Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 5/1/21**
(See policy history boxes for previous effective dates)

Title: Computer-Aided Evaluation as an Adjunct to Magnetic Resonance Imaging of the Breast

Description/Background

Magnetic resonance imaging (MRI) of the breast may be used to: screen women at high risk of breast cancer, to detect the extent of disease in women diagnosed with breast cancer who are eligible for breast-conserving surgery, and to monitor the impact of breast cancer treatment. While MRI of the breast has been shown to have high sensitivity in detecting breast lesions, it has a high false positive rate because of the difficulty in distinguishing between benign and malignant lesions. The use of computer-aided evaluation (CAE) as an adjunct to MRI is designed to assist radiologists' interpretation of contrast-enhanced MRI of the breast, improving specificity while maintaining high sensitivity.

Benefits of improved detection and measurement with MRI include: reduction in biopsy rates when MRI-detected lesions are identified as benign; reduction in reoperation rates identifying when tissue that should be removed is clearly identified; and reduction in time needed to interpret breast MRI images.

CAE systems for MRI are designed to facilitate the interpretation of MRIs by detecting patterns of contrast enhancement across a series of images, which in turn may help identify lesions and their likelihood of being malignant. There are 2 aspects of enhancement (also called kinetics): (1) Within the first 1 to 2 minutes of the contrast injection, how quickly does the lesion enhance? and (2) What is the subsequent pattern of enhancement?[1] Malignant lesions demonstrate a rapid enhancement in contrast within the first 1 to 2 minutes after the contrast injection, followed by a washout period in which the contrast fades within minutes. Benign lesions exhibit a slow progressive rise in intensity, with no washout of the contrast.

A large number, potentially hundreds 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 pick a region of interest and look at the enhancement pattern. There may be variations across radiologists in the regions of interest selected and in the precise definition of the region of interest. CAE systems use color-coding and differences in hue to indicate the pattern of enhancement for each pixel in the breast image, thereby allowing radiologists to analyze enhancement patterns systematically.

Regulatory Status:

Several CAE systems for use with MRI of the breast have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Examples of FDA-cleared devices include:

- SpectraLook®, part of iCAD's VersaVue® Enterprise Suite (iCAD) was cleared for marketing by FDA through the 510(k) process in 2012. The VersaVue Suite is intended for postprocessing of magnetic resonance images as a means for visualizing these images. A previous version of this device, 3TP (3Time Point) was FDA-cleared in 2008.
- CADstream® (Merge Healthcare) was cleared for marketing by FDA through the 510(k) process in 2003, at which time it was distributed by Confirma (Kirkland, WA).
- Aegis™ Breast (Sentinelle Medical; now from Hologic) was cleared for marketing by FDA through the 510(k) process in 2007. However, in the 510(k) documents, the manufacturer states that the primary goal of the technology is "to identify where and how deep a biopsy or localization needle should be inserted into an imaged breast."
- DynaCAD for Breast (MRI Devices; now from Invivo) was cleared for marketing by FDA through the 510(k) process in 2004.

The FDA in January 2020 reclassified "medical imaging analyzers, including computer-assisted/aided detection (CADe) devices, for mammography breast cancer)" … from class III to II. A medical imaging analyzer "is a prescription device that is intended to mark, highlight, or in any other manner direct the clinicians' attention to portions of a radiology image that may reveal abnormalities during interpretation of patient radiology images by the clinicians. This device incorporates pattern recognition and data analysis capabilities and operates on previously acquired medical images. This device is not intended to replace the review by a qualified radiologist, and is not intended to be used for triage, or to recommend diagnosis. Under this final order, the medical image analyzer is a prescription use only device."

Medical Policy Statement

The use of computer-aided evaluation for interpretation of contrast-enhanced magnetic resonance imaging (MRI) of the breast is considered experimental/investigational**.** Although it may be safe, its effectiveness has not been proven.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

77048 77049

Rationale

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

COMPUTER-AIDED EVALUATION AS AN ADJUNCT TO MAGNETIC RESONANCE IMAGING

Clinical Context and Test Purpose

Magnetic resonance imaging (MRI) of the breast may be used: (1) to screen women at high risk for breast cancer, (2) to distinguish between malignant and benign lesions in women with suspected breast cancer, and (3) to provide more detailed views of lesions in women diagnosed with breast cancer who are planning treatment. The purpose of computer-aided evaluation (CAE) as an adjunct to MRI of the breast is to assist with the interpretation of the images, with the goal of improving the specificity of MRIs while maintaining high sensitivity.

