

## Breast Cancer Imaging: Mammography, MRI, and Breast Ultrasound

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**Breast cancer screening is essential in lowering breast-cancer related mortality and the prevalence of invasive and advanced breast cancer in high risk women. High risk women should receive a screening that is based on at least three imaging modalities, i.e., mammography, magnetic resonance imaging and ultrasonography, for the primary prevention of breast cancer. The use of these three modalities allows for the early detection of breast cancer or precancerous lesions.**



### Risk Factors for Breast Cancer

It is estimated that **1 in 8 women** in the United States will develop breast cancer. Thus, it is prudent to identify these cases at an early stage for time management. Identification of the cases at an early stage is achieved via **screening for breast cancers** and via **identification of risk factors** among selected women. The following factors have been shown to increase the risk of developing breast cancer.

#### **Prior diagnosis**

Women who have been diagnosed with lobular carcinoma in situ on a previous biopsy study or women who have had a breast lesion requiring evaluation in one breast are at an

increased risk of developing breast cancer in the contralateral breast. Additionally, recurrent breast cancer in the ipsilateral breast is more likely compared to the occurrence of breast cancer in a healthy woman with no previous history of breast cancer.

### **Positive family history of breast cancer**

Women with a family history of breast cancer have a 13 % lifetime risk of developing breast cancer, whereas those with two first degree relatives diagnosed with breast cancer have a 21 % lifetime risk of developing breast cancer. **Women with a positive family history of breast cancer with a specific genetic mutation might develop breast cancer during the reproductive years or when they are old.**

### **Genetic mutations**

Certain genetic mutations are known to put the patient at a **significantly higher risk** of breast cancer compared to the general population. For instance, women who carry the **BRCA1 or BRCA2 genes** are at a significantly higher risk of breast cancer. Mutations in the **PTEN gene, TP53 gene, MSH2 gene and MLH1 gene** also put the woman at an increased risk of developing breast cancer.

Therefore, **women with a documented family history of a genetic abnormality associated breast or reproductive system cancers should be screened for these specific genes.** If the woman is found to be positive for one of the previously mentioned genes, she should receive breast cancer imaging screening at a considerably younger age compared to women who do not have such genetic abnormalities.

### **Increased exposure to estrogen hormone**

Increased exposure to estrogen hormone triggers breast cellular hyperplasia that may tip over into metaplasia and development of breast cancer. The factors that indicate an increased exposure to estrogen include early menarche, late menopause, nulliparity, use of oral contraceptive pills, and use of hormonal replacement therapy.

**Other risk factors** for breast cancer include radiation exposure, obesity, alcohol use and advanced age > 40 years.

## Breast Imaging as a Screening Tool for Women at High Risk for Cancer

Randomized clinical trials showed a clear benefit from breast cancer screening in lowering cancer-related mortality and morbidity. The most studied imaging modalities are:

- Mammography
- Breast magnetic resonance imaging
- Ultrasonography

### Imaging features of breast cancer

- Masses
- Microcalcifications—5 or more punctate calcifications within a 1 cm area
- Architectural distortion

## Terminology used for masses

- **Mass:** 75 % of the margins are visualized on 2 views
- **Focal asymmetry:** Seen on 2 views, but 75 % of the margins are not seen
- **Asymmetry:** Seen on only 1 view

