Magnetic resonance imaging (MRI) of the breast is performed using MRI scanners and intravenous MRI contrast agents, together with specialized breast coils. This policy addresses the use of breast MRI for breast cancer imaging.

Note: This policy only addresses the use of breast MRI for clinical indications related to detection or diagnosis of breast cancer. The use of MRI to monitor silicone gel-filled breast implants for leaks or ruptures, which may be done without contrast enhancement, is addressed in Blue Shield of California Medical Policy: Magnetic Resonance Imaging to Monitor Integrity of Silicone-Gel-Filled Breast Implants.

MRI for Screening Purposes

MRI of the breast may be considered medically necessary for screening for breast cancer in patients with any of the following conditions [1]:

- Known BRCA1 or BRCA2 gene mutation
- High risk of BRCA1 or BRCA2 mutation due to a known presence of the mutation in relatives
- Personal history of or a first-degree relative with Li-Fraumeni syndrome, Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome
- High risk (lifetime risk > 20% or 5-year risk of ≥ 3%) of developing breast cancer as identified by models that are largely defined by family history
- Received radiation therapy to the chest between 10 and 30 years of age
MRI for Diagnostic Purposes

MRI of the breast may be considered medically necessary for any of the following indications:

- For detection of a suspected occult breast primary tumor in patients with axillary nodal adenocarcinoma (i.e., negative mammography and physical exam) [3].
- In patients with a new diagnosis of breast cancer to evaluate the contralateral breast when clinical and mammographic findings are normal [4].
- For preoperative tumor mapping of the involved (ipsilateral) breast to evaluate the presence of multicentric disease in patients with clinically localized breast cancer who are candidates for breast-conservation therapy (see Policy Guidelines section) [7].
- For presurgical planning in patients with locally advanced breast cancer including ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) before and after completion of neoadjuvant chemotherapy to permit tumor localization and characterization, response to treatment, and potential for breast conserving therapy [8].
- To determine the presence of pectoralis major muscle/chest wall invasion in patients with posteriorly located tumors [10].
- To evaluate a documented abnormality of the breast before obtaining an MRI-guided biopsy when there is documentation that other methods, such as palpation, mammogram, or ultrasound, are not able to localize the lesion for biopsy [12].

MRI of the breast is considered investigational for all of the following indications:

- As a screening technique in average-risk patients [2]
- As a screening technique for the detection of breast cancer when the sensitivity of mammography is limited (i.e., dense breasts, breast implants, scarring after treatment for breast cancer) [2]
- For the diagnosis of low-suspicion findings on conventional testing not indicated for immediate biopsy and referred for short-interval follow-up [5]
- For the diagnosis of a suspicious breast lesion in order to avoid biopsy [6]
- To determine response during neoadjuvant chemotherapy in patients with locally advanced breast cancer [9]
- For the evaluation of residual tumor in patients with positive margins after lumpectomy [11]

Policy Guidelines

General

A first degree relative is defined as the parents, brothers, sisters, or children of an individual.

Breast MRI exams should be performed and interpreted by an expert breast imaging team working together with the multidisciplinary oncology treatment team.

As noted, breast MRI exams require a dedicated breast coil and the use of contrast by radiologists familiar with the optimal timing sequences and other technical aspects of image interpretation. The breast MR imaging center also should have the ability to perform MRI-guided biopsy and/or wire localization of findings detected by MRI.

Preoperative MRI in patients with localized disease apparently results in higher rates of mastectomy and lower rates of BCT. There is uncertainty from the available evidence on
whether outcomes are improved by changing to a more extensive operation. If biopsies are performed on all MRI-identified lesions, and if shared patient decision making is used for altering the surgical approach, then the probability of improved outcomes is increased.

Consideration of BRCA1 and BRCA2 gene mutation testing should be given for women who have a family history suspected of having the BRCA1 or BRCA2 mutation, which has not been identified. (For further reference see Blue Shield of California Medical Policy: Genetic Testing for Hereditary Breast and/Ovarian Cancer).

Risk Assessment Tools

If a risk assessment model value is not documented; Blue Shield of California (BSC) will use the National Cancer Institute (NCI) Breast Cancer Risk Assessment Tool available at: *www.cancer.gov/bcrisktool/

A number of risk assessment tools based mainly on family history can assist practitioners in estimating breast cancer risk and include the Claus,(1) modified Gail,(2) Tyrer-Cuzick,(3) and BRCAPRO(4) models.

Note: The tool should not be used to calculate breast cancer risk for women who have already had a diagnosis of breast cancer, lobular carcinoma in situ (LCIS), or ductal carcinoma in situ (DCIS).

The member information required to calculate risk of breast cancer includes:

- Age
- Age at time of first menstrual period
- Age at time of her first live birth
- First degree relatives with a history of breast cancer
- History and number of breast biopsies performed
- Diagnosis of atypical hyperplasia with at least one breast biopsy
- Ethnicity/Race

BI-RADS Classification

The Breast Imaging Reporting and Data System (BI-RADS) provides a standardized classification system for mammograms:

<table>
<thead>
<tr>
<th>BI-RADS Category</th>
<th>Assessment</th>
<th>Clinical Management Recommendation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Assessment incomplete</td>
<td>Need to review prior studies and/or complete additional imaging</td>
</tr>
<tr>
<td>1</td>
<td>Negative</td>
<td>Continue routine screening</td>
</tr>
<tr>
<td>2</td>
<td>Benign finding</td>
<td>Continue routine screening</td>
</tr>
<tr>
<td>3</td>
<td>Probably benign finding</td>
<td>Short-term follow-up mammogram at 6 months, then every 6-12 months for 1 to 2 years</td>
</tr>
<tr>
<td>4</td>
<td>Suspicious abnormality</td>
<td>Perform biopsy, preferably needle biopsy</td>
</tr>
<tr>
<td>5</td>
<td>Highly suspicious of malignancy; appropriate action should be taken</td>
<td>Biopsy and treatment, as necessary</td>
</tr>
</tbody>
</table>
Known biopsy-proven malignancy, treatment pending

Assure that treatment is completed

**Benefit Application**

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program (FEP)) prohibit Plans from denying Food and Drug Administration (FDA) - approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

**Rationale**

Magnetic resonance imaging (MRI) of the breast can be used for screening, detection, and/or diagnosis of breast cancer. It can be used as a replacement for mammography screening, or can be used as an additional imaging test alone or in combination with other imaging modalities.

**Screening Uses**

- Detection of breast cancer in patients who are at high genetic risk for breast cancer
- Detection of breast cancer in patients who have breast characteristics limiting the sensitivity of mammography (i.e., dense breasts, implants, or scarring after treatment for breast cancer)

MRI of the breast has been investigated as a screening tool in specific higher-risk subgroups of patients. First, it has been studied in patients considered to be at high genetic risk of breast cancer, such as those with known BRCA1 or BRCA2 genetic mutations or with a family history consistent with a hereditary pattern of breast cancer. Screening for breast cancer often begins at an earlier age in these patients, and mammography is considered less sensitive in younger patients due to the prevalence of dense breast tissue. In addition, screening MRI has been suggested for patients who may or may not be at increased risk but who have breast tissue characteristics that limit the sensitivity of mammographic screening. These characteristics are dense breast tissue, breast implants, or scarring after breast-conserving therapy (BCT). BCT consists of breast-conserving surgery (BCS) followed by radiotherapy (RT).

[1] Magnetic Resonance Imaging as a Screening Tool in Patients at High Risk for Breast Cancer

There is a large body of published evidence on this question. The original policy was based on a 2003 Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessment. This Assessment concluded that for high-risk women, the evidence appears to show at least equivalent performance for MRI in terms of sensitivity in detecting breast cancer compared with mammography. In 2 published studies, however, there were only 15 cases of cancer. In both studies, MRI detected 100% of cancer cases, and mammography detected 33%. Recent abstracts show findings...
consistent with superior sensitivity of MRI and either equivalent or slightly inferior specificity.

Other studies since the 2003 TEC Assessment have corroborated the improved sensitivity of MRI compared with mammography in high-risk women. In a 2012 prospective Canadian trial of 496 women with known BRCA 1/2 mutations who were screened between 1997 and 2002, the sensitivity of MRI versus mammography was 74% and 35%, respectively (p=0.02); sensitivity improved during the period of 2003 to 2009 to 94% versus 9%, respectively (p<0.001). The authors attributed the decline in sensitivity for mammography to the fact that MRI was identifying very small cancers that are difficult to detect on mammography. Although direct benefit of MRI screening among this population has not been proven, such a benefit might be inferred by knowledge of the sensitivity and specificity of this test, along with knowledge of the benefits of mammography developed through several lines of evidence including randomized controlled trials (RCTs). A modeling study found that using MRI to screen women with BRCA 1/2 mutations conferred a substantial mortality benefit among women between 25 and 60 years of age.

