How should we screen for breast cancer? Mammography, ultrasonography, MRI

■ ABSTRACT

Of the imaging techniques currently available to evaluate women for breast disease, mammography remains the mainstay of breast cancer screening, but recent guidelines have included magnetic resonance imaging (MRI) for the screening of some women at high risk. Whole-breast ultrasonography for screening has not been established as useful and so should not be offered routinely to patients.

■ KEY POINTS

Most major medical organizations recommend starting routine screening mammography for women at age 40.

If a screening mammogram is abnormal or has findings of unclear significance, the patient should be referred for diagnostic mammography.

If a palpable breast mass is discovered, the patient should be referred for diagnostic mammography and ultrasonography.

Breast MRI can be considered in addition to mammography for screening in high-risk patients, such as women with a BRCA gene mutation, a strong family history of breast cancer or a personal history of ovarian cancer, or women who have received high-dose chest radiation, such as mantle radiotherapy for Hodgkin disease. Other high-risk groups in which breast MRI is currently being studied are women with a personal history of breast cancer, women with a history of atypical duct hyperplasia or lobular carcinoma in situ, and women with an elevated Gail breast cancer risk assessment score.

The answer to how we should screen for breast cancer is, “Very carefully.” No screening procedure is perfect, women vary greatly in their breast cancer risk, and screening may lead to unnecessary procedures and alarm. Therefore, physicians must carefully consider which screening regimen is right for each patient.

While many issues surrounding breast cancer screening are still unresolved, general guidelines have now been implemented on the basis of data accrued over many years. In this article, we summarize the most current guidelines and also comment briefly on screening examinations that hold promise but have not yet earned a place in routine breast cancer screening.

Breast cancer survival has improved over the past few decades. In the 1940s, the 5-year survival rate for early-stage localized disease (no lymph node involvement or metastasis) was 72%, which has improved to 97% today. This improvement in survival is in large measure attributable to the increased and effective use of screening mammography in asymptomatic patients, with improved treatment protocols also playing a role. Early detection of breast cancer, ie, before it is clinically apparent, is important both to patients and to their physicians. In this article, we also examine how the careful use of breast imaging techniques—mammography, ultrasonography, and magnetic resonance imaging (MRI)—can improve breast cancer detection in women.

■ WHO SHOULD UNDERGO MAMMOGRAPHIC SCREENING?

Experts have long agreed that screening mammography reduces the rate of death
Current breast biopsy techniques

**CORE NEEDLE BIOPSY**
A large-bore automated cutting needle is used to remove three to five solid cylindrical tissue samples (“cores”). For adequate samples, a 14-gauge or larger needle is used. These procedures are performed with guidance by ultrasonography, stereotactic imaging, or MRI. In most cases this is the preferred method of biopsy, since it usually provides adequate tissue for tumor grading and performance of receptor studies, both of which are important in formulating the patient’s treatment plan.

**FINE-NEEDLE ASPIRATION**
A smaller-bore (usually 18- or 20-gauge) needle is used to obtain cytologic samples from a suspicious breast mass. This is technically easy to perform but is less used by radiologists now that automated core-biopsy instruments are more widely available. Fine-needle aspiration can often make the diagnosis of malignancy but does not provide sufficient tissue for more detailed studies, and thus generally necessitates obtaining a second (core) biopsy specimen for study before definitive treatment can be planned. In addition, the satisfactory interpretation of cytologic specimens requires pathologists with special expertise in cytopathology. Fine-needle aspiration is not recommended for the evaluation of suspected ductal carcinoma in situ.

**EXCISIONAL BIOPSY**
This procedure is performed by a surgeon in the operating room, usually to remove the entire mass or suspicious area. Excisional biopsy requires preoperative wire localization if the lesion is not palpable.

