Clinical Policy Bulletin: Magnetic Resonance Imaging (MRI) of the Breast

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Policy

I. Aetna considers magnetic resonance imaging (MRI), with or without contrast materials, of the breast medically necessary for members who have had a recent (within the past year) conventional mammogram and/or breast sonogram, in any of the following circumstances where MRI of the breast may affect their clinical management:

A. For individuals who received radiation treatment to the chest between ages 10 and 30 years, such as for Hodgkin disease, Wilm's tumors; or

B. To assess tumor location, size, and extent before and/or after neoadjuvant chemotherapy in persons with locally advanced breast cancer, for determination of eligibility for breast conservation therapy; or

C. To detect implant rupture in symptomatic members; or

D. To detect suspected local tumor recurrence in members with breast cancer who have undergone mastectomy and breast reconstruction with an implant; or

E. To detect local tumor recurrence in individuals with breast cancer who have radiographically dense breasts or old scar tissue from previous breast surgery that compromises the ability of combined mammography and ultrasonography; or

F. To detect the extent of residual cancer in the recently post-operative breast with positive pathological margins after incomplete lumpectomy when the member still desires breast conservation and local re-excision is planned; or

G. To evaluate persons with lobular carcinoma in situ (LCIS) or ductal carcinoma in situ (DCIS); or
H. To guide localization of breast lesions to perform needle biopsy when suspicious lesions exclusively detected by contrast-enhanced MRI can not be visualized with mammography or ultrasonography; or

I. To localize the site of primary occult breast cancer in individuals with adenocarcinoma suggestive of breast cancer discovered as axillary node metastasis or distant metastasis without focal findings on physical examination or on mammography/ultrasonography; or

J. To map the extent of primary tumors and identify multi-centric disease in persons with localized breast cancer (stage I or II, T0-1 N0-1 M0) prior to surgery (lumpectomy versus mastectomy).

II. Aetna considers breast MRI a medically necessary adjunct to mammography for screening of women considered to be at high genetic risk of breast cancer because of any of the following:

A. Carry or have a first-degree relative who carries a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes); or

B. Confirmed presence of BRCA1 or BRCA2 mutation; or

C. First degree blood relative with BRCA1 or BRCA2 mutation and are untested; or

D. Have a lifetime risk of breast cancer of 20 to 25 % or more using standard risk assessment models (BRCAPRO, Claus model, Gail model, or Tyrer-Cuzick); or

E.

III. Aetna considers breast MRI medically necessary to detect intra-capsular (silent) rupture of silicone gel-filled breast implants. Screening for silent intra-capsular rupture more frequently than every 2 years is not considered medically necessary.

IV. Aetna considers breast MRI experimental and investigational for all other indications, including any of the following, because there is insufficient scientific evidence to support its use:

A. To confirm implant rupture in symptomatic individuals whose ultrasonography shows rupture, especially with implants more than 10 years old (ultrasound sufficient to proceed with removal); or

B. To differentiate benign from malignant breast disease, especially clustered micro-calcifications; or

C. To differentiate cysts from solid lesions (ultrasound indicated); or

D. To evaluate breasts before biopsy in an effort to reduce the number of surgical biopsies for benign lesions; or

E. Surveillance of asymptomatic individuals with breast cancer who have completed primary therapy and who are not at high genetic risk of breast cancer; or

F. To provide an early prediction of response to adjuvant breast cancer chemotherapy in guiding choice of chemotherapy regimen; or

G. Dermatomyositis as an indication for use of MRI for breast cancer screening; or

H. To screen for breast cancer in members with average risk of breast cancer; or...
I. To screen BRCA-positive men.

V. Aetna considers computer-aided detection of malignancy with MRI of the breast experimental and investigational because its clinical value has not been established.

See also CPB 0584 - Mammography.

Background

Mammography is the only screening test proven to lower breast cancer morbidity and mortality. Although mammography is an effective screening tool, it does have limitations, especially in women with dense breasts. New imaging techniques are being developed to overcome these limitations, enhance cancer detection, and improve patient outcome. Digital mammography, computer-aided detection (CAD), breast ultrasound, and breast magnetic resonance imaging (MRI) are frequently used adjuncts to mammography in today's clinical practice.

