KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria
Breast MRI with and without Computer-Aided Detection (CAD)

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	Magnetic Resonance Imaging (MRI) (220.2)
Local Coverage Determinations (LCD)	None
Local Coverage Article	None
KPWA Medical Policy	Due to the absence of a NCD, LCD, or other coverage guidance specific to breast MRI, KPWA has chosen to use their own Clinical Review Criteria for ***indications for breast MRI***, for medical necessity determinations. Use the Non-Medicare criteria below.

For Non-Medicare Members

I. Breast MRI may be indicated for **ONE or more of the following**:
   A. Breast abnormality evaluation needed, as indicated by **ONE or more of the following**:
      Note: If an area of distortion is found on mammography, a breast ultrasound should be the next step to confirm. If breast ultrasound shows a correlate, that area can then be biopsied under ultrasound guidance. If a breast ultrasound biopsy cannot be done of the area for some reason or is unsuccessful, and tomosynthesis guided or stereotactic guided breast biopsy is also not an option, consultation with a breast surgeon is recommended. MRI is not indicated in this situation.
      1. A single 6-month MRI for f/u if requested by the radiologist who attempted or performed the original MRI guided biopsy
      2. Breast MRI is covered for members with suspected silicone (not saline) implant leaks or rupture when **ALL** of the following have been met:
         a. Implants were placed as a result of **ONE of the following**:
            - Medically necessary lumpectomy or complete or partial mastectomy due to disease, injury or illness (such as breast cancer, chronic and severe fibrocystic disease, or infection unresponsive to medical therapy, chest wall surgery, or trauma) resulting in significant deformity;
            - Prophylactic mastectomy to prevent the onset of breast cancer when a clinical determination has been made that there is a high risk for breast cancer
         b. Records must document need for this test for evaluation and management
         c. A recent mammogram and/or ultrasound (depending on local breast center protocol) does not confirm leakage
         d. The leakage is not the result of a cosmetically placed implant as this would be a complication of a non-covered service
         e. It is not being requested for routine surveillance of a silicone implant
      3. Nipple Discharge, a breast MRI is indicated when **ALL of the following** conditions are met:
         a. Discharge is clear or bloody
         b. Discharge is unilateral and coming from a single duct

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c. Discharge is spontaneous (i.e., does not happen only with expression) and persistent (i.e., not a single episode)
d. Discharge is reproducible on exam
e. Mammography and ultrasound have been completed and did not detect a pathologic etiology. *If mammography, ultrasound or ductography were done, and was abnormal, MRI would not be indicated

B. Breast cancer diagnosis (new within the last 3 months) and **ONE or more** of the following:

1. After positive nipple-areolar biopsy for Paget disease, to define extent of disease and identify additional disease
2. Assessment of tumor response to neoadjuvant (preoperative) chemotherapy to determine appropriateness of breast-conserving surgery to assist with surgical planning
3. Evaluation of a newly diagnosed invasive breast cancer (e.g., lobular, ductal) (see below**).
4. Evaluation of a newly diagnosed DCIS and there is documentation that the patient is requesting breast conserving surgery (see below**).
5. Post lumpectomy, (within 6 weeks) for assessment of residual disease with the finding of close or positive margins on pathology.

C. Occult breast cancer, suspected (e.g., unknown primary), as indicated by **ALL of the following**:
1. Diagnosis of adenocarcinoma or carcinoma not otherwise specified in **ONE or more of the following**:
   a. Axillary lymph nodes
   b. Supraclavicular lymph nodes
2. Mammogram and breast ultrasound show no evidence of cancer.
3. No palpable breast mass suitable for biopsy

D. Annual MRI for breast cancer screening for **One or more of the following**:

Not indicated for patients who have undergone bilateral mastectomy for risk reduction or for treatment.

1. A lifetime risk of 20% or greater, as defined by validated models such as the following models: Tyrer-Cuzick, Gail Model, BRCAPro, Claus.
   a. The specific risk model must be documented in the clinical notes
   b. If member has had breast or ovarian cancer diagnosed after age 50, calculate the risk *prior* to the diagnosis
2. Carrier of high-risk[A] breast cancer gene mutation (including but not limited to: BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11, TP53)
3. Personal history of radiation to chest between ages 10 and 30 years
4. Annual MRI is indicated for individual with a personal history of breast cancer (including DCIS), diagnosed at or before age 50 and treated with breast conservation therapy of the affected breast (lumpectomy). Patients treated with mastectomy (unilateral or bilateral) would not routinely qualify.
5. Other high-risk family history of breast cancer, as indicated by **ONE or more of the following**:
   - Male relative with breast cancer
   - Untested first-degree relative [A*] of BRCA1 or BRCA2 mutation carrier
   - Woman not of Ashkenazi Jewish ancestry, with **ONE or more of the following**:
     i. First-degree [A*] or second-degree [B*] relative with breast cancer and **ONE or more of the following**:
        - Diagnosed at age 45 years or younger
        - Diagnosed at age 50 years or younger, with limited family history [C*]
        - Diagnosed at age 50 years or younger, who in turn has one or more close blood relatives [D*] with breast cancer, with at least one diagnosed at age 50 years or younger (29)
        - Diagnosed at age 50 years or younger, who in turn has one or more close blood relatives [D*] with epithelial ovarian [E*] cancer diagnosed at any age
        - Diagnosed at age 60 years or younger, with triple-negative breast cancer [F*]

