HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: MRI FOR BREAST CANCER DIAGNOSIS

DATE: 5/9/2013; reaffirmed 1/14/2016

This coverage guidance was created under HERC's 2013 coverage guidance process and does not include strength of recommendation, a GRADE-informed framework or coverage guidance development framework.

As a part of the coverage guidance monitoring process, the HERC decided on 1/14/2016 (see Appendix A) to reaffirm the existing coverage guidance and reconsider the need to update the topic during the regular two-year review cycle.

HERC COVERAGE GUIDANCE

In women with recently diagnosed breast cancer, preoperative or contralateral MRI of the breast should not be a covered service.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. In addition to an evidence-based guideline developed by the Evidence-based Guideline Subcommittee and a health technology assessment developed by the Heath Technology Assessment Subcommittee, coverage guidance may utilize an existing evidence report produced in the last 5 years by the Agency for Healthcare Research and Quality, the Medicaid Evidence-based Decisions Project or the Washington Health Technology Assessment Program.

EVIDENCE SOURCE

Washington State Health Care Authority Health Technology Assessment Program. (2010). *HTA Report: Breast MRI in diagnosis and treatment of cancer in women at high*

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risk. Olympia, WA: Health Technology Assessment Program. Retrieved May 7, 2012, from http://www.hta.hca.wa.gov/documents/breast_mri_072310_final.pdf

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

In 2009, an estimated 192,370 cases and 40,170 deaths occurred in women with breast cancer. In 2002, the United States Preventive Services Task Force found adequate evidence of film mammography's sensitivity and specificity and evidence of mammography's effectiveness in decreasing breast cancer mortality in women at average risk and concluded that film mammography was the standard for detecting breast cancer in women at average risk of developing breast cancer. In women recently diagnosed with breast cancer, MRI has been used to evaluate the contralateral breast, and has also been used to assist with treatment planning prior to definitive treatment. Whether these uses of breast MRI improve patient outcomes is not clear, and is the focus of this report.

Evidence Review

Detecting Contralateral Breast Cancer in Women Recently Diagnosed
MRI detects contralateral breast lesions in a substantial proportion of women with breast cancer, but does not reliably distinguish benign from malignant findings. This evidence review identified the following results:

- Detection of suspicious findings (true positives plus false positives): 9.3% (95% CI, 5.8% to 14.7%)
- Incremental cancer detection rate (ICDR): 4.1% (95% CI, 2.7% to 6.0%)
- PPV, 47.9% (95% CI, 31.8% to 64.6%)
- True positive: false positive ratio, 0.92 (95% CI, 0.47 to 1.82).

Some women will undergo treatment changes based on false positive tests, with one study reporting that 6.9% of women with changes in treatment based on MRI were found to have benign lesions. There were no RCTs which assessed the effect of adding MRI to conventional breast cancer screening on mortality rates.

Changes in Treatment in Women with Recently Diagnosed Breast Cancer
Preoperative MRI testing in women with recently diagnosed breast cancer will change treatment plans for some women (15.7%). Conversion of wide local excision to more extensive surgery will occur in up to 11.3% of women, and conversion from wide excision to mastectomy will occur in up to 8.1% of women. In women with breast cancer

with dense breast tissue, microcalcifications suspicious for carcinoma in situ or discordance between mammography and ultrasound, MRI may add clinical information which may alter treatment plans (44.3% of the time in one retrospective observational study).

Changes in Treatment – Incomplete Excision
Adding MRI will change treatment plans and result in more extensive surgery for some women, but may not change incomplete excision rates or breast cancer recurrence rates. The evidence is insufficient to determine whether MRI affects the rate of incomplete cancer excision because it is conflicting. One study found no difference between groups while another found an 18% decrease in re-excision rates in women who underwent MRI preoperatively. The study reporting of no difference between groups may have been underpowered to find a difference if one existed. The evidence is insufficient to determine whether changes in treatment plans based on the results of preoperative MRI testing are beneficial.