An expert panel convened by the American Cancer Society recommended the use of MRI for screening women at a 20 to 25% or greater lifetime risk for breast cancer (Saslow et al, 2007). The panel states that, in addition to mammography, annual screening using MRI is recommended for women who:

- Carry or have a first-degree relative who carries a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes)
- Have a BRCA 1 or 2 mutation
- Have a first-degree relative with a BRCA 1 or 2 mutation and are untested
- Have a lifetime risk of breast cancer of 20 to 25% or more using standard risk assessment models
- Received radiation treatment to the chest between ages 10 and 30, such as for Hodgkin Disease

The ACS guidelines recommend use of MRI in addition to, not in place of, mammography for screening high-risk women (Saslow et al, 2007). The guidelines explain that all of the clinical trials screened participants with both MRI and mammography at the same time. The guidelines state that there is no evidence to support one approach over the other. "For the majority of women at high risk, it is critical that MRI screening be provided in addition to, not instead of, mammography, as the sensitivity and cancer yield of MRI and mammography combined is greater than for MRI alone."

The guideline provides information about 3 risk assessment models available for calculating breast cancer risk (BRCAPRO, Claus model, and Tyrer-Cuzick). Software for each model is available online (see Appendix below). The 3 risk models utilize different combinations of risk factors, are derived from different data
sets, and vary in the age to which they calculate cumulative breast cancer risk. As a result, they may generate different risk estimates for a given patient. This variability is an indicator that the risk models provide approximate, rather than precise, estimates of breast cancer risk. According to ACS guidelines, each of the risk models can be used for the purpose of identifying patients who would benefit from breast MRI screening (Saslow et al, 2007). In addition, the Gail model is widely used in research studies and clinical counseling to predict a woman’s lifetime risk of developing breast cancer. Calculation of a 5-year and lifetime breast cancer risk according to the Gail model can be performed by accessing the National Cancer Institute’s website (http://www.nci.nih.gov) and searching for information on breast cancer risk.

The ACS panel also identified several risk subgroups for which the available data are insufficient to recommend either for or against MRI screening (Saslow et al, 2007). They include women with a personal history of breast cancer, carcinoma in situ, atypical hyperplasia, and extremely dense breasts on mammography.

Although ultrasound is sufficient to confirm rupture of breast implants in women with symptoms, MRI may be necessary to detect intra-capsular rupture of silicone gel-filled breast implants in asymptomatic women. The sensitivity of plastic surgeons familiar with implants to diagnose rupture is 30 % compared to 89 % for MRI (Holmich et al, 2005). The FDA therefore recommends that women with silicone gel-filled breast implants have regular breast MRIs over their lifetime to screen for silent rupture. The FDA-approved labeling of silicone gel-filled breast implants recommends that the first MRI be performed 3 years post-operatively, then every 2 years thereafter. The FDA recommends that the MRI have at least a 1.5 Tesla magnet, a dedicated breast coil, and a radiologist experienced with breast implant MRI films for signs of rupture.

Houssami et al (2008) reviewed the evidence on MRI in staging the affected breast to determine its accuracy and impact on treatment. These researchers estimated summary receiver operating characteristic curves, positive predictive value (PPV), true-positive (TP) to false-positive (FP) ratio, and examined their variability according to quality criteria. Pooled estimates of the proportion of women whose surgery was altered were calculated. Data from 19 studies showed MRI detects additional disease in 16 % of women with breast cancer (n = 2,610). Magnetic resonance imaging incremental accuracy differed according to the reference standard (RS; p = 0.016) decreasing from 99 % to 86 % as the quality of the RS increased. Positive predictive value was 66 % (95 % confidence interval [CI]: 52 % to 77 %) and TP:FP ratio was 1.91 (95 % CI: 1.09 to 3.34). Conversion from wide local excision (WLE) to mastectomy was 8.1 % (95 % CI: 5.9 to 11.3), from WLE to more extensive surgery was 11.3 % in multi-focal/multi-centric disease (95 % CI: 6.8 to 18.3). Due to MRI-detected lesions (in women who did not have additional malignancy on histology) conversion from WLE to mastectomy was 1.1 % (95 % CI: 0.3 to 3.6) and from WLE to more extensive surgery was 5.5 % (95 % CI: 3.1 to 9.5). The authors concluded that MRI staging causes more extensive breast surgery in an important proportion of women by identifying additional cancer, however there is a need to reduce FP MRI detection. They stated that randomized trials are needed to determine the clinical value of detecting additional disease which changes surgical treatment in women with apparently localized breast cancer.
In a review on the utility of MRI for the screening and staging of breast cancer, Patani and Mokbel (2008) stated that while MRI can facilitate local staging, especially the evaluation of ipsilateral multi-centric or multi-focal lesions as well as synchronous contralateral disease that may be missed by conventional imaging; however, efficacy with respect to clinically relevant and patient oriented end-points has yet to be addressed in the context of clinical trials.