The question addressed in this evidence review is: Does the use of CAE as an adjunct to MRI of the breast improve the net health outcome in women at risk for breast cancer, with suspected breast cancer, or with a breast cancer diagnosis compared with MRI interpretation without CAE?

The following PICO was used to select literature to inform this review.

Patients
The relevant populations of interest are:

- Women at increased risk for breast cancer, which includes those with:
  - *BRCA1* or *BRCA2* variant
  - A first-degree relative with a *BRCA1* or *BRCA2* gene
  - Radiotherapy to the chest area between the ages of 10 and 30
  - Li-Fraumeni, Cowden, *PTEN* hamartoma tumor syndrome or Bannayan-Riley-Ruvalcaba syndromes
  - *PALB2*, *PTEN*, or *TP53* variants
  - Greater than 20% lifetime risk of invasive breast cancer based on family history.[2]
- Women with suspected breast cancer
- Women with a breast cancer diagnosis who are planning treatment.

Interventions
The comparator of interest is CAE as an adjunct to breast MRI. CAE systems use color-coding and differences in hue to indicate the pattern of enhancement in the tissues, thereby allowing radiologists to analyze enhancement patterns systematically.

CAE is administered in a tertiary care center or a specialty MRI center.

Comparators
The following test is currently being used to make decisions about managing women with or at risk of breast cancer: breast MRI without CAE.

CAE is administered in a tertiary care center or imaging center.

Outcomes
To assess clinical validity, the outcomes of interest are comparisons of sensitivity and specificity of MRI of the breast, with and without the use of CAE.

To assess clinical utility, the primary outcomes of interest are improvements in overall survival and breast cancer-specific mortality. Also of interest is the avoidance of invasive procedures, as outlined below:

- For women at increased risk of breast cancer, the incremental increase in the detection of breast cancer using CAE, compared with MRI interpretation without CAE, may result in earlier less invasive treatment.
- For women with suspected breast cancer, the incremental increase in malignancy detection using CAE, compared with MRI interpretation without CAE, may be reflected in lower biopsy rates or lower rates of further work-ups.
- For women with a breast cancer diagnosis who are planning treatment, the incremental increase in information on the extent of the disease (eg, size and location of lesions) using CAE, compared with MRI interpretation without CAE, may influence the surgical decision (eg, lumpectomy vs mastectomy).

Clinical follow-up of at least 1 to 2 years is necessary to monitor suspicious lesions or progression of tissue adjacent to resected malignant lesions.

Study Selection Criteria
For the evaluation of clinical validity of CAE as an adjunct to MRI, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of a CAE device approved by the Food and Drug Administration
- Included a suitable reference standard (pathologic confirmation of breast cancer)
- Patients' clinical characteristics were described
- Patient selection criteria were described.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

To demonstrate the impact of computer-aided evaluation (CAE) in the diagnosis of breast cancer, studies that compare sensitivity and specificity of magnetic resonance imaging (MRI) with and without the use of CAE systems are needed. Such studies can demonstrate the incremental diagnostic accuracy of CAE compared to no CAE. Ideally, these studies should be prospective and should evaluate a population of patients similar to that presenting for breast cancer screening or diagnosis in a clinical setting.

Systematic Reviews
Two systematic reviews identified have evaluated clinical validity. One is a TEC Assessment (2006)[3] and the other as a systematic review by Dorrius et al (2011).[4] The TEC Assessment did not pool results; ranges of sensitivities and specificities from studies that evaluated the distinction between malignant and benign lesions are reported in Table 1. A study by Deurloo et al (2005) included in the TEC Assessment (2006), evaluated women with pathologically proven breast cancer who were scheduled for breast-conserving therapy, in order to use MRI to detect additional findings.[5] Reviewers reported that MRI detected other lesions or larger lesions in 48 (41%) of the women. Dorrius et al (2011) conducted meta-analyses on all radiologists and on subgroups by the level of experience, with and without CAE on the ability to distinguish between malignant and benign lesions (Table 2). Statistical heterogeneity was moderate to substantial (I^2 range, 56%-83%) for all results except for the specificity of residents' readings both with and without CAE, which had low-to-moderate statistical heterogeneity (I^2 range, 24%-33%). Sub-group analyses showed that the use of CAE did not improve the sensitivity and specificity among experienced radiologists; however, radiologists in training experienced improved, but not statistically significant, increases in sensitivity with CAE compared to not using CAE.