A recent study considered the separate effects of screening mammography and of adjuvant therapy on the breast cancer death rate, drawing on the experience of multiple institutions. From 1975 to 2000, the overall reduction in breast cancer deaths was 24%. The study estimated that the portion of the reduction attributed to screening mammography ranged from 28% to 65% (median 46%), with the rest attributed to the use of adjuvant therapy. The variability in the reduction of the death rate was attributed to variations in the inclusion criteria of the participating groups: eg, some groups included patients with ductal carcinoma in situ, and other studies included only patients with invasive carcinoma.

**General recommendations for mammographic screening**
Screening mammography should begin at age 40. This recommendation is supported by major medical organizations, including the American Cancer Society, the American College of Radiology, the National Cancer Institute, the American College of Obstetricians and Gynecologists, and the American Medical Association. In our practice, we follow the American College of Radiology recommenda-
tions for routine screening at yearly intervals.

Screening mammography is most effective between ages 50 and 59 and should be routinely recommended.

There is no established upper age limit to the beneficial use of screening mammography. According to the 2004 revised American College of Radiology guidelines, \(^8\) “It is unclear at what age, if any, women cease to benefit from screening mammography. Because this age is likely to vary depending on the individual’s overall health, the decision as to when to stop routine mammography screening should be made on an individual basis by each woman and her physician.\(^8\)” The American Cancer Society further recommends that “as long as a woman is in reasonably good health and would be a candidate for treatment, she should continue to be screened with mammography."\(^9\)

Special recommendations

If a patient has a first-degree relative who has had breast cancer, screening mammography should commence 10 years earlier than the age at which that relative was diagnosed, or at age 25, whichever is older. For example, if the patient’s mother was diagnosed with breast cancer at age 39, screening mammography for her daughters should begin at age 29.

Patients with a personal history of atypical duct hyperplasia or lobular carcinoma in situ are candidates for increased surveillance, usually including a clinical breast examination and mammography every 6 months. (High-risk patients may also be candidates for breast MRI, as discussed later in this article).

Patients who have received high-dose chest radiation (mantle radiotherapy) are at increased risk of developing radiation-induced breast cancer. For this reason, a woman with a diagnosis of Hodgkin lymphoma for example, who received mantle radiotherapy, should begin mammographic screening 8 years after her radiation treatment.

‘Mammogram density’ is now considered a risk factor for breast cancer. In fact, the risk associated with mammogram density may be greater than the risk from many other risk factors.\(^10\)–\(^13\) Mammogram density is thought to be an inherited phenomenon,\(^14\) but it can also be caused by hormone therapy. Women on long-term hormone therapy are called back more often for further evaluation and have a higher rate of benign breast biopsies carried out to evaluate suspicious findings.\(^15\)

The addition of breast ultrasonography or MRI in selected cases of mammogram density may be useful. Digital mammography may also play a role in patients with mammogram density and is currently undergoing evaluation in large-scale trials.\(^16\) Its clinical usefulness has yet to be fully elucidated.

**WHAT HAPPENS IF THE MAMMOGRAM SHOWS AN ABNORMALITY?**

Screening mammography may detect a mass lesion, suspicious microcalcifications, focal asymmetry, or architectural distortion. It may detect lymph nodes of abnormal size, contour, or density. It may also detect more subtle changes such as skin thickening. If any of these findings is noted, diagnostic mammography is recommended.

About 10% of women who undergo screening mammography are called back for further evaluation. Of these patients, around 10% will have a breast biopsy, of which 25% to 40% will be positive for breast cancer.\(^17\),\(^18\) Using estimates from the Mammography Quality Standards Act guidelines, of 1,000 asymptomatic patients screened by mammography, 2 to 10 patients will be shown to have breast cancer. This range allows for variations encountered in different screening populations.

**WHEN SHOULD WE ORDER DIAGNOSTIC MAMMOGRAPHY?**

If a patient presents with a breast complaint, or if an abnormality is noted on the clinical breast examination, then diagnostic mammography should be ordered. In contrast to screening mammography, which consists of two standard views of each breast, diagnostic mammography includes extra views or studies tailored to evaluate the finding in question.

