

6.01.29	Magnetic Resonance Imaging for Detection and Diagnosis of Breast Cancer		
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Section:	6.0 Radiology	Page:	Page 1 of 32

Policy Statement

Note: All policy statements below refer to performing magnetic resonance imaging (MRI) of the breast with contrast and a breast coil. MRI of the breast without a breast coil, regardless of the clinical indication, is considered **investigational**. See additional comments in Policy Guidelines about the breast imaging team and the need for breast MRI centers to perform MRI-guided biopsy and localization.

MRI for Screening Uses

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

- Lobular carcinoma in situ
- A known *BRCA1* or *BRCA2* variant
- High risk of *BRCA1* or *BRCA2* variant due to a known presence of the variant in relatives
- Another gene variant associated with high risk, e.g., *TP53* (Li-Fraumeni syndrome), *PTEN* (Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome), *CDH1*, and *STK11*, *ATM*, *CHEK2*, and *PALB2* or who have a first-degree relative with one of these syndromes
- High risk (lifetime risk about greater than or equal to 20% or 5-year risk of greater than or equal to 3%) of developing breast cancer as identified by models that are largely defined by family history
- Received radiotherapy to the chest between 10 and 30 years of age

*(National Cancer Care Network [NCCN], www.nccn.org, clinical practice guidelines in oncology: genetic/familial high-risk assessment: breast and ovarian. v2.2017)

MRI for Detection Uses

MRI of the breast may be considered **medically necessary** for detection of a suspected occult breast primary tumor in patients with axillary nodal adenocarcinoma (i.e., negative mammography and physical exam).

MRI of the breast may be considered **medically necessary** in patients with a new diagnosis of breast cancer to evaluate the contralateral breast when clinical and mammographic findings are normal.

MRI for Treatment-Related Uses

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

- 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)
- Presurgical planning in patients with locally advanced breast cancer (before and after completion of neoadjuvant chemotherapy) to permit tumor localization and characterization
- To determine the presence of pectoralis major muscle/chest wall invasion in patients with posteriorly located tumors
- To evaluate a documented abnormality of the breast before obtaining an MRI-guided biopsy when there is documentation that other methods, such as palpation or ultrasound, are not able to localize the lesion for biopsy

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

- As a screening technique in average-risk patients

- As a screening technique for the detection of breast cancer when the sensitivity of mammography (i.e., mammography using low-dose x-rays for imaging) is limited (i.e., dense breasts, breast implants, scarring after treatment for breast cancer)
- For the diagnosis of low-suspicion findings on conventional testing not indicated for immediate biopsy and referred for short-interval follow-up
- For the diagnosis of a suspicious breast lesion in order to avoid biopsy
- To determine response during neoadjuvant chemotherapy in patients with locally advanced breast cancer
- For the evaluation of residual tumor in patients with positive margins after initial lumpectomy or breast conservation surgery

Policy Guidelines

High-Risk Considerations

There is no standardized method for determining a woman's risk of breast cancer that incorporates all possible risk factors. There are validated risk prediction models, but they are based primarily on family history. Some known risk factors confer a high risk by themselves.

A number of other factors may increase the risk of breast cancer but do not by themselves indicate high risk. It is possible that combinations of these factors may be indicative of high risk, but it is not possible to give quantitative estimates of risk. As a result, it may be necessary to individualize the estimate of risk, whereby one would need to take into account the numerous risk factors. A number of risk factors, not individually indicating high risk, are included in the National Cancer Institute Breast Cancer Risk Assessment Tool (also called the Gail model). Risk factors in the model can be accessed online (<http://www.cancer.gov/bcrisktool/Default.aspx>).

National Comprehensive Cancer Network guidelines state there is insufficient evidence for any recommendations for breast magnetic resonance imaging (MRI) for patients with the following variants: *BARD1*, *FANCC*, *MRE11A*, *MUTYH*, *NF1*, *NBN*, *RAD50*, *SMARCA*, or *XRCC2*. Moreover, there are conflicting data on risks associated with a *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM* gene deletion (NCCN clinical practice guidelines in oncology: genetic/familial high-risk assessment: breast and ovarian. v.2.2017.

[https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf]).

General

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

Considerations for Performing MRI

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 MRI center also should have the ability to perform MRI-guided biopsy and/or wire localization of findings detected by MRI.

Considerations for Preoperative MRI

Preoperative MRI in patients with localized disease results in higher rates of mastectomy and lower rates of breast-conserving therapy. 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/or Ovarian Cancer Syndrome [BRCA1 or BRCA2]).

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 Tool⁷⁸ available at:

*<http://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

The Breast Imaging Reporting and Data System (BI-RADS) Classification

The Breast Imaging Reporting and Data System (BI-RADS) provides a standardized classification system for mammograms⁷⁹:

BI-RADS Category	Assessment	Clinical Management Recommendation(s)
0	Incomplete	Additional imaging evaluation needed before final assessment
1	Negative	No lesion found (routine follow-up)
2	Benign finding	No malignant features; e.g. cyst (routine follow-up for age, clinical management)
3	Probably benign finding	Malignancy is highly unlikely, e.g. fibroadenoma (initial short interval follow-up)
4	Suspicious abnormality	Low to moderate probability of cancer, biopsy should be considered
5	Highly suggestive of malignancy	Almost certainly cancer, appropriate action should be taken
6	Known cancer	Biopsy proven malignancy, prior to institution of therapy

Coding

The following specific CPT codes describe magnetic resonance imaging of the breast:

- **77058:** Magnetic resonance imaging, breast, without and/or with contrast material(s); unilateral
- **77059:** Magnetic resonance imaging, breast, without and/or with contrast material(s); bilateral

Description

Magnetic resonance imaging (MRI) of the breast is performed using scanners and intravenous imaging contrast agents in combination with specialized breast coils. This evidence review only addresses the use of breast MRI for clinical indications related to detection or diagnosis of breast cancer.

Note: This policy only addresses the use of breast MRI for clinical indications related to detection, and 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 the Integrity of Silicone-Gel-Filled Breast Implants.

Related Policies

- Computer-Aided Evaluation of Malignancy with Magnetic Resonance Imaging of the Breast
- Digital Breast Tomosynthesis
- Magnetic Resonance Imaging to Monitor the Integrity of Silicone Gel-Filled Breast Implants

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)] prohibits 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.

Regulatory Status

MRI of the breast can be performed using commercially available magnetic resonance scanners and intravenous magnetic resonance contrast agents. Specialized breast coils such as the Access Breast Coil 4/SMS (Confirma, Kirkland, WA) and magnetic resonance-compatible equipment for performing biopsy have been developed and cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process. The Food and Drug Administration determined that these devices are substantially equivalent to predicate devices for use "in conjunction with a magnetic resonance imager (MRI) to produce diagnostic and interventional images of the breast, chest wall and axillary tissues that can be interpreted by a trained physician."¹

Rationale

Background

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of the breast can be used to screen, detect, and/or diagnosis of breast cancer. MRI can be used as a replacement for mammography screening, or it can be used as an additional imaging test alone, or it can be used in combination with other imaging modalities. Each of these potential uses is described below.

