NH, Borel Rinkes IH, Zuithoff NP, et al. Meta-analysis of MR imaging in the diagnosis of breast lesions. Radiology 2008; 246:116.
63. Comstock CE, Gatsonis C, Newstead GM, et al. Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening. JAMA 2020; 323:746.
64. Pinker K, Helbich TH, Morris EA. The potential of multiparametric MRI of the breast. Br J Radiol 2017; 90:20160715.
65. Rahbar H, Zhang Z, Chenevert TL, et al. Utility of Diffusion-weighted Imaging to Decrease Unnecessary Biopsies Prompted by Breast MRI: A Trial of the ECOG-ACRIN Cancer Research Group (A6702). Clin Cancer Res 2019; 25:1756.
66. Benndorf M, Baltzer PA, Vag T, et al. Breast MRI as an adjunct to mammography: Does it really suffer from low specificity? A retrospective analysis stratified by mammographic BI-RADS classes. Acta Radiol 2010; 51:715.
67. Houssami N, Ciatto S, Macaskill P, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 2008; 26:3248.
68. Sardanelli F, Podo F, Santoro F, et al. Multicenter surveillance of women at high genetic breast cancer risk using mammography, ultrasonography, and contrast-enhanced magnetic resonance imaging (the high breast cancer risk italian 1 study): final results. Invest Radiol 2011; 46:94.
69. Bleicher RJ, Ciocca RM, Egleston BL, et al. Association of routine pretreatment magnetic resonance imaging with time to surgery, mastectomy rate, and margin status. J Am Coll Surg 2009; 209:180.
70. Holland R, Veling SH, Mravunac M, Hendriks JH. Histologic multifocality of Tis, T1-2 breast carcinomas. Implications for clinical trials of breast-conserving surgery. Cancer

1985; 56:979.

71. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347:1233.
72. Veronesi U, Saccozzi R, Del Vecchio M, et al. Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. N Engl J Med 1981; 305:6.
73. Sarrazin D, Lê MG, Arriagada R, et al. Ten-year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. Radiother Oncol 1989; 14:177.
74. van Dongen JA, Voogd AC, Fentiman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. J Natl Cancer Inst 2000; 92:1143.
75. Jacobson JA, Danforth DN, Cowan KH, et al. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. N Engl J Med 1995; 332:907.
76. Blichert-Toft M, Rose C, Andersen JA, et al. Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. Danish Breast Cancer Cooperative Group. J Natl Cancer Inst Monogr 1992; :19.
77. Turnbull L, Brown S, Harvey I, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. Lancet 2010; 375:563.
78. Turnbull LW, Brown SR, Olivier C, et al. Multicentre randomised controlled trial examining the cost-effectiveness of contrast-enhanced high field magnetic resonance imaging in women with primary breast cancer scheduled for wide local excision (COMICE). Health Technol Assess 2010; 14:1.
79. Morris EA. Should we dispense with preoperative breast MRI? Lancet 2010; 375:528.
80. Shin HC, Han W, Moon HG, et al. Limited value and utility of breast MRI in patients undergoing breast-conserving cancer surgery. Ann Surg Oncol 2012; 19:2572.
81. Weber JJ, Bellin LS, Milbourn DE, et al. Selective preoperative magnetic resonance imaging in women with breast cancer: no reduction in the reoperation rate. Arch Surg 2012; 147:834.
82. Feigelson HS, James TA, Single RM, et al. Factors associated with the frequency of initial total mastectomy: results of a multi-institutional study. J Am Coll Surg 2013; 216:966.
83. Kuhl CK, Strobel K, Bieling H, et al. Impact of preoperative breast MR imaging and MR-guided surgery on diagnosis and surgical outcome of women with invasive breast cancer with and without DCIS component. Radiology 2017; 284:645.

84. Landercasper J, Linebarger JH, Ellis RL, et al. A quality review of the timeliness of breast cancer diagnosis and treatment in an integrated breast center. J Am Coll Surg 2010; 210:449.

85. Zhang M, Sun S, Mesurolle B. The impact of pre-operative breast MRI on surgical waiting time. PLoS One 2017; 12:e0169756.

86. Gonzalez V, Sandelin K, Karlsson A, et al. Preoperative MRI of the breast (POMB) influences primary treatment in breast cancer: a prospective, randomized, multicenter study. World J Surg 2014; 38:1685.

87. Sung JS, Li J, Da Costa G, et al. Preoperative breast MRI for early-stage breast cancer: effect on surgical and long-term outcomes. AJR Am J Roentgenol 2014; 202:1376.

88. Lai HW, Chen CJ, Lin YJ, et al. Does Breast Magnetic Resonance Imaging Combined With Conventional Imaging Modalities Decrease the Rates of Surgical Margin Involvement and Reoperation?: A Case-Control Comparative Analysis. Medicine (Baltimore) 2016; 95:e3810.

89. Peters NH, van Esser S, van den Bosch MA, et al. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: the MONET - randomised controlled trial. Eur J Cancer 2011; 47:879.

90. Houssami N, Turner R, Morrow M. Preoperative magnetic resonance imaging in breast cancer: meta-analysis of surgical outcomes. Ann Surg 2013; 257:249.

91. Katipamula R, Degnim AC, Hoskin T, et al. Trends in mastectomy rates at the Mayo Clinic Rochester: effect of surgical year and preoperative magnetic resonance imaging. J Clin Oncol 2009; 27:4082.

92. Hawley ST, Jagsi R, Morrow M, et al. Social and clinical determinants of contralateral prophylactic mastectomy. JAMA Surg 2014; 149:582.

93. Sorbero ME, Dick AW, Beckjord EB, Ahrendt G. Diagnostic breast magnetic resonance imaging and contralateral prophylactic mastectomy. Ann Surg Oncol 2009; 16:1597.