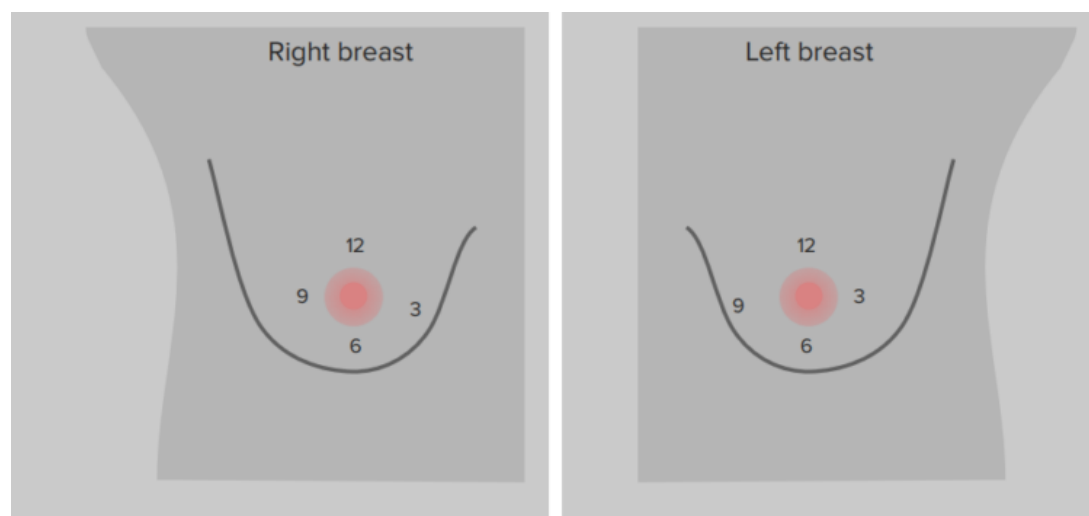
## Protocols for palpable abnormalities

- **Age  $\geq$  30:** Diagnostic mammogram/tomosynthesis & breast ultrasound
- **Age  $\leq$  30:** Breast ultrasound only
- **Pregnant patient:** Breast ultrasound only
- **Breastfeeding patient:** Breast ultrasound +/- diagnostic mammogram/tomosynthesis; patient should be instructed to feed or pump just prior to mammogram
- **Axillary lump:** Diagnostic mammogram/tomosynthesis and breast ultrasound

## Localizing breast lesions

If there is a vague or large area, then it may be localized by a quadrant. If there is a focal area, then it will be localized by an o'clock position and distance from the nipple in centimeters.

**Note:** Ultrasound is used as an adjunct to mammography for focal areas of concern and focal mammographic abnormalities. It is not commonly used alone due to the high false-positive rate of ultrasound.



Localizing breast lesions by an o'clock position. Image by Lecturio.

## Breast biopsies

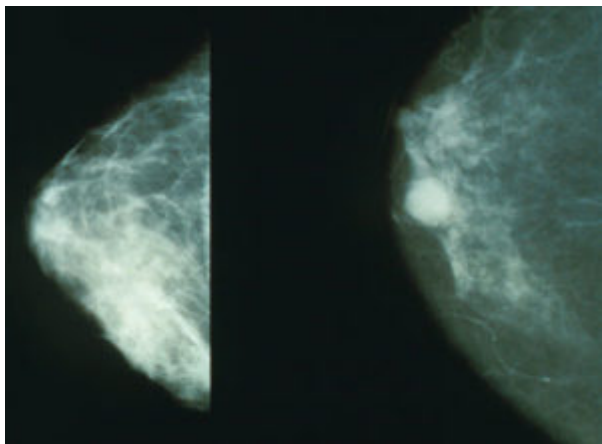
Breast masses are almost always biopsied using image-guided needle biopsy. Breast imaging and breast image-guided biopsies allow for a full evaluation prior to surgery. If type and extent of disease are known, then usually only one surgery is needed. Prior to breast needle biopsies, a surgical biopsy was performed to diagnose the problem and then another surgery was performed to fully remove the lesion.

**Types of breast biopsies are:**

- Ultrasound-guided
- Stereotactic (mammographically guided)
- MRI-guided

Biopsy is performed using the method that the lesion is seen best on. Ultrasound-guided biopsies are most common as masses are best seen on ultrasound.

## Mammography



[Image](#): "Mammo breast cancer" by Morning2k. License: [Public domain](#)

Mammography was constantly shown to allow for the early detection of breast cancer or precancerous lesions before they develop into invasive breast cancer. Nowadays, it is **recommended to start the routine annual mammography screening after the age of 40 years**. The American College of Obstetricians and Gynecologists recommended annual mammography screening for breast cancer in all women aged between 40 and 49 years.

The **main question regarding mammography screening in high-risk women for breast cancer is whether the age to start screening should be lowered**. A recent study has shown that women who are considered as high risk for breast cancer who received annual mammography after 30 years of age and up to 39 years of age had a cancer detection rate of 3.4 per 1000. Surprisingly, the cancer detection rate by mammography in high-risk women aged between 40 and 49 years is around 3.3 per 1000.

Based on this, one can clearly deduct that **commencing routine annual mammography screening at the age of 30 years, 10 years younger than your typical screened woman, is certainly beneficial to the patient**.

The issue with using mammography in women younger than 40 years of age is the reduced sensitivity and specificity due to the presence of a denser breast in young women. Therefore, **many women who get a mammogram before the age of 40 years (up to 8.6 %) will need a second assessment exam (recall rate)**.