This indication also incorporates several American Cancer Society (ACS) consensus recommendations for use of breast MRI. Two indications are related to use of MRI in rare genetic syndromes. In these uncommon conditions, breast cancer often occurs in premenopausal women, with risks as high as 50%. Thus, the lifetime risk threshold of 20% to 25% or greater for using MRI is thought to be met by patients with Li-Fraumeni syndrome (mutations of TP53 gene) and their first-degree relatives, and by patients with Cowden syndrome (i.e., Bannayan-Riley-Ruvalcaba syndrome; mutations of PTEN gene) and their first-degree relatives. Use of MRI in these situations also is included in National Comprehensive Cancer Network (NCCN) guidelines on genetic/familial high-risk assessment. The third ACS consensus recommendation is for use of MRI in those who received radiation therapy to the chest between the ages of 10 and 30 years. The risk of breast cancer in these patients can be quite high but depends on the age at treatment, radiation dose, and concomitant use of chemotherapy. Travis et al. (2005) estimated that the cumulative absolute risks of breast cancer for a survivor of Hodgkin lymphoma who was treated at age 25 years with a chest radiation dose of at least 40 Gy without alkylating agents are 1.4% at age 35, 11.1% at age 45, and 29.0% at age 55; more recent treatment approaches using lower doses of radiation and limited fields are associated with lower risks. NCCN guidelines related to breast cancer screening in those who received thoracic radiotherapy (RT) between the ages of 25 and 30 recommend clinical examination and mammography beginning 8 to 10 years after RT, or starting at age 40, whichever comes first, along with annual MRI.

Sensitivity of MRI for detecting breast cancer may vary with the type of lesion. Kuhl et al. (2007) reported results for the diagnosis of ductal carcinoma from a prospective series in a single, specialized referral center. Over a 5-year period, 7,319 women who were referred to this center received MRI in addition to mammography for diagnostic assessment and screening. A total of 193 women (2.6%) received a final surgical pathology diagnosis of pure ductal carcinoma in situ (DCIS). Of those, 167 (87%) had undergone both imaging tests preoperatively; 93 (56%) of these cases were diagnosed by mammography and 153 (92%) by MRI (p<0.001). Of 89 high-grade DCIS lesions, 43 (48%) were missed by mammography but detected by MRI; 2 lesions (2%) were missed by MRI but detected by mammography. MRI was significantly more sensitive than mammography in detecting high- (98% vs 52%; p<0.001) and intermediate-grade (91% vs 59%; p=0.013) DCIS, but not for detecting low-grade DCIS (80% vs 61%; p=0.13). The authors noted that their results were not representative of the typical screening setting.
They also indicated that a multi-institutional trial would be needed to further investigate the role of MRI for diagnosing DCIS in a screening population and to determine the impact of MRI screening on outcomes such as recurrence rates and mortality. It should be noted that in 2010, the Society of Breast Imaging and the American College of Radiology (ACR) jointly recommended annual screening with both MRI and mammography for high-risk women.(15)

King et al. (2013) retrospectively reviewed the clinical course of 776 women at Memorial Sloan-Kettering who were diagnosed with lobular carcinoma in situ and offered screening by annual mammography alone (n=321) or mammography plus MRI (n=455). At a median follow-up of 58 months, detection of incident cancers was similar between screening groups (13% each). The proportion of DCIS detected compared with invasive cancers detected also was similar between groups (p=0.69). In patients with lobular carcinoma in situ at increased risk for breast cancer, screening with MRI and mammography did not increase the detection of incident cancers compared with mammography alone.

In summary, MRI is more sensitive than mammography or ultrasonography in detecting malignancy. Because of the high likelihood of malignancy among women at high risk for breast cancer, the benefits of detecting cancer earlier with MRI outweigh the disadvantages of incurring more unnecessary workups and biopsies due to false positive results.

[2] MRI of the Breast as a Screening Test for Detecting Breast Cancer in Patients With Average Risk, or Who Have Breast Characteristics Limiting the Sensitivity of Mammography

Evidence for this question is based on a 2004 TEC Assessment(17) and a number of more recent articles. The sensitivity of mammography is limited in patients after breast-conserving therapy (BCT); therefore, there is the potential for improved sensitivity with MRI. However, additional prospective studies are needed to confirm this and to identify patient subsets most likely to benefit from MRI evaluation given the relatively low incidence of recurrence.

Discussion continues on the possible use of MRI to screen women with dense breasts. This debate is driven in part by the recognition that women who have dense breasts have an elevated cancer risk. In 3 nested case control studies with 1,112 matched case-control pairs, the authors estimated that the adjusted odds ratio (OR) for detecting breast cancer among women with density in 75% or more of the mammogram versus those with density in less than 10% of the mammogram was 4.7 (95% confidence interval [CI]: 1.0 to 7.4). These cancers were detected through screening or during a period of less than 12 months after a negative screening examination. In younger women (<56 years), 26% of all breast cancers were in patients with density evident in 50% or more of the mammogram.(18)

In the 2012 American College of Radiology Imaging Network (ACRIN) 6666 trial, mammography alone was compared with mammography plus ultrasound in women 25 years or older with at least heterogeneously dense breast tissue and at least 1 other breast cancer risk factor.(19) Half (54%) of women had a personal history of breast cancer. In a substudy, women who completed 3 rounds of screening and did not have contraindications or renal impairment were asked to undergo contrast-enhanced MRI within 8 weeks of the last screening mammography. Six hundred twenty-seven women consented and were eligible for the substudy, and 612 (98%) completed the needed tests; 16 cancers were found in these women. Sensitivity increased from 44% (95% CI: 20
to 70) for mammography plus ultrasound to 100% (95% CI: 79 to 100; p=0.004) when MRI was added. Specificity declined from 84% (95% CI: 81 to 87) for mammography plus ultrasound to 65% (95% CI: 61 to 69; p<0.001) for all 3 tests. Over the 3-year study period, another 9 cancers were identified between screening tests, and 2 additional cancers were identified off-study.

In a 2009 retrospective study, MRI accuracy was evaluated in patients who had dense breasts and suspected breast cancer or inconclusive evaluations at a single institution in Italy.(20) The criterion standard was histology at 6- and/or 18-month follow-up. MRI was compared with mammography or ultrasound. About half of women were found to have breast cancer. Of 238 patients, 97 (41%) had all 3 imaging tests. Sensitivity and specificity were 98% and 95%, respectively, for MRI; 73% and 45%, respectively, for mammography; and 86% and 41%, respectively, for ultrasound. In this study, MRI was used to evaluate patients suspected of having breast cancer or with equivocal results from other modalities, including clinical examination. Although specificity was relatively high and the negative predictive value (NPV) in this selected population was 98%, this study does not provide sufficient evidence to use MRI as a substitute for biopsy in these patients, as the authors themselves state.

Joint recommendations from the Society of Breast Imaging and ACR suggest that the addition of ultrasound to screening mammography “may be useful for incremental cancer detection” for women for whom dense breast is their only risk factor.(15) MRI is not mentioned in this context. However, in the ACR’s 2012 Appropriateness Criteria for breast imaging,(21) MRI for intermediate-risk women (15%-20% lifetime risk of breast cancer) was rated 7 on a scale from 1 to 9 (in which 7, 8, and 9 are considered usually appropriate); mammography was rated 9. In contrast, MRI was rated 9 for women with high lifetime risk of breast cancer (> = 20%) and 3 (usually not appropriate) for average-risk women.

For average-risk women, benefits of increased detection probably do not outweigh harms. Because the prevalence of breast cancer is extremely low in average-risk young women, screening with a test such as MRI that has inferior specificity would result in a lower positive predictive value (PPV) and many more false-positive results. Compared with mammography, there would be greater numbers of workups and biopsies with increased anxiety and morbidity if MRI screening were to be applied to young, average-risk women.

In summary, in the average-risk population or among women with breast characteristics limiting the sensitivity of mammography, the incremental effects of adjunctive MRI screening remain uncertain. There is a potential for harm in this patient population given the low overall prevalence of breast cancer and the larger numbers of false-positive results that may increase unnecessary biopsies.

**Other Detection Uses**

- Detection of a suspected occult breast primary tumor in patients with axillary nodal adenocarcinoma and negative mammography and clinical breast exam
  - Breast MRI has been advocated to help detect suspected occult primary breast cancer in patients with adenocarcinoma in the axillary lymph nodes after mammography and physical exam have failed to reveal a breast tumor. Localization of a breast primary might permit BCT instead of presumptive mastectomy.
- Detection of breast cancer in the contralateral breast of patients with breast cancer
Patients with a diagnosed breast cancer are at higher risk for a synchronous or subsequent breast cancer in the contralateral breast, and breast MRI has been suggested as a more sensitive screening test compared with mammography.