Computer-aided detection has been used to aid radiologists’ interpretation of contrast-enhanced MRI of the breast, which is sometimes used as an alternative to mammography or other screening and diagnostic tests because of its high sensitivity in detecting breast lesions, even among those in whom mammography is less accurate (e.g., younger women and those with denser breasts). However, MRI has a high FP rate because of the difficulty in differentiating between benign and malignant lesions. The use of CAD may also reduce the time needed to interpret breast MRI images, which currently takes much longer than reading mammograms.

The BlueCross and BlueShield Association’s Technology Evaluation Center (TEC) Medical Advisory Panel (2006) assessed the evidence on the use of CAD with MRI of the breast by comparing the sensitivity, specificity, and recall rate (percentage of patients asked to come back for further evaluation) of MRI with and without the use of commercially available CAD systems in detecting malignant lesions, evaluating the extent of disease in women with cancer, or gauging the impact of treatment. According to this assessment, many of the studies on the use of CAD with MRI of the breast mainly reported on the development of CAD systems, or testing new CAD approaches. The assessment noted that few of them evaluated commercially available CAD systems. Several of those that did, reported on the development and testing of approaches that underlie one of the commercially available systems (3TP); the assessment stated that it is not clear to what degree the current 3TP system has or has not been modified compared to these earlier approaches.

Although the studies had to have separate testing data sets to be included in the TEC assessment, these data sets often were enriched with more cancer cases or consisted exclusively of cases in which lesions had been found. The TEC assessment found, as a result, the range of sensitivities and specificities cannot be applied to the populations usually found in a clinical setting. The TEC assessment also found that many of the studies of CAD systems were retrospective, and reported primarily on their development and testing; thus, these studies lacked the rigor and generalizability of a large, prospective, well-designed study.

The TEC assessment stated that the literature is unclear on how CAD systems are to be used. In the case of CAD with mammography, the radiologist reads the original films first, makes a diagnosis, and then reviews the CAD results. The TEC assessment explained that, because CAD is not 100 % sensitive, lesions detected by mammography both before the use of CAD and after viewing the CAD results may be worked up. Thus, CAD can add to the sensitivity of mammography, but not its specificity. The TEC assessment noted, however, with MRI of the breast, the sensitivity is already high, and the focus is mainly on enhancing the specificity. In some studies, it appears that CAD was intended as an adjunct to the initial MRI reading, just as with CAD and mammography. In other studies, it was proposed as a way of speeding up the MRI reading process, and the precise protocol to be followed in reading the MRI images is unclear. In addition, unlike in the case of
CAD with mammography, in the documents regarding the FDA clearance it did not specify that CAD must be added only after an initial reading of the images alone, although it did say for one system that "patient management decisions should not be made based solely on the results of the CADstream analysis". The TEC assessment observed that the impact of CAD on the accuracy of MRI of the breast may depend partly on how the CAD results are incorporated into the reading and diagnostic process.

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel concluded that there is insufficient evidence to evaluate if the use of CAD systems would maintain or increase the sensitivity, specificity, and recall rates of MRI of the breast. The TEC assessment concluded that, given the inability to evaluate these intermediate outcomes, it is impossible to evaluate the impact of CAD on health outcomes such as treatment success and survival of patients with breast cancer.

There is limited evidence on the predictive value of preoperative MRI in persons who are newly diagnosed with early stage breast cancer, and no consistent evidence that a pre-operative breast MRI confers a benefit to the patient by improving clinical outcomes or surgical procedures. Lehman et al (2009) stated that use of breast MRI in the pre-operative evaluation of patients recently diagnosed with breast cancer has increased significantly over the past 10 years because of its well-documented high sensitivity for detecting otherwise occult breast cancer in the affected and contralateral breasts. However, published research reports on the impact of this improved cancer detection are limited. Equally important are growing concerns that the quality of breast MRI may vary significantly across practice sites, and therefore the published value of MRI may not be achieved for many patients.

These researchers described the peer-reviewed, published clinical research trials evaluating breast MRI in patients with newly diagnosed breast cancer on which the National Comprehensive Cancer Network (NCCN) practice guidelines on breast cancer were based. The current NCCN guidelines (2011) recommend that breast MRI be considered for patients with a newly diagnosed breast cancer to evaluate the extent of cancer or presence of multi-focal or multi-centric cancer in the ipsilateral breast; and for screening of the contralateral breast cancer at the time of initial diagnosis (category 2B).