Screening Uses

Screening uses include screening for breast cancer in patients who are at high genetic risk for breast cancer; screening also benefits patients who have breast characteristics that limit the sensitivity of a mammography.

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 women with known *BRCA1* or *BRCA2* genetic variants 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 a mammographic screening (these characteristics are dense breast tissue, breast implants, or scarring after breast-conserving therapy [BCT]). BCT consists of breast-conserving surgery followed by radiotherapy.

Detection Uses

The following are examples of how to detect 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.

The following are examples of how to detect 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.
- Diagnosis of low-suspicion findings on conventional testing not indicated for immediate biopsy but referred for short-interval follow-up

The following are examples of how to detect breast cancer in the case of:

- Low-suspicion findings on conventional testing not indicated for immediate biopsy but referred for short-interval follow-up
- Further characterization of suspicious breast lesion to avoid biopsy

Treatment-Related Uses

The following are potential treatment-related uses of breast MRI:

- 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 breast-conserving surgery followed by radiotherapy
- 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. Patients 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 2 years to demonstrate the stability of benign findings or to detect progression; progression would indicate 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 can only be seen on 1 mammographic view (ie, the lesion cannot be seen in other views or on an ultrasound). Patients who fall under this category have a lesion that is not palpable, and therefore, percutaneous biopsy localization cannot be performed. Instead, MRI would be used to localize the suspicious lesion and permit biopsy (this technique would presumably lead to earlier diagnosis of breast cancer as opposed to waiting until the lesion was visible on 2 mammographic views or on ultrasound). The previously described scenario is an infrequent occurrence, so the evidence base addressing this use is mainly anecdotal, but the clinical rationale supporting this use is good.

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

Patients with locally advanced breast cancer are usually offered neoadjuvant chemotherapy to reduce tumor size and 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 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. A decline in 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 the 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 would also 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 whether 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 oriented and marked to direct re-excision if margins are shown to contain tumor; however, when the 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 the residual tumor as a guide to re-excision when surgical margins are positive for tumor.

Literature Review

Assessment of a diagnostic technology typically focuses on 3 categories of evidence: (1) technical reliability (test-retest reliability or interrater reliability); (2) clinical validity (sensitivity, specificity, and positive and negative predictive value) in relevant populations of patients; and (3) clinical utility (ie, demonstration that the diagnostic information can be used to improve health outcomes). The following is a summary of the literature to date.

Screening Uses

Clinical Context and Test Purpose

The question addressed in this portion of the evidence review is whether use of magnetic resonance imaging (MRI) as an adjunct to screen for breast cancer improves the net health outcome compared with standard mammographic techniques. Specifically, does the use of MRI improve diagnostic accuracy compared with standard screening mammography methods, and is this degree of increased accuracy likely to improve health outcomes via earlier diagnosis and treatment?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is asymptomatic individuals being screened for breast cancer. Evaluation is stratified by those at high risk of breast cancer, those at average risk of breast cancer, and those with characteristics limiting the accuracy of the mammography (e.g., dense breasts).

Interventions

The intervention of interest is MRI as an adjunct to screening with mammography.

Comparators

The comparator of interest is mammography alone.

Outcomes

The outcomes of interest for diagnostic accuracy include test accuracy and test validity (i.e., sensitivity, specificity). Primary outcomes of interest for clinical utility are overall mortality and breast cancer–specific mortality. Another outcome of interest for clinical utility is resource utilization (e.g., need for additional testing or procedures).

Timing

MRI would be performed as an adjunct to routine screening; timing can be guided by national guidelines on breast cancer screening.

Setting

The test would be performed in an outpatient imaging setting.

Technical Reliability

The technical reliability of MRI devices is well-accepted.

Clinical Validity and Clinical Utility

Screening Individuals at High Risk of Breast Cancer

The original evidence review was based on a 2003 Blue Cross Blue Shield Association Technology Evaluation Center (TEC).² This Assessment concluded that for high-risk women, the evidence appeared to show equivalent or better 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.^{3,4} In both studies, MRI detected 100% of cancer cases; mammography detected 33%. Further, abstracts in both studies revealed 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.⁵⁻¹⁰ In addition, Chiarelli et al (2014) found higher diagnostic accuracy for detecting breast cancer in high-risk women with MRI plus mammography compared with mammography alone.¹¹

To evaluate sensitivity and specificity of screening MRI in women ages 50 years or older with high breast cancer risk, Phi et al (2015) conducted an individual patient data meta-analysis of 6 trials in women with *BRCA1* and *BRCA2* variants (N=1951; 22% >age 50 years).¹² Literature was searched in April 2013. Screening examinations were obtained annually in all 6 trials. Sensitivity of mammography, MRI, and the combination of the two appeared similar in women regardless of age. However, specificity of all 3 imaging modalities was statistically superior in women age 50 years or older compared with women younger than 50 years; specificity of MRI in older vs younger women was 89% (95% confidence interval [CI], 84% to 92%) vs 84% (95% CI, 78% to 88%), respectively. Sensitivity and specificity of combination MRI plus mammography were similar to those of MRI alone in both age groups.

Sensitivity of MRI for detecting breast cancer may vary by type of lesion. Kuhl et al (2007) reported on results for the diagnosis of ductal carcinoma from a prospective series in a single, specialized referral center.¹³ Over a 5-year period, 7319 women who were referred to this center received MRI in addition to mammography for diagnostic assessment and screening. A total of 193 (2.6%) women 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 (2%) lesions 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 important 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 jointly recommended annual screening with both MRI and mammography for high risk women.¹⁴

King et al (2013) et al retrospectively reviewed the clinical course of 776 women at a single institution who were diagnosed with lobular carcinoma in situ and offered screening by annual mammography alone ($n=321$) or mammography plus MRI ($n=455$).¹⁵ 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.

Section Summary: Screening Individuals at High Risk of Breast Cancer

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

Screening Individuals at Average Risk of Breast Cancer

In a systematic review of literature conducted for the 2016 U.S. Preventive Services Task Force breast cancer screening recommendation update, no randomized controlled trials (RCTs) or nonrandomized observational studies identified evaluated adjunctive MRI for screening average-risk women for breast cancer.¹⁶ Thus, there is a lack of published evidence on MRI screening of average-risk women. Because the prevalence of breast cancer is extremely low in average-risk young women, screening with a test such as MRI that has lower 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 with adjunctive MRI screening applied to young, average-risk women.