Other Detection Uses

[3] MRI of the Breast for Detection of a Suspected Occult Breast Primary Tumor With Axillary Nodal Adenocarcinoma When There is a Negative Mammography and Physical Exam

Evidence for this question is based on a 2004 TEC Assessment(17) and 1 subsequent article. The Assessment concluded that, in this small subgroup of patients, adjunctive use of breast MRI allowed a substantial portion of patients (25%-61%) to avoid the morbidity of mastectomy; risk of unnecessary biopsy was estimated to be 8%.

A 2010 meta-analysis of studies on the use of MRI in patients with mammographically occult breast cancer and an axillary metastasis evaluated 8 retrospective studies with a total of 220 patients.(22) In 7 studies, a potential primary lesion was detected in a mean of 72% of cases (range: 36-86). Pooling individual patient data yielded a sensitivity of 90% (range: 85-100) in detecting an actual malignant tumor. Specificity, however, was a pooled value of 31% (range: 22-50).

In summary, the use of MRI to guide breast-conserving surgery (BCS) rather than presumptive mastectomy appears to offer the substantial benefit of breast conservation for those patients in whom MRI detects the primary tumor.

[4] MRI to Detect Breast Cancer in the Contralateral Breast of Patients With Established Breast Cancer

In 2007, Lehman et al. reported results of the ACRIN-A6667 trial on “MRI Evaluation of the Contralateral Breast in Women with a Recent Diagnosis of Breast Cancer.”(23) They found that 30 (3%) of 969 women with a recent diagnosis of unilateral breast cancer were found to have contralateral cancer at the time of initial diagnosis using MR imaging. Contralateral lesions were not detected by mammography or physical exam. Eighteen (60%) of the 30 cancers were invasive, and 12 (40%) were DCIS. In this study, 121 patients (12.5%) had biopsies, with a positive biopsy rate of 24.8%. With 1-year follow-up, sensitivity of MRI was 91% and specificity was 88%. Results of this study in a diverse group of patients were similar to the findings of others.

Liberman et al. (2003) reported on 212 women who had negative mammograms of the asymptomatic contralateral breast and found 12 cancers (prevalence: 5%) on MRI, including 6 DCIS and 6 infiltrating carcinomas.(24) However, the PPV of these findings was only 20%, with a specificity of 76%. Lehman et al. (2005) found 4 contralateral cancers in 103 patients; in this study, 10 biopsies were done.(25)

These data align with ACR practice guidelines(26) and a consensus statement from the American Society of Breast Surgeons.(27)

In summary, although long-term outcomes of these contralateral breast cancers are not fully known, important changes in management will occur as a result of these findings, which should lead to improved outcomes. That is, in addition to the presumed benefits of early detection, simultaneous treatment of synchronous cancers can occur rather than multiple treatments on separate occasions.
Medical Policy

Diagnostic Uses

- Diagnosis of low-suspicion findings on conventional testing not indicated for immediate biopsy but referred for short-interval follow-up
- Diagnosis of a suspicious breast lesion to avoid biopsy
- Preoperative tumor mapping (e.g., detection of multicentric disease [in a separate quadrant of the breast]) in patients with clinically localized breast cancer who are considered candidates for BCS followed by radiation therapy (RT)
- Preoperative tumor mapping in patients with locally advanced breast cancer before and after completion of neoadjuvant chemotherapy
- Evaluation of response during neoadjuvant chemotherapy in patients with locally advanced breast cancer
- Diagnosis of suspected chest wall involvement in posteriorly located tumors
- Evaluation of residual tumor after lumpectomy with positive surgical margins

Patients with abnormal findings on mammography are categorized according to the level of suspicion of the findings. Those with low-suspicion findings are often recommended to undergo short-interval follow-up after 3 to 6 months instead of immediate biopsy. This follow-up may continue for a period of 2 years to demonstrate stability of benign findings or to detect progression, indicating the need for biopsy. MRI of the breast has been investigated as a technique to further characterize low-suspicion breast lesions, so that patients with MRI-negative lesions may be reassured and avoid the need for prolonged follow-up and those with MRI-positive lesions may be referred for early biopsy, possibly leading to earlier diagnosis and treatment.

Breast lesions detected by clinical exam or mammography that are considered suspicious frequently are referred for biopsy; however, only a minority of such biopsies reveal breast cancer due to the relatively low specificity of clinical and radiologic exams. MRI of the breast has been investigated as a technique to further characterize suspicious breast lesions so that patients with benign lesions may be spared a biopsy procedure. One infrequent situation (niche use), in which MRI of the breast may be helpful and improve health outcomes is in the management of patients who have a suspicious lesion that is seen on only 1 mammographic view and subsequently recommended for biopsy; however, the lesion cannot be seen in other views or on ultrasound, so percutaneous biopsy localization cannot be performed. MRI would be used, in this situation, to localize the suspicious lesion and permit biopsy and would presumably lead to earlier diagnosis of breast cancer compared with waiting until the lesion was visible on 2 mammographic views or on ultrasound. This is an infrequent occurrence, so the evidence base addressing this use is mainly anecdotal, but the rationale supporting this use is good.

Patients with localized breast cancer are considered candidates for BCS followed by RT. However, mastectomy may be considered in patients with multicentric disease. MRI has been investigated as a technique to assess the extent of tumor in the breast, specifically to detect multicentric disease as an aid to surgical planning.

Patients with locally advanced breast cancer generally are offered neoadjuvant chemotherapy in the hope of reducing tumor size to permit BCT. Evaluation of tumor size and extent using conventional techniques (i.e., mammography, clinical examination, ultrasonography) is suboptimal, and breast MRI has been proposed as a means to more accurately determine tumor size for surgical planning. MRI before chemotherapy is used to document tumor location, so that the tumor can be optimally evaluated after chemotherapy, especially if the size and degree of contrast enhancement are greatly
Medical Policy

reduced: Tumors that respond to chemotherapy get smaller and may even disappear; however, actual reduction in size is a delayed finding, and earlier changes in tumor vascularity have been observed in chemotherapy-responsive tumors. Reduction in the degree of contrast enhancement on MRI has been noted in tumors relatively early in the course of chemotherapy. This MRI finding as an early predictor of tumor response has been explored as a means to optimize choice of chemotherapeutic agent (e.g., to alter chemotherapy regimen if the tumor appears unresponsive).

Tumors located near the chest wall may invade the pectoralis major muscle or extend deeper into chest wall tissues. Typically, modified radical mastectomy removes only the fascia of the pectoralis muscle; however, tumor involvement of the muscle also would necessitate removal of the muscle (or a portion of it). In smaller tumors, it is necessary to determine how closely the tumor abuts the pectoralis muscle and whether it invades the muscle to determine whether there is an adequate margin of normal breast tissue to permit BCT. Breast MRI has been suggested as a means of determining pectoralis muscle/chest wall involvement for surgical planning and to assist in the decision of whether or not to use neoadjuvant chemotherapy.

BCT includes complete removal of the primary tumor along with a rim of normal surrounding tissue. Pathologic assessment of surgical margins is performed on excisional specimens to determine whether the tumor extends to the margins of resection. Surgical specimens are generally oriented and marked to direct re-excision if margins are shown to contain tumor; however, when tumor is not grossly visible, the extent of residual tumor within the breast can only be determined through repeat excision and pathologic assessment. MRI has been proposed to evaluate the presence and extent of residual tumor as a guide to re-excision when surgical margins are positive for tumor.


Evidence for this question is based on a 2004 TEC Assessment.(17) Available evidence suggests that adjunctive MRI may be very sensitive and specific in patients with low-suspicion findings on conventional testing and may provide a useful method to select patients for biopsy or to avoid prolonged short-interval follow-up. However, none of the available studies used prospective methods appropriate to patient populations to directly compare the sensitivity and specificity of short-interval mammographic follow-up with MRI and to determine the effects of adjunctive MRI on cancer detection rate and biopsy rate.

Well-designed prospective confirmatory studies would be necessary to permit conclusions regarding the effect this adjunctive use of breast MRI has on health outcomes.

In summary, insufficient evidence is available on the use of MRI to diagnose low-suspicion findings on conventional testing that are not indicated for immediate biopsy.

[6] MRI of the Breast to Further Characterize Suspicious Breast Lesions

Evidence on this question is based on TEC Assessments from 2000,(28) 2001,(29) and 2004.(17) Studies addressed a group of patients who have breast lesions of sufficient suspicion to warrant recommendation to undergo biopsy for diagnosis. Therefore, MRI results are assumed to have an impact on the decision whether or not to undergo definitive biopsy, considered the criterion standard.