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- Epithelial ovarian [E*] cancer
- First-degree [A*] or second-degree [B*] relative with 2 breast primaries, with the first primary diagnosed at age 50 years or younger
- First-degree [A*] or second-degree [B*] relative with breast cancer diagnosed at any age, who in turn has **One** or more of the following:
  i. Two or more close blood relatives [D*] with breast or epithelial ovarian [E*] cancer diagnosed at any age
  ii. One or more close male blood relatives [D*] with breast cancer
- First-degree [A] or second-degree relative [B*] with breast cancer who is of ethnicity associated with deleterious mutations, including Icelandic, Hungarian, Swedish, and Dutch
- First-degree [A*] or second-degree relative [B*] with breast or ovarian cancer diagnosed at any age, who in turn has 2 or more close blood relatives [D*] with pancreatic cancer diagnosed at any age

a. First-degree [A*] or second-degree relative [B*] with pancreatic cancer diagnosed at any age, who in turn has 2 or more close blood relatives [D*] with ONE or more of the following:
   - Breast cancer diagnosed at any age
   - Ovarian cancer diagnosed at any age
   - Pancreatic cancer diagnosed at any age

b. Third-degree relative [H*] with breast or epithelial ovarian [E*] cancer, who in turn has **ONE or more of the following**:
   - One close blood relative [D*] with epithelial ovarian [E*] cancer and another close blood relative [D*] with breast cancer diagnosed at age 50 years or younger
   - Two or more close blood relatives [D*] with breast cancer, with at least one diagnosed at age 50 years or younger
   - Two or more close blood relatives [D*] with epithelial ovarian [E*] cancer

c. Woman of Ashkenazi Jewish ancestry, with **One or more of the following**:
   - One or more first-degree relatives [A*] with breast cancer or epithelial ovarian cancer
   - Two or more second-degree relatives, [B*] on same side of family, [I*] with breast cancer
   - Two or more second-degree relatives, [B*] on same side of family, [I*] with epithelial ovarian cancer

d. Patient has diagnosis of, or has first-degree relative [A] with, **One or more of the following**:
   - Bannayan-Riley-Ruvalcaba syndrome
   - Cowden syndrome
   - Li-Fraumeni syndrome

* See below for the definition:
A - First-degree relatives consist of male or female parents, siblings, or children
B - Second-degree relatives consist of male or female grandparents, grandchildren, aunts, uncles, nieces, nephews, or half- siblings
C - Examples of a limited family history include fewer than 2 first-degree or second-degree female relatives or fewer than 2 female relatives in either maternal or paternal ancestry surviving beyond 45 years of age. (
D - Close blood relatives include first-degree, second-degree, or third-degree relatives on the same side of the family
E - A triple-negative breast cancer is one that is estrogen receptor-negative, progesterone receptor-negative, and human epidermal growth factor receptor 2-negative
F - Two primaries may be either bilateral disease or 2 or more clearly separate ipsilateral tumors, either synchronous or asynchronous
H - Third-degree relatives consist of first cousins, great-aunts, great-uncles, great-grandchildren, or great-grandparents
I - Each side of the family, maternal or paternal, should be considered independently

**Ideally, this should be ordered after discussion with the patient about risks and benefits or per recommendation of a multidisciplinary care conference, if available.

"Don't routinely order breast MRI in new breast cancer patients." per The American Society of Breast Surgeons Choosing Wisely initiative:

After a new diagnosis of breast cancer, breast MRI can be useful in selected patients to aid treatment decisions. However, there is a lack of evidence that routine use of MRI lessens cancer recurrence, death from cancer or the need for re-operation

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after lumpectomy surgery. The routine use of MRI is associated with an increased need for subsequent breast biopsy procedures, delays in time to treatment and higher cost of care. Increased mastectomy rates can occur if the MRI finds additional cancers or indeterminate findings cause patient anxiety, leading to patient requests for mastectomy.

(https://www.choosingwisely.org/clinician-lists/breast-surgeons-mris-in-new-breast-cancer-patients/)

Routine Surveillance of Silicone Breast Implants
Breast MRI is not covered for routine surveillance of silicone breast implants. The FDA made a recommendation (not a requirement) when they re-approved silicone implant use that members receive periodic breast MRIs. The FDA did not fund this screening. The choice of silicone vs saline is a patient preference and the use of MRI in this case cannot be described as medically necessary.

Computer-aided detection applied to breast MRI
No longer requires review

If requesting this service, please send the following documentation to support medical necessity:

- Documentation to support medical necessity (i.e., family history, prior treatment, genetic testing results, other imaging studies and diagnostic results, etc.)
- Applicable CPT code(s)

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Breast Cancer Screening and Lesions:
Mammography has been the standard tool used for breast cancer imaging. Community breast cancer screening programs have found an overall sensitivity of 75% and a specificity of 92%. The sensitivity of mammography in randomized trials is in the range of 68-88% (Elmore et al., 2005).