Lehman and colleagues (2007) conducted a study to examine if MRI could improve on clinical breast examination and mammography in detecting contralateral breast cancer soon after the initial diagnosis of unilateral breast cancer. A total of 969 women with a recent diagnosis of unilateral breast cancer and no abnormalities on mammographic and clinical examination of the contralateral breast underwent breast MRI. The diagnosis of MRI-detected cancer was confirmed by means of biopsy within 12 months after study entry. The absence of breast cancer was determined by means of biopsy, the absence of positive findings on repeat imaging and clinical examination, or both at 1 year of follow-up. MRI detected clinically and mammographically occult breast cancer in the contralateral breast in 30 of 969 women who were enrolled in the study (3.1%). The sensitivity of MRI in the contralateral breast was 91%, and the specificity was 88%. The negative predictive value of MRI was 99%. A biopsy was performed on the basis of a positive MRI finding in 121 of the 969 women (12.5%), 30 of whom had specimens that were positive for cancer (24.8%); 18 of the 30 specimens were positive for
invasive cancer. The mean diameter of the invasive tumors detected was 10.9 mm. The additional number of cancers detected was not influenced by breast density, menopausal status, or the histologic features of the primary tumor. The authors concluded that MRI can detect cancer in the contralateral breast that is missed by mammography and clinical examination at the time of the initial breast-cancer diagnosis.

Bernard and associates (2010) evaluated the prevalence of synchronous, occult contralateral breast cancer detected by MRI but not by mammography or clinical breast examination in women with newly diagnosed breast cancer, including those aged 70 years or older. These investigators reviewed MRI results for women with newly diagnosed breast cancer who underwent bilateral breast MRI after negative mammography and clinical examination. The prevalence of pathologically confirmed contralateral carcinoma diagnosed solely by MRI was determined and analyzed in the context of age, breast density, family history, menopausal status, and primary-tumor characteristics. Logistic regression was used to explore the association between contralateral carcinoma and potential patient risk factors. A total of 425 women were evaluated, of whom 129 (30%) were aged 70 years or older. A contralateral biopsy was recommended and performed solely on the basis of MRI in 72 of the 425 women (17%). Sixteen of these 72 women (22%) had pathologically confirmed carcinoma, including 7 in the older subgroup. The prevalence of clinically and mammographically occult contralateral carcinoma detected by MRI was 3.8% (16/425) overall and 5.4% (7/129) in the group of older women. When potential risk factors for contralateral breast cancer were evaluated, post-menopausal status was the only significant predictor of contralateral cancer detected by MRI (p = 0.016). The authors concluded that contralateral breast screening with MRI should be considered in post-menopausal women with newly diagnosed breast cancer, even those aged 70 years or older at diagnosis.

On the other hand, Houssami and Hayes (2009) noted that randomized controlled trials (RCTs) have shown equivalent survival for women with early stage breast cancer who are treated with breast-conservation therapy (local excision and radiotherapy) or mastectomy. Decades of experience have shown that breast-conservation therapy provides excellent local control based on defined standards of care. Magnetic resonance imaging has been introduced in pre-operative staging of the affected breast in women with newly diagnosed breast cancer because it detects additional foci of cancer that are occult on conventional imaging. The median incremental (additional) detection for MRI has been estimated as 16% in meta-analysis. In the absence of consensus on the role of pre-operative MRI, these investigators reviewed data on its detection capability and its impact on treatment. They outlined that the assumptions behind the adoption of MRI, namely that it will improve surgical planning and will lead to a reduction in re-excision surgery and in local recurrences, have not been substantiated by trials. Evidence consistently shows that MRI changes surgical management, usually from breast conservation to more radical surgery; however, there is no evidence that it improves surgical care or prognosis. Emerging data indicate that MRI does not reduce re-excision rates and that it causes FPs in terms of detection and unnecessary surgery; overall there is little high-quality evidence at present to support the routine use of pre-operative MRI. The authors concluded that RCTs are needed to establish the clinical, psychosocial, and long-term effects of MRI and to show a
related change in treatment from standard care in women newly affected by breast cancer.