Available evidence did not show that this use of breast MRI would improve health outcomes. Considering the relative ease of breast biopsy, the sensitivity of breast MRI
would have to be virtually 100% to confidently avoid biopsy. Although MRI performs well, it is clear that the sensitivity is not 100%. False negative results tend to occur, particularly in certain subcategories, such as DCIS, but invasive carcinomas may fail to enhance on MRI, also leading to false negative results. The potential harm to health outcomes of failing to diagnose breast cancer or at least of delaying the diagnosis of breast cancer is of significant concern. The TEC Assessment concluded that potential benefits of sparing a fraction of patients from unnecessary biopsy does not outweigh potential harms considering the current level of diagnostic performance of breast MRI.

A fairly large study by Bluemke et al. (2004) addressing this issue was released after the 2004 TEC Assessment but did not change conclusions. (30) Based on MRI results from 821 patients, sensitivity was 88.1% and specificity was 67.7%.

A systematic review published in 2011 analyzed 69 studies including 9298 women. (31) Pooled sensitivity was 90% (95% CI, 88 to 92), and pooled specificity was 75% (95% CI, 70 to 79). Pooled positive likelihood ratio of an abnormal MRI for malignancy was 3.6 (95% CI, 3.0 to 4.2), and pooled negative likelihood ratio was 0.12 (95% CI, 0.09 to 0.15). For breast cancer or high-risk lesions versus benign lesions, the area under the curve for MRI was 0.91.

In summary, MRI for evaluation of suspicious breast lesions has a relatively high sensitivity and a moderately high specificity. However, the NPV is not sufficient to preclude the need for biopsy. Therefore, the use of MRI for further characterization of suspicious lesions is not likely to change clinical management. In addition, the fairly high rate of false positives will lead to substantial numbers of unnecessary biopsies.

[7] MRI of the Breast as a Preoperative Mapping Technique to Identify Multicentric Disease in Patients With Clinically Localized Breast Cancer

Evidence for this question originally was based on a 2004 TEC Assessment. (32) Since then, a large amount of research has been published on this issue, including 2 RCTs. The 2004 TEC Assessment concluded that ipsilateral MR imaging at the time of diagnosis did not meet TEC criteria because there was insufficient evidence to permit conclusions about the effect on health outcomes of adding MRI to the standard staging workup of early stage invasive breast cancer. However, as noted in the Assessment, long-term recurrence rates after modified radical mastectomy compared with BCS plus whole breast irradiation did differ, with lower long-term recurrence rates after mastectomy. For example, the National Cancer Institute (NCI) USA trial (N=247) reported 18-year locoregional recurrence rates of 25.6% for BCT versus 9.5% for modified radical mastectomy. (33) The National Cancer Institute Italy trial (N=701) reported 20-year local recurrence rates of 2.3% for radical mastectomy and 8.8% for BCT. (34) These differences were both statistically significant with p values less than 0.01. Studies have shown that 2% to 15% of women newly diagnosed with breast cancer would have multicentric disease detected on MRI.

As a result of these findings, there was controversy regarding the use of MRI preoperatively for patients diagnosed with breast cancer. (35-43) Although these studies were not sufficient to determine the effect on health outcomes, they suggested a mechanism by which outcomes may be improved. If additional foci of malignancy are detected, then the use of MRI may lead to improved surgical decision making and a reduction in re-excisions due to foci of malignancy that were missed at the initial evaluation. (37)

Numerous observational studies have estimated the frequency of additional findings when preoperative MRI is performed and the incidence of change in clinical and
surgical management. Only a few observational studies are prospective. A prospective case series of 74 patients who had newly diagnosed invasive breast cancer and preoperative MRI was published by Barchie et al. in 2011. The incidence of mastectomy increased from 29% to 53% as a result of MRI scans. In another prospective study of 119 patients from Germany, preoperative MRI changed clinical management in 40%. Seventeen patients (14%) had mastectomies instead of BCS, and 8 (7%) had an extended excision.

A 2008 meta-analysis of 19 observational studies (total N=2610) reported quantitative estimates of incremental findings on MRI and incidences of resulting changes in clinical management. Median prevalence of additional ipsilateral cancer foci detected by preoperative MRI was 16% (interquartile range [IQR], 11-24). Conversion from BCT to mastectomy occurred in 8.1% (95% CI, 5.9 to 11.3) of patients, and change to a more extensive local surgery occurred in 11.3% (95% CI, 6.8 to 18.3). Of additional mastectomies, 1.1% may have been clinically inappropriate, as judged by lack of extensive disease on histopathology. The rate of possibly inappropriate change to a wider local excision was estimated to be 5.5%.

In 2012, Plana et al. published another systematic review and meta-analysis of 50 publications reporting on 10,811 women. In this analysis, additional disease was detected in the ipsilateral breast in 20% of women and in the contralateral breast in 6%. Of the additional lesions detected, approximately two-thirds were malignant and one-third were benign by final histopathology, for a PPV of 66%. Based on MRI findings, 8% of women were appropriately referred for mastectomy rather than BCT, and 2% were inappropriately referred for mastectomy.

Two RCTs evaluated the short-term benefit of preoperative MRI in women with localized breast cancer. A multicenter RCT from the U.K. (the COMICE trial) examined the impact of presurgical MRI on the need for additional treatment within 6 months. This study was an open, parallel-group trial conducted at 45 centers in the U.K. and enrolled 1623 women with biopsy-proven breast cancer who were scheduled for wide local excision BCT. Of 816 patients in the MRI group, 58 (7%) underwent mastectomy as a result of MRI findings and/or patient choice, compared with 10 patients (1%) in the no-MRI group that underwent mastectomy as a result of patient choice. There was no statistically significant reduction in reoperation rates in those who received MRI scans (19% in both groups; OR=0.96; 95% CI, 0.75 to 1.24; p=0.77). In the MRI group, 19 patients (2%) had a “pathologically avoidable” mastectomy, defined as a mastectomy based on MRI results showing more extensive disease, but histopathology showed only localized disease. Twelve months after surgery, there was no statistically significant difference in quality of life between the 2 groups. This RCT and 3 other comparative studies were included in a 2014 meta-analysis of individual patient data (total N=3180). Most patients (62%-93%) had localized, invasive disease and received BCT and systemic chemotherapy. After a median follow-up of 2.9 years (IQR, 1.6-4.5), there was no difference in estimated 8-year ipsilateral local (adjusted hazard ratio [HR], 0.88; 95% CI, 0.52 to 1.51; p=0.65) or distant (adjusted HR=1.18; 95% CI, 0.76 to 2.27; p=0.48) recurrence-free survival overall or in patients who received BCT only.

A second RCT, the MONET trial, was published by Peters et al. in 2011. This study randomized 463 patients with suspicious, nonpalpable breast lesions identified on mammography or ultrasound to either prebiopsy MRI or usual care. Of 207 evaluable patients in the MRI group, 11 additional suspicious lesions were identified on MRI and were occult on other imaging studies. All 11 of these additional lesions underwent biopsy, with 2 (18%) positive for malignancy. The incidence of mastectomy was similar between
the 2 groups (32% vs 34%, p=NS), as was the incidence of BCS (68% vs 66%). The incidence of re-excisions due to positive tumor margins was unexpectedly greater in the MRI group compared with the control group (34% vs 12%, p=0.008).

Both RCTs and 7 other comparative studies were included in a 2013 meta-analysis (total N=3738) that compared preoperative MRI with standard preoperative assessment in women with newly diagnosed breast cancer.(48) Results were reported separately for 6 studies that included patients with breast cancers of any type (n=3112) and 3 studies that included patients with invasive lobular histology only (n=626). The proportion of patients who had mastectomy was significantly greater in preoperative-MRI groups, both for patients with any type of breast cancer (26% vs 18%; adjusted OR=1.51; 95% CI, 1.21 to 1.89; p<0.001) and for patients with invasive lobular cancer only (43% vs 40%; adjusted OR=1.64; 95% CI, 1.04 to 2.59; p=0.034). This increase was due to increased initial mastectomy because the odds of conversion from BCS to mastectomy were not significantly different between MRI and no-MRI groups. Similarly, the odds of having re-excision surgery after initial BCS did not differ statistically between groups, both for patients with any type of breast cancer and for those with invasive lobular cancer only. Statistical measures of between-study heterogeneity were not reported. In unadjusted analysis, the odds of re-excision surgery after initial BCS were significantly greater in patients with invasive lobular cancer who did not have preoperative MRI (11% vs 18%; unadjusted OR=0.56; 95% CI, 0.33 to 0.95; p=0.031); however, because the OR was not statistically significant in adjusted analysis, this result is not considered definitive.

Fortune-Greeley et al. (2014) retrospectively examined case records of 20,332 women with invasive breast cancer in the Surveillance Epidemiology and End Results-Medicare-linked dataset.(49) Twelve percent of patients had a preoperative MRI. Among patients with invasive lobular carcinoma, but not with other histologic types, preoperative breast MRI was associated with lower odds of reoperation after initial partial mastectomy (adjusted OR=0.59; 95% CI, 0.40 to 0.86).