Reasons to refer a patient for diagnostic mammography include an abnormal screening mammogram, a breast mass or thickening on palpation, focal breast pain, clear or bloody
nipple discharge, nipple retraction, a concerning palpable lymph node, or abnormal skin changes such as erythema or peau d’orange. If a breast mass is palpated, an ultrasonographic examination is ordered in addition to diagnostic mammography (FIGURES 1–3).

If diagnostic mammography or ultrasonography reveals suspicious findings, biopsy is recommended (see “Current breast biopsy techniques,” page 898). In a small number of cases in which suspicion of cancer is very low, a conclusion of “probably benign” may be given, with recommendations for short-term follow-up.

A PALPABLE MASS WITH NEGATIVE MAMMOGRAPHIC AND ULTRASONOGRAPHIC STUDIES

What should be done when a mass is palpable, but mammographic and ultrasonographic studies are negative? This will depend on the situation. Often, ultrasonography will show the palpable lump to be a normal fibrous ridge or a region of benign asymmetry that corresponds definitely to the palpable findings. In these cases, no further workup is needed. But if clinical suspicion remains high despite the negative imaging results, biopsy should be considered.

Fine-needle aspiration is an easy, minimally invasive way to obtain a sample of a palpable mass. It can be performed in the office. Core biopsy can be carried out on a palpable mass using imaging guidance in order to assure a safe trajectory for the cutting needle.

If the palpable mass is not easily accessible (eg, if it is close to the chest wall or in the axil-
la), or if the patient is very anxious, an exci-
sional biopsy can be performed to remove the
entire mass.

No imaging technique can exclude breast
cancer with 100% accuracy. This is true for
mammography, ultrasonography, and MRI.

ULTRASONOGRAPHY IN BREAST CANCER
SCREENING: ADJUNCTIVE ROLE ONLY

Should we use ultrasonography to screen for
breast cancer? In a word, no. The rationale
and limitations summarized below—from the
Position Statement on Screening Breast
Sonography in Dense Breasts, promulgated by
the Society of Breast Imaging19—reflect the
expert consensus on this issue.

Screening mammography is an important
tool, but it can miss some breast cancers, espe-
cially in women with dense breast tissue. For
this reason, it was thought that ultrasono-
graphic screening might improve breast can-
cer detection rates.20 Indeed, breast ultra-
sonography can detect some invasive cancers
that mammography and physical examination
miss, but the number of cancers found with
ultrasonography alone remains small. Also,
ultrasonography does not detect most micro-
calcifications, which are the typical findings
in ductal carcinoma in situ. In fact, 75% of
cancers missed by ultrasonography were du-
tal carcinoma in situ and 25% were invasive
carcinomas.

In addition, the results of ultrasonography
can vary widely, depending on the expertise
of the technician. Indeterminate findings can
lead to the increased use of costly and perhaps
unnecessary interventions. There are at pres-
ent no data to support whole-breast ultrasono-
graphic screening to decrease breast cancer
death rates. A study by the American College
of Radiology Imaging Network (called ACRIN Study 6666) is under way to investi-
gate this issue.

Screening for breast cancer should begin
with mammography. Ultrasonography can be
added to evaluate a mass or to clarify focal
mammographic findings. According to a posi-
tion statement of the Society of Breast
Imaging,19 it “has not been established that
women will benefit from the incorporation of
sonography into routine breast cancer screen-
ing programs... At the present time, it is not
the standard of care to offer or perform this
examination.” In our practice, we do not rec-
ommend or offer screening with breast ultra-
sonography.

MAGNETIC RESONANCE IMAGING
AND BREAST CANCER SCREENING

What is breast MRI?
MRI uses magnetic fields along with radiofre-
cuency transmitters and receivers to produce
cross-sectional images of the human body. To
image the breast, specialized imaging receivers
(“coils”) that encompass each breast are used.

For cancer detection protocols, a contrast
agent that contains gadolinium is injected
intravenously to help identify tissues that
“handle” the agent in an abnormal way, which
is a possible sign of the neovascularity seen in
many breast cancers. MRI involves no ioniz-
ing radiation, and most patients tolerate the
contrast agent well.

