

# BREAST IMAGING FOR SCREENING AND DIAGNOSING CANCER

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[Instructions for Use](#) ⓘ

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## Related Commercial Policies

- [Omnibus Codes](#)
- [Preventive Care Services](#)

## Community Plan Policy

- [Breast Imaging for Screening and Diagnosing Cancer](#)

## COVERAGE RATIONALE

### The following are proven and medically necessary:

- Digital mammography for patients with dense breast tissue
- Breast magnetic resonance imaging (MRI) for patients at high risk for breast cancer as defined as having any of the following:
  - Personal history of atypical breast histologies
  - Family history or genetic predisposition for breast cancer
  - Prior therapeutic thoracic radiation therapy
  - Dense breast tissue with any one of the following risk factors:
    - Lifetime risk of breast cancer of  $\geq 20\%$ , according to risk assessment tools based on family history
    - Personal history of BRCA1 or BRCA 2 gene mutations
    - First-degree relative with a BRCA 1 or BRCA 2 gene mutation but not having had genetic testing themselves
    - Prior therapeutic thoracic radiation therapy between ages of 10-30
    - Personal history of Li Fraumeni Syndrome, Cowden syndrome or Bannayan-Riley-Ruvalcaba syndrome or a first-degree relative with one of these syndromes
- Breast ultrasound as an aid for radiologists to localize breast lesions and in guiding placement of instruments for cyst aspiration and percutaneous breast biopsies

### The following are unproven and not medically necessary due to insufficient evidence of efficacy:

- Breast magnetic resonance imaging (MRI) for patients with dense breast tissue not accompanied by defined risk factors as described above
- Magnetic resonance elastography (MRE) for breast cancer screening or diagnosis
- Scintimammography for breast cancer screening or diagnosis
- Electrical impedance scanning (EIS) for the detection of breast cancer
- Computer-aided detection (CAD) as an aid for radiologists to interpret contrast-enhanced magnetic resonance imaging (MRI) of the breast
- Breast ultrasound for routine breast cancer screening including patients with dense breast tissue
- Computer-aided detection (CAD) is unproven and/or not medically necessary as an aid for radiologists to detect breast cancer during ultrasound
- Computer-aided tactile breast imaging
- Automated breast ultrasound system

## APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan

document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

CPT Code	Description
0422T	Tactile breast imaging by computer-aided tactile sensors, unilateral or bilateral
76376	3D rendering with interpretation and reporting of computed tomography, magnetic resonance imaging, ultrasound, or other tomographic modality with image postprocessing under concurrent supervision; not requiring image postprocessing on an independent workstation
76377	3D rendering with interpretation and reporting of computed tomography, magnetic resonance imaging, ultrasound, or other tomographic modality; image postprocessing under concurrent supervision; requiring image postprocessing on an independent workstation
76391	Magnetic resonance (e.g., vibration) elastography
76498	Unlisted magnetic resonance procedure (e.g., diagnostic, interventional)
76499	Unlisted diagnostic radiographic procedure
76641	Ultrasound, breast, unilateral, real time with image documentation, including axilla when performed; complete
76642	Ultrasound, breast, unilateral, real time with image documentation, including axilla when performed; limited
77046	Magnetic resonance imaging, breast, without contrast material; unilateral
77047	Magnetic resonance imaging, breast, without contrast material; bilateral
77048	Magnetic resonance imaging, breast, without and with contrast material(s), including computer-aided detection (CAD real-time lesion detection, characterization and pharmacokinetic analysis), when performed; unilateral
77049	Magnetic resonance imaging, breast, without and with contrast material(s), including computer-aided detection (CAD real-time lesion detection, characterization and pharmacokinetic analysis), when performed; bilateral
77065	Diagnostic mammography, including computer-aided detection (CAD) when performed; unilateral
77066	Diagnostic mammography, including computer-aided detection (CAD) when performed; bilateral
77067	Screening mammography, bilateral (2-view study of each breast), including computer-aided detection (CAD) when performed

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HCPCS Code	Description
S8080	Scintimammography (radioimmunosциntigraphy of the breast), unilateral, including supply of radiopharmaceutical