Table 1. Characteristics of Systematic Reviews Assessing Clinical Validity

Study	Literature Search	Design	Study Population	Purpose of Studies	Reference Standard	Blinding of Assessors
TEC Assessment (2006)[3,]	Mar 2006	4 prospective studies (307 women)	• Women with lesions not yet pathologically proven (3 studies) • Women with pathologically proven cancer scheduled for BCT (1 study)	• Distinguish between malignant and benign lesions • Determine if additional findings might change treatment strategy	Pathology results	2 studies had blinded assessors; 2 studies had unblinded assessors
Dorrius et al (2011)[4,]	Dec 2010	3 prospective and 7 retrospective studies (895 women; 1264 lesions)	Women with benign or malignant breast lesions who had MRI	Distinguish between malignant and benign lesions	Pathology results	Not discussed

BCT: breast-conserving therapy; MRI: magnetic resonance imaging.

Table 2. Results of Systematic Reviews Assessing Clinical Validity

Study	No. of Studies	*Clinical Validity (95% CI), %*	
		Sensitivity	***Specificity***
TEC Assessment (2006)[3,]			
Without computer-aided evaluation	2	91-93[a]	82-93[a]
With computer-aided evaluation	2	87-92[a]	84-86[a]
Dorrius et al (2011)[4,]			
All radiologists, magnetic resonance imaging	4	82 (72 to 90)	81 (74 to 87)
All radiologists, magnetic resonance imaging + computer-aided evaluation	8	89 (83 to 93)	81 (76 to 85)
Experienced radiologists, magnetic resonance imaging	4	89 (78 to 94)	86 (79 to 91)
Experienced radiologists, magnetic resonance imaging + computer-aided evaluation	8	89 (81 to 94)	82 (76 to 87)
Resident, magnetic resonance imaging	3	72 (62 to 81)	79 (69 to 86)
Resident, magnetic resonance imaging + computer-aided evaluation	3	89 (80 to 94)	78 (69 to 84)

CI: confidence interval. [a] Range.

Retrospective Diagnostic Accuracy Studies

Larger representative diagnostic accuracy studies published after the 2011 systematic review are described next. All studies are retrospective analyses that included populations of patients not reflective of those seen in clinical care. Most were conducted in Asia where protocols may differ from those used in the United States. Tables 3 and 4 present study characteristics and diagnostic accuracy results.

Yun et al (2016) in South Korea conducted a respective study of 124 patients newly diagnosed with breast cancer.[6] Patients underwent conventional MRI and MRI with CAE as part of a preoperative assessment of the extent of breast cancer. A commercially available CAE device

was used (CADstream). Images were evaluated by 2 experienced radiologists blinded to histopathology results or patient characteristics.

Song et al (2015) in Korea retrospectively evaluated 86 patients with invasive breast cancer using MRI alone, MRI plus CAE, mammography, ultrasound computed tomography, and fluorine 18 fluorodeoxyglucose with positron emission tomography.[7] For MRI plus CAE, the CADstream device was used, and pathologic analysis was used, as the reference standard. Two experienced radiologists blinded to the pathology report independently evaluated each image and final decisions reached by consensus.

Liu et al (2014) retrospectively compared radiologists' readings of 3.0-Tesla MRI images with readings by CAE (DynaCAD) in 78 consecutive patients with newly diagnosed breast lesions at a single institution in China.[8] Three experienced radiologists blinded to histologic diagnosis performed MRI readings and 3 radiologists performed CAE readings; it is unclear whether these were the same radiologists. Results may be applicable only to patients with lesions greater than 0.8 cm and possibly only to readings made by 3.0-Tesla MRI.

Lehman et al (2013) reported on a U.S.-based multicenter, retrospective study of 9 experienced and 11 inexperienced radiologists who read a set of dynamic contrast-enhanced breast MRIs twice, once with and once without CADstream.[9] Specificity (BI-RADS category 3 [considered negative]) did not change with the addition of CAE for either group.