In 2016, Health Quality Ontario published a systematic review on MRI as an adjunct to mammography for women who are not at high risk of breast cancer.¹⁷ Reviewers searched for studies evaluating screening breast MRI as an adjunct to mammography compared with mammography alone. Studies needed to use pathology results as a reference standard for positive tests and clinical follow-up as a reference standard for negative tests. In addition, studies needed to report one or more outcomes of interest which included effectiveness outcomes (e.g., mortality, health-related quality of life, screening-related harms) and diagnostic outcomes (e.g., sensitivity, specificity), and biopsy and recall rates. Reviewers did not find any studies that met eligibility criteria. They concluded that there is a lack of evidence to inform the questions of the diagnostic accuracy of MRI plus mammography vs MRI alone and the impact of adjunct screening MRI on health outcomes in patients at less than high risk of breast cancer.

Section Summary: Screening of Individuals at Average Risk of Breast Cancer

There is a lack of evidence on MRI screening for average-risk women; systematic reviews did not identify any RCTs or nonrandomized comparative studies. Moreover, the PPV of screening tests would likely be lower in this lower prevalence population and there would be higher false-positive rates, morbidity, and anxiety.

Screening when Breast Characteristics Limit the Sensitivity of Mammography

Evidence for individuals with limited sensitivity of mammography is based on a 2004 Blue Cross Blue Shield Association Technology Evaluation Center (TEC)¹⁸ 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 adjunctive MRI. However, additional prospective studies are needed to confirm this and to identify patient subsets most likely to benefit from adjunctive MRI evaluation given the relatively low incidence of recurrence.

Discussion continues on the possible use of adjunctive MRI to screen women with dense breasts. In the 2012 ACRIN (American College of Radiology Imaging Network) 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 sub study, 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 sub study, 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.

Section Summary: Screening When Breast Characteristics Limit the Sensitivity of Mammography

There is a lack of prospective studies on the diagnostic accuracy of MRI vs mammography in patients who have had BCT. For women who are not otherwise at high risk of breast cancer but have breast characteristics that limit the sensitivity of mammography, the evidence on MRI screening is lacking.

Detection Uses

Clinical Context and Test Purpose

The question addressed in this portion of the evidence review is whether use of MRI as an adjunct to detect breast cancer in the ipsilateral or contralateral breast improves the net health outcome compared with standard techniques. Specifically, does MRI improve the diagnostic

accuracy beyond standard evaluation methods for detecting breast cancer and is this degree of increased accuracy likely to improve health outcomes via earlier diagnosis, better patient management decisions, and more appropriate treatment?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with suspicious lesions or with breast cancer in 1 breast.

Interventions

The intervention of interest is MRI examination as an adjunct to standard evaluation methods.

Comparators

The comparators of interest are mammography and clinical assessment.

Outcomes

The outcomes of interest for diagnostic accuracy include test accuracy and test validity (i.e., sensitivity, specificity). Primary outcomes of interest for clinical utility are the avoidance of invasive procedures (e.g., biopsy, mastectomy), the ability to detect cancer that would require additional or earlier treatment, and overall mortality and breast cancer-specific mortality rates.

Timing

MRI would be performed after a positive breast cancer screening or diagnostic examination.

Setting

The test would be performed in an imaging setting.

Technical Reliability

The technical reliability of MRI devices is well-accepted.

Clinical Validity and Clinical Utility

Detecting Suspected Occult Breast Primary Tumor with Axillary Nodal Adenocarcinoma with a Negative Mammography and Physical Exam

Evidence on detection of suspected occult breast cancer is based on a 2004 Blue Cross Blue Shield Association Technology Evaluation Center (TEC)¹⁸ and a subsequent meta-analysis. 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 systematic review of studies on the use of MRI in patients with mammographically occult breast cancer and an axillary metastasis evaluated 8 retrospective studies (total N=220 patients).²⁰ 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 31% (range, 22%-50%).

Section Summary: Detecting Suspected Occult Breast Primary Tumor with Axillary Nodal Adenocarcinoma with 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.

Detecting Contralateral Breast Cancer after Established Breast Cancer

In 2007, Lehman et al reported on results of the ACRIN-A6667 trial.²¹ They reported 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 MRI. 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 (12.5%) patients 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.²² 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.²³

Section Summary: Detecting Contralateral Breast Cancer after Established Breast Cancer

The available evidence suggests that adjunctive MRI can identify contralateral breast cancers in women with negative mammograms. A trial with nearly 1000 women found that MRI had high sensitivity and reasonably high specificity for identifying contralateral lesions not detected by mammography or physical examination. Although long-term outcomes of contralateral breast cancers are not fully known, important changes in management will occur as a result of the findings, and these management changes 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.

Detecting Breast Cancer in the Case of Low-Suspicion Findings on Conventional Mammography

Evidence on low-suspicion findings is based on a 2004 Blue Cross Blue Shield Association Technology Evaluation Center (TEC).¹⁸ Available evidence has suggested 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.

Section Summary: Detecting Breast Cancer in the Case of Low-Suspicion Findings on Mammography

A TEC Assessment found insufficient evidence on the use of MRI to diagnose low-suspicion findings on conventional testing that are not indicated for immediate biopsy. Well-designed prospective confirmatory studies would be necessary to permit conclusions on the effect this adjunctive use of breast MRI on health outcomes.

Detecting Breast Cancer by Further Characterizing Suspicious Breast Lesions

Evidence on further characterization based on Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessments from 2000,²⁴ 2001,²⁵ and 2004.¹⁸ 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 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 not be detected 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 the potential benefits of sparing a fraction of patients from unnecessary biopsy did not outweigh potential harms considering the current level of diagnostic performance of breast MRI.²⁵

A fairly large study by Bluemke et al (2004)²⁶ addressing this patient population with suspicious breast lesions was released after the 2004 TEC Assessment but did not change conclusions. Based on MRI results from 821 patients, sensitivity was 88.1% and specificity was 67.7%.

In a 2009 retrospective study, MRI accuracy was evaluated in patients who had dense breasts and suspected breast cancer or inconclusive evaluations from other modalities.²⁷ 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. Although specificity was relatively high and the negative predictive value (NPV) in this selected population was 98%, this study does not provide sufficient evidence that MRI can be used as a substitute for biopsy in these patients.

A systematic review published in 2011 analyzed 69 studies including 9298 women.²⁸ Pooled sensitivity was 90% (95% CI, 88% to 92%), and pooled specificity was 75% (95% CI, 70% to 79%). The 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 vs benign lesions, the area under the curve (AUC) for MRI was 0.91.