To lower the recall rate, we recommend comparing the current mammography images with previous mammography images for the same patient. Comparing to previous examinations lowers the recall rate to 3.66 %.

**Mammography is superior to magnetic resonance imaging** in the detection of early precancerous regions, such as intraductal carcinoma in situ, which is characterized by

small microcalcifications on mammography.

Finally, women with BRCA mutations should receive mammography routine screening starting at the age of 25 years. If the quality of the mammograms is very low due to the very dense breast at that age, one can:

- Compare different mammograms focusing more on changes rather than the isolated interpretation of a single mammogram
- Compare the results of the mammogram with magnetic resonance imaging
- Use ultrasonography for screening purposes

## Screening guidelines

Ideally, women should be screened every year beginning at the age of 40 and continuing as long as they have a life expectancy of 10 years or more. 7 large randomized controlled trials have shown a 30 % decrease in deaths from breast cancer due to screening mammography. However, this is not done in many parts of the world due to the expense of annual screening.

- Performed on patients with no clinical breast symptoms
- 4 total images, 2 on each breast:
  - MLO: Medial-lateral oblique
  - CC: Cranial caudal
- CC images: top part shows lateral aspect of the breast

**Note:** Standard screening mammogram (4 views) will emit the same amount of radiation that you normally receive in three months of exposure to your surroundings or one transatlantic flight.

## Diagnostic Mammogram

For a woman presenting clinical evidence of breast disease, palpable mass or other symptoms, or an abnormality seen on screening mammogram, additional tailored images are obtained to further evaluate the area of concern. Abnormalities that lead to concern include:

- Palpable mass
- Pain
- Discharge
- Skin thickening
- Skin or nipple retraction
- Abnormality on screening mammogram

## Breast density

The breast tissues are made of fibroglandular tissue and fatty tissue. The density of the breast tissue is based on the amount of fibroglandular tissue that is present. Fibroglandular tissue appears white.

Given on all mammograms:

- Almost entirely fatty
- Scattered fibroglandular
- Heterogeneously dense
- Extremely dense

**Note:** Dense breast tissues decrease the sensitivity of mammography and are thought to have at least a slightly increased risk of developing breast cancer.

## Tomosynthesis

- 3D mammography
- Used in addition to standard or 2D mammography
- Increase the sensitivity of mammography especially in women with dense breast tissue
- Expensive upgrade to a standard mammography machine

## Birads categories

Birads categories are final assessment categories and assigned to every mammography report.

0	Need additional imaging evaluation or prior mammogram for comparison
1	Negative
2	Benign
3	Probably benign (< 2 % chance of malignancy), short-interval follow-up recommended
4	Suspicious abnormality (2—95 % chance of malignancy), biopsy should be considered
5	Highly suggestive of malignancy (> 95 % chance of malignancy), appropriate action should be taken
6	Known biopsy has proven malignancy

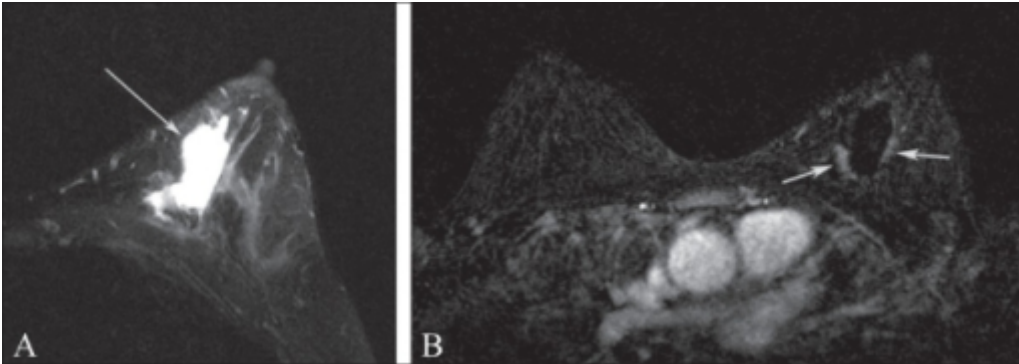
## Magnetic Resonance Imaging

In contrast to a mammography, the utility and benefits of magnetic resonance imaging studies, such as screening tools for breast cancer in high-risk women, are based on low-evidence research such as:

- Case series
- Descriptive studies
- Prospective observational studies

Randomized clinical trials were not performed to assess the efficacy of magnetic resonance imaging in screening for breast cancer in healthy or high-risk women.