In summary, for patients with localized disease by standard preoperative assessment, MRI will detect additional foci of disease in the ipsilateral or contralateral breast with a frequency in the range of 10% to 20%. Detection of additional disease can lead to changes in surgical treatment, most importantly a change from BCS to mastectomy. Because of the high false positive rate, current recommendations state that a biopsy of MRI-identified lesions should be undertaken before a decision on the type of surgery is made, to reduce the number of inappropriate mastectomies. If conversions to mastectomy are appropriate based on extent of disease, then patients in the MRI group would be expected to show lower rates of local recurrence and reoperations. Two RCTs evaluated short-term outcomes of a preoperative MRI versus no MRI and did not show that short-term reoperation rates were decreased in the MRI group. Further intermediate-to long-term studies are needed to determine whether outcomes are improved by preoperative MRI scanning.

The overall evidence is uncertain on whether MRI may improve outcomes when used as part of a preoperative assessment for localized disease. If biopsies are performed on all MRI-identified lesions, and if shared patient decision making is used for altering the surgical approach, then the probability of improved outcomes is increased. Therefore, under these circumstances, MRI of the breast may be considered medically necessary for preoperative assessment of women with localized disease by conventional imaging.

[8] MRI for Preoperative Tumor Mapping in Patients With Locally Advanced Breast Cancer Before and After Completion of Neoadjuvant Chemotherapy
Evicience on this question is based on a 2004 TEC Assessment(50) and more recent publications. Compared with conventional methods of evaluating tumor size and extent (i.e., mammography, clinical exam, ultrasound), MRI of the breast provides an estimation of tumor size and extent that is at least as good as or better than that based on alternatives. Drew et al. (2001) found MRI to be 100% sensitive and specific for defining residual tumor after chemotherapy.(51) Conversely, mammography achieved 90% sensitivity and 57% specificity (mammography results considered equivocal), and clinical exam was only 50% sensitive and 86% specific. Similarly, Partridge et al. (2002) reported correlations of residual tumor size by histopathology of 0.89 with MRI and 0.60 with clinical exam.(52)

MRI results were well-correlated with results of histopathologic assessment (criterion standard) with correlation coefficients of 0.72 to 0.98; however, MRI is not intended as a replacement for histopathologic assessment.

A 2008 study of 51 patients compared MRI determination of tumor response after neoadjuvant therapy with pathologic results from BCT or mastectomy.(53) Interestingly, MRI correctly diagnosed 18 (95%) of 19 pathologic complete responses (CRs) among HER2-positive patients and 8 (50%) of 16 pathologic CRs among HER2-negative patients (p<0.005). In other words, MRI's accuracy in determining CR to neoadjuvant chemotherapy was greater among HER2-positive patients. The authors noted that false negatives were more likely when residual disease was in the form of scattered cells or small foci, which occurred more often in HER2-negative patients. MRI accuracy in detecting CR also varied by chemotherapeutic regimen used. These conclusions were based on small numbers with “suboptimal” spatial resolution and would need to be replicated in larger studies before being applied to clinical practice.

In a 2010 retrospective study of 208 patients undergoing neoadjuvant therapy, MRI indicated CR in 64 patients, but 36 (56%) of these had residual disease on pathology.(54) Conversely, MRI indicated residual disease in 144 patients, but no invasive cancer cells were found on pathology review in 14 (10%), 5 of whom had DCIS. Sensitivity of MRI to detect residual invasive cancer was 78% (95% CI, 0.71 to 0.83), and specificity was 67% (95% CI, 0.51 to 0.79). Furthermore, in 22% of all patients, tumor size on MRI differed by more than 20 mm from pathology measurement. Such discrepancies could alter treatment choice from mastectomy to BCT or more rarely, from BCT to mastectomy. MRI appeared to be most accurate in patients with triple-negative tumors, then HER2-positive tumors, and least accurate in patients with estrogen receptor (ER)-positive tumors. Patients in this study may overlap with participants in the 2011 study by Loo et al.,(55) described next.

Marinovich et al. (2013) conducted a systematic review with meta-analysis to assess the accuracy of MRI for predicting pathologic tumor size after neoadjuvant chemotherapy.(56) Literature was searched to February 2011, and 19 studies were included (total N=958). Median correlation coefficient was 0.70 (range, 0.21-0.92). In pooled analysis of 5 studies (total N=528), MRI overestimated tumor size by a small amount (mean difference, 0.1 cm; 95% CI, -0.1 to 0.3). There was no evidence of statistical heterogeneity (P=0%). By a pooled variance calculation, the authors determined that 95% of pathologic measurements fell within -4.2 cm to +4.4 cm of MRI measurements. In 2 studies that compared both MRI and ultrasound with pathologic tumor size (total N=256 and 220, respectively), performance of MRI and ultrasound was comparable.

Lobbes et al. (2013) reported a systematic review of 35 studies (total N=2359) reporting on the ability of MRI to predict tumor size after neoadjuvant chemotherapy.(57)
Literature was searched to July 1, 2012. Median correlation coefficient was 0.70 (range, 0.21-0.98). Variation in size between MRI and pathology ranged from -1.4 cm to +2.0 cm.

In summary, using breast MRI instead of conventional methods to guide surgical decisions regarding BCT versus mastectomy after neoadjuvant chemotherapy would be at least as beneficial and may lead more frequently to appropriate surgical treatment.

[9] MRI of the Breast to Evaluate Response During Neoadjuvant Chemotherapy in Patients With Locally Advanced Breast Cancer

Evidence for this question is based on a 2004 TEC Assessment,(50) subsequent studies, and an ACRIN trial. The most important use of MRI would be to reliably identify patients whose tumors are not responding to neoadjuvant chemotherapy (high NPV) to avoid added morbidity associated with continued ineffective chemotherapy. Such chemotherapy may be discontinued or changed to an alternative and potentially effective regimen. MRI is harmful if it falsely suggests a lack of response (low specificity) and leads to premature discontinuation of effective chemotherapy.

The ACRIN 6657/I-SPY trial enrolled 206 women aged 26 to 68 years with invasive breast cancer ≥3 cm or larger who were receiving anthracycline-based neoadjuvant chemotherapy, with or without a taxane.(58) MRIs were performed at 4 time points: before chemotherapy, after 1 cycle of chemotherapy, between the anthracycline-based regimen and the taxane, and after all chemotherapy but before surgery. Various MRI parameters were evaluated for their ability to predict pathologic outcome. Results were reported as the difference in predictive ability for residual cancer burden, a composite pathologic index, between MRI parameters and clinical size predictors at the same time points. MRI findings were a stronger predictor of pathologic outcomes than clinical assessment, with the largest difference being tumor volume after the first chemotherapy cycle and a difference in the area under the receiver operating characteristic curve (AUC) of 0.09; corresponding AUC values after the third and fourth MRIs were 0.07 and 0.05. Similar findings were reported for predicting pathologic CR. However, implications of these findings for treatment and outcomes are uncertain and were not addressed in this study.

The 2004 TEC Assessment reported a total of 6 studies (total N=206) that performed breast MRI during the course of chemotherapy. MRI outcomes for response to chemotherapy were based on either reduction in tumor size or reduction in contrast enhancement. Three studies(59-61) reported NPV results of 38%, 83%, and 100%, respectively; however, the 2 lower estimates were from prospective studies, and the highest estimate was from a retrospective study.

A 2005 study(62) examined whether MRI measurements of tumor volume and diameter predicted response to neoadjuvant chemotherapy and recurrence-free survival (RFS), but results did not change the conclusions reached in the 2004 Assessment. The authors found that initial (prechemotherapy) and final volumes were the strongest predictors of RFS. Early changes in MRI volume or diameter showed a trend of association (p=0.7 or 0.8) with RFS but were not statistically significant. However, of 62 enrolled patients, only 32 (52%) were included in the analysis of early response. Several other studies on the ability of MRI to gauge response to neoadjuvant chemotherapy did not include MRIs during chemotherapy, when changes in therapy might be considered.

A 2011 study of 188 women who underwent MRI scans before and during neoadjuvant chemotherapy compared the ability of MRI to detect response to treatment by breast cancer subtype.(55) The authors concluded that change in the largest diameter of enhancement on MRI was associated with tumor response among patients with triple-
negative and HER2-positive tumors but not among patients with more common ER-positive/HER2-negative tumors.