Two single-institution, prospective cohort studies examined the diagnostic accuracy of breast MRI for lesions identified on mammography or ultrasound. Strobel et al (2015) in Germany included lesions characterized as Breast Imaging Reporting and Data System (BI-RADS) category 4 by conventional workup in 340 women.²⁹ Most women were postmenopausal (61%), had no previous breast biopsy (64%), or family history of breast cancer (62%), and underwent initial evaluation for routine screening (88%). Of 353 lesions, 135 (38%) were biopsied; lesions down-graded to BI-RADS categories 1, 2, or 3 on MRI were followed-up with imaging for 18 months, except for pure clustered microcalcifications (without accompanying mass), which was biopsied or was followed-up with imaging for 24 months at patient discretion; none of the lesions monitored progressed during follow-up. Overall incidence of malignancy including DCIS was 20% (n=69). MRI down-graded 256 (28%) of 353 lesions, confirmed 37 (11%) lesions, and upgraded 50 (14%) lesions. PPV of MRI was 73% compared with 19% for conventional imaging. NPV of MRI was 99% (and could not be calculated for conventional imaging). For pure clustered microcalcifications, sensitivity was 89% (25/28 lesions) and the false-negative rate was 12% (3/28 lesions). False-positive MRI findings resulted in biopsy for 5 (1.5%) of 340 women.

In a similar study, Li et al (2014) in China included 84 women with BI-RADS categories 3, 4, or 5 microcalcifications on mammography.³⁰ Most patients were premenopausal (81%), had no family history of breast cancer (83%), and underwent initial evaluation for routine screening (56%). All lesions were biopsied surgically (n=91). Incidence of malignancy including DCIS was 46%. PPV of MRI was 87% compared with 60% for mammography. NPV of MRI was 91%.

Section Summary: Detecting Breast Cancer by Further Characterizing Suspicious Breast Lesions
MRI for evaluation of suspicious breast lesions has a relatively high sensitivity and a moderately high specificity. However, it has not yet been established whether the NPV is sufficient to preclude the need for biopsy. Although 2 more recent studies reported NPVs greater than 90% in certain types of breast lesions, these studies were conducted in single, non-U.S. institutions that require replication in larger, multicenter trials. Therefore, the use of MRI to further characterize suspicious lesions is currently unlikely to alter clinical management. In addition, the fairly high rate of false positives will lead to substantial numbers of unnecessary biopsies.

Treatment-Related Uses

Clinical Context and Test Purpose

The question addressed in this portion of the evidence review is whether use of MRI evaluation as an adjunct to guide treatment planning (e.g., surgical approach) for patients with known or

suspected breast cancer improves the net health outcome compared with standard techniques. Specifically, does MRI as an adjunct to standard methods for pretreatment planning, posttreatment evaluation, or evaluation of response to treatment improve the diagnostic accuracy, and is this degree of increased accuracy likely to improve health outcomes?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant populations of interest are individuals with suspicious lesions and individuals with breast cancer.

Interventions

The intervention of interest is MRI as an adjunct to standard evaluation methods.

Comparators

The relevant comparators of interest are mammography, clinical assessment, and/or pathologic inspection.

Outcomes

The relevant outcomes of interest for diagnostic accuracy include test accuracy and test validity (i.e., sensitivity, specificity). Primary outcomes of interest for clinical utility include avoidance of invasive procedures (e.g., biopsy, mastectomy), the ability to detect cancer requiring additional or earlier treatment, and overall mortality and breast cancer-specific mortality rates.

Timing

MRI would be performed after identification of suspicious breast lesions, or before or after treatment for breast cancer.

Setting

The test would be performed in an outpatient imaging setting.

Technical Reliability

The technical reliability of MRI devices is well-accepted.

Clinical Validity and Clinical Utility

Preoperative Mapping to Identify Multicentric Disease with Clinically Localized Breast Cancer

Evidence on preoperative mapping was based on a 2004 Blue Cross Blue Shield Association Technology Evaluation Center (TEC).³¹ The TEC Assessment concluded that ipsilateral MRI 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.

Subsequently, several meta-analyses have evaluated evidence on additional disease detected by MRI and changes in clinical management, most of which were by the same research group.³²⁻³⁶ The most recent and comprehensive meta-analysis was published by Houssami et al (2017).³⁴ Studies included in the review were comparative (randomized or nonrandomized), evaluated preoperative MRI vs an alternative approach that did not include MRI, and reported quantitative data on surgical outcomes. The primary end point for the meta-analysis was whether patients underwent mastectomy as surgical treatment. Secondary end points were re-excision rates after BCS, positive margins after BCS, and receipt of contralateral prophylactic mastectomy.

Nineteen studies met the inclusion criteria—3 RCTs and 16 nonrandomized comparative studies. For the primary study end point, a pooled analysis of 15 studies (n=85,975 patients) found significantly greater odds of receiving mastectomy after preoperative MRI than after no MRI (odds ratio [OR], 1.39; 95% CI, 1.23 to 1.57; $p<0.001$). Findings were the same in analyses stratified by publication dates, suggesting that the higher mastectomy rates were not limited to older studies conducted when MRI-guided biopsy was less common. In an analysis limited to patients with invasive lobular cancer, there was no significant difference in the odds of mastectomy (6 studies: pooled OR=1.00; 95% CI, 0.75 to 1.33; $p=0.988$) or the odds of re-excision (5 studies, OR=0.65; 95% CI, 0.35 to 1.24; $p=0.192$).

Among the secondary outcomes, a pooled analysis of 3 studies found a significantly higher odds of contralateral prophylactic mastectomy after MRI (OR=1.91; 95% CI, 1.25 to 2.91). There were no significant differences between groups on other secondary outcomes (i.e., re-excision rates, positive margins, reoperation rates).

One meta-analysis has addressed breast cancer recurrence rates. This 2014 meta-analysis, published by Houssami et al in 2014, analyzed individual patient data from 4 studies—1 RCTs and 3 nonrandomized comparative studies (total N=3180 patients).³⁶ Most patients (62%-93%) had localized, invasive disease and received BCT and systemic chemotherapy. After a median follow-up of 2.9 years (interquartile range [IQR], 1.6-4.5 years), 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.

Reoperation Rates

A description of the 3 RCTs included in the 2017 Houssami meta-analysis (described above) is as follows.

A 2010 multicenter RCT from the U.K. (COMICE trial) examined the impact of presurgical MRI on the need for additional treatment within 6 months.³⁷ 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 (1%) patients in the no-MRI group who underwent mastectomy by 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 (2%) patients had a “pathologically avoidable” mastectomy, defined as a mastectomy based on MRI results showing more extensive disease, but histopathology showing only localized disease. Twelve months after surgery, there was no statistically significant difference in quality of life between groups.

A second RCT, the MONET trial, was published by Peters et al in 2011.³⁸ It randomized 463 patients with suspicious, nonpalpable breast lesions identified on mammography or ultrasound to 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 additional lesions underwent biopsy, with 2 (18%) positive for malignancy. The incidence of mastectomy was similar between groups (32% vs 34%, $p=0.776$), as was the incidence of BCS (68% vs 66%). The incidence of re-excisions due to positive tumor margins was significantly greater in the MRI group (34%) compared with the control group (12%; $p=0.008$).