94. Iacconi C, Galman L, Zheng J, et al. Multicentric Cancer Detected at Breast MR Imaging and Not at Mammography: Important or Not? Radiology 2016; 279:378.

95. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med 2007; 356:1295.

96. Brennan ME, Houssami N, Lord S, et al. Magnetic resonance imaging screening of the contralateral breast in women with newly diagnosed breast cancer: systematic review and meta-analysis of incremental cancer detection and impact on surgical management. J Clin Oncol 2009; 27:5640.

97. Houssami N, Hayes DF. Review of preoperative magnetic resonance imaging (MRI) in breast cancer: should MRI be performed on all women with newly diagnosed, early

stage breast cancer? CA Cancer J Clin 2009; 59:290.

98. Miller BT, Abbott AM, Tuttle TM. The influence of preoperative MRI on breast cancer treatment. Ann Surg Oncol 2012; 19:536.
99. Pediconi F, Catalano C, Roselli A, et al. Contrast-enhanced MR mammography for evaluation of the contralateral breast in patients with diagnosed unilateral breast cancer or high-risk lesions. Radiology 2007; 243:670.
100. Solin LJ, Orel SG, Hwang WT, et al. Relationship of breast magnetic resonance imaging to outcome after breast-conservation treatment with radiation for women with early-stage invasive breast carcinoma or ductal carcinoma in situ. J Clin Oncol 2008; 26:386.
101. Pilewskie M, Olcese C, Eaton A, et al. Perioperative breast MRI is not associated with lower locoregional recurrence rates in DCIS patients treated with or without radiation. Ann Surg Oncol 2014; 21:1552.
102. Fancellu A, Turner RM, Dixon JM, et al. Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma in situ. Br J Surg 2015; 102:883.
103. Greenwood HI, Wilmes LJ, Kelil T, Joe BN. Role of Breast MRI in the Evaluation and Detection of DCIS: Opportunities and Challenges. J Magn Reson Imaging 2020; 52:697.
104. Yoon GY, Choi WJ, Kim HH, et al. Surgical Outcomes for Ductal Carcinoma in Situ: Impact of Preoperative MRI. Radiology 2020; 295:296.
105. Lam DL, Smith J, Partridge SC, et al. The Impact of Preoperative Breast MRI on Surgical Management of Women with Newly Diagnosed Ductal Carcinoma In Situ. Acad Radiol 2020; 27:478.
106. Yeh ED, Slanetz PJ, Edmister WB, et al. Invasive lobular carcinoma: spectrum of enhancement and morphology on magnetic resonance imaging. Breast J 2003; 9:13.
107. DeMartini W, Lehman C. A review of current evidence-based clinical applications for breast magnetic resonance imaging. Top Magn Reson Imaging 2008; 19:143.
108. Kim DY, Moon WK, Cho N, et al. MRI of the breast for the detection and assessment of the size of ductal carcinoma in situ. Korean J Radiol 2007; 8:32.

Topic 808 Version 41.0

GRAPHICS

BI-RADS assessment categories

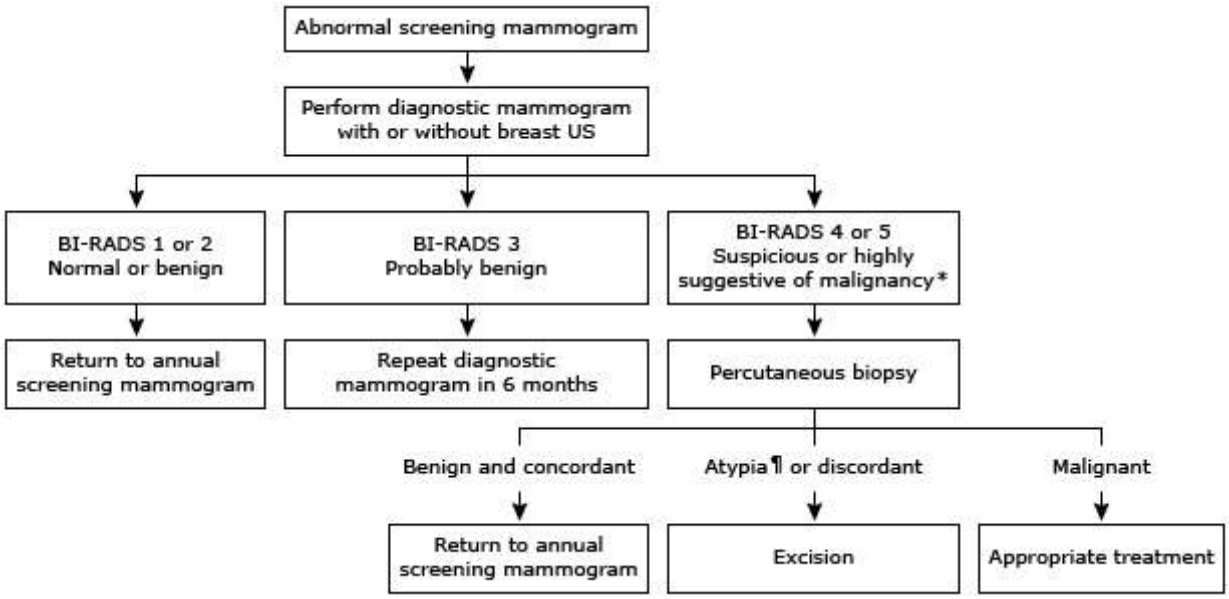
Assessment	Management	Likelihood of cancer
Category 0: Incomplete – Need additional imaging evaluation and/or prior mammograms for comparison	Recall for additional imaging and/or comparison with prior examination(s)	N/A
Category 1: Negative	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 3: Probably benign	Short-interval (6-month) follow-up or continued surveillance mammography	>0 but ≤2% likelihood of malignancy
Category 4: Suspicious	Tissue diagnosis*	>2 but <95% likelihood of malignancy
Category 4A: Low suspicion for malignancy		>2 to ≤10% likelihood of malignancy
Category 4B: Moderate suspicion for malignancy		>10 to ≤50% likelihood of malignancy
Category 4C: High suspicion for malignancy		>50 to <95% likelihood of malignancy
Category 5: Highly suggestive of malignancy	Tissue diagnosis*	≥95% likelihood of malignancy
Category 6: Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

BI-RADS: Breast Imaging-Reporting and Data System.

