Health Technology Clinical Committee
Findings and Coverage Decision
Topic: **Breast MRI**
Meeting Date: **August 20th, 2010**
Final Adoption: **October 22nd, 2010**

Number and Coverage Topic

20100820A – Breast MRI

HTCC Coverage Determination

Breast MRI is a **covered benefit with conditions** consistent with the criteria identified in the reimbursement determination.

HTCC Reimbursement Determination

❖ Limitations of Coverage

Breast MRI is a covered benefit for screening for breast cancer, with a minimum of 11 months between screenings in women at high risk of breast cancer. Women at high risk are defined as:

- A personal history or strong family history of breast cancer;
- A genetic mutation of BRCA 1, BRCA2, TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes);
- GAIL model lifetime cancer risk of 20% or higher; or
- History of radiation treatment to the chest between ages 10 and 30, such as for Hodgkin's disease.

❖ Non-Covered Indicators

- N/A

❖ Agency Contact Information

Agency	Contact Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plan	1-800-762-6004
Health and Recovery Services Administration	1-800-562-3022

Health Technology Background

The Breast MRI topic was selected and published in December 2009 to undergo an evidence review process. The evidence based technology assessment report indicates that in 2009, an estimated 192,370 cases and 40,170 deaths occurred in women with breast cancer (National Cancer Institute, 2010) in the US. 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 based on randomized controlled trials (RCTs) and concluded that film mammography was the standard for detecting breast cancer in women at average risk of developing breast cancer (USPSTF 2002). Aim of Evidence Review: To systematically review, critically appraise and analyze research evidence regarding the accuracy, efficacy, effectiveness and safety of MRI in the detection of breast cancer in women at high risk for developing breast cancer. *High risk* – high risk for developing breast cancer is variously defined in clinical trials but frequently refers to women: with a calculated lifetime risk of 20% or greater; with a calculated risk of greater than 1% per year; with genetic BRCA1 or BRCA2 mutation; with a history of breast cancer; and with a family history consistent with a hereditary breast cancer syndrome. Other risk factors such as age, ethnicity, age at menarche, previous breast biopsy, parity, age at first birth are included in some risk calculation models.

Key Points – Safety: No reliable evidence for harm from increased radiation exposure; no reliable evidence to suggest that gadolinium-based contrast agents are associated with adverse outcomes in the fetus, infants or children; no reliable evidence for meaningful adverse psychological outcomes from false-positive MRI test results in women at high risk for breast cancer; and no reliable evidence for increased cancer in women with breast implants. Key Points – Cost and Cost Effectiveness: Adding MRI to mammographic breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs; accurately predicting mortality reduction and other health outcomes in high-risk women may not be possible unless results from valid RCTs become available; cost per QALYs gained range from approximately $25,000 to $311,000 depending upon assumptions about various costs, yearly risk, mortality reduction with the addition of MRI, frequency of screening, etc. The evidence based technology assessment report focused on two recent large systematic reviews (Lord, 2007 and Warner, 2008) found to be of acceptable quality. The evidence based technology assessment report identified 7 expert treatment guidelines and a CMS policy.

In June 2010, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed Breast MRI report is 83 pages, and identified a relatively large amount of literature.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on August 20, reviewed the report, including peer and public feedback, and heard public and agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at http://www.hta.hca.wa.gov under the committee section.

Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The committee concludes that the best available evidence on breast MRI has been collected and summarized. The evidence is presented below:

- The evidence based technology assessment report indicates that in 2009, an estimated 192,370 cases and 40,170 deaths occurred in women with breast cancer (National Cancer Institute, 2010) in the US.
- The evidence based technology assessment report summarized the evidence on accuracy and efficacy of MRI compared with conventional techniques for detecting breast cancer and its role in reducing breast cancer mortality and other meaningful health outcomes in women at increased risk for breast cancer based on abnormal mammogram, palpable breast anomaly or relevant demographic and clinical risk factors. Current practice as reflected through clinical guidelines does not support routine use of MRI in screening average risk women.
- Evidence included in the technology assessment review was obtained through systematic searches of the medical literature for relevant systematic reviews including meta-analyses, other diagnostic studies, randomized controlled trials and economic studies. Selected national guidelines and previous technology assessment were also summarized in the technology assessment report.
- The evidence based technology assessment report focused on two recent large systematic reviews (Lord, 2007 and Warner, 2008) found to be of acceptable quality.
    - Lord 07: 5 adequate studies involving a total of 2059 patients were included in the review of MRI accuracy in screening women at high risk. No studies addressed mortality or recurrence or earlier stage disease.
    - Warner 08: 11 included studies involving xx patients were included in the review of MRI accuracy in screening women at high risk. No studies addressed mortality, recurrence, or earlier stage disease.
    - Two additional studies were included in the review: Brennan 09 involved 22 studies of 3,253 women with breast cancer and Lehman 07 involving 969 women comparing detection in the contralateral breast with MRI compared to conventional screening.
    - Definition of high risk women varied among studies from gene mutation BRCA 1 and/or BRCA 2; previous history of breast cancer; family history of breast cancer; other gene mutations; lifetime risk of breast cancer over 20% or 25%
    - Trials assessed efficacy of MRI in screening of women at high risk when added to (not substitute) conventional screening usually mammography +/- ultrasound, +/- clinical breast exam
- The evidence based technology assessment report identified 7 expert treatment guidelines and a CMS policy.
- The committee also reviewed information provided by the state agencies; public members; and heard comments from the evidence reviewer, HTA program, agency medical directors and the public.

2. Is the technology safe?

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is safe. Summary of committee considerations follows.

- The evidence based technology assessment report reported several key outcomes related to safety of MRI in screening women at high risk of breast cancer, including: harms of test itself (no radiation, but contrast agents); psychological harms from screening, false positives and false negatives; harms by and from change in treatment, including unnecessary treatment (biopsy) with false positives; harms related to over diagnosis.
- The evidence based technology assessment report concluded that no evidence was found to suggest that MRI radiation exposure results in adverse outcomes for women at high risk of breast cancer being screened with MRI. The evidence from observation studies suggests that gadolinium-based agents (with the possible exception of gadodiamide) may be safely used as MRI contrast agents in non-pregnant adults without chronic kidney disease (CKD).
- The report concludes that insufficient evidence exists to conclude that false-positive breast cancer screening tests or recalling patients for false positive tests leads to clinically meaningful negative psychological outcomes.
    - One narrative review of 313,967 women at average risk for breast cancer reported no long-term symptoms of depression in women with false positive mammograms (Brewer, 2007).
- No other evidence was reported on the harms of unnecessary treatment and over diagnosis. Evidence about change in treatment discussed in efficacy.

3. Is the technology effective?

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is effective. Summary of committee considerations follows.

- The evidence about the efficacy and effectiveness included outcomes of: diagnostic accuracy (sensitivity and specificity); reduction in mortality; reduced need for other tests; changes in treatment plan; excision and re-excision rates; and cancer recurrence rates.
- Overall: The evidence based technology assessment report concluded that adding yearly screening with MRI to mammographic screening will increase detection of breast cancer. The increase in cancer detection is offset by a higher rate of false positive tests, benign breast biopsies, and more extensive surgeries, including an increase in more unnecessary mastectomies; no reliable evidence exists on reduction in mortality, recurrence, or re-excision rates.
- Diagnostic accuracy: The evidence based technology assessment report concluded that adding yearly screening with MRI to mammographic screening will increase detection of breast cancer. Based on higher quality evidence about sensitivity, the addition of MRI to annual breast cancer screening with mammography will
    - Detect an estimated additional 2 to 5 breast cancer per 100 screenings.
    - Add more false positives, resulting in 11 additional benign biopsies per 100 screening rounds.
- Diagnostic accuracy in contralateral breast: The evidence based technology assessment report concluded that MRI detects contralateral breast lesions in 9% more women than mammography alone, but does not reliably distinguish benign from malignant findings with a positive predictive value of 47%.
- Reduction of need for other tests: The evidence based technology assessment report concluded that insufficient evidence exists to conclude that, in high risk women, the addition of MRI to mammographic screening reduces the need for mammography or ultrasound. Current trials and convention focus on addition of MRI, not replacement test.
- Change in treatment: The evidence is borderline quality, but sufficient to conclude that adding MRI screening in high risk women and preoperative MRI testing in women with recently