In a 2014 RCT by Gonzalez et al in Sweden, 440 women underwent surgical treatment of invasive breast cancer with or without presurgical breast MRI.³⁹ Breast MRI provided incremental information that altered treatment plan in 40 (18%) of 220 patients in the MRI group. Conversion from planned BCS to mastectomy occurred more often in the MRI group (20%) than in the control group (10%; $p=0.024$). However, more patients in the MRI group had planned BCS at baseline (70%) than in the control group (60%; $p=0.036$). Ipsilateral reoperation rate was 5% in the

MRI group vs 15% in the control group ($p < 0.001$). Reoperation rates among those initially planned for BCS were 5% and 22%, respectively ($p < 0.001$).

In addition to the RCTs, 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.⁴⁰ Twelve percent of patients had a preoperative MRI. Among patients with invasive lobular carcinoma, but not 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).

Section Summary: Preoperative Mapping to Identify Multicentric Disease with Clinically Localized Breast Cancer

Preoperative MRI as an adjunct to mammography and clinical assessment identifies additional foci of ipsilateral breast cancer and results in a higher rate of mastectomy. For example, a 2017 meta-analysis of 17 studies found significantly higher odds of receiving mastectomy after preoperative MRI vs no MRI in women with breast cancer. Follow-up studies reported mixed results, including no significant reduction in reoperations rates after MRI while other studies reported lower odds of reoperation in patients with invasive lobular carcinoma. No significant differences in ipsilateral local or distant recurrence-free survival after MRI-guided treatment were found in meta-analyses. However, there might have been insufficient power in the available data to detect differences in the overall population and further studies may help determine if particular subgroups derive greater benefit.

Guiding Surgical Decisions after Neoadjuvant Chemotherapy

Evidence on guiding surgical decisions is based on a 2004 Blue Cross Blue Shield Association Technology Evaluation Center (TEC)⁴¹ 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.⁴² 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 on correlations of residual tumor size by histopathology of 0.89 with MRI and 0.60 with clinical exam.⁴³ 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.

Several systematic reviews have been published after the 2004 TEC Assessment. Most recently, in 2015, Marinovich et al published an individual patient data meta-analysis of agreement between MRI and pathologic tumor size and other evaluation methods after neoadjuvant chemotherapy.⁴⁴ To be eligible for inclusion, studies had to evaluate at least 15 patients undergoing neoadjuvant chemotherapy who were evaluated with MRI and at least 1 other test (i.e., mammography, ultrasound, clinical examination) after surgery. Studies also had to report residual tumor size (i.e., longest diameter). Twenty-four studies met inclusion criteria, and individual patient data were available for 8 of these studies ($n=300$ patients). The pooled mean difference (MD) in size estimates between MRI and pathology (8 studies, $n=243$ patients) was 0.0 cm; 95% CI, -0.1 to 0.2 cm). In 4 studies comparing size estimates of mammography and pathology, the MD was 0.0 cm, but the 95% CI was wider (-0.3 to 0.4 cm). In 5 studies ($n=123$ patients) reporting on the MD between ultrasound and pathology, the pooled estimate was -0.3 cm (95% CI, -0.6 to 0.1 cm). The largest size variance was for studies (3 studies, $n=107$ patients) comparing clinical examination with pathology (pooled MD = -0.8 cm; 95% CI, -1.5 to -0.1 cm).

Previously, Lobbes et al (2013) reported on a systematic review of 35 studies (total $N=2359$ patients) reporting on the ability of MRI to predict tumor size after neoadjuvant chemotherapy.⁴⁵ Literature was searched to July 2012. Median correlation coefficient was 0.70 (range, 0.21-0.98). Variation in size between MRI and pathology ranged from -1.4 to +2.0 cm.

Section Summary: Guiding Surgical Decisions after Neoadjuvant Chemotherapy

Studies, including a 2015 meta-analysis, found that MRI results are well-correlated with pathologic assessment for measuring residual tumor size after neoadjuvant chemotherapy, and that MRI performed better than conventional methods. Using breast MRI instead of conventional methods to guide surgical decisions regarding BCT vs mastectomy after neoadjuvant chemotherapy would be at least as beneficial and might lead more frequently to appropriate surgical treatment.

Evaluating Response to Neoadjuvant Chemotherapy with Locally Advanced Breast Cancer

Evidence on the use of MRI to assess response to chemotherapy is based on a 2004 Blue Cross Blue Shield Association Technology Evaluation Center (TEC),⁴¹ 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 (2012) enrolled 206 women ages 26 to 68 years with invasive breast cancer 3 cm or larger who were receiving anthracycline-based neoadjuvant chemotherapy, with or without a taxane.⁴⁶ 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 (AUROC) of 0.09; corresponding AUROC values after the third and fourth MRIs were 0.07 and 0.05. Similar findings were reported for predicting pathologic complete response (pCR). However, implications of these findings for treatment and outcomes are uncertain and were not addressed in this trial.

The 2004 TEC Assessment reported on 6 studies (total N=206 patients) that performed breast MRI during the course of chemotherapy.⁴¹ MRI outcomes for response to chemotherapy were based on either reduction in tumor size or reduction in contrast enhancement. Three studies⁴⁷⁻⁴⁹ 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 study⁵⁰ examined whether MRI measurements of tumor volume and diameter predicted response to neoadjuvant chemotherapy and recurrence-free survival, but results did not change the conclusions reached in the 2004 Assessment.⁴¹ The authors found that initial (prechemotherapy) and final volumes were the strongest predictors of recurrence-free survival. Early changes in MRI volume or diameter only showed a trend of association ($p=0.7$ or 0.8) with recurrence-free survival. 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 with treatment by breast cancer subtype.⁵¹ The authors concluded that change in the largest diameter of enhancement on MRI was associated with tumor response among patients with triple-negative and human epidermal growth factor receptor 2 (HER2)-positive tumors but not among patients with more common estrogen receptor-positive/HER2-negative tumors.

Marinovich et al (2012) reviewed the literature on this topic to February 2011.⁵² Thirteen studies were included. They were heterogeneous in MRI parameters used, thresholds for identifying response, and definitions of pathologic response. Reviewers 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 2013.⁵³ Literature was searched to February 2011, and 44 studies (total N=2949 patients) assessing the ability of MRI to discriminate residual breast tumor after neoadjuvant chemotherapy from 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 AUROC was 0.88, and diagnostic odds ratio was 17.9 (95% CI, 11.5 to 28.0). (A diagnostic odds ratio 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, 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, 8 studies reported on measures of diagnostic accuracy.⁴⁵ Median sensitivity, defined as the proportion of patients with pCR correctly classified by MRI, was 42% (range, 25%-92%). Median specificity, defined as the proportion of patients without pCR 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.⁵⁴ 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 a retrospective review of patients with *HER2*-negative breast cancer, Charehbili et al (2014) assessed diagnostic accuracy of contrast-enhanced MRI for detecting pathologic response to neoadjuvant chemotherapy.⁵⁵ All patients had participated in an RCT that evaluated neoadjuvant chemotherapy (docetaxel, adriamycin, and cyclophosphamide [TAC]) with and without zoledronic acid. Of 250 randomized patients, 194 (78%) were included in the diagnostic accuracy study. Incidence of pCR was 21%. At the completion of neoadjuvant chemotherapy (6 cycles), area under the curve was 0.63 (95% CI, 0.52 to 0.74), and sensitivity, specificity, PPV, and NPV were 43%, 84%, 37%, and 87%, respectively. Accuracy for pCR was 76%.