* Practice guidelines recommend biopsy for all BI-RADS 4 and 5 lesions. If there are clinical factors (eg, age, comorbidities, etc) for which the patient, in consultation with the clinician, chooses to defer biopsy, the reasoning should be documented in the medical record.

Graphic 100197 Version 10.0

Management algorithm for patients with abnormal mammograms



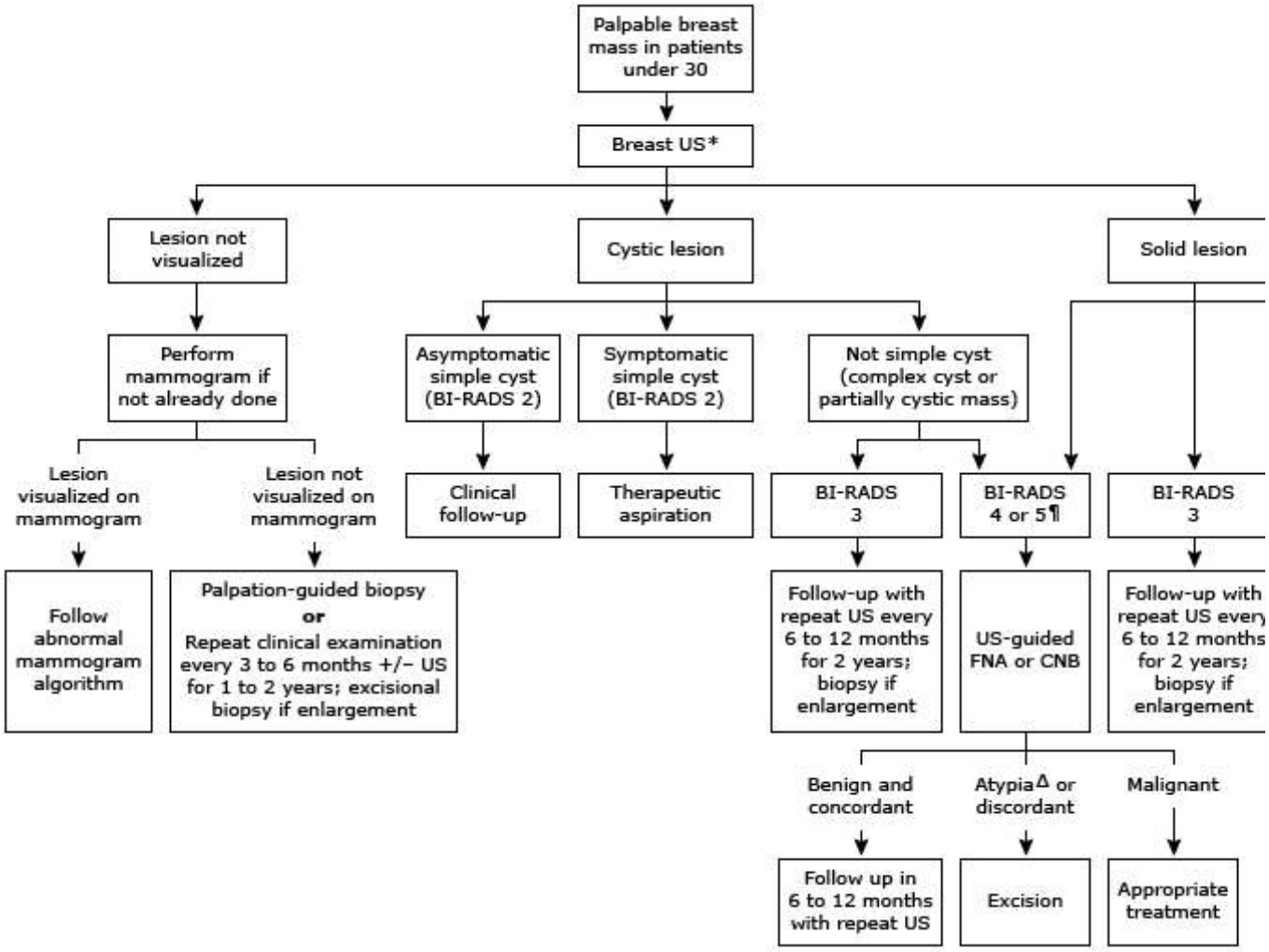
US: ultrasound; BI-RADS: Breast Imaging-Reporting and Data System.

* BI-RADS 4C and 5 lesions require surgical evaluation prior to percutaneous biopsy. The presence and size of a mass may influence the choice of biopsy method.

¶ Not all high-risk benign lesions require surgical excision; practices also vary between excision and observation for lesions with atypia. Refer to UpToDate topic on atypia and lobular carcinoma in situ for details.

Graphic 65978 Version 4.0

Diagnostic algorithm for palpable breast abnormalities in women less than 3 age



US: ultrasound; BI-RADS: Breast Imaging-Reporting and Data System; FNA: fine needle aspiration; CNB: c needle biopsy.