Marinovich et al. (2012) reviewed the literature on this topic to February 2011. Thirteen studies were included. Studies were heterogeneous in MRI parameters used, thresholds for identifying response, and definitions of pathologic response. The authors could not reach definitive conclusions because of limitations in study design and data reporting. This group conducted a subsequent systematic review with meta-analysis in 2013. Literature was searched to February 2011, and 44 studies (total N=2949) assessing the ability of MRI to discriminate residual breast tumor after neoadjuvant chemotherapy from pathologic complete response (pCR) were identified. Median MRI sensitivity, defined as the proportion of patients with residual tumor correctly classified by MRI, and specificity, defined as the proportion of patients with pCR classified by MRI as absence of residual tumor, were 0.92 (IQR, 0.85-0.97) and 0.60 (IQR, 0.39-0.96), respectively. Specificity increased when a relative threshold for defining negative MRI (i.e., contrast enhancement equal to or less than normal breast tissue) was used rather than an absolute threshold (complete absence of MRI enhancement) with little decrement to sensitivity. Pooled area under the receiver operating curve was 0.88, and diagnostic OR was 17.9 (95% CI, 11.5 to 28.0) (A diagnostic OR of 1 indicates no discriminatory ability; higher values indicate better test performance.) Accuracy decreased when residual DCIS was included in the definition of pCR. Statistical measures of between-study heterogeneity were not reported. A subset of studies compared MRI with other imaging modalities (mammography and ultrasound) and clinical exam; however, 95% CIs for pooled analyses were very large, rendering conclusions uncertain.

In the 2013 systematic review by Lobbes et al. just discussed, 8 studies reported measures of diagnostic accuracy. Median sensitivity, defined as the proportion of patients with pCR (responders) correctly classified by MRI, was 42% (range, 25-92). Median specificity, defined as the proportion of patients without pCR (nonresponders) correctly classified by MRI, was 89% (range, 50-97). Median (range) PPV and NPV were 64% (50%-73%) and 87% (71%-96%), respectively.

De Los Santos et al. (2013) conducted a retrospective review of 746 women who received neoadjuvant chemotherapy and preoperative MRI. Incidence of pCR was 24%. Sensitivity, specificity, PPV, and NPV of MRI for detecting pCR were 83%, 47%, 47%, and 83%, respectively. Accuracy, defined as the correct proportion of all MRI results (true positive plus true negative, divided by the number of MRI scans performed), was 80%.

In summary, there is insufficient evidence to determine whether breast MRI can reliably predict lack of response to neoadjuvant chemotherapy. There is a large amount of variability in reported performance characteristics of MRI in published studies, leaving uncertainty regarding the true accuracy of MRI for this purpose. Furthermore, evidence would need to show that any resulting change in patient management (e.g., discontinuation of chemotherapy or change to a different regimen) would improve outcomes.

[10] MRI to Diagnose Suspected Chest Wall Involvement in Posteriorly Located Tumors

Morris et al. (2000) prospectively studied 19 patients with posteriorly located breast tumors suspected to involve the pectoralis major muscle based on either mammography or clinical exam. Thirteen of these tumors were thought to be fixed to the chest wall on clinical exam, and 12 appeared to have pectoral muscle involvement on mammography. MRI results were compared with surgical and pathologic findings. The presence of abnormal enhancement within the pectoralis major muscle on MRI was
100% sensitive and 100% specific for identifying 5 tumors that actually involved the pectoralis major muscle.

Two other retrospective studies(67,68) reported on 4 cases in which MRI was able to determine involvement of the chest wall with 100% accuracy.

In summary, given the high level of diagnostic accuracy for MRI, as compared with criterion standard and conventional alternative techniques, the evidence is considered sufficient to conclude that breast MRI improves net health outcome.

[11] MRI to Evaluate Residual Tumor After Lumpectomy With Positive Surgical Margins

Evidence for this question comprises several observational studies, most of which are retrospective. Seven studies evaluated the diagnostic performance of MRI to detect residual disease after previous biopsy or lumpectomy.(69-75) Histopathologic examination on re-excision was used as the criterion standard. Most of these studies, including 1 prospective study, reported poor sensitivity and specificity of MRI for detection of residual disease. Two studies that reported more favorable results(70,74) had methodologic issues that limited the influence of reported results. Three of these studies(69,73,75) were conducted at the same institution and accrued patients during similar time periods, so overlap of reported patients may exist.

Lee et al. (2004) prospectively studied 80 patients eligible for BCT who had close or positive margins on lumpectomy and were scheduled for re-excision lumpectomy.(72) In this study, MRI was 61% sensitive and 70% specific for detection of residual tumor. The finding of extensive tumor on MRI led to mastectomy in 6 patients (7.5%), but it is difficult to determine from the publication what proportion of these cases had false positive MRI results. Bedrosian et al. (2003) retrospectively studied 70 patients before re-excision and found that MRI had 57% sensitivity and 60% specificity.(69) MRI prompted wider than initially planned surgical excision in 11 cases, but 10 of these (91%) turned out to be false positive MRI results. Kawashima et al. (2001) studied 50 patients and reported 66% sensitivity and 81% specificity.(71) Orel et al. (1997) included 47 patients with questionable or positive margins after biopsy and found that MRI had 54% sensitivity and 62% specificity for residual tumor at the biopsy site.(73) Similarly, sensitivity and specificity were low for identification of residual tumor anywhere in the breast (64% and 58%, respectively). Weinstein et al. (2001) reviewed 14 cases of invasive lobular carcinoma that had prior excisional biopsy and found that MRI had 57% sensitivity and 0% specificity for identifying residual disease.(75)

Frei et al. (2000) retrospectively studied 68 patients with positive margins and examined the relationship between when MRI was performed after initial surgery and diagnostic performance of MRI for residual disease.(70) However, this study excluded 3 patients with technically inadequate MRI studies and has discrepancies in reported results in the publication. Sensitivity of MRI ranged from 89% to 95%, with slight improvements noted with longer time intervals after initial surgery. Specificity was initially 52% for MRI performed at least 7 days after lumpectomy; when analysis was restricted to MRI conducted at least 28 days after lumpectomy, the specificity of MRI increased to 75%. Soderstrom et al. (1997) retrospectively examined 19 patients with various indications for MRI, including 11 patients with close or positive margins after surgery, and found MRI was 100% sensitive and 71% specific for identification of residual tumor.(74) The authors noted that MRI overestimated the extent of tumor in 1 patient who was counted as a true positive.
In summary, available evidence is not sufficient to permit conclusions about whether MRI improves net health outcomes when used to identify the presence and/or extent of residual disease after lumpectomy and before re-excision.

**Other Suggested Uses for MRI of the Breast**

Some have suggested that MRI may be useful before accelerated partial-breast irradiation (APBI), to identify patients with multicentric tumors that would not fall within the radiotherapy field. However, neither the equivalence of APBI to whole-breast irradiation nor the utility of MRI in this context have been demonstrated. In a consensus statement on APBI, a Task Group from the American Society for Radiation Oncology “agreed that there were insufficient data to justify recommendation of routine breast MRI for patients selected for APBI.”

**Ongoing Clinical Trials**

A search of online site ClinicalTrials.gov for “breast cancer MRI” or “breast carcinoma MRI” yielded 124 studies currently recruiting participants. Examples include:

- One study (NCT01716247) with a target enrollment of 1000 is comparing MRI with contrast-enhanced mammography among women with an increased risk of breast cancer.
- Another study (NCT01300585) of 100 patients is using MRI in an effort to identify how breast glands are attached to the overlying skin. This information may be useful to identify candidates for alveolar- or nipple-sparing surgery versus conventional mastectomy.
- A randomized trial (NCT01805076) is comparing surgical and recurrence outcomes in patients with stage 1 or 2 breast cancer who undergo mammography and ultrasound or mammography, ultrasound, and breast MRI to determine surgical procedure (BCS or mastectomy). Targeted enrollment is 536 women.

**Summary**

**Magnetic resonance imaging as a screening tool in patients at high risk for breast cancer:** Magnetic resonance imaging (MRI) is more sensitive than mammography or ultrasonography in detecting malignancy. Because of the high likelihood of malignancy among women at high risk for breast cancer, the benefits of detecting cancer earlier with MRI outweigh the disadvantages of incurring more unnecessary workups and biopsies due to false positive results.

**MRI of the breast as a screening test for detecting breast cancer in patients with average risk, or who have breast characteristics limiting the sensitivity of mammography:** In the average-risk population or among women with breast characteristics limiting the sensitivity of mammography, the incremental effects of adjunctive MRI screening remain uncertain. There is a potential for harm in this patient population given the low overall prevalence of breast cancer and the larger numbers of false positive results that may increase unnecessary biopsies.

**MRI of the breast for detection of a suspected occult breast primary tumor with axillary nodal adenocarcinoma when there is a negative mammography and physical exam:** The use of MRI to guide breast-conserving surgery (BCS) rather than presumptive mastectomy appears to offer the substantial benefit of breast conservation for those patients in whom MRI detects the primary tumor.
MRI to detect breast cancer in the contralateral breast of patients with established breast cancer: Although long-term outcomes of these contralateral breast cancers are not fully known, important changes in management will occur as a result of these findings, which should lead to improved outcomes. That is, in addition to the presumed benefits of early detection, simultaneous treatment of synchronous cancers can occur rather than multiple treatments on separate occasions.