Section Summary: Evaluating Response to Neoadjuvant Chemotherapy with Locally Advanced Breast Cancer

Studies, including systematic reviews, have not found sufficient 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 uncertain 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.

Evaluating Suspected Chest Wall Involvement

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.⁵⁶ Thirteen 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 reported on 4 cases in which MRI was able to determine involvement of the chest wall with 100% accuracy.^{57,58}

Section Summary: Evaluating Suspected Chest Wall Involvement

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

Evaluating Residual Tumor after Lumpectomy or Breast Conservation Surgery

Evidence on evaluating residual tumor comprises several observational studies, most of which were retrospective. Histopathologic examination on re-excision was used as the criterion standard. Most studies reported poor sensitivity and specificity of MRI for detection of residual disease. Three studies were conducted at the same institution and accrued patients during similar time periods, so overlap reporting may exist.⁵⁹⁻⁶¹

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.⁶² 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 (7.5%) patients, 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.⁵⁹ MRI prompted wider than initially planned surgical excision in 11 cases, 10 (91%) of which turned out to be false-positive MRI results. Kawashima et al (2001) studied 50 patients and reported 66% sensitivity and 81% specificity.⁶³ 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.⁶⁰ 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.⁶¹

Two studies, published in or before 2000, that reported more favorable results had methodologic issues limiting the influence of reported results.^{64,65} Frei et al (2000) retrospectively studied 68 patients with positive margins and examined the relation between when MRI was performed after initial surgery and diagnostic performance of MRI for residual disease.⁶⁴ This study excluded 3 patients with technically inadequate MRI studies and had publication discrepancies in reported results. 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.⁶⁵ The authors noted that MRI overestimated the extent of tumor in 1 patient who was counted as a true-positive.

In 2017, Krammer et al published a retrospective study evaluating breast MRI to assess residual disease in 175 patients who had been candidates for BCS and had positive surgical margins.⁶⁶ MRIs were read independently by 2 radiologists, both of whom had access to the pathology report from the initial surgery and any prior breast imaging. Pathology findings served as the criterion standard. For reader 1, the sensitivity and specificity of detecting residual disease was

63% and 75%, respectively. For reader 2, sensitivity and specificity were 83% and 64%, respectively. The interobserver agreement was moderate ($\kappa=0.56$).

Section Summary: Evaluating Residual Tumor after Lumpectomy or Breast Conservation Surgery
Available evidence is not sufficient to permit conclusions whether use of MRI identifies the presence and/or extent of residual disease after lumpectomy or BCS and before re-excision. Most studies were retrospective, and most reported poor sensitivity and specificity of MRI for detection of residual disease. Two studies reporting more favorable results had methodologic issues that limited the influence of reported results.

Evaluating and Localizing Lesions Prior to Biopsy

Use of MRI to evaluate lesions prior to biopsy is infrequent. MRI is used in this situation to permit biopsy and breast cancer diagnosis sooner than waiting until the lesion is visible on 2 mammographic views or on ultrasound or becomes palpable. The evidence base addressing this use is mainly anecdotal.

De Lima Docema et al (2014) used contrast-enhanced MRI to locate occult tumors in 25 patients selected from a group who had undergone breast MRI for suspicious incidental MRI findings at a single institution in Brazil.⁶⁷ Sentinel lymph node mapping and tumor resection was done simultaneously. Malignant tumors were confirmed in 15 (60%) patients, including 4 patients with DCIS. Survival outcomes were not reported.

Section Summary: Evaluating and Localizing Lesions Prior to Biopsy

Although the evidence base addressing this use of MRI is mainly anecdotal, the rationale supporting its use is good. Improved health outcomes are expected by enabling earlier diagnosis of breast cancer. A small cohort study in Brazil identified malignant tumors in 60% of patients with MRI-detected occult lesions using contrast-enhanced MRI.

Summary of Evidence

Screening Uses

For individuals who are asymptomatic with high risk of breast cancer who receive MRI as an adjunct to screen for breast cancer, the evidence includes a systematic review (Blue Cross Blue Shield Association Technology Evaluation Center (TEC) and subsequent diagnostic accuracy studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Studies have found that 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 unnecessary workups and biopsies due to false-positive results. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic with average risk of breast cancer who receive MRI as an adjunct to screen for breast cancer, the evidence includes a systematic review. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. The systematic review did not identify any randomized control trials or nonrandomized comparative studies evaluating MRI for screening average-risk women. Moreover, the diagnostic accuracy of screening tests would likely be lower in this lower prevalence population and there would be higher false-positive rates, morbidity, and anxiety. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with characteristics limiting accuracy of mammography (e.g., dense breasts) who receive MRI as an adjunct to screen for breast cancer, the evidence includes a systematic review (TEC Assessment) and subsequent diagnostic accuracy studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. There is a lack of prospective studies on the diagnostic accuracy of MRI vs mammography in patients who have had breast-conserving therapy. For women who are not at high risk of breast

cancer but whose breast characteristics might limit the sensitivity of mammography, the evidence on MRI screening is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

Detection Uses

For individuals who have suspected occult breast primary tumor with axillary nodal adenocarcinoma with negative mammography who receive MRI as an adjunct to detect breast cancer eligible for breast-conserving therapy, the evidence includes a systematic review (TEC Assessment) and subsequent meta-analysis. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. The studies found that adjunctive use of breast MRI to guide breast-conserving surgery rather than preemptive mastectomy allowed a substantial portion of patients to avoid the morbidity of mastectomy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have breast cancer who receive adjunctive MRI of the contralateral breast, the evidence includes cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. A study of nearly 1000 patients found that MRI could detect contralateral breast cancer with a high degree of accuracy. Although long-term outcomes of these contralateral breast cancers are not fully known, important changes in management will occur (e.g., simultaneous treatment of synchronous cancers) as a result of these findings, which should lead to improved outcomes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have low-suspicion findings on conventional mammography who receive MRI as an adjunct to detect breast cancer, the evidence includes a systematic review (TEC Assessment). Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. The TEC Assessment concluded that, although the available studies suggested reasonably high diagnostic accuracy, none of the studies used prospective methods in appropriate study populations or appropriate comparison interventions such as short-interval mammographic follow-up. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have suspicious breast lesions who receive MRI as an adjunct to further characterize lesions, the evidence includes a systematic review (TEC Assessment) and subsequent cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Studies have found that MRI for evaluation of suspicious breast lesions has a relatively high sensitivity and a moderately high specificity. However, it has not yet been established that the negative predictive value is sufficient to preclude the need for biopsy. Although 2 recent studies have reported negative predictive values greater than 90% in certain types of breast lesions, these were non-U.S., single-institution studies that require replication in larger, multicenter trials. Therefore, the use of MRI to further characterize suspicious lesions is currently unlikely to alter clinical management. In addition, the moderately high rate of false-positives will lead to substantial numbers of unnecessary biopsies. The evidence is insufficient to determine the effects of the technology on health outcomes.