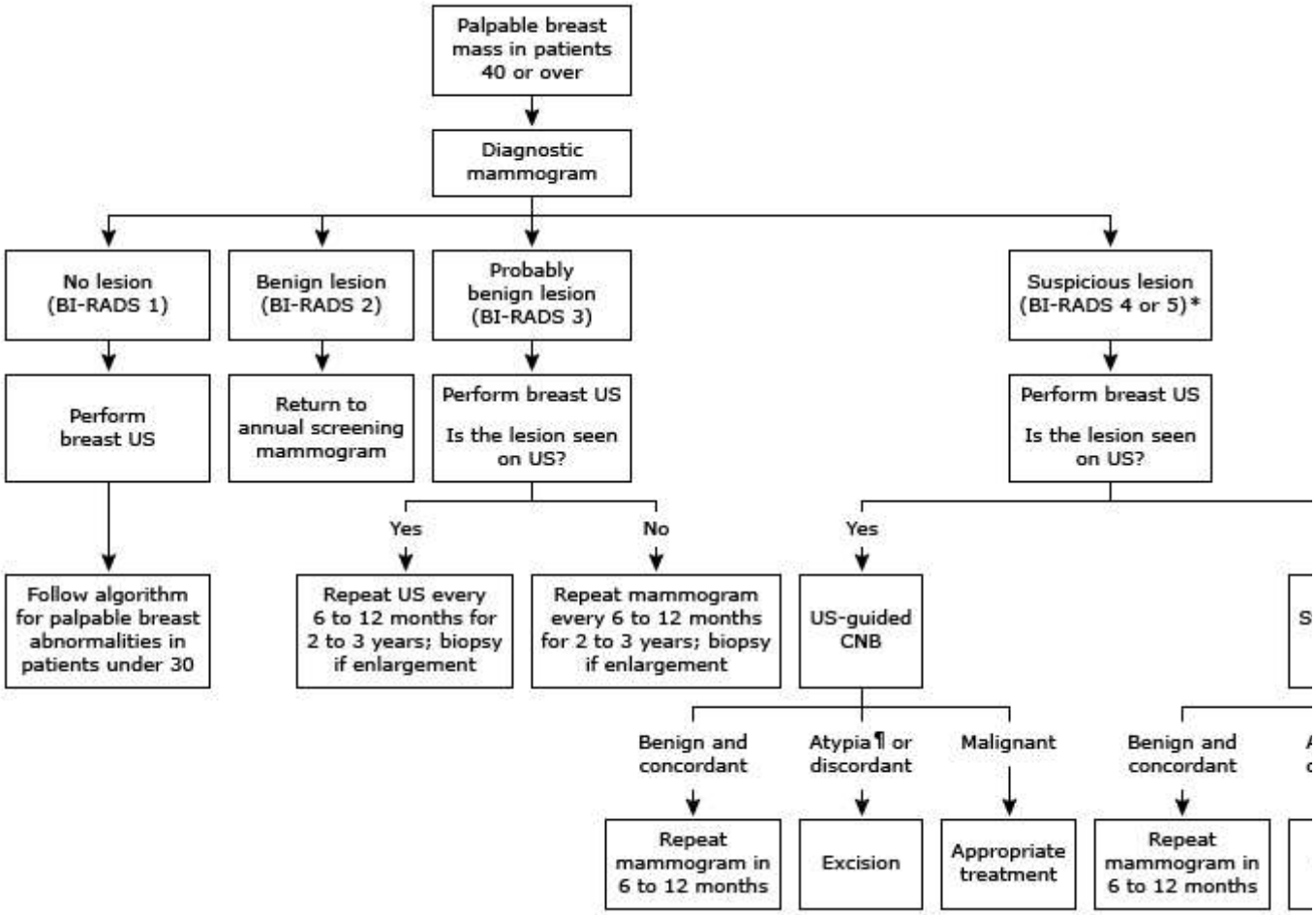
* Palpable lesions may also undergo needle sampling. However, the US-first approach illustrated here is

¶ BI-RADS 4C and 5 lesions require surgical evaluation prior to percutaneous biopsy. The presence and s mass may influence the choice of biopsy method.

Δ Not all high-risk benign lesions require excision; practices also vary between excision and observation f with atypia. Refer to UpToDate topic on atypia and lobular carcinoma in situ for details.

Graphic 54674 Version 4.0

Diagnostic algorithm for palpable breast abnormalities in patients aged 40 y



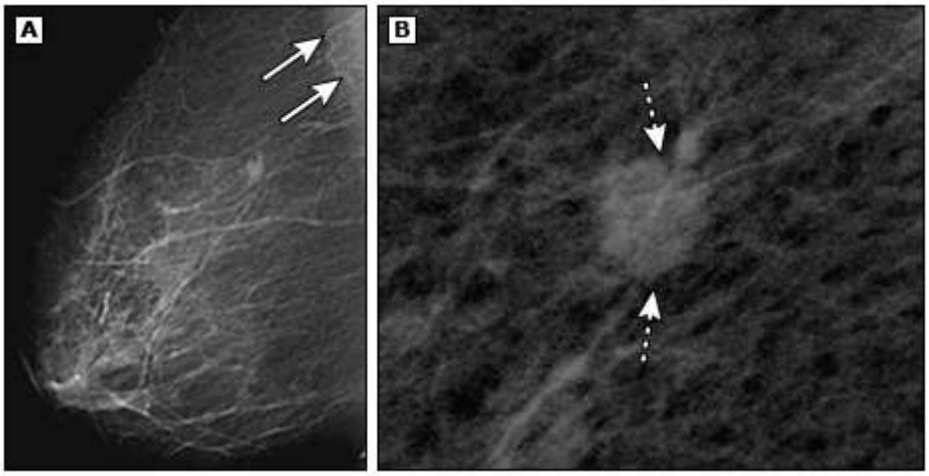
BI-RADS: Breast Imaging-Reporting and Data System; US: ultrasound; CNB: core needle biopsy.

* BI-RADS 4C and 5 lesions require surgical evaluation prior to percutaneous biopsy. The presence and si influence the choice of biopsy method.

¶ Not all high-risk benign lesions require surgical excision; practices also vary between excision and obse with atypia. Refer to UpToDate topic on atypia and lobular carcinoma in situ for details.