Changes in Treatment – Recurrence Rates
The evidence regarding the effect of preoperative MRI testing in women with early invasive breast cancer on recurrence rates is inconclusive. One retrospective observational study reported a 5.6% reduction in recurrence rates in patients receiving preoperative MRI before breast conservation surgery. Another larger observational study found that MRI was not associated with a lower recurrence rate or 8-year rate of local failure.

Safety
Gadolinium-based MRI contrast agents appear to be safe. There is no evidence of adverse events associated with MRI radiation exposure. We found no evidence that breast implants increase the risk of developing breast cancer. The evidence is insufficient to conclude that false-positive breast cancer screening or testing results lead to clinically meaningful negative psychological outcomes.

Technical and Provider Issues in MRI Testing
The evidence is insufficient to establish technical MRI specifications or provider qualifications.

[Evidence Source]

Overall Summary

MRI of the breast identifies contralateral breast lesions in women who have been recently diagnosed with breast cancer and may result in a change in treatment plans, but some women will undergo those changes based on false positive tests, and whether those changes are beneficial is unknown. Preoperative MRI testing in women with

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recently diagnosed breast cancer may change treatment plans, but there is no clear evidence that it changes incomplete excision rates or breast cancer recurrence rates. There is no evidence of a benefit on mortality with contralateral or preoperative MRI of the breast.

PROCEDURE

MRI of the Breast

DIAGNOSES

Breast cancer

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Codes	
V10.3	Personal history of malignant neoplasm, breast
V16.3	Family history of malignant neoplasm, breast
V76.10	Special screening for malignant neoplasms, breast, unspecified
V76.19	Special screening for malignant neoplasms, breast, other screening breast examination
V84.01	Genetic susceptibility to malignant neoplasm of breast
174.0-9	Malignant neoplasm of female breast
233.0	Carcinoma in situ of breast
ICD-9 Volume 3 (procedure codes)	
None	
CPT Codes	
77058	MRI breast, with or without contrast, unilateral
77059	MRI breast, with or without contrast, bilateral
HCPCS Codes	
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

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Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

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Appendix A: 2015 Rescanning Summary

HERC decision (1/14/2016): Reaffirm the existing coverage guidance and reconsider the need to update it during the regular two-year review cycle.

Bottom Line: Additional evidence suggests that MRI in patients with recently diagnosed breast cancer does not improve clinical outcomes, but may result in false-positive test results and overtreatment with more aggressive surgical procedures.

Scope Statement:

Population description	Adults with recently diagnosed breast cancer *Population scoping notes: None*
Intervention(s)	Breast MRI *Intervention exclusions: None*
Comparator(s)	Usual care, including other imaging modalities
Outcome(s) (up to five)	**Critical:** All-cause mortality, cancer-specific mortality **Important:** Progression-free survival, false-positive test results, quality of life *Considered but not selected for GRADE table: Change in surgical or non-surgical treatment plan*
Key questions	1. What is the comparative effectiveness of breast MRI after the diagnosis of breast cancer for improving patient outcomes? 2. What are the harms of breast MRI after the diagnosis of breast cancer? Contextual Question 1. How often do the results of MRI after breast cancer diagnosis lead to changes in the surgical or non-surgical treatment plan?

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Scanning Results

1. Alberta Provincial Breast Tumour Team. (2012). *Magnetic resonance imaging for breast cancer screening, pre-operative assessment, and follow-up*. Edmonton (Alberta): Alberta Health Services, Cancer Care. Retrieved from http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-br007-mri.pdf

Citation 1 is an Alberta Health Services clinical practice guideline addressing the use of MRI for screening, pre-operative assessment, or follow-up of breast cancer. It offers the following pertinent guidance:

"Pre-operative MRI may be considered in the following circumstances:

- Biopsy proven axillary nodal adenocarcinoma with no primary identified on mammography, ultrasound, and physical examination.
- Discordant clinical and mammogram/ultrasound findings.