The procedure. The patient lies prone on
a padded table that contains the two breast
coils. The breasts are positioned within the
coils, sometimes with mild compression to
maintain constant positioning. The table is
advanced into the magnet and a preselected
series of scans is carried out, both before and
after the injection of contrast material. The
entire study takes about 40 to 50 minutes,
with about half of that time devoted to
patient preparation, placement of a small-
gauge intravenous catheter, and patient posi-
tioning. The scans are acquired rapidly, but
image reconstruction and post-processing
continue after the patient has left the scanner.

Contraindications to MRI include
implant expanders, cardiac pacemakers, neu-
rostimulator devices, extreme claustrophobia,
and morbid obesity.

What are the disadvantages of breast MRI?
An important disadvantage of breast MRI is
the rate of false-positive results. The sensitiv-
ity of breast MRI is high but the specificity is
low. Breast cysts, fibroadenomas, papillomas,
and fibrocystic changes may all appear as
abnormalities on contrast images, resulting in
unnecessary biopsies. In a study of breast MRI
in high-risk women, many of whom were

No imaging study can exclude breast cancer with 100% accuracy
young and had very dense breast tissue, screening MRI led to three times as many benign breast biopsies as mammography.\textsuperscript{21} However, one could argue that in high-risk populations the sensitivity of mammography is quite low and may be of limited value, making MRI an imperfect but better tool.\textsuperscript{22}

Another disadvantage of breast MRI is that it does not detect microcalcifications, which are often associated with ductal carcinoma in situ. These calcifications are readily apparent on mammography. Breast MRI is also not sensitive in detecting lobular cancers.

A recent study in Germany in high-risk women found breast MRI to have a sensitivity of 92\% in detecting ductal carcinoma in situ (DCIS),\textsuperscript{23} but in general DCIS remains a mammographic diagnosis.

Other major drawbacks to using breast MRI include cost and limited access. Fees for breast MRI range from $3,000 to $4,000, which is 10 times that of mammography. Unlike mammography, breast MRI is not routinely covered by insurance. Screening MRI protocols have yet to be developed, and access to breast MRI remains limited.

Who is a candidate for screening with MRI? The average lifetime risk of breast cancer for an American woman is now one in seven.\textsuperscript{17} However, the risk of breast cancer in women with a BRCA1 gene mutation is 3.2\% by age 30, 19\% by age 40, 50\% by age 50, and 85\% by age 70. The lifetime risk for carriers of BRCA1 or BRCA2 mutations is 50\% to 85\%.\textsuperscript{24} Breast cancers in women with a mutation often occur at a young age, are “aggressive” with a high nuclear grade, and lack estrogen receptors.\textsuperscript{25} At the time of diagnosis, half of these breast cancers have already spread to axillary lymph nodes.\textsuperscript{22}

Up to this point, strategies to follow these patients have included bilateral prophylactic mastectomy, prophylactic chemotherapy with tamoxifen, and early surveillance, ie, beginning clinical breast examinations and mammographic screening at age 25 to 30.

The usefulness of breast MRI in these high-risk patients is now being studied. Investigators in the United Kingdom looked at mammography vs contrast-enhanced MRI in 649 asymptomatic women with a known BRCA1, BRCA2, or TP53 mutation or a strong family history of breast cancer. MRI was significantly more sensitive (77\% vs 40\%) but less specific (81\% vs 93\%) than mammography. In particular, MRI was significantly more sensitive than mammography in patients with a BRCA1 mutation and their first-degree relatives (92\% vs 23\%).\textsuperscript{21,26}

Screening breast MRI is proving to be a useful adjunct to mammography in patients with a BRCA mutation. In addition to these patients, the American Cancer Society has recently recommended that other high-risk patients pursue breast MRI. These include women with a 20 \% to 25 \% or greater lifetime risk of breast cancer: ie, women with a strong family history of breast cancer or ovarian cancer and women with a history of mantle radiotherapy for Hodgkin disease.\textsuperscript{27}

Insurance often covers the cost of breast MRI for patients in these high-risk groups. High-risk patients can also obtain breast MRI under research protocols in which there is no charge to the patient.