Due to limitations in the sensitivity of mammography, there has been research into alternative imaging modalities, particularly for women at high-risk of breast cancer. Interest in more accurate screening tests has grown since the identification of the BRCA1 and BRCA2 genes in the mid-1990s. Population-based studies have found that women with BRCA1 mutations have a approximately a 65% risk of developing breast cancer by age 70, and women with BRCA2 mutations have a 45% risk (Saslow et al., 2006). Mammography may not be adequate for detecting breast cancer in women with the BRCA1/2 mutation. In a study of BRCA1/2 mutation carriers who underwent annual mammography, screening detected only 5 out of 9 cases of breast cancer; the remaining were interval cancers (Brekelmans et al., 2001).

Contrast-enhanced magnetic resonance imaging (MRI) is proposed as an adjunct to mammography for women at high-risk of breast cancer. Breast MRI involves the injection of a contrast agent, usually gadolinium. Breast carcinomas tend to enhance, or get brighter, following injection of the contrast agent. MRI may be able to detect small breast lesions missed by mammography. However, contrast-enhanced MRI may not be able to distinguish between breast carcinoma and benign disease which also enhance, thus reducing the specificity of MRI.

The American Cancer Society (ACS) issued guidelines in May 2007 on breast screening with MRI as an adjunct to mammography (Saslow et al., 2007). The recommendations include:

- Annual screening for women with a lifetime risk of ≥20-25%, BRCA mutation or untested first-degree relative of BRCA carrier.
- No recommendation for or against screening women with a lifetime risk of 15-20%.
- Recommendation against screening women with <15% lifetime risk due to insufficient evidence.

The ACS recommends the BRCAPRO or other model largely dependent on family history be used to determine lifetime risk. BRCAPRO is a computer program on a statistical model for estimating an individual's probability of carrying a BRACA1/2 mutation on the basis of their own cancer status, and the history of breast and ovarian cancer among her first- and second-degree relatives (Berry et al., 2002). Other risk models, such as the Gail

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model risk calculator, which is also based on family history, may be easier to use in the primary care setting. An individual's risk level may vary with the different models (Saslow et al., 2007).

The Kaiser Permanente breast clinic already generally recommends MRI screening for women with known BRCA mutations, who are a first-degree relative of a BRCA carrier but are untested or have a 30-49% lifetime risk.

Silicone Implant Leakage:
Silicone-gel breast implants were first available for commercial use in the early 1960s. It is estimated that 1.5 to 2 million women in the United States have received an artificial breast implant, and the number is growing. Almost four-fifths of these women received the implant for cosmetic purposes to enhance or remodel breast shape, or to correct traumatic or congenital deformities. In only 20% of the cases they received it for breast reconstruction after mastectomy. At least three major generations and over 200 models of silicone gel-filled breast implants have been manufactured. The differences between the generations are primarily in the types of silicone gel and thickness of elastometric shell. The first generation of silicone gel-filled implants (early 1960s to the mid 1970s) had a thick elastometric shell with firm silicone gel. The second generation (mid 1970s to late 1980s) had a thin elastometric shell, and a less viscous gel. The third generation (mid 1980s to date) has a multilayer shell with a barrier layer and thick cohesive viscous silicone gel. In 1993 a newer generation of highly cohesive silicone implants (Style 410) was developed, however it is widely used in Europe and other countries, but not in the US (Brown 2002, Belli 2002, Scaranelo 2004, Gamper 2007, Gorczyca 2007).

Silicone implants may have psychological benefits but could be associated with local complications and systemic effects. Local implant-related complications include wound infection, hematomas, sensory nerve injury, capsular contracture, and implant rupture. The latter is a well-known complication and could range from focal rupture involving pinhole sized holes, through large visible tears, to complete disintegration of the implant shell. Implant rupture can be divided into two major categories: intracapsular (80-90% of all ruptures) and extracapsular. Unlike rupture, gel bleed is microscopic escape of silicone particles through the intact silicone envelope, in the absence of gross holes or tears. This is usually confined to the fibrous capsule that forms around the implant. Implant age, and design were found to be the most important factors associated with rupture. Other potential causes of rupture include trauma, mammography, and history of closed capsulotomy. The age of implant at rupture varied between reports between 4 and 22 years, with means also varying between studies from 11 to 16 years (Cher 2001, Samuels 1994, Gorczyca 2007).

Silicone gel-implant rupture may be clinically silent and pass unnoticed by the patient and the physician. It could remain undetected for years especially when it is contained within the fibrous capsule. A symptomatic rupture may present with local symptoms as breast pain, nodules, capsular contracture, and change in symmetry, size, or shape of the breast. Silicone gel granulomas and chronic disseminated granulomatous inflammation have been associated with implant rupture and gel migration. The potential health implications of silicone implant rupture are greatly debated. Some researchers reported that seepage of silicone and distant migration of the free silicone may lead to serious symptoms and foreign body reactions. Others indicated that it is harmless and does not lead to significant clinical symptoms or activate the humoral immune system (Ahn 2003, Holmich 2004, Gampper 2007).