Table 3. Characteristics of Retrospective Studies Assessing Clinical Validity

Study	Country	Dates	Study Population	Number	Reference Standard	Outcomes
Yun et al (2016)[6],	South Korea	2011-2014	Women who underwent MRI and MRI with CAE for presurgery assessment of breast cancer	124 women (34 ALN-positive; 90 ALN-negative)	Pathology results	Identify malignant vs benign ALN in patients with breast cancer
Song et Al (2015)[7],	South Korea	2008-2012	Women with invasive breast cancer who underwent MRI, MRI with CAE, mammography, US, CT, and FDG-PET	86 women	Pathology results	Lymph node status, overall accuracy of imaging techniques
Liu et al (2014)[8],	China	2010-2011	Women diagnosed with breast lesions who underwent MRI and MRI with CAE	78 women (93 lesions)	Pathology results	Identify malignant vs benign breast lesions
Lehman et al (2013)[9],	U.S.	NR	Radiologists (9 experienced, 11 novices) interpreting MRIs, with and without CAE	27 benign and 43 malignant lesions	Pathology results	Identify malignant vs benign breast lesions

ALN: axillary lymph nodes; CAE: computer-aided evaluation; CT: computed tomography; FDG-PET: fluorine 18 fludeoxyglucose positron emission tomography; MRI: magnetic resonance imaging; NR: not reported; US: ultrasound.

Table 4. Results of Retrospective Studies Assessing Clinical Validity

Study	Outcome	N	Clinical Validity (95% CI), %			
			Sensitivity	***Specificity***	***PPV***	***NPV***
Yun et al (2016)[6],	Malignant/benign ALN	124				
MRI			82.4	85.6	68.3	92.7
MRI + CAE			91.2	94.4	86.1	96.6

Song et al (2015)[7,]	Lymph node status	86				
Mammography			36.2	86.8	76.2	54.1
Ultrasound			61.4	92.3	90.0	67.3
Computed tomography			63.6	78.9	77.8	65.2
MRI			61.4	73.7	73.0	62.2
MRI + CAD			47.7	68.4	63.6	53.1
FDG-PET			47.7	81.6	75.0	57.4
	Multifocality evaluation	86				
Mammography			66.7	89.5	NR	NR
Ultrasound			83.3	71.3	NR	NR
Computed tomography			66.7	79.0	NR	NR
MRI			100.0	61.8	NR	NR
MRI + CAE			100.0	77.6	NR	NR
FDG-PET			33.3	93.4	NR	NR
Liu et al (2014)8,a	Malignant/benign lesions	93				
MRI			73.1	75.6	79.2	68.9
MRI + CAE			90.4	82.9	87.0	87.2
Lehman et al (2013)9,	Malignant/benign lesions	70				
Experienced, MRI			84 (78 to 90)	61 (52 to 71)	78 (74 to 82)	70 (64 to 76)
Experienced, MRI + CAE			91 (88 to 95)	62 (52 to 72)	80 (76 to 83)	81 (76 to 87)
Novice, MRI			77 (71 to 84)	67 (58 to 76)	79 (76 to 83)	64 (59 to 70)
Novice, MRI + CAE			83 (77 to 90)	63 (56 to 71)	79 (75 to 82)	70 (64 to 75)

ALN: axillary lymph nodes; CAE: computer-aided evaluation; CI: confidence interval; FDG-PET: fluorine 18 fludeoxyglucose positron emission tomography; MRI: magnetic resonance imaging; NPV: negative predictive value; NR: not reported; PPV: positive predictive value.
[a] Calculated by BCBSA.

The purpose of the limitations tables (Tables 5 and 6) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

Table 5. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Yun et al (2016)[6,]					1.Follow-up duration not sufficient (no clinical follow-up)
Song et al (2015)[7,]					1. Follow-up duration not sufficient (no clinical follow-up)
Liu et al (2014)[8,]				3. Did not report key clinical validity outcomes (calculated by BCBSA)	1. Follow-up duration not sufficient (no clinical follow-up)
Lehman et al (2013)[9,]					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest.
[c] Comparator key: 1. Classification thresholds not defined; 2. Not compared to credible reference standard; 3. Not compared to other tests in use for same purpose.
[d] Outcomes key: 1. Study does not directly assess a key health outcome; 2. Evidence chain or decision model not explicated; 3. Key clinical validity outcomes not reported (sensitivity, specificity, and predictive values); 4. Reclassification of diagnostic or risk categories not reported; 5. Adverse events of the test not described (excluding minor discomforts and inconvenience of venipuncture or noninvasive tests).
[e] Follow-Up key: 1. Follow-up duration not sufficient with respect to natural history of disease (true-positives, true-negatives, false-positives, false-negatives cannot be determined).