In our practice, candidates for annual screening breast MRI include:

- Women who carry a BRCA mutation
- Women with a strong family history of breast cancer
- First-degree relatives of a BRCA carrier, but untested
- Women with a strong family history or a personal history of ovarian cancer

Ultrasonography can clarify a focal finding on the clinical exam or mammogram

\begin{figure}
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\includegraphics[width=\textwidth]{mammogram.png}
\caption{This mammogram shows mild asymmetry of the left breast.}
\end{figure}
• Women who were treated for Hodgkin disease with radiation to the chest.
• Women known to have a hereditary breast cancer syndrome and their first-degree relatives.

Screening MRI is currently under investigation in patients with a history of atypical duct hyperplasia or lobular carcinoma in situ or with an elevated Gail score (ie, a 5-year risk of developing breast cancer ≥ 1.7%).

In carefully selected cases, MRI may be helpful in the evaluation of equivocal or suspicious mammographic findings; however, detailed mammographic evaluation and ultrasonography should be done first.

Important note: Breast MRI may not detect some in situ carcinomas and other low-grade benign or malignant lesions and is only an adjunct to mammography. Breast MRI should never be offered as a substitute for conventional screening mammography.

![Breast MRI shows abnormal enhancement of a single lesion corresponding in size and location to the left mammographic asymmetry.](image)

**FIGURE 5.** Breast MRI shows abnormal enhancement of a single lesion corresponding in size and location to the left mammographic asymmetry.

**MRI is not a substitute for conventional screening mammography**

**BREAST CANCER SCREENING GUIDELINES AS APPLIED IN DAILY PRACTICE**

A 56-year-old white woman is seen at the breast center for her annual examination and mammographic evaluation. She is considered at high risk because of a family history of breast cancer—her mother and sister—and her elevated 5-year Gail score (5.0%).

Her breast examination is negative and her mammogram shows mild asymmetry on the left (**FIGURE 4**). Because she is at high risk, breast MRI is ordered and reveals a small mass on the left near the area of asymmetry (**FIGURE 5**).

She is taken to surgery and is found to have a 5-mm breast cancer with negative axillary lymph nodes. She undergoes radiation therapy and begins anastrozole (Arimidex) therapy. Cytotoxic chemotherapy was not necessary.

**PATIENTS WITH BREAST CANCER: ANOTHER HIGH-RISK GROUP**

No discussion of breast MRI would be complete without mentioning another high-risk group: patients with breast cancer.

A study of breast MRI in women recently diagnosed with breast cancer found that MRI detected contralateral breast cancer in up to 10% of women initially diagnosed with unilateral breast cancer. The contralateral breast cancers in these women were missed by both clinical and mammographic evaluation.

These results suggest that breast MRI may be a valuable tool in evaluating women at the time of the initial breast cancer diagnosis. However, more evidence is needed from large-scale clinical trials before clinicians can recommend routine screening MRI for long-term follow-up of patients with a personal history of breast cancer.

**MUCH WORK IS YET TO BE DONE**

In a report just released by the American Cancer Society, the breast cancer mortality rate decreased by 2.2% per year between 1990 and 2004. However, in African American women the breast cancer death rate declined by only 1.6% per year and remained unchanged among Asian Americans/Pacific Islanders and Alaskans/Native Americans. Reasons for the differences in mortality rates remain unclear, and further research is needed. In the same report, it appears that breast cancer incidence is more complex than previously thought. Access to mammography and the
decline in hormone therapy use may be contributing factors. The decrease in screening mammogram rates is also of concern. Almost one-third of American women are not undergoing mammographic screening at appropriate intervals. Most women who are not having routine mammograms are not receiving a recommendation for mammography from their physician. We must continue to communicate to our patients the importance of routine screening mammography and offer our high-risk patients additional breast imaging when appropriate.

**REFERENCES**


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