## DESCRIPTION OF SERVICES

Mammography is a specific type of imaging that uses a low-dose x-ray system for examination of the breasts. This is considered the best available method for early detection of breast cancer, particularly in the case of small or nonpalpable lesions. An abnormal screening mammogram requires a diagnostic test to confirm whether cancer is present. Lesions that are suggestive of cancer are evaluated with tissue biopsy. If a noninvasive diagnostic test is available that can accurately exclude cancer; many women with an abnormal mammogram could avoid biopsy. Therefore, efforts to develop adjuvant imaging procedures continue. This policy will focus on magnetic resonance elastography, scintimammography, electrical impedance scanning and computer-aided detection for MRI, automated breast ultrasound and ultrasound for breast cancer screening and the diagnosis of breast cancer. (American Cancer Society (ACS), 2016)

The National Cancer Institute (2017) estimates that about 40 percent of women undergoing screening mammography have dense breasts. These women have an increased risk of breast cancer, with detection usually at a more advanced and difficult to treat stage.

Mammography is a low-dose X-ray imaging method of the breast. However, mammograms of dense breasts can be difficult to interpret. Fibroglandular breast tissue and tumors both appear as solid white areas on mammograms. As a result, dense breast tissue may obscure smaller tumors, potentially delaying detection of breast cancer. (ACS, 2016)

### **Breast Magnetic Resonance Imaging (MRI)**

MRI is a non-invasive imaging modality that uses magnetic and radiofrequency fields to image body tissue producing very detailed, cross-sectional pictures of the body. Inconsistent with CT, MRI uses no ionizing radiation and is generally a safe procedure. MRI is sometimes used in combination with mammography. (National Institute of Biomedical Imaging, 2017)

### **Magnetic Resonance Elastography (MRE) of the Breast**

MRE of the breast is a phase-contrast-based MRI technique that is based upon quantitative differences in the mechanical properties of normal and malignant tissues. Specifically, the elastic modulus of breast cancer tissue is approximately 5- to 20-fold higher than that of the surrounding fibroglandular tissue, i.e., breast cancers are usually harder than normal tissues. This difference can be measured by applying a known stressor and measuring the resulting deformation. MRE is performed by a radiologist in an MRI suite equipped with the electromechanical driver and integrated radiofrequency coil unit. (ACS, 2016)

### **Breast Specific Gamma Imaging (BSGI)**

BSGI, also known as scintimammography (SMM) or molecular breast imaging (MBI) is a noninvasive diagnostic technology that detects tissues within the breast that accumulate higher levels of a radioactive tracer that emit gamma radiation. The test is performed with a gamma camera after intravenous administration of radioactive tracers. Scintimammography has been proposed primarily as an adjunct to mammography and physical examination to improve selection for biopsy in patients who have palpable masses or suspicious mammograms. (ACS, 2016)

### **Electrical Impedance Scanning (EIS)**

EIS was developed as a confirmatory test to be used in conjunction with mammography. The device detects abnormal breast tissue using small electrical currents. Since malignant tissue tends to conduct more electricity than normal tissue, the electrical current produced creates a conductivity map of the breast which automatically identifies sites that appear suspicious. The transmission of electricity into the body is via an electrical patch on the arm or a handheld device which travels to the breast. This is measured by a probe on the surface of the skin. (ACS, 2016)

### **Computer-Aided Detection with MRI of the Breast**

In contrast to CAD systems used with mammography, CAD analysis with MRI creates a 2- or 3-dimensional (2-D, 3-D) color-coded image that is overlaid on the MRI image to mark potentially malignant areas of the breast which allows the radiologist to compare the enhanced image to the original MRI. (ACS, 2016)

### **Breast Ultrasound**

Ultrasound, also known as sonography, is an imaging method using sound waves rather than ionizing radiation to a part of the body. For this test, a small, microphone-like instrument called a transducer is placed on the skin (which is often first lubricated with ultrasound gel). It emits sound waves and picks up the echoes as they bounce off body tissues. The echoes are converted by a computer into a black and white image on a computer screen. Ultrasound is useful for evaluating some breast masses and is the only way to tell if a suspicious area is a cyst (fluid-filled sac) without placing a needle into it to aspirate (draw out) fluid. Cysts cannot accurately be diagnosed by physical exam alone. Breast ultrasound may also be used to help doctors guide a biopsy needle into some breast lesions. (ACS, 2016)