Table 6. Study Design and Conduct Limitations

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
Yun et al (2016)[6]						
Song et al (2015)[7]						
Liu et al (2014)[8]						
Lehman et al (2013)[9]	1. No description of how radiologists were recruited to participate in study	1. Blinding of radiologists not discussed				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).
[b] Blinding key: 1. Not blinded to results of reference or other comparator tests.
[c] Test Delivery key: 1. Timing of delivery of index or reference test not described; 2. Timing of index and comparator tests not same; 3. Procedure for interpreting tests not described; 4. Expertise of evaluators not described.
[d] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[e] Data Completeness key: 1. Inadequate description of indeterminate and missing samples; 2. High number of samples excluded; 3. High loss to follow-up or missing data.
[f] Statistical key: 1. Confidence intervals and/or p values not reported; 2. Comparison with other tests not reported.

Section Summary: Clinically Valid

A TEC assessment (2006) found insufficient literature on the use of MRI with CAE to detect malignant lesions of the breast, and a 2011 systematic review did not find statistically significant differences in diagnostic accuracy with CAE plus MRI and MRI alone. Several studies were published after the systematic review and most also did not find that CAE plus MRI, resulted in statistically significant improvements in diagnostic accuracy. Studies were retrospective in nature and tended to include women already diagnosed with breast cancer. Additionally, studies did not include clinical follow-up.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials.

Retrospective Studies

While no prospective trials were identified, 2 retrospective analyses, evaluating disease-specific survival have been identified. Nam et al (2018)[10] and Kim et al (2017)[11] reviewed the medical records of women with invasive breast cancer who had undergone MRI with a commercially available CAE system (Table 7). Univariate and multivariate Cox proportional hazards modeling were conducted to evaluate the association between CAE-generated kinetic features and survival. Kinetic features in the model included: peak signal intensity, early-phase enhancement (medium or rapid), and delayed-phase enhancement (persistent, plateau, and washout). Clinical and pathological variables, such as age, T stage, N stage, histologic grade, estrogen-receptor status, human epidermal growth factor 2 status, and lymphovascular invasion were added to the model. Table 8 presents the results of the analyses.

Table 7. Characteristics of Retrospective Studies Assessing Clinical Utility

Study	Country	Dates	Study Population	N	Outcomes	Median FU, mo
Nam et al (2018)[10]	Taiwan	2011	Women with invasive breast cancer who underwent preoperative MRI with CAE	301	Association between kinetic features of CAE and DFS	55
Kim et al (2017)[11]	South Korea	2012-2013	Women with newly diagnosed invasive breast cancer who had undergone MRI and surgery	329	Association between kinetic features of CAE and recurrence and DFS	50

CAE: computer-aided evaluation; DFS: disease-free survival; FU: follow-up; MRI: magnetic resonance imaging

Table 8. Multivariate Cox Proportional Hazard Analysis of Clinical, Pathologic, and CAE-Generated Kinetic Parameters With Survival

Study	Hazard Ratio	95% Confidence Interval	p
Nam et al (2018)[10]			
Peak enhancement	1.004	1.001 to 1.006	0.013
T stage			
1	Reference		
2	1.669	0.737 to 3.779	0.220
3	3.046	0.524 to 17.698	0.215
4	0	0 to ¥	0.998
N stage			
0	Reference		
1	1.267	0.534 to 3.004	0.591
2	0.851	0.185 to 3.914	0.836
3	3.040	0.872 to 10.598	0.081
Histologic grade			
1	Reference		
2	3.227	0.704 to 14.784	0.131
3	3.162	0.596 to 16.775	0.176
Molecular subtype			
Luminal	Reference		
HER2 enriched	3.538	0.314 to 39.828	0.306
Triple-negative	21.060	2.675 to 165.780	0.004

Adjuvant endocrine therapy			
Yes	Reference		
No	3.282	0.409 to 26.305	0.263
Kim et al (2017)11,			
Tumor size	0.993	0.766 to 1.287	0.959
Axillary lymph node			
Positive	0.976	0.46 to 2.237	0.954
Negative	Reference		
Histologic grade			
3	1.098	0.502 to 2.404	0.814
1 or 2	Reference		
Lymphovascular invasion			
Positive	3.011	1.302 to 6.962	0.010
Negative	Reference		
Ki-67 protein status			
High (≥14%)	1.202	0.511 to 2.823	0.674
Low (<14%)	Reference		
Adjuvant endocrine therapy			
No	1.741	0.815 to 3.718	0.152
Yes	Reference		
Peak enhancement	1.001	1.000 to 1.002	0.004
Angio-volume	1.006	0.987 to 1.026	0.510
Washout component	1.029	1.005 to 1.054	0.017