Furthermore, Solin (2010) stated that for the woman with a newly diagnosed early stage breast cancer, the routine use of pre-operative breast MRI is not indicated beyond conventional breast imaging (i.e., mammography with correlation ultrasound as indicated). There is no consistent evidence that a pre-operative breast MRI confers a benefit to the patient by improving clinical outcomes or surgical procedures. In a meta-analysis of studies reporting on the use of pre-operative breast MRI for the patient with an established index cancer, multi-focal or multi-centric disease was found on breast MRI in 16% of the patients, a rate substantially higher than the rate of local recurrence after breast conserving surgery plus definitive radiation treatment. In the largest retrospective study of patients treated with breast conserving surgery plus radiation, no gain was found for adding a breast MRI to conventional breast imaging. No randomized clinical trial has been designed to evaluate long-term clinical outcomes associated with adding a pre-operative breast MRI. Adding pre-operative breast MRI can alter clinical management in ways that are potentially harmful to patients (e.g., increased ipsilateral mastectomies, increased contralateral prophylactic mastectomies, increased work-ups, and delay to definitive surgery). The authors concluded that the routine use of pre-operative breast MRI is not warranted for the typical patient with a newly diagnosed early stage breast cancer.

There are no clinical studies of breast MRI in BRCA-positive men. Neither the American Cancer Society guidelines nor the National Comprehensive Cancer Network (NCCN) guidelines recommend breast MRI screening for men.

Wurzinger et al (2005) evaluated the MRI appearance of phyllodes breast tumors and to differentiate them from fibro-adenomas. MR images were obtained on a 1.5-T imager. T1- and T2-weighted sequences and dynamic 2D fast-field echo T1-weighted sequences were performed. MR images of 23 patients with 24 phyllodes breast tumors (1 malignant, 23 benign) were analyzed with respect to morphology and contrast enhancement. The tumors were compared with the MRI appearance of 81 fibro-adenomas of 75 patients. Well-defined margins were seen in 87.5% of the phyllodes tumors and 70.4% of the fibro-adenomas, and a round or lobulated shape in 100% and 90.1%, respectively. A heterogeneous internal structure was observed in 70.8% of phyllodes tumors and in 49.4% of fibro-adenomas. Non-enhancing internal septations were found in 45.8% of phyllodes tumors and 27.2% of fibro-adenomas. A significantly greater increase in signal was seen on T2-weighted images in the tissue surrounding phyllodes tumors (21%) compared with fibro-adenomas (1.2%). Most of both lesions appeared with low signal intensity on T1- and T2-weighted images. After the administration of contrast material, 33.3% of phyllodes tumors and 22.2% of fibro-adenomas showed a suspicious signal intensity-time course. The authors concluded that phyllodes breast tumors and other fibro-adenomas can not be precisely differentiated on breast MRI. Phyllodes tumors have benign morphologic features and contrast enhancement characteristics suggestive of malignancy in 33% of cases.

Biondi et al (2009) stated that phyllodes tumors are unusual biphasic fibro-epithelial neoplasms of the breast, accounting for less than 1% of all breast tumors and raising issues of diagnosis and therapeutic choice. They can grow quickly and
when the maximum diameter is greater than 10 cm, they are known as giant phyllodes tumors. Ultrasound, mammography and fine needle aspiration are not effective. A potentially useful diagnostic modality is MRI. Core tissue biopsy or incisional biopsy represent the preferred means of pre-operative diagnosis. Conservative treatment can be effective also in giant tumors depending upon the size of the tumor and the breast if a complete excision with an adequate margin of normal breast tissue can be achieved, so avoiding local recurrence often accompanied by worse histopathology. The authors reported the case of a giant benign phylloide tumor of the breast treated with conservative surgery, quadrantectomy and oncoplasty. No local recurrence at 4 years follow-up.

An UpToDate review on “Phyllodes tumors of the breast” (Grau et al, 2011) states that the role of MRI in the diagnosis and management of phyllodes tumors is not clear. A retrospective study of 30 patients with biopsy confirmed phyllodes tumors showed that malignant phyllodes tumors are seen as well-circumscribed tumors with irregular walls, high signal intensity on T1-weighted images and low signal intensity on T2-weighted images. Cystic change may be seen as well. Interestingly, a rapid enhancement pattern is seen more commonly with benign rather than malignant phyllodes tumors, which is the opposite of the pattern seen with adenocarcinomas of the breast. When the diagnosis of a phyllodes tumor has been made on core biopsy, breast MRI may prove helpful in determining the extent of disease and facilitating pre-operative planning. However, the use of breast MRI in surgical planning for phyllodes tumors is controversial as there are very little data on its role in this setting as they are so rare.

Furthermore, the NCCN Clinical Practice Guideline on breast cancer (2011) mentions the use of ultrasonography and mammography for the work-up of patients with phyllodes tumor; but does not mention the use of MRI in the management of these patients.