Pre-operative MRI may be used in the following situations where the patient desires breast conserving surgery and:

- There is high risk for multifocal/multicentric disease.
- The extent of disease is unclear.

MRI may be used for breast cancer evaluation before, during and after neoadjuvant therapy to help evaluate response to systemic treatments.

- MRI may overestimate response to neoadjuvant chemotherapy and should not be used to plan post-chemotherapy breast conserving surgery.
- MRI accurately predicts lack of response to neoadjuvant chemotherapy and may be used to support a change in therapy. "

2. Brasic, N., Wisner, D. J., & Joe, B. N. (2013). Breast MR imaging for extent of disease assessment in patients with newly diagnosed breast cancer. *Magnetic Resonance Imaging Clinics of North America, 21*(3), 519-32.

Citation 2 is a non-systematic narrative review of MRI for breast cancer. It would not meet criteria for inclusion in an updated coverage guidance.

3. Bruening, W., Uhl, S., Fontanarosa, J., Reston, J., Treadwell, J., & Schoelles, K. (2012). *Noninvasive diagnostic tests for breast abnormalities: Update of a 2006 review.* Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from www.effectivehealthcare.ahrq.gov/reports/final.cfm

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Citation 3 is an AHRQ review of various non-invasive imaging modalities for evaluation of abnormalities identified on routine screening. The review does not explicitly address MRI for patients with recently diagnosed breast cancer and is therefore out of scope.

4. Chen, X., Li, W. L., Zhang, Y. L., Wu, Q., Guo, Y. M., & Bai, Z. L. (2010). Meta-analysis of quantitative diffusion-weighted MR imaging in the differential diagnosis of breast lesions. *BMC Cancer, 10*, 693.

Citation 4 is a SR of a quantitative diffusion weighted MR technique for the diagnosis of breast cancer. It is therefore out of scope.

5. Cooper, K. L., Meng, Y., Harnan, S., Ward, S. E., Fitzgerald, P., Papaioannou, D., … Lorenz, E. (2011). Positron emission tomography (PET) and magnetic resonance imaging (MRI) for the assessment of axillary lymph node metastases in early breast cancer: systematic review and economic analysis. *Health Technology Assessment, 15*(4), 1-134.

Citation 5 is a SR and economic evaluation of PET, MRI, and various lymph node sampling techniques for the diagnosis of axillary lymph node metastases. The summary sensitivity and specificity of MRI ranged from 64%-98% and 73%-100% respectively depending on the MR technique used. In the cost-effectiveness analysis, MRI was the dominant strategy, though this British economic analysis may be too indirect to influence new coverage guidance.

6. Harnan, S. E., Cooper, K. L., Meng, Y., Ward, S. E., Fitzgerald, P., Papaioannou, D., … Wyld, L. (2011). Magnetic resonance for assessment of axillary lymph node status in early breast cancer: a systematic review and meta-analysis. *European Journal of Surgical Oncology, 37*(11), 928-36.

Citation 6 is a SR of studies examining MRI for the assessment of axillary lymph node status in early stage breast cancer. The sensitivity and specificity of ultrasmall super-paramagnetic iron oxide MRI were 98% and 96% respectively. However, the authors conclude that “current estimates of sensitivity and specificity do not support replacement of SLNB [sentinel lymph node biopsy] with any current MRI technology in this patient group.

7. Houssami, N., Turner, R., Macaskill, P., Turnbull, L. W., McCready, D. R., Tuttle, T. M., … Solin, L. J. (2014). An individual person data meta-analysis of preoperative magnetic resonance imaging and breast cancer recurrence. *Journal of Clinical Oncology, 32*(5), 392-401.

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Citation 7 is a patient-level MA of the effects of preoperative MRI on local and distant recurrence in patients with breast cancer. At eight years, there was no difference in local or distant recurrence in the MRI and no-MRI groups.