Treatment-Related Uses

For individuals who have clinically localized breast cancer who receive MRI for preoperative mapping to identify multicentric disease, the evidence includes randomized controlled trials, systematic reviews, and prospective cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Studies have found that, for patients with clinically localized breast cancer, MRI can detect additional areas of disease in the ipsilateral or contralateral breast beyond that detected by standard imaging; further, MRI is associated with a higher rate of mastectomy. Follow-up studies have reported mixed results including no significant reduction in reoperations rates after MRI while other studies

have reported lower odds of reoperation in patients with invasive lobular carcinoma. No significant differences in ipsilateral local or distant recurrence-free survival after MRI-guided treatment were found in meta-analyses. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have locally advanced breast cancer undergoing neoadjuvant chemotherapy who receive MRI to guide surgical decisions after neoadjuvant chemotherapy, the evidence includes diagnostic accuracy studies and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Both a 2004 TEC Assessment and a 2015 systematic review and meta-analysis found that MRI results were well-correlated with pathologic assessment for measuring residual tumor size after neoadjuvant chemotherapy. The 2015 meta-analysis also found that MRI performed better than conventional methods. Using breast MRI instead of conventional methods to guide surgical decisions on breast-conserving therapy vs mastectomy after neoadjuvant chemotherapy would be at least as beneficial and may lead to appropriate surgical treatment more often. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have locally advanced breast cancer undergoing neoadjuvant chemotherapy who receive MRI to evaluate response to chemotherapy, the evidence includes diagnostic accuracy studies and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Studies, including systematic reviews, have not found that there is sufficient 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 about 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, change to a different regimen) would improve outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have posteriorly located breast tumors who receive MRI to diagnose chest wall involvement, the evidence includes cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Only a few small studies were identified, but MRI was 100% accurate for identifying chest wall involvement compared with the criterion standard. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have positive surgical margins after lumpectomy or breast conservation surgery who receive MRI to evaluate residual tumor, the evidence includes cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. The studies, most of which were retrospective, generally reported poor sensitivity and specificity with MRI for detection of residual disease compared with the criterion standard. The studies with the most favorable findings had methodologic issues that limited the influence of reported results. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a suspicious breast lesion recommended for biopsy but not localizable by mammography or ultrasonography who receive MRI to evaluate and localize the lesion prior to biopsy, the evidence includes a cohort study. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. A small cohort study in Brazil identified malignant tumors in 60% of patients with MRI-detected occult lesions using contrast-enhanced MRI. Although there is little published evidence supporting this indication, improved health outcomes are expected by enabling earlier diagnosis of breast cancer for suspicious lesions where other good options are not available. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Current National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (v.2.2017),⁶⁸ breast cancer screening and diagnosis (v.1.2017),⁶⁹ and genetic assessment of those at high risk of breast and/or ovarian cancer (v.2.2017)⁷⁰ list the following indications for breast magnetic resonance imaging (MRI).

Screening:

- Recommend Annual MRI Screening (Based on Evidence):
 - *BRCA* mutation, commence at age 25-29 y
 - First-degree relative of *BRCA* carrier, but untested: commence at age 25-29 y
 - Lifetime risk 20% or greater, as defined by models that are largely dependent on family history
- Recommend Annual MRI Screening (Based on Expert Consensus Opinion):
 - Radiation to chest between 10 and 30 years
 - Li-Fraumeni syndrome and first-degree relatives
 - Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives
 - >20% risk of breast cancer based on gene and/or risk level--*ATM*, *CDH1*, *CHEK2*, *PALB2*, *PTEN*, *STK11*, *TP53*
- Consider MRI screening for LCIS [lobular carcinoma in situ] and ALH [atypical lobular hyperplasia]/ADH [atypical ductal hyperplasia] based on emerging evidence if lifetime risk ≥20%
- Insufficient evidence to Recommend for or Against MRI Screening:
 - Lifetime risk 15%-20%, as defined by models that are largely dependent on family history
 - Heterogeneously or extremely dense breast on mammography
 - Women with a personal history of breast cancer, including ductal carcinoma in situ (DCIS)
- Recommend Against MRI Screening (Based on Expert Consensus Opinion):
 - Women at <15% lifetime risk⁶⁹

NCCN guidelines also state there is insufficient evidence for any recommendations for use of breast MRI for patients with the following genetic variants: *BARD1*, *FANCC*, *MRE11A*, *MUTYH*, *NF1*, *NBN*, *RAD50*, *SMARCA*, or *XRCC2*. Moreover, there are conflicting data on risks associated with a *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM* gene deletion.⁷⁰

Diagnosis⁶⁸:

- Optional MRI for women with nipple discharge, no palpable mass and a BI-RADS rating of 1-3
- To consider MRI for women with skin changes with a suspicion of inflammatory breast cancer or Paget's disease with BI-RADS 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 identify primary cancer in women with axillary nodal adenocarcinoma or with Paget disease of the nipple with 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:

- 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

American Cancer Society

The American Cancer Society guide on early detection of breast cancer, last revised in 2016, has recommended the following on MRI⁷¹:

"A breast MRI is mainly used for women who have been diagnosed with breast cancer, to help measure the size of the cancer, look for other tumors in the breast, and to check for tumors in the opposite breast. For certain women at high risk for breast cancer, a screening MRI is recommended along with a yearly mammogram. MRI is not recommended as a screening tool by itself because it can miss some cancers that a mammogram would find. Although MRI can find some cancers not seen on a mammogram, it's also more likely to find something that turns out not to be cancer (called a false positive). False-positive findings have to be checked out to know that cancer isn't present. This means more tests and/or biopsies. This is why MRI is not recommended as a screening test for women at average risk of breast cancer, because it would mean unneeded biopsies and other tests for many of these women."

American College of Radiology

The American College of Radiology has appropriateness criteria for breast imaging, which were developed in 2012 and last updated in 2016 (see Table 1).⁷² The relative radiation level also is reported, which is irrelevant for MRI.