The clinical diagnosis of asymptomatic implant rupture can be challenging. It was reported that less than one third of ruptures in asymptomatic patients can accurately be detected by experienced plastic surgeons. The gold standard for diagnosing an implant rupture is removal and examination of the implant. Mammography, ultrasonography, computed tomography, and magnetic resonance imaging have all been used in the diagnosis of silicone breast implant rupture. Each was reported to have its specific indications, advantages, and limitations. The type of silicone implant may also be a factor in choosing the modality for evaluating its integrity.

Mammography is a rapid inexpensive test, used routinely for screening, and can easily detect free silicone within the breast parenchyma due to extracapsular rupture. It, however, has a small radiation risk, and limited ability to detect intracapsular rupture which accounts for 80-90% of implant failures. The dense silicone is not easily penetrated by the X-ray energies used for typical screening mammography (Samuels 1994, Gampper 2007, Gorczyca 2007).

Ultrasonography is inexpensive, does not use ionizing radiation, can detect intracapsular rupture, and may also detect small amounts of free silicone mixed within the surrounding breast tissues. However, its usefulness for detecting implant rupture depends on the experience of the operator, type of equipment used, as well as other technical factors. It was also reported that ultrasonography may have its limitations in the evaluation of the posterior aspect of the implant, pectoralis muscle and chest wall (Belli 2002, Gorczyca 2007).
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MRI does not use ionizing radiation, has the ability to detect implant rupture, and to localize extensive free silicone. It can also be used with severe capsular contracture. Specialized breast coils increase the image quality and reduce scan time. However, it was reported that MRI cannot detect microscopic silicone leakage (gel bleeds). It is expensive, less available, less comfortable for the patient, and cannot be used among those with pacemakers, or other internal metallic devices that are not compatible with the MRI. Some patients may be claustrophobic and are unable to complete the examination (Beekman 1999, Gorczyca 2007, Gampper 2007)

FDA recommends MRI, with a dedicated breast coil and a magnet of at least 1.5 Tesla, as the current method of choice for detecting silent rupture of silicone gel implant. This is recommended to be performed three years after the implant, then every 2 years thereafter. The FDA also recommends the removal of ruptured breast implants.

With Computer-Aided Detection (CAD):
(Background information quoted from Blue Cross Blue Shield Association Technology Evaluation Center, BCBSA TEC report, June 2006)

Over the past decade, MRI of the breast has been studied in a variety of clinical settings, including both benign and malignant conditions of the breast…While MRI has a very high sensitivity for detecting lesions, its specificity is variable and often quite low because of the difficulty in distinguishing between benign and malignant lesions. The sensitivity for detection of invasive carcinoma overall is above 90%, while specificities between 37% and 90% have been reported (Deurloo et al. 2005a). The low specificity is particularly challenging in younger women, who are more likely to have enhancing benign lesions (Gilhuijs et al., 2002) …

Some investigators have incorporated additional criteria into the determination of MRI results in an attempt to increase the specificity without compromising sensitivity (Liberman 2004; Nunes et al. 2001). Descriptive features of lesion morphology such as those used in X-ray mammography may be helpful in this regard. For example, lesions with irregular or spiculated margins are characteristically malignant, while lesions with smooth, regular margins are usually benign (Nunes et al. 1997a) …CAD systems for MRI… provide easier ways of interpreting the patterns of contrast enhancement and washout across a series of images, which in turn may help identify lesions and their likelihood of being malignant. In contrast to CAD systems used with mammography, CAD for MRI is not aimed primarily at identifying lesions for consideration by a radiologist. Unlike the subtle appearance of lesions on mammography, most cancers enhance on MRI. The challenge is determining which lesions are benign and which are malignant. A large number of images are produced during MRI of the breast: images are taken at varying 'depths' throughout each breast multiplied by the number of times the breast is imaged to capture different time points in the enhancement process… Radiologists view the images to detect suspicious areas, and then they can pick a region of interest and look at the enhancement pattern. However, there may be variations across radiologists in the regions of interest selected and in the precise definition of the region of interest. CAD systems, in contrast, use color-coding and differences in hue to indicate the patterns of enhancement for each pixel in the breast image. It thereby may allow the radiologist to analyze the enhancement patterns systematically, although there is some question about how effective it is in reducing interobserver variability (Gabriel et al. 2005). Some CAD programs apparently incorporate morphological characteristics as well to estimate a probability of malignancy…"

There are several FDA-approved CAD systems for use with MRI of the breast. These include:

- CADstream (Confirma, Inc. Kirkland, WA). Originally cleared in 2003. CADstream version 4.0 was cleared in 2008.
- MRI Soft Tissue Motion Correction Software (Siemens Medical Solutions. Malvern, PA). Cleared September 2005.
- Z3D (Clario Medical Imaging): Cleared September 2008.