MRI of the breast for the diagnosis of low-suspicion findings on conventional testing that are not indicated for immediate biopsy: Insufficient evidence is available on the use of MRI to diagnose low-suspicion findings on conventional testing not indicated for immediate biopsy.

MRI of the breast to further characterize suspicious breast lesions: MRI for evaluation of suspicious breast lesions has a relatively high sensitivity and a moderately high specificity. However, the negative predictive value is not sufficient to preclude the need for biopsy. Therefore, the use of MRI for further characterization of suspicious lesions is not likely to change clinical management. In addition, the fairly high rate of false positives will lead to substantial numbers of unnecessary biopsies.

MRI of the breast as a preoperative mapping technique to identify multicentric disease in patients with clinically localized breast cancer: For patients with localized disease by standard preoperative assessment, MRI will detect additional foci of disease in the ipsilateral or contralateral breast with a frequency in the range of 10% to 20%. Detection of additional disease can lead to changes in surgical treatment, most importantly a change from BCS to mastectomy. Because of the high false positive rate, current recommendations state that a biopsy of MRI-identified lesions should be undertaken before a decision on the type of surgery is made, to reduce the number of inappropriate mastectomies. If conversions to mastectomy are appropriate based on extent of disease, then patients in the MRI group would be expected to show lower rates of local recurrence and reoperations. Two randomized controlled trials evaluated short-term outcomes of a preoperative MRI versus no MRI and did not show that short-term reoperation rates were decreased in the MRI group. Further intermediate- to long-term studies are needed to determine whether outcomes are improved by preoperative MRI scanning.

The overall evidence is uncertain on whether MRI may improve outcomes when used as part of a preoperative assessment for localized disease. If biopsies are performed on all MRI-identified lesions, and if shared patient decision making is used for altering the surgical approach, then the probability of improved outcomes is increased. Therefore, under these circumstances, MRI of the breast may be considered medically necessary for preoperative assessment of women with localized disease by conventional imaging.

MRI for preoperative tumor mapping in patients with locally advanced breast cancer before and after completion of neoadjuvant chemotherapy: Using breast MRI instead of conventional methods to guide surgical decisions regarding BCT versus mastectomy after neoadjuvant chemotherapy would be at least as beneficial and may lead more frequently to appropriate surgical treatment.

MRI of the breast to evaluate response during neoadjuvant chemotherapy in patients with locally advanced breast cancer: There is insufficient evidence to determine whether breast MRI can reliably predict lack of response to neoadjuvant chemotherapy. Furthermore, evidence would need to show that any resulting change in patient management (e.g., discontinuation of chemotherapy or change to a different regimen) would improve outcomes.
MRI to diagnose suspected chest wall involvement in posteriorly located tumors: Given the high level of diagnostic accuracy for MRI, as compared with criterion standard and conventional alternative techniques, the evidence is considered sufficient to conclude that breast MRI improves net health outcome.

MRI to evaluate residual tumor after lumpectomy with positive surgical margins: Available evidence is not sufficient to permit conclusions about whether MRI improves net health outcomes when used to identify the presence and/or extent of residual disease after lumpectomy and before re-excision.

Guidelines and Other Recommendations

ACS

The ACS guide on early detection of breast cancer, last revised January 31, 2014, recommends the following regarding use of MRI screening of the breast(77):

- Women at high risk (greater than 20% lifetime risk according to risk assessment tools that are based mainly on family history) should receive annual MRI and mammogram.
- For women at moderately increased risk (15%-20% lifetime risk), evidence is insufficient to make a recommendation for or against annual MRI screening. If MRI is used, it should be in addition to, not instead of, a screening mammogram.
- Annual MRI screening is not recommended for women whose lifetime risk of breast cancer is less than 15%.

ACR

ACR has appropriateness criteria for breast imaging, which were updated in November 2013 and cover 5 clinical conditions.(21) For each indication, imaging modalities are assigned a rating from 1 to 9: 1, 2, and 3 are usually not appropriate; 4, 5, and 6 may be appropriate; 7, 8, and 9 are usually appropriate. The relative radiation level also is reported, which is not relevant for MRI.

**Table 1. American College of Radiology Appropriateness Criteria for Breast Cancer Screening**

<table>
<thead>
<tr>
<th>Specific Indications</th>
<th>MRI Rating</th>
<th>Other Ratings ≥ MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk women: women with a BRCA gene mutation and their untested first-degree relatives, women with a history of chest irradiation between the ages of 10 and 30 years, women with 20% or greater lifetime risk of breast cancer</td>
<td>9 with and without contrast</td>
<td>Mammography [9]</td>
</tr>
<tr>
<td>Intermediate-risk women: women with personal history of breast cancer, lobular neoplasia, atypical ductal hyperplasia, or 15%-20% lifetime risk of breast cancer</td>
<td>7 with and without contrast</td>
<td>Mammography [9]</td>
</tr>
<tr>
<td>Average-risk women: women with &lt;15% lifetime risk of breast cancer, breasts not dense</td>
<td>3 with and without contrast</td>
<td>Mammography [9]</td>
</tr>
</tbody>
</table>

*MRI (magnetic resonance imaging) with contrast (and in some cases without) was rated a 1 or 2 for all indications for initial diagnostic workup of breast microcalcifications, nonpalpable mammographic findings (except microcalcifications), palpable breast masses, and stage 1 breast carcinoma.
ACR also released a practice guideline on breast MRI in 2008.(26) Among the indications listed are the following:

- For patients with a new breast malignancy: MRI screening of the contralateral breast in patients with a new breast malignancy may be used as a diagnostic tool to identify more completely the extent of disease in patients with a recent breast cancer diagnosis.
- Evaluating extent of disease: To determine the extent of disease and the presence of multifocality and multicentricity in patients with invasive carcinoma and DCIS; to evaluate whether there is invasion deep to fascia; to assess potentially positive margins postlumpectomy; and to determine treatment response and the extent of residual disease before, during, and/or after neoadjuvant chemotherapy but before surgical treatment.
- Additional evaluation: To search for recurrence of cancer among women with a prior history of breast cancer and suspicion of recurrence, when clinical, mammographic, and/or sonographic findings are inconclusive; to search for the primary tumor when patients present with metastatic disease and/or axillary adenopathy and there are no mammographic or physical findings of primary breast carcinoma; to localize/confirm lesion when other imaging is inconclusive and biopsy is not feasible (e.g., possible distortion on only 1 mammographic view); to evaluate suspected cancer recurrence in patients with tissue transfer flaps (rectus, latissimus dorsi, gluteal) after breast reconstruction; to guide interventional procedures such as vacuum-assisted biopsy and preoperative wire localization for lesions that are occult on mammography or sonography.

In 2010, the Society of Breast Imaging and ACR jointly recommended that high-risk women be screened annually with both MRI and mammography.(15)

American Society of Clinical Oncology

ASCO guidelines for follow-up and management after primary treatment of breast cancer were published in 2006.(78) In 2013, the guidelines were updated with systematic review of the literature through March 2012, and no revisions were made.(79) The guidelines recommended against the use of breast MRI “for routine follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.”(79) Furthermore, “The decision to use breast MRI in high-risk patients should be made on an individual basis depending on the complexity of the clinical scenario.”(78)

International Late Effects of Childhood Cancer Guideline Harmonization Group

In 2013, an International Guideline Harmonization Group from 9 countries published evidence-based recommendations for breast cancer surveillance in female survivors of childhood, adolescent, and young adult cancer who received chest irradiation before age 30 years and have no genetic predisposition to breast cancer.(80) The authors found concordance among previous guidelines to initiate annual breast MRI exams beginning at age 25 or 8 years after radiation. Based on systematic review of the literature to August 2011 and expert consensus, the authors recommended mammography, breast MRI, or both for surveillance. (Strong recommendation based on high-quality evidence with a low degree of uncertainty.) The authors acknowledged that “no prospective studies have assessed the use of MRI screening in this population.” The recommendation is therefore based on extrapolation of evidence from patients with hereditary risk for breast cancer.
NCCN guidelines on breast cancer[81] and breast cancer screening[13] were most recently updated in 2014 and 2013, respectively. These guidelines list the following indications for breast MRI:

- **Screening**
  - To consider annual MRI screening as an adjunct to mammography beginning at age 30 for women with lifetime risk of breast cancer >20% based on models depending primarily on family history (e.g., Claus, BRCAPRO, BOADICEA, Tyrer-Cuzick).
  - Annual MRI screening is recommended as an adjunct to mammogram and clinical breast exam for women who had prior thoracic radiotherapy between the ages of 10 and 30 years, beginning 8 to 10 years following radiation therapy, or starting at age 40, whichever comes first.
  - For women with a pedigree suggestive of or known genetic predisposition, annual mammogram and MRI are recommended beginning at age 25 or based on the earliest age of onset in the family.
  - Annual MRI screening also is recommended for those with Li-Fraumeni syndrome and their first-degree relatives, as well as those with Cowden and Bannayan-Riley-Ruvalcaba syndromes and their first degree relatives.
  - There is insufficient evidence to recommend for or against MRI screening among women with a lifetime risk of 15% to 20%; lobular carcinoma in situ or atypical lobular hyperplasia; atypical ductal hyperplasia; heterogeneously or extremely dense breast on mammography; or women with a personal history of breast cancer, including DCIS.
  - NCCN guidelines recommend against MRI screening of women with less than a 15% lifetime risk of breast cancer.