Graphic 74666 Version 4.0

Medial lateral oblique mammographic view

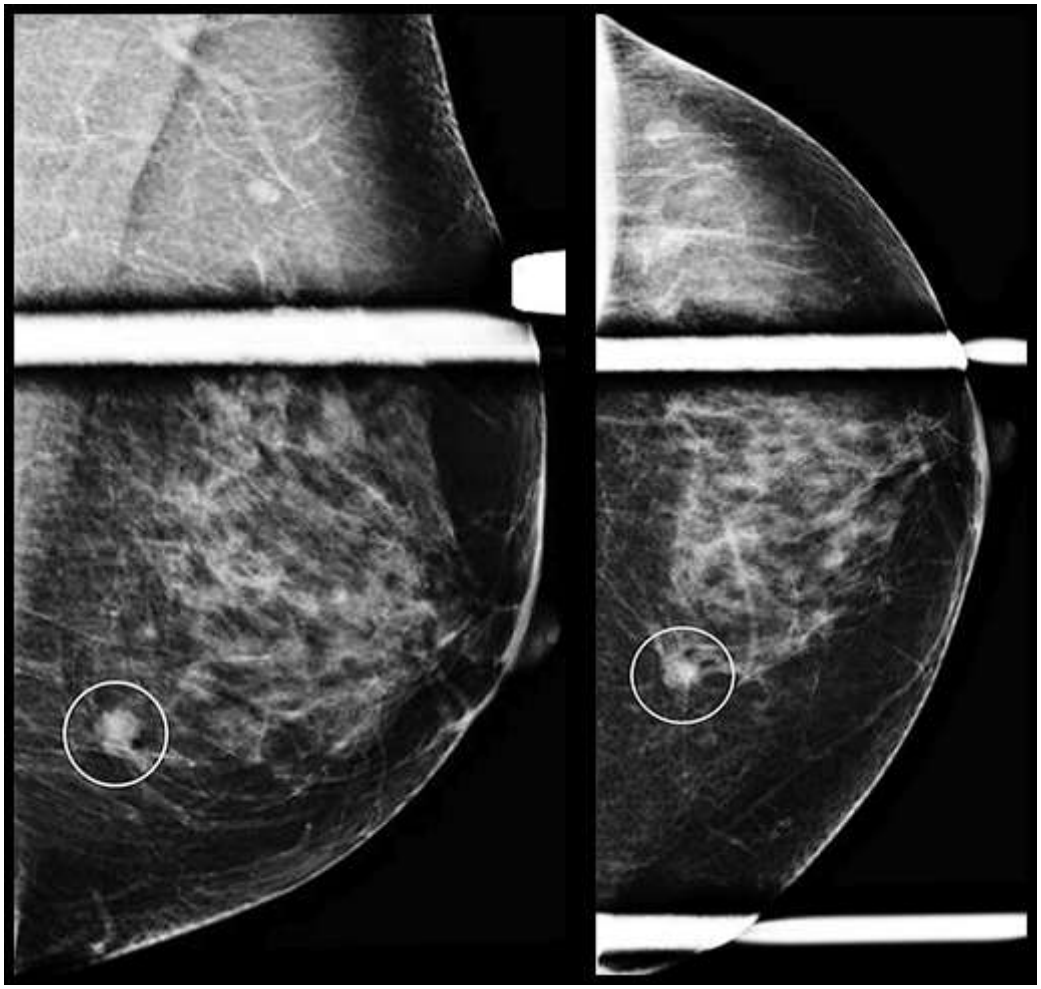


These images illustrate the benefits of spot compression and magnification. In the left panel (A), a medial lateral oblique (MLO) mammographic image, there is a mass at the posterior edge of the film (arrows), which is incompletely characterized. The borders of the lesion can be better characterized with regional spot compression and magnification. The spot magnification MLO view (B) shows that the lesion has irregular borders (dashed arrows) and spiculation. In addition, associated microcalcifications are seen. The lesion can now be characterized as suspicious, BI-RADS 4C, requiring biopsy. Pathology revealed infiltrating duct cell carcinoma with papillary features.

BI-RADS: Breast Imaging-Reporting and Data System.

Graphic 74424 Version 6.0

Mammogram of early breast cancer

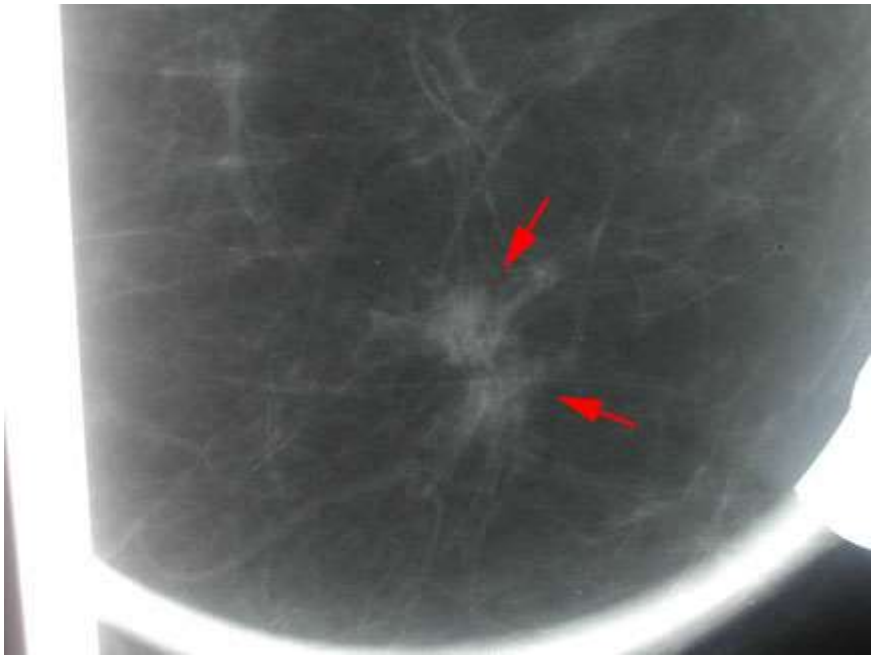


Digital spot compression views of the left breast demonstrate a small spiculated nodule (circle) in the lower inner quadrant.