8. Houssami, N., Turner, R., & Morrow, M. (2013). Preoperative magnetic resonance imaging in breast cancer: meta-analysis of surgical outcomes. *Annals of Surgery, 257*(2), 249-55.

Citation 8 is a SR of studies on the effects of preoperative MRI on surgical outcomes. The authors conclude that "evidence showed that MRI significantly increased mastectomy rates and suggests an unfavorable harm-benefit ratio for routine use of preoperative MRI in BC [breast cancer]. We found weak evidence that MRI reduced re-excision surgery in patients with ILC [invasive lobular cancer] — although this was at the expense of increased mastectomies—and overall patient benefit from MRI in ILC is not clear from this study."

9. Institute for Clinical Systems Improvement (ICSI). (2012). Diagnosis of breast disease. Bloomington, MN: ICSI. Retrieved from https://www.icsi.org/_asset/v9l91q/DxBrDis.pdf

Citation 9 is an ICSI report on the initial diagnosis of breast cancer. It is therefore out of scope.

10. Medeiros, L. R., Duarte, C. S., Rosa, D. D., Edelweiss, M. I., Edelweiss, M., Silva, F. R., … Rosa, M. I. (2011). Accuracy of magnetic resonance in suspicious breast lesions: a systematic quantitative review and meta-analysis. *Breast Cancer Research & Treatment, 126*(2), 273-85.

Citation 10 is a SR examining the use of MRI for the initial diagnosis of suspicious breast lesions identified on screening. It is therefore out of scope.

11. Meng, Y., Ward, S., Cooper, K., Harnan, S., & Wyld, L. (2011). Cost-effectiveness of MRI and PET imaging for the evaluation of axillary lymph node metastases in early stage breast cancer. *European Journal of Surgical Oncology, 37*(1), 40-6. Retrieved from http://ac.els-cdn.com/S0748798310005238/1-s2.0-S0748798310005238-main.pdf?_tid=709ff45c-4211-11e5-a1ee-00000aacb360&acdnat=1439508017_3059855702ecf908c89280499139c38e

Citation 11 is a cost-effectiveness study of MRI of imaging vs sentinel lymph node biopsy for evaluation of axillary lymph node metastases in early breast cancer. The summary sensitivity and specificity of MRI were both 90%. From the perspective of the British NHS, MRI was the most cost-effective strategy for diagnosing axillary lymph

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node metastases, but this British economic analysis may be too indirect to influence new coverage guidance.

12. Parsyan, A., Algahtani, A., Mesurolle, B., & Meterissian, S. (2013). Impact of preoperative breast MRI on surgical decision making and clinical outcomes: a systematic review. *World Journal of Surgery, 37*(9), 2134-9.

Citation 12 is a SR of studies examining the effects of preoperative MRI on surgical decision-making and clinical outcomes. The authors conclude that "Preoperative MRI is a highly sensitive but nonspecific method that leads to changes in surgical management with increased numbers of more extended surgical interventions. It appears that a relatively large proportion of MRI-driven changes in surgical management result in overtreatment without conclusively proven beneficial effects on such clinical outcomes as decrease in reoperation rates or improved patient survival."

13. Plana, M. N., Carreira, C., Muriel, A., Chiva, M., Abraira, V., Emparanza, J. I., … Zamora, J. (2012). Magnetic resonance imaging in the preoperative assessment of patients with primary breast cancer: systematic review of diagnostic accuracy and meta-analysis. *European Radiology, 22*(1), 26-38.

Citation 13 is a systematic review of studies of MRI in the preoperative assessment of breast cancer. The authors conclude that "MRI shows high diagnostic accuracy, but MRI findings should be pathologically verified because of the high FP [false positive] rate. Future research on this emerging technology should focus on patient outcome as the primary end-point."