CAE: computer-aided evaluation; *HER2*: human epidermal growth factor 2

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.
Decisions for biopsies may be changed as a result of CAE; Biopsies may be performed in areas of abnormality identified by CAE not seen on standard MRI. This might, in turn, improve the detection rate for malignancies. However, the number of unnecessary biopsies might increase when CAE is used if the test falsely identifies abnormalities.

Section Summary: Clinically Useful

Two retrospective analyses were identified that evaluated associations between CAE-generated kinetic features and survival among women with invasive breast cancer. Median follow-up was less than 5 years. Higher peak enhancement was associated with lower survival rates. However, peak enhancement was also associated with stage and histologic grade, so the incremental value of CAE-generated information remains unclear. Furthermore, there is insufficient information to formulate a model of indirect evidence to support clinical utility. Thus, the utility of CAE plus MRI in clinical care cannot be determined from the literature.

Summary of Evidence

For individuals with risk of breast cancer, with suspected breast cancer, or diagnosed with breast cancer, who receive CAE as an adjunct to breast MRI, the evidence includes diagnostic accuracy studies, retrospective studies, and systematic reviews. Relevant outcomes are disease-specific survival, test validity, and resource utilization. The most recent systematic review (2011) did not find a statistically significant improvement in sensitivity and specificity of CAE as an adjunct to MRI vs MRI alone. Moreover, retrospective studies published resulted in statistically significant improvement in diagnostic accuracy compared with MRI alone. Studies were generally conducted in women already diagnosed with breast cancer; there is less literature on breast cancer detection. However, there are no comparative studies evaluating the impact of CAE with MRI on patient management decisions or health outcomes compared with MRI alone. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Current breast cancer guidelines from the National Comprehensive Cancer Network do not address the use of CAE for contrast-enhanced MRI. These guidelines include those on breast cancer (v.6.2020),[12] breast cancer risk reduction (v.1.2020)[13] breast cancer screening and diagnosis (v.1.2020),[2] and the genetic/familial high risk assessment: breast, ovarian and pancreatic cancer (v.2.2021).[14]

American College of Radiology

The American College of Radiology (2016) amended its 2011 practice parameter for the use of MRI-guided breast interventional procedures.[15] There were no recommendations on use of computer-aided evaluation with breast MRI.

The American College of Radiology (2018) revised practice parameter for the Performance of Contrast-Enhanced Magnetic Resonance Imaging (MRI) of the Breast[16] states that computer-aided detection (CAD) software is commonly used at image interpretation to manage large datasets and highlight kinetic information.

U.S. Preventive Services Task Force Recommendations

U.S. Preventive Services Task Force recommendations for Breast Cancer: Screening (January 11, 2016) does not address computer-aided evaluation as an adjunct to MRI of the breast.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov did not identify any ongoing or unpublished trials that would likely influence this review.

Government Regulations

National:

There is no national coverage determination for computer-aided evaluation of malignancy with magnetic resonance imaging of the breast.

Local:

There is no local coverage determination for computer-aided evaluation of malignancy with magnetic resonance imaging of the breast.

The 2021 CMS Physician Fee Schedule has fees associated with codes 77048, 77049.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Computer-Aided Detection Mammography (Retired)
- Digital Breast Tomosynthesis (3-D Mammography)
- Magnetic Resonance Imaging for Detection and Diagnosis of Breast Cancer

References

1. Cheng L, Li X. Breast magnetic resonance imaging: kinetic curve assessment. Gland Surgery. Feb 2013;2(1):50-53. PMID 25093457
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer Screening and Diagnosis. Version https://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf Accessed 1/11/2021
3. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Computer-Aided Detection of Malignancy with Magnetic Resonance Imaging of the Breast. TEC Assessments 2006; Volume 21, Tab 4.
4. Dorrius MD, Jansen-van der Weide MC, van Ooijen PM, et al. Computer-aided detection in breast MRI: a systematic review and meta-analysis. Eur Radiol. Aug 2011;21(8):1600-1608. PMID 21404134
5. Deurloo EE, Peterse JL, Rutgers EJ et al. Additional breast lesions in patients eligible for breast-conserving therapy by MRI: impact on preoperative management and potential benefit of computerised analysis. Eur J Cancer. Jul 2005; 41(10):1393-401. PMID 15913987
6. Yun SJ, Sohn YM, Seo M. Differentiation of benign and metastatic axillary lymph nodes in breast cancer: additive value of MRI computer-aided evaluation. Clin Radiol. Apr 2016;71(4):403 e401-407. PMID 26875621