Courtesy of Pierre J Sasson, MD.

Graphic 74338 Version 5.0

Mammogram spiculated mass

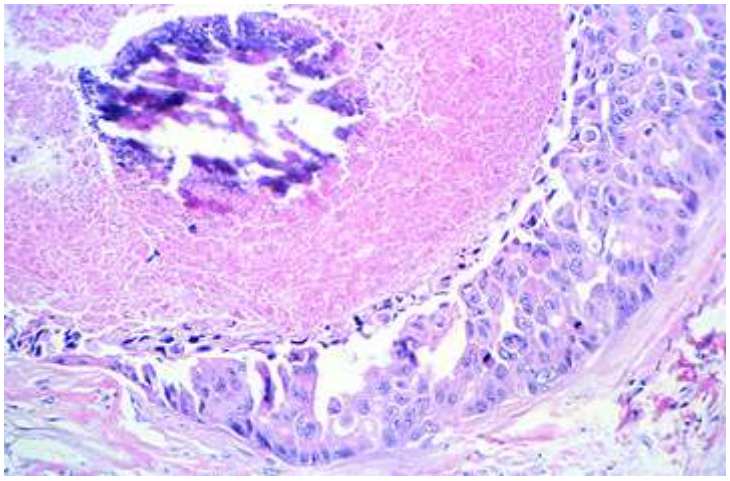


Spot magnification view of a mammogram showing 2 small adjacent interconnected spiculated masses (red arrows). Pathology revealed tubular carcinoma. Tubular carcinoma characteristically appears spiculated on mammogram and is often associated with satellite lesions.

Courtesy of Lisa E Esserman, MD.

Graphic 57593 Version 3.0

Comedo ductal carcinoma in situ

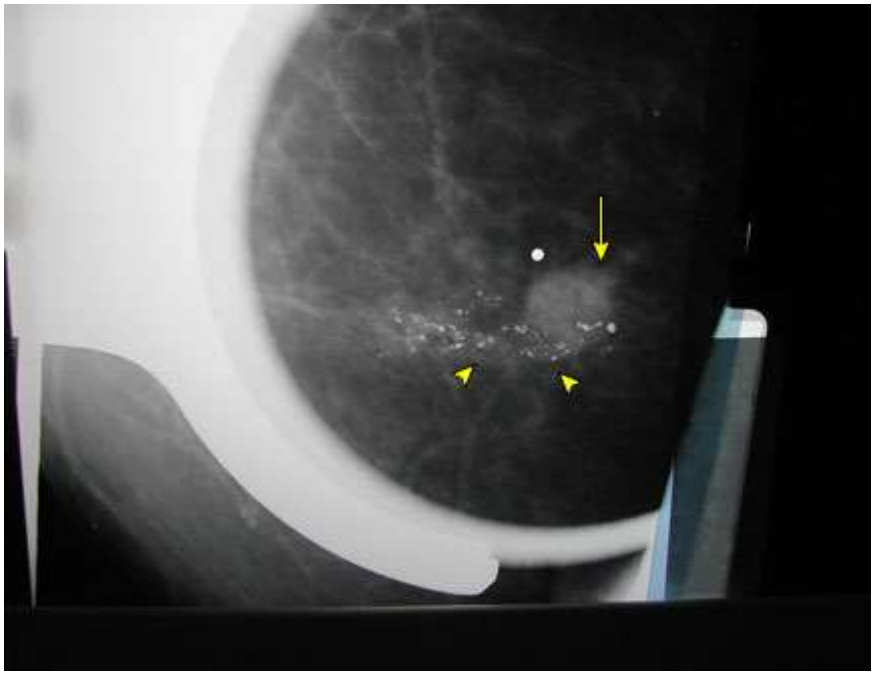


Light microscopic specimen of comedo ductal carcinoma in situ shows a large central area of necrosis that is focally calcified. The nuclei are poorly differentiated (high grade).

Courtesy of Stuart Schnitt, MD.

Graphic 77048 Version 2.0

Mammogram grouped calcifications A

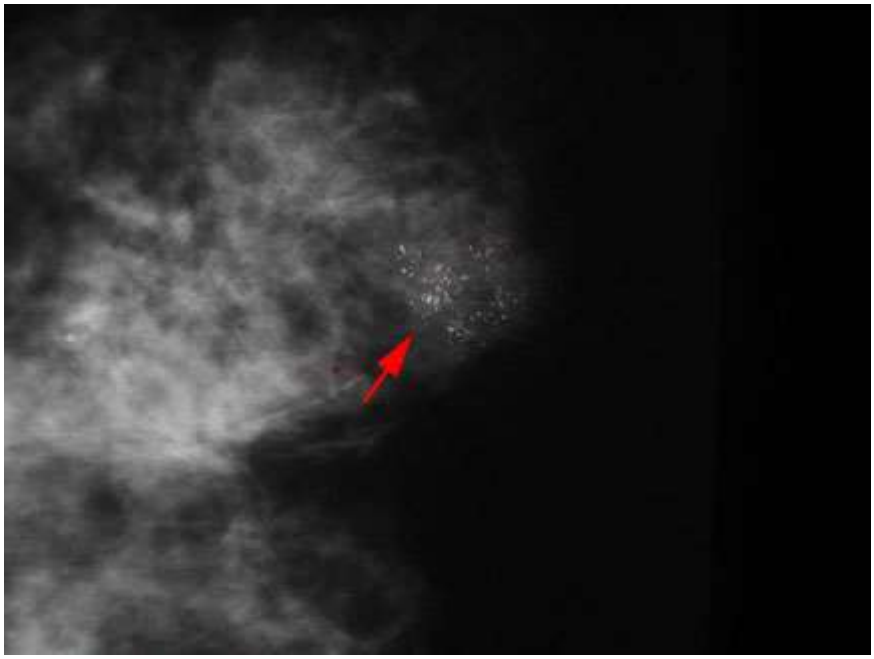


Spot compression view of a mammogram showing a high-density spiculated mass (arrow) with heterogeneous linear clacifications in a ductal distribution (arrowheads). These "casting" calcifications are characteristic of high-grade ductal carcinoma in situ (DCIS). Pathology revealed infiltrating duct cell carcinoma with DCIS, comedo type.