In a retrospective cohort study, Weber and colleagues (2012) examined the effect of pre-operative MRI on the reoperation rate in women with operable breast cancer. Women with operable breast cancer treated by a single surgeon between January 1, 2006, and December 31, 2010 were included in this study; selective pre-operative MRI based on breast density and histologic findings were carried out. Main outcome measures were reoperation rate and pathologically avoidable mastectomy at initial operation. Of 313 patients in the study, 120 underwent pre-operative MRI. Patients undergoing MRI were younger (mean age, 53.6 versus 59.5 years; p < 0.001), were more often of non-Hispanic white race/ethnicity (61.7 % versus 52.3 %, p < 0.05), and more likely had heterogeneously dense or very dense breasts (68.4 % versus 22.3 %, p < 0.001). The incidence of lobular carcinoma (8.3 % in the MRI group versus 5.2 % in the no MRI group, p = 0.27) and the type of surgery performed (mastectomy versus partial mastectomy, p = 0.67) were similar in both groups. The mean pathological size of the index tumor in the MR imaging group was larger than that in the no MRI group (2.02 versus 1.72 cm, p = 0.009), but the extent of disease was comparable (75.8 % in the MR imaging group versus 82.9 % in the no MRI group had pathologically localized disease, p = 0.26). The reoperation rate was similar between the 2 groups (19.1 % in the MRI group versus 17.6 % in the no MRI group, p = 0.91) even when stratified by breast density (p = 0.76), pT2 tumor size (p = 0.35), or lobular carcinoma histologic findings (p = 0.26). Pathologically avoidable mastectomy (multi-focal or multi-
centric MRI and uni-focal histopathological findings) was observed in 12 of 47 patients (25.5%) with pre-operative MRI who underwent mastectomy. The authors concluded that the selective use of pre-operative MRI to decrease reoperation in women with breast cancer is not supported by these data. In a considerable number of patients, MRI over-estimated the extent of disease.

Plana et al (2012) estimated the diagnostic accuracy of MRI in detecting additional lesions and contralateral cancer not identified using conventional imaging in primary breast cancer. These investigators conducted a systematic review and meta-analyses to estimate diagnostic accuracy indices and the impact of MRI on surgical management. A total of 50 articles were included (n = 10,811 women). MRI detected additional disease in 20% of women and in the contralateral breast in 5.5%. The summary PPV of ipsilateral additional disease was 67% (95% CI: 59 to 74%). For contralateral breast, the PPV was 37% (95% CI: 27 to 47%). For ipsilateral lesions, MRI devices greater than or equal to 1.5 Tesla (T) had higher PPV (75%, 95% CI: 64 to 83%) than MRI with less than 1.5 T (59%, 95% CI: 53 to 71%). Similar results were found for contralateral cancer, PPV 40% (95% CI: 29 to 53%) and 19% (95% CI: 8 to 39%) for high- and low-field equipments, respectively. True-positive MRI findings prompted conversion from wide local excision (WLE) to more extensive surgery in 12.8% of women while in 6.3% this conversion was inappropriate. The authors concluded that MRI shows high diagnostic accuracy, but MRI findings should be pathologically verified because of the high FP rate. They stated that future research on this emerging technology should focus on patient outcome as the primary end-point.

Prevos et al (2012) examined if MRI can identify pre-treatment differences or monitor early response in breast cancer patients receiving neoadjuvant chemotherapy. PubMed, Cochrane library, Medline and Embase databases were searched for publications until January 1, 2012. After primary selection, studies were selected based on pre-defined inclusion/exclusion criteria. Two reviewers assessed study contents using an extraction form. In 15 studies, which were mainly under-powered and of heterogeneous study design, 31 different parameters were studied. Most frequently studied parameters were tumor diameter or volume, K (trans), K(ep), V(e), and apparent diffusion coefficient (ADC). Other parameters were analyzed in only 2 or less studies. Tumor diameter, volume, and kinetic parameters did not show any pre-treatment differences between responders and non-responders. In 2 studies, pre-treatment differences in ADC were observed between study groups. At early response monitoring significant and non-significant changes for all parameters were observed for most of the imaging parameters. The authors concluded that evidence on distinguishing responders and non-responders to neoadjuvant chemotherapy using pre-treatment MRI, as well as using MRI for early response monitoring, is weak and based on under-powered study results and heterogeneous study design. Thus, the value of breast MRI for response evaluation has not yet been established.