Medical Technology Assessment Committee (MTAC)

MRI in the Diagnosis of Breast Cancer and Breast Lesion

02/13/2002: MTAC REVIEW

Evidence Conclusion: All studies reviewed were retrospective, had several limitations, and data were obtained from records. Tan's study showed that MRI had an impact on the clinical management in almost one fifth of the patients. MRI findings were false positive among 61.5 % of the patients who underwent an additional surgery, which was a mastectomy in one case. Olson's study showed that MRI had a sensitivity of 95%, and specificity of 80%. These were based on data obtained from patients who underwent additional breast surgery, not all the sample. The clinical usefulness of a diagnostic test depends not only on its accuracy but also its reliability i.e. the

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consistency of interpretation on different occasions and by different observers. Mussurakis' study shows that all readers achieved a high sensitivity in cancer detection, their specificity however was much lower. The study also revealed a significant inter-observer variability in the interpretation of breast MRI. The high false positive rates, i.e. low specificity, and high inter-observer variability indicate that MRI, with its current limitations, is not an accurate or a reliable technology, compared to the gold standard of biopsy. Randomized trials, with a large study population will be required to confirm the findings and define the patients most likely to benefit from MRI. Moreover, further efforts are needed to improve, and standardize the indications, techniques, and image interpretation.

Articles: The search yielded 63 articles. Selection was based on study type. The majority were reviews, editorials, letters, and commentaries. The literature did not reveal any randomized controlled trials or longitudinal studies.

The following articles were selected for critical appraisal: Tan J E, Schnall M D, et al. Role of magnetic resonance imaging and magnetic resonance imaging-guided surgery in the evaluation of patients with early-stage breast cancer for breast conservation treatment. *Am J Clin Oncol* 1999; 22(4): 414-18 See Evidence Table. Olson JA, Morris EA, et al. Magnetic resonance imaging facilitates breast conservation for occult breast cancer. *Annals of Surgical Oncology* 2000; 7(6): 411-15 See Evidence Table. Mussurakis S et al. Observer variability in the interpretation of contrast enhanced MRI of the breast. *The British Journal of Radiology*1996; 69: 1009-16. See Evidence Table.

The use of MRI in the diagnosis of breast cancer and breast lesions does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

06/04/2007: MTAC REVIEW

MRI in the Diagnosis of Breast Cancer and Breast Lesion

Evidence Conclusion: The major prospective studies comparing screening asymptomatic women at moderate-to-high risk of breast cancer with MRI and mammography are summarized in Table 1. All of these studies were judged to be of reasonable validity. All studies were prospective and eligibility criteria included an assessment of risk based on genetic and family history factors. In addition, all of the studies included an independent evaluation of MRI and mammograms. The gold standard was biopsy/histology for positive tests in all studies. Gold standards for negative tests varied. Most studies used 1-year follow-up of negative tests to identify false negatives; Kuhl et al., 2005 used 6 months' follow-up. The Lehman et al., 2005 study was the weakest for several reasons. This is the only study in which the authors did not attempt to verify the accuracy of negative tests. In addition, only 4 cases of cancer were identified, a number too small for statistical analysis. The absolute difference in the breast cancer detection rate between combined testing with MRI and mammography and mammography alone ranged from 1% (Kriege et al., 2004) to 5% (Warner et al., 2004; Kuhl et al. 2005). The Kriege study included moderate-to-high risk women (≥15% lifetime risk) whereas the other two studies included only high-risk women. None of the studies reported whether the difference in the breast cancer detection rate with MRI plus mammography versus mammography alone was statistically significant. The recall rate (proportion of women called back for follow-up testing) ranged from 4% to 8% higher with MRI screening than with mammography-alone screening. None of the studies reported the recall rate with combined screening, but this would likely reflect the higher MRI rates. The sensitivity and specificity of combined screening with MRI and mammography versus mammography alone was reported in two studies. Leach et al., 2005 found a higher sensitivity with combined screening (94% versus 40%) and a lower specificity (77% versus 93%). Kuhl et al. (2005) also found a higher sensitivity with combined testing than mammography alone (93% versus 33%) and similar levels of specificity with the two methods (96% and 97%). Neither study reported p-values for the difference in sensitivity and specificity. The Kuhl et al., 2005 study did a sub-analysis by level of risk (see Table 2). The risk categories were moderate-risk (20% lifetime risk) and high-risk (21-40% lifetime risk). The sensitivity of combined screening was 100% in both the moderate and high-risk groups. This was substantially higher than the sensitivity with mammography alone, 50% for the moderate risk group and 25% for the high-risk group. Specificities of combined screening and mammography alone were similar for both risk levels. This analysis is limited in that it is based on a small number of cancer cases, only 6 for the moderate-risk group. This results in imprecise and unreliable statistics and should be viewed as preliminary data. For example, mammography correctly detected 3/6 cancers (50%); if only one additional cancer had been identified, the sensitivity would be dramatically altered to 4/6 (67%). Conclusion There is no high-grade evidence on whether combined screening with MRI and mammography improves health outcomes such as breast cancer mortality or overall mortality. The available evidence from 6 prospective studies suggests that combined screening of asymptomatic women at moderate-to-high risk of breast cancer with MRI plus mammography results in a 1-5% absolute increase in the cancer detection rate over mammography alone. The recall rate is substantially higher with MRI alone (4-8%) and would thus be higher with combined screening. Findings of 2 prospective studies are that combined screening substantially improves sensitivity compared to mammography alone and