Courtesy of Lisa E Esserman, MD.

Graphic 75424 Version 5.0

Mammogram grouped calcifications B

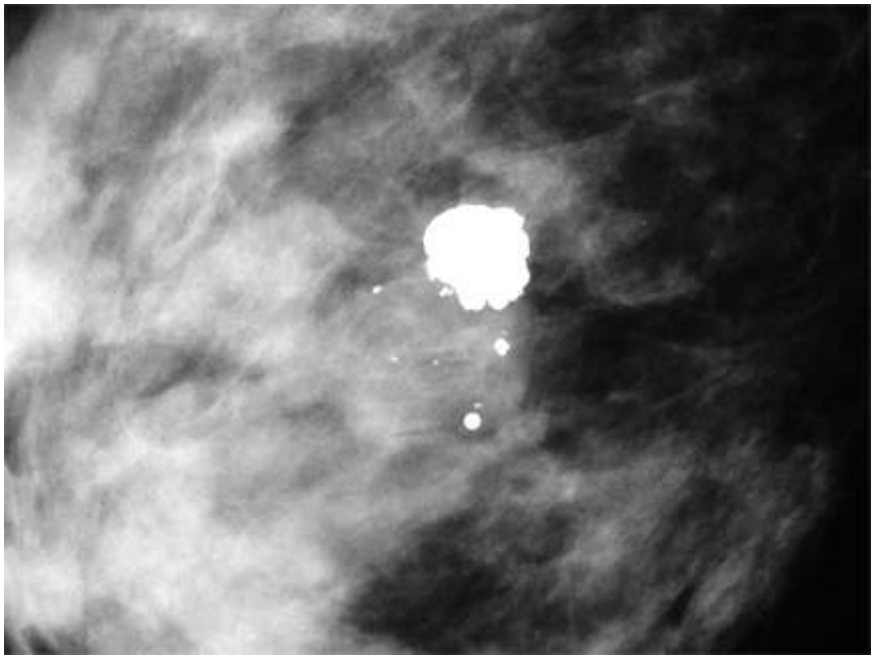


Magnified craniocaudal mammogram showing linear branching calcifications in a segmental distribution (red arrow). Grouped microcalcifications such as these are highly suggestive of carcinoma, and the linear branching is suggestive of a ductal lesion. Biopsy confirmed a high-grade ductal carcinoma in situ (DCIS).

Courtesy of Lisa E Esserman, MD.

Graphic 66876 Version 3.0

Mammographic calcifications

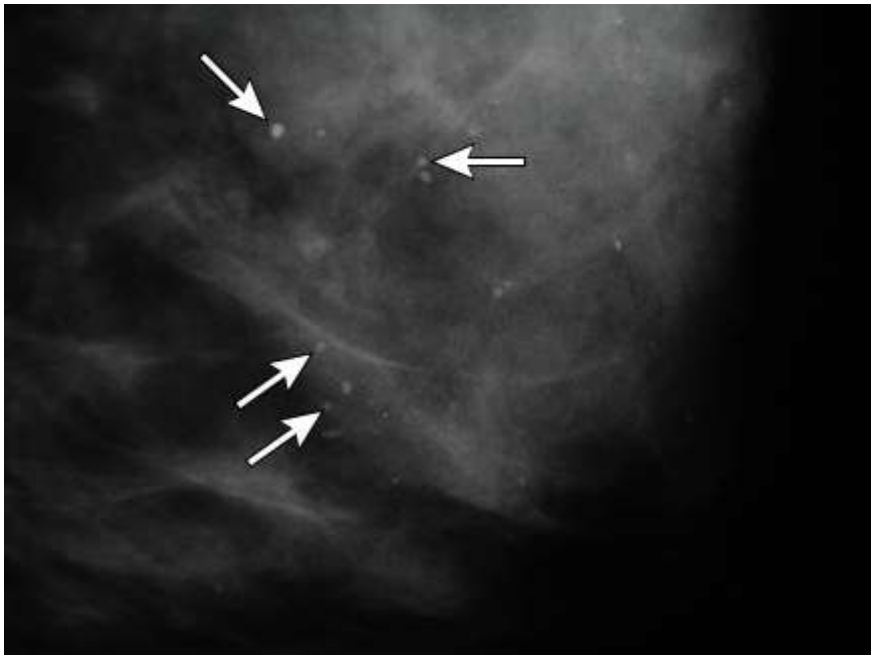


Medial lateral oblique view mammogram demonstrates a classic benign, partially calcified fibroadenoma with typical coarse, popcorn-like calcifications. These findings are not suspicious and do not require biopsy.

Courtesy of Lisa Esserman, MD.