7. Song SE, Seo BK, Cho KR, et al. Computer-aided detection (CAD) system for breast MRI in assessment of local tumor extent, nodal status, and multifocality of invasive breast cancers: preliminary study. Cancer Imaging. Feb 08 2015;15:1. PMID 25888983
8. Liu YH, Xu L, Liu LH, et al. 3.0T MR-CAD: Clinical Value in Diagnosis of Breast Tumor Compared with Conventional MRI. J Cancer. Jul 2014;5(7):585-589. PMID 25057309
9. Lehman CD, Blume JD, DeMartini WB, et al. Accuracy and Interpretation Time of Computer-Aided Detection Among Novice and Experienced Breast MRI Readers. Am J Roentgenol. Jun 2013;200(6):W683-W689. PMID 23701102
10. Nam SY, Ko ES, Lim Y, et al. Preoperative dynamic breast magnetic resonance imaging kinetic features using computer-aided diagnosis: Association with survival outcome and tumor aggressiveness in patients with invasive breast cancer. PLoS One. Apr 2018;13(4):e0195756. PMID 29649266
11. Kim JJ, Kim JY, Kang HJ, et al. Computer-aided diagnosis-generated kinetic features of breast cancer at preoperative MR imaging: association with disease-free survival of patients with primary operable invasive breast cancer. Radiology. Jul 2017;284(1):45-54. PMID 28253106
12. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: breast cancer. Version 6.2020; September 8, 2020. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Accessed 1/11/21
13. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: breast cancer risk reduction. Version 1.2020; May 29, 2020 https://www.nccn.org/professionals/physician_gls/pdf/breast_risk.pdf Accessed 1/11/21
14. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Genetic/familial high-risk assessment: breast and ovarian. Version 2.2021; November 20, 2020. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf Accessed 1/11/21
15. Committee on Practice Parameters – Breast Imaging, American College of Radiology, Newell MS, et al. ACR Practice Guideline for the Performance of Magnetic Resonance Imaging-Guided Breast Interventional Procedures. 2016 (revised); https://www.acr.org/-/media/ACR/Files/Practice-Parameters/MR-Guided-Breast.pdf. Accessed 1/11/21.
16. ACR Practice Parameter for the Performance of Contrast-Enhanced Magnetic Resonance Imaging (MRI) of the Breast. Revised 2018. https://www.acr.org/-/media/ACR/Files/Practice-Parameters/MR-Contrast-Breast.pdf Accessed 1/11/21

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 1/11/21, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/08	3/6/08	5/1/08	Joint policy established
7/1/09	4/21/09	5/11/09	Routine maintenance
3/12/11	12/13/11	12/21/11	Routine maintenance
9/1/13	6/19/13	6/26/13	Routine maintenance
7/1/15	4/24/15	5/8/15	Routine maintenance Changed “detection” to “evaluation” in policy title and policy statement References and rationale updated
7/15/16	4/19/16	4/19/16	Routine approval
1/1/17	10/11/16	10/11/16	Routine review
1/1/18	10/19/17	10/19/17	Routine maintenance
1/1/19	10/16/18	10/16/18	Routine maintenance Title changed to “Computer-Aided Evaluation as an Adjunct to Magnetic Resonance Imaging of the Breast.” Previous title: Computer-Aided Evaluation of Malignancy with Magnetic Resonance Imaging of the Breast.
5/1/19	2/19/19		Code update: 0159T deleted as of 12/31/18; 77048 and 77049 effective as of 1/1/19.
5/1/20	2/18/20		Routine maintenance
5/1/21	2/16/21		Policy retired. Original CPT code on this policy, 0159T, was specific to computer-aided detection. The current codes on this policy are not specific to CAD only.

Next Review Date: This policy is retired and no longer subject to routine review

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: COMPUTER-AIDED EVALUATION AS AN ADJUNCT TO MAGNETIC RESONANCE IMAGING OF THE BREAST

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.