The American Society of Clinical Oncology’s clinical practice guideline update on “Breast cancer follow-up and management after primary treatment” (Khatcheressian et al, 2013) provided recommendations on the follow-up and management of patients with breast cancer who have completed primary therapy with curative intent. A systematic review of the literature published from March 2006 through March 2012 was completed using Medline and the Cochrane Collaboration Library.
An Update Committee reviewed the evidence to determine whether the recommendations were in need of updating. There were 14 new publications that met inclusion criteria: 9 systematic reviews (3 included meta-analyses) and 5 RCTs. After its review and analysis of the evidence, the Update Committee concluded that no revisions to the existing ASCO recommendations were warranted. Regular history, physical examination, and mammography are recommended for breast cancer follow-up. Physical examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter. For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy. Thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed. The use of complete blood counts, chemistry panels, bone scans, chest radiographs, liver ultrasounds, pelvic ultrasounds, computed tomography scans, [(18)F] fluorodeoxyglucose-positron emission tomography scans, MRI, and/or tumor markers (carcinoembryonic antigen, CA 15-3, and CA 27.29) is not recommended for routine follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.

Korteweg et al (2011) evaluated the feasibility of 7-T breast MRI by determining the intrinsic sensitivity gain compared with 3-T in healthy volunteers and explored clinical application of 7-T MRI in breast cancer patients receiving neoadjuvant chemotherapy (NAC). In 5 volunteers, the signal-to-noise ratio (SNR) was determined on proton density MRI at 3-T using a conventional 4-channel bilateral breast coil and at 7-T using a dedicated 2-channel unilateral breast coil, both obtained at identical scan parameters. Subsequently, consecutive breast cancer patients on NAC were included. The 7-T breast MRI protocol consisted of diffusion-weighted imaging, 3-D high-resolution (450 μm isotropic) T1-weighted fat-suppressed gradient-echo sequences and quantified single voxel (1)H-magnetic resonance spectroscopy. Morphology was scored according to the MRI Breast Imaging-Reporting and Data System (BI-RADS)-lexicon, and the images were compared with 3-T and histopathologic findings. Image quality was evaluated using a 5-point scale. A 5.7-fold higher SNR was measured at 7-T than at 3-T, which reflected the advantages of a higher field strength and the use of optimized radiofrequency coils. Three breast cancer patients were included and received a total of 13 7-T MRI examinations. The image quality of the high-resolution examinations was at least satisfactory, and good to excellent in 9 of the 13 examinations performed. More anatomic detail was depicted at 7-T than at 3-T. In 1 case, a fat plane between the muscle and tumor was visible at 7-T, but not at the clinically performed 3-T examination, suggesting that there was no muscle invasion, which was confirmed by pathology. Changes in tumor apparent diffusion coefficient values could be monitored in 2 patients and were found to increase during NAC, consistent with published results from studies at lower field strengths. Apparent diffusion coefficient values increased respectively from 0.33 × 10(-3) mm(2)/s to 1.78 × 10(-3) mm(2)/s after NAC and from 1.20 × 10(-3) mm(2)/s to 1.44 × 10(-3) mm(2)/s during NAC. Choline concentrations as low as 0.77 mM/kg(water) could be detected. In 1 patient, choline levels showed an overall decrease from 4.2 mM/kg (water) to 2.6 mM/kg(water) after NAC and the tumor size decreased correspondingly from 3.9 × 4.1 × 5.6 cm(3) to 2.0 × 2.7 × 2.4 cm(3). All 7-T MRI findings were consistent with pathology analysis. The authors concluded that
dedicated 7-T breast MRI is technically feasible, can provide more SNR than at 3-T, and has diagnostic potential.

An UpToDate review on “MRI of the breast and emerging technologies” (Slanetz, 2014) states that “High field strength MRI -- High field strength magnets (3-Tesla and 7-Tesla) provide higher signal to noise ratios than conventional breast MRI, performed with 1.5-Tesla field strength magnets. The high field strength magnets result in higher spatial resolution and improved detection of breast cancers <5 mm in size than conventional techniques. However, there are no large prospective trials that show clinical advantage for high field strength MRI. In addition, the lack of widespread availability of higher field magnets limits applicability to clinical practice”.

Appendix

Breast Cancer Staging:

Information about breast cancer staging is available from the National Cancer Institute at the following website:

Breast Cancer Risk Assessment Models:

Software for each of the breast cancer models referenced the American Cancer Society guidelines (Saslow et al, 2007) is available via the internet:

BRCAPRO Version 4.3. Available
at: http://www4.utsouthwestern.edu/breasthealth/cagene/default.asp.
Claus model (BreastCa for Palm, version 1.0, copyright. 2001)
http://www.palmgear.com/index.cfm?
fuseaction=software.showsoftware&prodID=29820.