14. Prevos, R., Smidt, M. L., Tjan-Heijnen, V. C., van Goethem, M., Beets-Tan, R. G., Wildberger, J. E., & Lobbes, M. B. (2012). Pre-treatment differences and early response monitoring of neoadjuvant chemotherapy in breast cancer patients using magnetic resonance imaging: a systematic review. *European Radiology, 22*(12), 2607-16.

Citation 14 is a SR of studies examining the role of MRI for assessing response to neoadjuvant chemotherapy. The authors conclude that "[e]vidence on distinguishing responders and non-responders to neoadjuvant chemotherapy using pretreatment MRI, as well as using MRI for early response monitoring, is weak and based on underpowered study results and heterogeneous study design. Thus, the value of breast MRI for response evaluation has not yet been established."

15. Shao, Z., Wang, H., Li, X., Liu, P., Zhang, S., & Cao, S. (2013). Morphological distribution and internal enhancement architecture of contrast-enhanced magnetic resonance imaging in the diagnosis of non-mass-like breast lesions: a meta-analysis. *Breast Journal, 19*(3), 259-268.

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Citation 15 is a MA of studies examining MRI for the initial diagnosis of breast cancer in non-mass like breast lesions. It is therefore out of scope.

16. Wu, L. M., Hu, J. N., Gu, H. Y., Hua, J., Chen, J., & Xu, J. R. (2012). Can diffusion-weighted MR imaging and contrast-enhanced MR imaging precisely evaluate and predict pathological response to neoadjuvant chemotherapy in patients with breast cancer? *Breast Cancer Research & Treatment, 135*(1), 17-28.

Citation 16 is a SR and MA of studies examining the use of diffusion-weighted MRI and contrast-enhanced MRI for monitoring response to neoadjuvant chemotherapy. The authors conclude that DW-MRI is highly sensitive and CE-MRI is highly specific in predicting pathological response to neoadjuvant chemotherapy. The authors propose that future studies should examine the combination of these tests for assessing response to neoadjuvant treatment.

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Appendix A. Methods

Search Strategy

A full search of the core sources was conducted to identify systematic reviews, meta-analyses, technology assessments, and clinical practice guidelines using the terms "MRI breast," "MRI breast diagnos*," and "magnetic resonance imaging breast diagnos*." Searches of core sources were limited to citations published after 2009.

The core sources searched included:

- Agency for Healthcare Research and Quality (AHRQ)
- Blue Cross/Blue Shield Health Technology Assessment (HTA) program
- *BMJ Clinical Evidence*
- Canadian Agency for Drugs and Technologies in Health (CADTH)
- Cochrane Library (Wiley Interscience)
- Hayes, Inc.
- Medicaid Evidence-based Decisions Project (MED)
- National Institute for Health and Care Excellence (NICE)
- Tufts Cost-effectiveness Analysis Registry
- Veterans Administration Evidence-based Synthesis Program (ESP)
- Washington State Health Technology Assessment Program

A MEDLINE® (Ovid) search was conducted to identify systematic reviews, meta-analyses, and technology assessments published after the search dates of original evidence sources. The search was limited to publications in English published after 2009.

Searches for clinical practice guidelines were limited to those published since 2010. A search for relevant clinical practice guidelines was also conducted, using the following sources:

- Australian Government National Health and Medical Research Council (NHMRC)
- Centers for Disease Control and Prevention (CDC) – Community Preventive Services
- Institute for Clinical Systems Improvement (ICSI)
- National Guidelines Clearinghouse
- New Zealand Guidelines Group
- NICE
- Scottish Intercollegiate Guidelines Network (SIGN)
- United States Preventive Services Task Force (USPSTF)
- Veterans Administration/Department of Defense (VA/DOD)

Inclusion/Exclusion Criteria

Studies were excluded if they were not published in English, did not address the scope statement, or were study designs other than systematic reviews, meta-analyses, technology assessment, or clinical practice guidelines.