Multiple observational studies compared the efficacy of magnetic resonance imaging in the detection of early breast cancer compared to mammography. **Of all the breast cancers detected on magnetic resonance imaging, only 41 % were also detectable by mammography.**



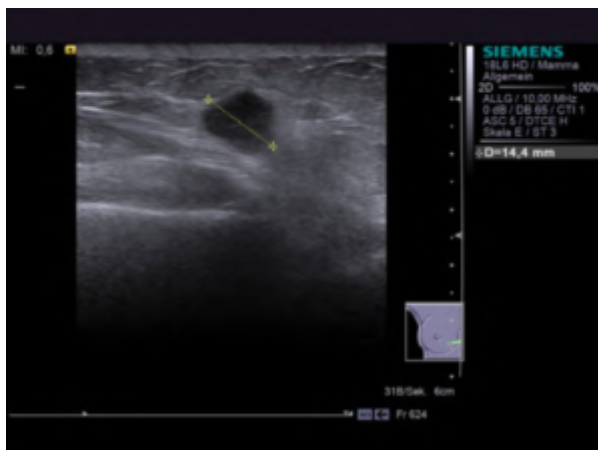
**Image:** “Axial T2W image (A) demonstrates a post-lumpectomy seroma cavity (arrow) in this patient with positive margins after conservation therapy for breast cancer. The axial DCE-MRI subtracted image demonstrates minimal thick, nodular enhancement in the posteromedial and lateral walls of the lumpectomy cavity (arrows). In this patient, re-excision of the cavity with attention to the areas noted on the DCE-MRI yielded negative margins ” by Ojeda-Fournier H, Comstock CE - Indian J Radiol Imaging (2009 Apr-Jun). License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

This result is based on seven huge observational studies from the Netherlands, Canada, the United Kingdom, Germany, Italy, Norway, and Austria. Despite the clear added benefit of magnetic resonance imaging in the detection of breast cancer, no sophisticated randomized clinical trials have been carried out so far.

**Similarly, magnetic resonance imaging of the breast is of low quality in younger women;** therefore, the current recommendation is to start magnetic resonance imaging in high-risk women with BRCA gene mutations at the age of 30.

False-positives with magnetic resonance imaging are more common. Of the identified lesions on magnetic resonance imaging, up to 8 % were later found to be benign.

## Ultrasonography



**Image:** “Triple-negative breast cancer in a 52 year old patient (G3, invasive ductal). The tumor appears as a lobulated, hypoechoic mass. The ligaments are displaced rather than disrupted. ” by Wojcinski S, Stefanidou N, Hillemanns P, Degenhardt F - BMC Womens Health (2013). License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

**As with magnetic resonance imaging, ultrasonography was only evaluated in observational studies** as a tool to screen for breast cancer. Women with an intermediate risk for breast cancer, i.e., a second degree relative with previous breast surgery for an unknown cause might benefit from early screening with ultrasonography instead of mammography or magnetic resonance imaging for two main reasons:

1. Mammography is based on X-ray and is therefore not risk-free.
2. Magnetic resonance imaging is very costly for a patient with an intermediate risk of developing breast cancer.

Very young women who are at high-risk for breast cancer should receive ultrasonography in addition to mammography and magnetic resonance imaging. The **goal is to combine the results of the different imaging modalities to make it possible to detect as many cancers as possible** before cancer becomes invasive. The added benefits of ultrasonography are based on cross-sectional and observational studies.

## Other Imaging Modalities for Screening for Breast Cancer

Patients who document a previous history of breast cancer might benefit from a positron emission tomography scan to screen for ipsilateral recurrent disease or contralateral breast cancer microscopic depositions.

High resolution computed tomography scans of the breast are also becoming a promising technique for the detection of early breast cancer in younger women whose magnetic resonance imaging studies and mammograms were not conclusive. Contrast-enhanced magnetic resonance imaging studies, or **contrast-enhanced computed tomography scans, are helpful in the differentiation between malignant and benign breast lesions.**

## References

Sickles EA. [The use of breast imaging to screen women at high risk for cancer](#). Radiologic clinics of North America. 2010. 48(5):859-78. doi: 10.1016/j.rcl.2010.06.012. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/20868890>

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