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may decrease specificity. Data on women at moderate risk of breast cancer (≤20% lifetime risk) are insufficient to draw conclusions about detection rate or diagnostic accuracy.
Articles: There were no randomized or non-randomized controlled trials that compared health outcomes in high-risk women who received screening with mammography alone versus screening with mammography plus MRI. As reported in the American Cancer Society review (Saslow et al., 2007), there were 6 published prospective studies examining diagnostic yield and/or sensitivity/specificity of mammography compared to MRI for asymptomatic women at moderate-to-high risk of breast cancer. These 6 studies were critically appraised and presented in a joint evidence table. The Kaiser Permanente national breast cancer screening guideline included the topic of breast MRI screening for high-risk women. They identified additional observational studies comparing mammography to MRI. These studies were not included in the MTAC review due to methodological limitations such as a retrospective design, small sample size or only a minority of the study population underwent MRI screening. *The studies reviewed include:* Kriege M et al. for the MRI Screening Study Group. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. NEJM 2004; 351: 427-437**.** See Evidence Table. Kuhl CK et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk of breast cancer. J Clin Oncol 2005; 23: 8469-8476. See Evidence Table. Leach MO et al. for the MARIBS Study Group. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet 2005; 365: 1769-1778. See Evidence Table. Lehman CD et al. for the International Breast MRI Consortium Working Group. Screening women at high risk of breast cancer with mammography and magnetic resonance imaging. Cancer 2005; 103: 1898-1895. See Evidence Table. Sardanelli F et al. for the High Breast Cancer Italian Trial (HIBCRIT). Multicenter comparative multimodality surveillance of women at genetic-familial high risk for breast cancer (HIBCRIT Study). Radiology 2007; 242: 698-715. See Evidence Table. Warner E et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound and mammography, and clinical breast examination. JAMA 2004; 292: 1317-1325. See Evidence Table.

The use of MRI in the screening of high risk patients for breast cancer and breast lesions does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

04/08/2008: MTAC REVIEW
MRI in the Diagnosis of Breast Cancer and Breast Lesion
Evidence Conclusion: *Diagnostic accuracy:* It is hard to determine the diagnostic accuracy of imaging studies used to assess the integrity of breast implants. Visual inspection of the implant after its surgical removal is considered the gold standard for ruptured implants. However, this would not apply to asymptomatic women, as it would not be appropriate or ethical to remove an implant with no evidence of leak or rupture. The majority of the studies on the diagnostic accuracy of MRI or other imaging tests were thus conducted among symptomatic women who requested or were advised to remove the implants. The meta-analysis and the studies reviewed show wide variations in the accuracy of MRI and its predictive values in detecting an implant rupture in symptomatic women. The studies had differences in the equipment used, imaging protocol, description of positive MRI, and surgical criteria for a diagnosis of rupture. There were also some interobserver variations as seen in Collis and colleagues' study (2007). Different generations of implants were used. These varied by manufacturer, model, longevity, long-term integrity of the implant, as well as the implantation site and position. The authors of the majority of studies did not indicate the generation of implants used. Only one study (Collis 2007) included patients who exclusively received the third-generation implants. Holmich (2005) also provided the proportion of women receiving each of the three implant generations. Results of studies among women who received earlier generation of implants might not be generalized to the generation(s) currently used. One other limitation of the studies is the inclusion of self-selected symptomatic women who were requesting removal or replacement of the implants. The higher prevalence of rupture among these women would overestimate the accuracy of the tests, and limit generalization of the results to similar groups of patients. The overall results of the published studies show that the sensitivity of MRI in detecting an implant rupture among symptomatic women ranged from 64% to 90%. The specificity of the test ranged from 43% to 100%, the positive predictive value from 57% to 100% and the negative predictive values from 79% to 90%. Ultrasound came next in its accuracy with a sensitivity ranging from 30% to 69% and specificity ranging from 64% to 81%. Mammography was found to have the lowest sensitivity ranging from 20% to 69%, but with a specificity of 82% to 93%. Collis et al's study among asymptomatic who responded to the invitation for MRI testing showed a wide variation in sensitivity (71-86%) and specificity (48-95%) depending on the radiologist who interpreted the test. This assessment was based only on implants that were surgically removed. *Diagnostic impact*: There is insufficient evidence to determine that MRI may influence the management decisions for detected implant leak. *Therapeutic impact:* There are no published studies on the impact of MRI detection of implant leak on health outcomes.
Conclusions:

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- MRI is moderately to highly sensitive, and more specific in detecting implant rupture among self-selected groups of symptomatic women**.** i.e. in confirming ruptures when suspected.
- There is insufficient evidence on the accuracy of MRI as a screening tool for detecting leak or rupture among asymptomatic women.
- There is insufficient evidence to determine that MRI may influence the management decisions for detected implant leak.
- There is insufficient evidence on the impact of MRI detection of implant leak on health outcomes.