- **Diagnosis**
  - For women under 30 with nipple discharge and no palpable mass, as well as a BIRADS rating of 1-3 on mammography +/- ultrasound, MRI or ductogram from a single duct are optional.
  - To consider MRI for women with skin changes with a suspicion of inflammatory breast cancer or Paget’s disease with BIRADS 1-3 on mammogram ± ultrasound and a benign punch biopsy of the skin or nipple.

- **Pretreatment evaluation**
  - To define extent of cancer or presence of multifocal or multicentric cancer in the ipsilateral breast, or as screening of the contralateral breast cancer at time of initial diagnosis (category 2B). There are no high-level data demonstrating that use of MRI to guide choice of local therapy improves outcomes (local recurrence or survival).
  - May be useful to detect additional disease in women with mammographically dense breasts, but “available data do not show differential detection rates by any subset by breast pattern (breast density) or disease type (e.g., DCIS, invasive ductal cancer, invasive lobular cancer).”
  - May be useful to identify primary cancer in women with axillary nodal adenocarcinoma breast and negative mammography, ultrasound, or clinical breast exam.

- **Treatment**
  - Before and after neoadjuvant therapy to evaluate extent of disease, response to treatment, and potential for breast-conserving therapy.

- **Surveillance**
Medical Policy

- Utility of follow-up screening in women with prior breast cancer is undefined. Generally, should only be considered for women with 20% lifetime risk of breast cancer.

False-positive findings on breast MRI are common. Surgical decisions should not be based solely on MRI findings. Additional tissue sampling of areas of concern identified by breast MRI is recommended.

- There are other indications for which breast MRI is considered optional (e.g., staging work-up for invasive cancer).

**U.S. Preventive Services Task Force**

In its recommendation statement for breast cancer screening, updated in December 2009, USPSTF concluded that “current evidence is insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as screening modalities for breast cancer.” (Recommendation Grade I: Evidence is currently insufficient to assess the balance of benefits and harms.) (82)

**References**


17. Blue Cross Blue Shield Association. Technology Evaluation Center (TEC) Assessment: Breast magnetic resonance imaging (MRI) for detection or diagnosis of primary or recurrent breast cancer. 2004; Volume 19, Tab 1.


50. Blue Cross Blue Shield Association, Technology Evaluation Center (TEC) Assessment: Breast MRI for management of patients with locally advanced breast cancer who are being referred for neoadjuvant chemotherapy. 2004; Volume19, Tab 7.


**Documentation Required for Clinical Review**

- History and physical and/or consultation notes including:
  - Age
  - Age at time of first live birth, if applicable
  - Age at time of first menstrual period
  - History and number of breast biopsies and pathology results
  - History of radiation therapy and at what age, if applicable
  - Reason for MRI
  - Relatives with a history of breast cancer
- Genetic testing reports (e.g., BRCA1 or BRCA2 testing), if applicable
- Pathology report(s), if applicable
- Radiology report(s) (e.g., mammogram, breast ultrasound)

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

**MN/IE**

The following service/procedure may be considered medically necessary in certain instances and investigational in others. Services may be medically necessary when policy criteria are met. Services are considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>CPT®</td>
<td>77058</td>
<td>Magnetic resonance imaging, breast, without and/or with contrast material(s); unilateral</td>
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<tr>
<td></td>
<td>77059</td>
<td>Magnetic resonance imaging, breast, without and/or with contrast material(s); bilateral</td>
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<td>Code</td>
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<td>C8903</td>
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<td>C8908</td>
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</tbody>
</table>

**HCPC**

| Procedure  | None |

**ICD-9**

| Procedure  | BH30Y0Z | Magnetic Resonance Imaging (MRI) of Right Breast using Other Contrast, Unenhanced and Enhanced |
| BH30YZZ    | BH31Y0Z | Magnetic Resonance Imaging (MRI) of Left Breast using Other Contrast, Unenhanced and Enhanced |
| BH31YZZ    | BH32Y0Z | Magnetic Resonance Imaging (MRI) of Bilateral Breasts using Other Contrast, Unenhanced and Enhanced |
| BH32YZZ    | BH32Y0Z | Magnetic Resonance Imaging (MRI) of Bilateral Breasts using Other Contrast, Unenhanced and Enhanced |

**ICD-10**

| Diagnosis  | C50.011 - C50.929 | Malignant neoplasm of female/male breast, code range |
| Diagnosis  | C79.81            | Secondary malignant neoplasm of breast                |
| Diagnosis  | D05.90 – D05.92   | Unspecified type of carcinoma in situ of breast, code range |

**ICD-10**

| Diagnosis  | 174.0 - 174.9 | Malignant neoplasm of female breast |
| Diagnosis  | 175.0 - 175.9 | Malignant neoplasm of male breast   |
| Diagnosis  | 198.81        | Secondary malignant neoplasm of breast |
| Diagnosis  | 233.0         | Carcinoma in situ of breast         |
| Diagnosis  | 611.72        | Lump or mass in breast              |
| Diagnosis  | V10.3         | Personal history of malignant neoplasm of breast |
| Diagnosis  | V16.3         | Family history of malignant neoplasm of breast |
| Diagnosis  | V84.01        | Genetic susceptibility to malignant neoplasm of breast |

**ICD-10**

| Diagnosis  | 174.0 - 174.9 | Malignant neoplasm of female breast |
| Diagnosis  | 175.0 - 175.9 | Malignant neoplasm of male breast   |
| Diagnosis  | 198.81        | Secondary malignant neoplasm of breast |
| Diagnosis  | 233.0         | Carcinoma in situ of breast         |
| Diagnosis  | 611.72        | Lump or mass in breast              |
| Diagnosis  | V10.3         | Personal history of malignant neoplasm of breast |
| Diagnosis  | V16.3         | Family history of malignant neoplasm of breast |
| Diagnosis  | V84.01        | Genetic susceptibility to malignant neoplasm of breast |

For dates of service on or after 10/01/2015
### Medical Policy

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<td>N63</td>
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<td>Z85.3</td>
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### Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>10/12/1994</td>
<td>New Policy Adoption</td>
<td>Medical Policy Committee</td>
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<tr>
<td>4/28/1998</td>
<td>No change</td>
<td>External Review</td>
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<tr>
<td>6/13/2001</td>
<td>BCBSA Medical Policy adoption</td>
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<tr>
<td>2/13/2002</td>
<td>Adopted BCBSA TEC for differential diagnosis of a breast lesion to avoid biopsy</td>
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<td>6/1/2003</td>
<td>Policy Review</td>
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<td>6/1/2005</td>
<td>Administrative Review</td>
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<td>6/28/2007</td>
<td>Policy Revision</td>
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<td>7/2/2007</td>
<td>Policy published.</td>
<td>Administrative Review</td>
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<td>5/16/2008</td>
<td>BCBSA Medical Policy Adoption. Revised ACS guidelines and lifetime risk figure</td>
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<td>9/25/2009</td>
<td>Policy Revision Criteria Revised</td>
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<td>• Combined Policies MRI of the Breast and Computer-Aided Detection with MRI of the Breast</td>
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<td>9/27/2013</td>
<td>Policy revision with position</td>
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change

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<tr>
<th>Date</th>
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<th>Responsible Party</th>
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<tr>
<td>8/29/2014</td>
<td>Policy title change from MRI of the Breast</td>
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<td>Policy revision with position change</td>
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</table>

Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California / Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a Split Evaluation, where a treatment, procedure or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

**Prior Authorization Requirements**

This service (or procedure) is considered **medically necessary** in certain instances and **investigational** in others (refer to policy for details).

For instances when the indication is **medically necessary**, clinical evidence is required to determine **medical necessity**.

For instances when the indication is **investigational**, you may submit additional information to the Prior Authorization Department.

Within five days before the actual date of service, the Provider MUST confirm with Blue Shield that the member’s health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member’s eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal www.blueshieldca.com/provider.

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.