Table 1. Appropriateness Criteria for Breast Cancer Screening^a

Specific Indications	MRI Rating	Mammography Rating
High risk women: women with a <i>BRCA</i> gene variant 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	9 with and without contrast (with mammography)	Mammography [9]
Intermediate-risk women: women with personal history of breast cancer, lobular neoplasia, atypical ductal hyperplasia, or 15%-20% lifetime risk of breast cancer	7 with and without contrast (with mammography)	Mammography [9]
Average-risk women: women with <15% lifetime risk of breast cancer, breasts not dense	3 with and without contrast	Mammography [9]

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.

MRI: magnetic resonance imaging.

^a MRI 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 I breast carcinoma.

The American College of Radiology also issued practice guidelines on breast MRI, which were last updated in 2013.⁷³ Among the indications listed are the following:

- For patients with a new breast malignancy - screening of the contralateral breast with RM 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: "MRI may be useful to determine the extent of disease and the presence of multifocality and multicentricity in patients with invasive carcinoma and ductal carcinoma in situ (DCIS)..."; to evaluate whether there is invasion deep to fascia; to assess potentially positive margins post lumpectomy; and to determine "before,

during, and/or after chemotherapy to evaluate treatment response and the extent of residual disease prior to 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 where there is “no mammographic or physical findings of primary breast carcinoma” for the “primary tumor” when patients present “with or axillary adenopathy and an occult primary”; to localize/confirm lesion when other imaging is “inconclusive” and “biopsy is not be performed (e.g., possible distortion on only one mammographic view...)”; to evaluate “suspected cancer recurrence in patients with tissue transfer flaps” (rectus, latissimus dorsi, gluteal) after breast reconstruction; and to guide “interventional procedures such as vacuum assisted biopsy and preoperative wire localization for lesions that are occult on mammography....”

American Society of Clinical Oncology

In 2006, the American Society of Clinical Oncology published guidelines for follow-up and management after primary treatment of breast cancer.⁷⁴ In 2013, the guidelines were updated with systematic review of the literature through March 2012, and no revisions were made.⁷⁵ 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.”⁷⁵ 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.”⁷⁴

International Late Effects of Childhood Cancer Guideline Harmonization Group

In 2013, an International Late Effects of Childhood Cancer 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.⁷⁶ 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.

U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force (USPSTF) published updated recommendations for breast cancer screening in 2016. The recommendations included the following statement on breast MRI⁷⁷:

“The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging, DBT [Digital Breast Tomosynthesis], or other methods in women identified to have dense breasts on an otherwise negative screening mammogram.”

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT02798796	Brazilian Randomized Study - Impact of MRI for Breast Cancer (BREAST-MRI)	372	Nov 2016 (ongoing)
NCT01929395	A Study to Evaluate the Use of Supine MRI Images in Breast Conserving Surgery	136	Dec 2017
NCT02244593	FAST MRI Study in Breast Cancer Survivors	300	Jun 2018
NCT01579552	Promoting Breast Cancer Screening in Women Who Survived Childhood Cancer	360	Jul 2018
NCT01716247	Comparison of Contrast Enhanced Mammography to Breast MRI in Screening Patients at Increased Risk for Breast Cancer	1000	Oct 2018
NCT01805076	MRI and Mammography Before Surgery in Patients with Stage I-II Breast Cancer	536	Sep 2019

NCT: national clinical trial.

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80. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 6.01.29 (September 2017).

Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- 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)

Post Service

- Results/reports of tests performed
- Procedure report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product 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 services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be 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.

Type	Code	Description
CPT®	77058	Magnetic resonance imaging, breast, without and/or with contrast material(s); unilateral
	77059	Magnetic resonance imaging, breast, without and/or with contrast material(s); bilateral
HCPCS	C8903	Magnetic resonance imaging with contrast, breast; unilateral
	C8904	Magnetic resonance imaging without contrast, breast; unilateral
	C8905	Magnetic resonance imaging without contrast followed by with contrast, breast; unilateral
	C8906	Magnetic resonance imaging with contrast, breast; bilateral
	C8907	Magnetic resonance imaging without contrast, breast; bilateral
	C8908	Magnetic resonance imaging without contrast followed by with contrast, breast; bilateral
ICD-10 Procedure	BH30Y0Z	Magnetic Resonance Imaging (MRI) of Right Breast using Other Contrast, Unenhanced and Enhanced
	BH30YZZ	Magnetic Resonance Imaging (MRI) of Right Breast using Other Contrast
	BH31Y0Z	Magnetic Resonance Imaging (MRI) of Left Breast using Other Contrast, Unenhanced and Enhanced
	BH31YZZ	Magnetic Resonance Imaging (MRI) of Left Breast using Other Contrast
	BH32Y0Z	Magnetic Resonance Imaging (MRI) of Bilateral Breasts using Other Contrast, Unenhanced and Enhanced
	BH32YZZ	Magnetic Resonance Imaging (MRI) of Bilateral Breasts using Other Contrast
ICD-10 Diagnosis	All Diagnoses	

Policy History

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

Effective Date	Action	Reason
10/12/1994	New Policy Adoption	Medical Policy Committee
04/28/1998	No change	External Review
06/13/2001	BCBSA Medical Policy adoption	Medical Policy Committee
02/13/2002	Adopted BCBSA TEC for differential diagnosis of a breast lesion to avoid biopsy	Medical Policy Committee
06/01/2003	Policy Review	Medical Policy Committee
06/01/2004	Adopted BCBSA TEC December 2003; Vol.18, No.15 as CTAF June 2004 consent agenda. Policy updated.	Medical Policy Committee
12/01/2004	Adopted BCBSA TEC September 2004; Vol.19, No.7. CTAF June 2004 consent agenda. Policy updated.	Medical Policy Committee
06/01/2005	Administrative Review	Administrative Review
06/28/2007	Policy Revision	Medical Policy Committee
07/02/2007	Policy published	Administrative Review
01/11/2008	Language clarification. Used NCI guidelines to determine risk. Position unchanged.	Medical Policy Committee
05/16/2008	BCBSA Medical Policy Adoption. Revised ACS guidelines and lifetime risk figure	Medical Policy Committee
09/25/2009	Policy Revision Criteria Revised Combined Policies MRI of the Breast and Computer-Aided Detection with MRI of the Breast	Medical Policy Committee
09/27/2013	Policy revision with position change	Medical Policy Committee
08/29/2014	Policy title change from MRI of the Breast Policy revision with position change	Medical Policy Committee
09/30/2015	Policy revision without position change	Medical Policy Committee
12/01/2016	Policy title change from Magnetic Resonance Imaging of the Breast Policy revision without position change	Medical Policy Committee
07/01/2017	Coding update	Administrative Review
12/01/2017	Policy revision without position change	Medical Policy Committee

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 (as applicable to your plan)
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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 be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.