Articles: The literature search revealed over 120 articles. Many were review articles or studies on and safety and durability of the silicone gel implants. The following questions were considered in screening the published articles:

1. What is the diagnostic accuracy of MRI in detecting silicone gel breast implant leak/rupture in asymptomatic and symptomatic women?
2. Would the detection of the implant rupture be using MRI influence management decisions?
3. Does the detection of the implant rupture using MRI have an impact on health outcome?

1. Diagnostic accuracy

The literature search revealed several studies dating back to the early 1990s. There were 2 meta-analyses, and a systematic review on the diagnostic accuracy of MRI for detecting implant rupture among symptomatic women. The more recent meta-analysis, as well as studies that were not included in the analysis and that verified MRI findings with visual inspection of implant after surgical removal were critically appraised. Two studies that included asymptomatic women with a breast implant were identified (Brown 2000, and Collis 2007). In Brown and colleagues' (2000), study, the majority (92%) of the implants was second generation implants, and in Collis et al's study all were 3rd generation implant type. Collis' study was selected for critical appraisal as the second-generation implants are known to be more prone to rupture, and the results of Brown's study may not be generalized to the other generations that are more commonly used.

2. Diagnostic impact

A small study on the clinical impact of MRI was identified and critically appraised.

3. Therapeutic impact

No studies on the impact of technology on patient outcomes were identified by the search.

The following studies were critically appraised:

Cher DJ, Conwell JA, Mandel JS. MRI for detecting silicone breast implant rupture: Meta-analysis and implications. *Ann Plast Surg* 2001; 47:367-380. See Evidence Table. Reynolds HE, Buckwalter KA, Jackson VP, et al. Comparison of mammography, sonography, and magnetic resonance imaging in the detection of silicone-gel breast implant rupture. *Ann Plast Surg.*1994; 33:247-257. See Evidence Table. Beekman WH, Hage JJ, van Amerongen AHM, et al. Accuracy of ultrasonography, and magnetic resonance imaging in detecting failure of breast implants filled with silicone gel. *Scand J Plast Reconstr Hand Surg* 1999; 33:415-418. See Evidence Table. Scaranelo AM, Marques AF, Smialowski EB, et al. Evaluation of the rupture of silicone breast implants by mammography, ultrasonography, and magnetic resonance imaging in asymptomatic patients: correlation with surgical findings. *Sao Paulo Med J* 2004; 122:41-47. See Evidence Table. Holmich LB, Vejborg I, Conrad C, et al. The diagnosis of breast rupture: MRI findings compared with findings of explanation. *Europ J Radiol*. 2005:213-225. See Evidence Table. Collis N, Phil M, Litherland J, et al. Magnetic resonance imaging and explantation investigation of long-term silicone gel implant integrity. *Plast Reconstr Surg* 2007; 120:1401-1406. See Evidence Table. Dobke MK, Middleton MS. Clinical impact of breast implant magnetic resonance imaging. *Ann Plast Surg.*1994; 33:241-246. See Evidence Table

The use of MRI in the detecting leakage from silicone implants does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

08/03/2009: MTAC REVIEW

MRI in the Diagnosis of Breast Cancer and Breast Lesion

Evidence Conclusion: Published studies by two research groups comparing the specificity of breast MRI with and without CAD assistance for distinguishing between benign and malignant lesions were reviewed. Williams et al. (2007) evaluated 155 breast lesions detected by MRI and found a statistically significant reduction in the false-positive rate (reduced 23%) with CAD enhancement at 100%. Meinel et al. (2006) evaluated 80 lesions and found a statistically significant increase in specificity (from 51% to 81%) when human readers were aided by CAD. A higher specificity (and corresponding low false-positive rate) would contribute to improved diagnosis since fewer women would be subject to unnecessary follow-up tests or procedures. No published studies, however, evaluated whether there was a reduction in the number of biopsies or other procedures, or whether use of CAD contributed to a change in diagnosis. The above findings are insufficient to draw conclusions about the use of CAD systems with breast MRI and its impact on health outcomes. The quantity of published studies is low, and sample sizes of

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individual studies are small. Only one research group, Williams et al. (2007) did a comparative analysis with a commercially available CAD system. Moreover, no studies are available on the impact of CAD-enhanced MRI on follow-up procedures or diagnosis.

Articles: The Pubmed search yielded 79 articles. One additional article was identified on the CADStream website (Lehman et al., 2006). BCBSA TEC conducted an assessment in 2006; their search in March of that year identified the same articles as the PubMed search. Most of the articles in the PubMed search were either review articles, dealt with related topics such as other types of cancer, or addressed CAD development of other technical aspects of CAD systems or MRI. Three empirical studies were identified that compared breast MR imaging with and without a CAD system. Two of the articles were published by the same research group (T. Lehman, W DeMartini, S Peacock and others) and the later article (2007) appears to also include lesions included in the earlier article (2006). The 2007 article by this group and the other comparative study were both critically appraised. References are as follows: Williams TC, DeMartini WB, Partridge SC et al. Breast MR imaging: Computer-aided evaluation program for discriminating benign from malignant lesions. Radiol 2007; 244: 94-103. See Evidence Table. Meinel LA, Stolpen AH, Berbaum KS et al. Breast MRI lesion classification: Improved performance of human readers with a backpropagation neural network computer-aided diagnosis (CAD) system. J Magn Reson Imaging 2007; 25: 89-95. See Evidence Table.