Graphic 65088 Version 3.0

Round mammographic calcifications



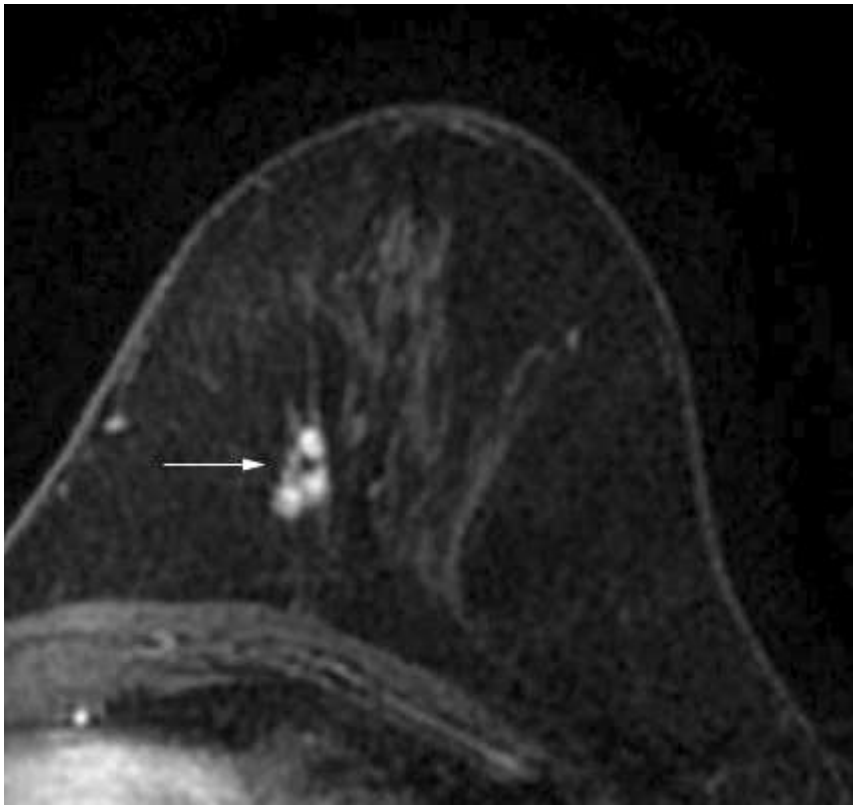
Magnified medial lateral oblique mammogram showing scattered, well-defined, round calcifications (arrows) that can be characterized as benign. These findings are benign and would be described as BI-RADS 2.

BI-RADS: Breast Imaging Reporting and Data System.

Courtesy of Lisa E Esserman, MD.

Graphic 52281 Version 6.0

MRI of early breast cancer



Left breast MRI demonstrates a mass with lobulated margins (arrow) and heterogeneous enhancement. There was rapid wash-in of intravenous gadolinium with a rapid washout on the delayed phase (suspicious enhancement curve).

MRI: magnetic resonance imaging.

Courtesy of Pierre J Sasson, MD.

Graphic 59469 Version 8.0

Preoperative MRI and positive margin rates

Study	Intervention		Positive margin rate		Re-excision rate	
	Arm	n	Percent	p value	Percent	p value
COMICE[1]	MRI	816	13*	NS	16	0.77
	No MRI	807	15*		19	
MONET[2]	MRI	74	NS	NS	45¶	0.069
	No MRI	75	NS		28¶	
	SOC	116	34		21	

MRI: magnetic resonance imaging; NS: not specified; SOC: standard of care.

* Positive margins stated are for invasive disease only.

¶ Re-excision rates stated are for re-excision (breast-conserving surgery) and conversion to mastectomy after initial surgery.

References:

1. *Turnbull L, Brown S, Harvey I, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: A randomised controlled trial. Lancet 2010; 375:563.*
2. *Peters NH, van Esser S, van den Bosch MA, et al. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: The MONET - randomised controlled trial. Eur J Cancer 2011; 47:879.*

Contributor Disclosures

Laura J Esserman, MD, MBA Grant/Research/Clinical Trial Support: Moderna [Ductal carcinoma in situ]. Consultant/Advisory Boards: Blue Cross/Blue Shield [Review evidence related to clinical benefits of new treatments]. All of the relevant financial relationships listed have been mitigated. **Bonnie N Joe, MD, PhD** Grant/Research/Clinical Trial Support: Kheiron Medical Technologies [Mammography]. All of the relevant financial relationships listed have been mitigated. **Anees B Chagpar, MD, MSc, MA, MPH, MBA, FACS, FRCS(C)** Consultant/Advisory Boards: Guardant Health [Breast cancer]; Merck [Breast cancer]; Novartis [Breast cancer]; Protean BioDiagnostics [Breast cancer]; Sanofi-Aventis [Breast cancer]. Speaker's Bureau: Merck [Breast cancer]. All of the relevant financial relationships listed have been mitigated. **Daniel F Hayes, MD** Equity Ownership/Stock Options: Inbiomotion [Breast cancer]. Patent Holder: Immunicon Corporation [Inventor]; University of Michigan [Inventor]; University of Michigan [Inventor]. Grant/Research/Clinical Trial Support: AstraZeneca [Breast cancer]; Menarini Silicon Biosystems, LLC [Breast cancer]; Pfizer [Breast cancer]. Consultant/Advisory Boards: Artiman Ventures [Breast cancer]; BioVeca [Breast cancer]; Cepheid [Breast cancer]; EPIC Sciences, Inc [Breast cancer]; Freenome, Inc [Colorectal cancer]; Guardant [Oncology]; Lexent Bio [Breast cancer]; L-Nutra [Breast cancer]; Macrogenics [Breast cancer]; OncoCyte [Biomarkers]; Predictus BioSciences [Breast cancer]; Tempus [Oncology]; Turnstone Biologics [Breast cancer]; Xilis [GI cancer]. Other Financial Interest: Menarini Silicon Biosystems [Royalties from licensing of patent – Breast cancer]. All of the relevant financial relationships listed have been mitigated. **Gary J Whitman, MD** Consultant/Advisory Boards: Siemens [Digital mammography, tomosynthesis, breast cancer]. All of the relevant financial relationships listed have been mitigated. **Wenliang Chen, MD, PhD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→