diagnosed breast cancer will change treatment plans for some women, however evidence is inconclusive as to whether the treatment change is beneficial.
  - 15.7% of women will have change in treatment
  - Wide local excision to more extensive surgery occurs in 11%
  - Wide excision to mastectomy occurs in 8%
  - Women with dense breasts may experience change (44% based on one retrospective study).
  - 7% of women with changes in treatment based on MRI had benign lesions
- Health Outcomes: The evidence is insufficient to conclude whether adding MRI screening in high risk women impacts health outcomes of mortality, recurrence, or re-excision.
  - Evidence on re-excision rates exists but is conflicting and low level, ranging from no difference to 18% decrease in re-excision in women who pre-operatively underwent MRI
  - Evidence on recurrence also conflicts with one study reporting a 5% reduction in recurrence rates while another larger study (both observational) showing no difference over 8 years.
  - No evidence assessed effect of adding MRI on mortality rates.

4. Special Populations?

- *Breast Implants:* the evidence based technology assessment report stated that insufficient evidence exists to conclude that breast implants increase the risk of developing breast cancer. Adding MRI to mammography appears to increase the detection rate for breast cancer in women with increased breast density.
- *Technical specifications and provider issues in MRI Testing:* the evidence is insufficient for establishing technical MRI specifications or establishing provider qualifications.

5. Is the technology cost-effective?

The committee discussed multiple key factors that were important for consideration in their overall decision on whether the technology has value and is cost-effective. Summary of committee considerations follows.

- The evidence based technology report concluded that adding MRI to mammography breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs.
  - Accurately estimating cost-effectiveness may not be possible because RCTs evaluating the mortality reduction with screening or testing women at high-risk for breast cancer have not been conducted.
- Washington state agency utilization and cost information indicated 5 year Breast MRI costs of $3,111,943 for UMP/PEP and $466,449 for DSHS.

6. Medicare Decision and Expert Treatment Guidelines

Committee reviewed and discussed the expert guidelines as identified and reported in the technology assessment report.

- Centers for Medicare and Medicaid Services (CMS), 2007 – annual breast cancer screening with clinical examination and mammography is covered by Medicare. Breast cancer screening with MRI is not covered as a routine preventive measure (preventive services must be specifically covered). However, breast MRI may be covered as a diagnostic procedure.
- Guidelines – 7 recent guidelines were identified providing specific recommendations for women at increased risk of breast cancer. Recommendations for this population were also found in the National Institute for Health and Clinical Excellence (NICE) database.

- Two guidelines were rated as high quality and are summarized:
  - (1) USPSTF, 2009 – if a woman has an abnormal mammographic finding on screening or a concerning finding on a physical examination, additional imaging and biopsy may be recommended. Additional imaging may help classify the lesion as a benign or suspicious finding to determine the need for biopsy.
    - The focus of the guideline was on women at average risk of breast cancer. Relevant evidence mentioned by the USPSTF is retrospective observational data and from expert opinion and is rated as medium risk or high risk of bias.
    - Breast MRI improved local staging in almost 20% of patients and that preoperative breast MRI studies may be particularly useful in surgical planning for, and managing of, patients with lobular carcinoma.
  - (2) National Cancer Institute, 2010 (last updated) – based on fair evidence, screening mammography in women aged 40 to 70 years decreases breast cancer mortality. The benefit is higher for older women, in part because their breast cancer risk is higher.
- One guidelines was rated as fair quality and are summarized below:
  - (1) NICE, 2006 – adding MRI to mammography increases sensitivity over mammography alone in screening for breast cancer in women at high risk; mammography may be useful adjunct to MRI in the high risk group; MRI is more sensitive than mammography in BRCA1 carriers; MRI combined with mammography is a cost-effective intervention in women with BRCA1 mutation aged 30-49; annual MRI combined with mammography is a cost-effective intervention in non-BRCA1 women aged 30-39 with an 8% or greater 10-year risk; and MRI combined with mammography is a cost-effective intervention in non-BRCA1 women aged 40-49 with a 20% or greater 10-year risk.
- Four guidelines were rated as low quality, those included: American College of Radiologists (ACR), 2010; European Society of Breast Cancer Specialists (EUSOMA) working group, 2010; National Comprehensive Cancer Network (NCCN), 2009 and American Cancer Society, 2007.