The use of computer-aided detection (CAD) applied to breast MRI does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Breast MRI surveillance in women with personal history of breast cancer

Date: 07/13/2020

Evidence Conclusion:

- There is insufficient evidence for or against annual surveillance breast MRI in less than 50 years old women with personal history of breast cancer who were diagnosed with invasive breast cancer.
- High-quality randomized controlled trials comparing annual surveillance breast MRI vs mammography in women <50 years old (even in women aged 50 years and older) with personal history of breast cancer who were diagnosed with invasive breast cancer are rare.
- In women (age 18+) with personal history of breast cancer, (some in this population had heterogeneously & extremely dense breast tissue, genetic/family history) who were diagnosed were invasive breast cancer or DCIS:
  - Although one cohort study indicates no difference in performance between annual surveillance MRI and mammography, retrospective studies suggest that MRI performance may be higher than mammography.
  - In addition, MRI results in increased recall and biopsy rates as well as false positive.
  - Cancer detection rate may be higher in patients undergoing MRI than in that undergoing mammography.
  - The findings also suggest that mammography combined with MRI may be more effective (with low specificity) than mammography alone but recall rate and biopsy rate are high.
  - It is also not clear who may benefit from surveillance breast MRI.
- Impact of MRI on survival was not assessed.

Articles: PubMed was searched through February 14, 2020 with the following search terms (with variations): (((Magnetic Resonance Imaging OR MRI)) AND (breast neoplasm OR breast cancer)) AND (follow-up OR postoperative). Search terms also included surveillance, follow-up, and breast MRI surveillance. The search was limited to English language publications and human populations. The search was filtered by RCTs, systematic review & meta-analysis, and observational studies. The reference lists of relevant studies were reviewed to identify additional publications. See Evidence Table.

The use of Breast MRI for surveillance in women with a personal history of breast cancer, diagnosed under the age of 50 does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Applicable Codes

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT® or HCPC Codes	Description
77046	Magnetic resonance imaging, breast, without contrast material; unilateral
77047	Magnetic resonance imaging, breast, without contrast material; bilateral

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77048	Magnetic resonance imaging, breast, without and with contrast material(s), including computer-aided detection (CAD real-time lesion detection, characterization and pharmacokinetic analysis), when performed; unilateral
77049	Magnetic resonance imaging, breast, without and with contrast material(s), including computer-aided detection (CAD real-time lesion detection, characterization and pharmacokinetic analysis), when performed; bilateral
C8903	Magnetic resonance imaging with contrast, breast; unilateral
C8905	Magnetic resonance imaging without contrast followed by with contrast, breast; unilateral
C8906	Magnetic resonance imaging with contrast, breast; bilateral
C8908	Magnetic resonance imaging without contrast followed by with contrast, breast; bilateral

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

****To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check**.

Date Created	Date Reviewed0	Date Last Revised
02/13/2002	06/07/2011 MDCRPC, 04/03/2012MDCRPC, 05/01/2012MDCRPC, 08/07/2012MDCRPC, 03/05/2013MDCRPC, 09/03/2013MPC, 05/06/2014MPC, 03/03/2015MPC, 08/04/2015MPC, 06/07/2016MPC, 04/04/2017MPC, 02/06/2018MPC, 01/08/2019MPC, 01/07/2020MPC, 01/05/2021MPC, 01/04/2022MPC, 01/10/2023MPC	06/06/2023

MDCRPC Medical Director Clinical Review and Policy Committee
MPC Medical Policy Committee

Revision History	Description
05/14/2015	Changed Breast Cancer Diagnosis criteria to include language that clarifies cancer must be newly diagnosed within the last 3 months.
08/04/2015	Criteria was modified for clarifications regarding requests for MR biopsies
09/02/2016	Added indication, “it is not being requested for routine surveillance of a silicone implant,” to criteria
01/09/2017	Revised indication to “evaluate response to neoadjuvant chemotherapy”
10/18/2018	Criteria was modified for clarifications under breast abnormality evaluation
01/28/2019	Computer-aided detection applied to breast MRI No longer requires review
12/27/2019	Codes deleted 77058, 77059, C8904, C8907, 0159T
03/02/2021	Added July 2020 MTAC Review. MPC approved to adopt Breast MRI criteria for members with a personal history of breast cancer diagnosed at the age of 50 or younger and elected to have a lumpectomy or partial mastectomy. Requires 60-day notice, effective date 08/01/2021.
05/03/2022	MPC approved to revise the criteria to include educational additions for *Breast Cancer Diagnosis*
10/17/2022	Clarification of breast center protocols
06/06/2023	MPC approved modifications to the existing MRI Breast criteria to align with recommendations from multiple guideline statements, including NCCN, regarding certain types of nipple discharge and the need for breast MRI to detect cancer. Requires 60-day notice, effective date 11/01/2023.

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