Breast cancer risk can also be estimated online using the Gail Model Breast Cancer Risk Assessment Tool available from the National Cancer Institute's website:

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

19085 Biopsy, breast, with placement of breast localization device(s) (eg, clip, metallic pellet), when performed, and imaging of the biopsy specimen, when performed, percutaneous; first lesion, including magnetic resonance guidance

19086 each additional lesion, including magnetic resonance guidance (List separately in addition to code for primary procedure)
19287 Placement of breast localization device(s) (eg clip, metallic pellet, wire/needle, radioactive seeds), percutaneous; first lesion, including magnetic resonance guidance

19288 each additional lesion, including magnetic resonance guidance (List separately in addition to code for primary procedure)

77058 Magnetic resonance imaging, breast, without and/or with contrast material(s); unilateral [not covered for screening of BRCA-positive men]

77059 bilateral [not covered for screening of BRCA-positive men]

CPT codes not covered for indications listed in the CPB:

+ 0159T Computer aided detection, including computer algorithm analysis of MRI image data for lesion detection/characterization, pharmacokinetic analysis, with further physician review for interpretation, breast MRI (List separately in addition to code for primary procedure)

Other CPT codes related to the CPB:

19100 - 19103 Breast biopsy

19120 - 19126 Excision breast lesion

19300 - 19307 Mastectomy procedures

19357 - 19369 Breast reconstruction

76641 Ultrasound, breast, unilateral, real time with image documentation, including axilla when performed; complete

76642 limited

77051 - 77057 Breast, mammography

88245 - 88269 Chromosome analysis

88271 - 88275 Molecular cytogenetics

Modifier 0A BRCA1 (hereditary breast/ovarian cancer)

Modifier 0B BRCA2 (hereditary breast cancer)

HCPCS codes covered if selection criteria are met:

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

Other HCPCS codes related to the CPB:

G0202 -  Mammography
G0206
L8600  Implantable breast prosthesis, silicone or equal
S3854  Gene expression profiling panel for use in the management of breast cancer treatment

ICD-9 codes covered if selection criteria are met:

174.0 - 175.9  Malignant neoplasm of breast
196.3  Secondary and unspecified malignant neoplasm of lymph nodes of axilla and upper limb
198.81  Secondary malignant neoplasm of breast
233.0  Carcinoma in situ of breast
759.6  Other hamartoses, not elsewhere classified [Cowden syndrome]
793.80, 793.89  Unspecified and other nonspecific abnormal findings on radiological and other examination of breast
996.54  Mechanical complications due to breast prosthesis
996.79  Other complications of internal (biological) (synthetic) prosthetic device, implant, and graft
V10.3  Personal history of malignant neoplasm of breast
V10.43  Personal history of malignant neoplasm of ovary
V15.3  Personal history of irradiation [to chest]
V16.3  Family history of malignant neoplasm of breast
V16.41  Family history of malignant neoplasm of ovary
V45.71  Acquired absence of breast and nipple
V50.41  Prophylactic breast removal
V50.42  Prophylactic ovary removal
V76.10  Special screening for malignant neoplasm breast, unspecified
V76.19  Other screening breast examination

V84.01  Genetic susceptibility to malignant neoplasm of breast [not covered for BRCA-positive men]

V84.02  Genetic susceptibility to malignant neoplasm of ovary

**ICD-9 codes not covered for indications listed in the CPB:**

- 217  Benign neoplasm of breast
- 238.3  Neoplasm of uncertain behavior of breast
- 610.0  Solitary cyst of breast
- 610.1  Diffuse cystic mastopathy
- 610.2  Fibroadenosis of breast
- 610.8  Other specified benign mammary dysplasia
- 611.9  Unspecified breast disorder
- 793.81  Mammographic microcalcification
- 799.9  Other unknown and unspecified cause of morbidity or mortality

**Other ICD-9 codes related to the CPB:**

- 610.3 - 611.9  Disorders of breast
- V15.89  Other specified personal history presenting hazards to health
- V43.82  Organ or tissue replaced by other means, breast
- V45.83  Breast implant removal status
- V58.11  Encounter for antineoplastic chemotherapy
- V67.2  Follow-up examination following chemotherapy
- V76.11  Screening mammogram for high-risk patient
- V76.12  Other screening mammogram
- V86.0  Estrogen receptor positive status [ER+] 
- V87.41  Personal history of antineoplastic chemotherapy

**The above policy is based on the following references:**


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