Committee Conclusions

Having made findings as to the most significant and relevant evidence regarding health outcomes, key factors and identified evidence related to those factors, primarily based on the evidence based technology assessment report, the committee concludes:

1. Evidence availability and technology features

The committee concludes that the best available evidence on Breast MRI has been collected and summarized.

- This evidence review summarized the evidence on the accuracy and efficacy of MRI compared with conventional techniques (mammography, sometimes with ultrasound and sometimes with clinical breast exam) for detecting breast cancer and its role in reducing breast cancer mortality and other meaningful health outcomes in women at increased risk for breast cancer.

2. Is it safe?

The committee concludes that the comprehensive evidence indicates that Breast MRI is equally safe to alternative tests. Key factors to the committee's conclusion included:

- The committee agreed that MRI screening in addition to mammography and/or other tests does not create additional radiation risk from the test itself, though there may be rare harms associated with the gadolinium-based MRI contrast agents.
- The addition of Breast MRI as a screening tool will result in additional false positives and treatment, including biopsy and potential harms from biopsy.

- The committee agreed that the psychological harms related to the testing may be present but were well tolerated.

3. Is it effective?

The majority of the committee concludes that the comprehensive evidence shows that Breast MRI is more effective treatment than other conventional medical treatments.

- The committee agreed that sufficient evidence exists to conclude that for women at high risk, adding yearly screening with MRI to mammographic screening increases detection of breast cancer, likely between 2 to 5 cancers per 100.
- The committee agreed that the increase in cancer detection is offset by a higher rate of false positive tests, about 10 in 100, which will lead to additional benign breast biopsies.
- The committee also agreed that Breast MRI changed treatment, including an increase in more extensive surgeries, including an increase in mastectomies, some of which may be unnecessary; and that evidence about the ultimate health impact of the changed treatment is inconclusive. For instance, re-excision rates varied widely from 5% to 50%.
- The committee agreed that there is no evidence about the effect of Breast MRI on mortality rates, but that mammography screening (early detection) does reduce mortality, and the evidence reviewed indicates more cancers are found through Breast MRI in high risk women.

4. Evidence about the technology's special populations, patient characteristics and adjunct treatment

The committee agreed that no compelling evidence exists to differentiate sub groups or special populations.

- The committee agreed with the evidence based report that there is inadequate evidence to conclude that patients with breast implants, increased breast density, or fibroglandular breast tissue benefit from Breast MRI or are at increased risk of breast cancer.

5. Is it cost-effective?

The committee concludes that the Breast MRI is unproven to be cost effective; agreeing with the comprehensive evidence review that no evidence based conclusions about cost effectiveness can be drawn.

- The evidence report adequately summarized the moderate quality evidence that because Breast MRI is a more expensive and additional test, adding Breast MRI will increase diagnostic and therapeutic costs.
- The evidence report also adequately summarized the poor cost-effectiveness evidence about whether Breast MRI screening in addition to mammography is cost effective largely because cost-effectiveness is highly dependent on mortality reduction and no evidence is available about mortality reduction.
- Committee acknowledged the state agency costs of breast cancer. Costs were nearly 3.6M and averaged $950 per treatment over the 5 years beginning in 2005.

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Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

The committee concluded that the current evidence on Breast MRI demonstrates that there is sufficient evidence to cover with conditions the use of Breast MRI in diagnosis and treatment of cancer in women at high risk. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Based on these findings, the committee voted 7 to 2 to cover with conditions Breast MRI. Breast MRI is a covered benefit for screening for breast cancer with a minimum of 11 months between screenings in women at high risk of breast cancer. Women at high risk are defined as:

1. A personal history or strong family history of breast cancer;
2. A genetic mutation of BRCA 1, BRCA2, TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes);
3. GAIL model lifetime cancer risk of 20% or higher; or
4. History of radiation treatment to the chest between ages 10 and 30, such as for Hodgkin's disease.

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to engage in a process for evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and takes public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State Health Technology Clinical Committee (HTCC) determines how selected health technologies are covered by several state agencies (RCW 70.14.080-140). These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.