### **Computer-Aided Detection (CAD) for Ultrasound**

CAD systems for ultrasound use pattern recognition methods to help radiologists analyze images and automate the reporting process. These systems have been developed to promote standardized breast ultrasound reporting. (ACS, 2016)

### **Computer-Aided Tactile Breast Imaging**

Tactile breast imaging includes placing a tactile array sensor in contact with the breast. As the clinician gently moves the hand-held sensor across the breast and underarm area, data signals are then processed into multi-dimensional color images that instantly appear on a computer screen in real-time, allowing the clinician to view the size, shape, hardness and location of suspicious masses immediately. (ACS, 2016)

### **Automated Breast Ultrasound**

Automated Breast Ultrasound is the first and only ultrasound system developed and US Food and Drug Administration (FDA) approved specifically for breast cancer screening in women with dense breast tissue who have not had previous breast biopsies or surgeries. It is used as an adjunct to mammography. The high center-frequency significantly

sharpens detail resolution while the ultra-broadband performance simultaneously delivers distinct contrast differentiation. (ACS, 2016)

## CLINICAL EVIDENCE

### **Digital Mammography**

#### ***Professional Societies***

#### **American College of Obstetricians and Gynecologists (ACOG, 2017)**

The American College of Obstetricians and Gynecologists recommends routine screening with use of digital mammography for women diagnosed with dense breasts. They do not recommend routine use of alternative or adjunctive tests to screening mammography in women with dense breasts who are asymptomatic and have no additional risk factors. The College strongly supports additional research to identify more effective screening methods that will enhance meaningful improvements in cancer outcomes for women with dense breasts and minimize false-positive screening results.

#### **Automated Breast Ultrasound System (ABUS)**

An archived 2013 Hayes report evaluating automated breast ultrasound system (ABUS), found that the results presented in the majority of the study abstracts report overall favorable results when using three-dimensional automated breast ultrasound. Further review is required to confirm abstract content and, therefore, conclusions about the safety and effectiveness of this technology cannot be made until a full assessment has been completed.

Hellgren et al. (2017) conducted a study to compare the sensitivity and specificity of Automated Breast Volume Scanners (ABVS) to handheld breast US for detection of breast cancer in the situation of recall after mammography screening. A total of 113 women, five with bilateral suspicious findings, undergoing handheld breast US due to a suspicious mammographic finding in screening, underwent additional ABVS. The methods were assessed for each breast and each detected lesion separately and classified into two categories: breasts with mammographic suspicion of malignancy and breasts with a negative mammogram. Results Twenty-six cancers were found in 25 women. In the category of breasts with a suspicious mammographic finding, the sensitivity of both handheld US and ABVS was 88% (22/25). The specificity of handheld US was 93.5% (87/93) and ABVS was 89.2% (83/93). In the category of breasts with a negative mammography, the sensitivity of handheld US and ABVS was 100% (1/1). The specificity of handheld US was 100% (102/102) and ABVS was 94.1% (96/102). The authors concluded that ABVS can potentially replace handheld US in the investigation of women recalled from mammography screening due to a suspicious finding. Due to the small size of this study population, further investigation with larger study populations is necessary before the implementation of such practice.

Kim et al (2016) conducted a prospective study to compare the diagnostic performance of handheld ultrasound (US) and an automated breast volume scanner (ABVS) as second-look US techniques subsequent to preoperative breast magnetic resonance imaging (MRI). From March to September 2014, both types of second-look US examinations were performed on 40 patients with breast cancer who had 76 additional suspicious lesions detected via preoperative breast MRI. Each second-look US modality was reviewed independently and the detection rate of each, the correlation between the detection rate, and the MRI factors (size, distance, and enhancement type) were evaluated. The detection rate of the ABVS was higher than that of handheld US for the second-look examination (94.7% versus 86.8%). Among the 76 total lesions, 7 were only identified by the ABVS, 1 was only found by handheld US, and 3 were not detected by either the ABVS or handheld US. When we analyzed the correlation between the detection rate and MRI factors, the only meaningful factor was the enhancement type. The ability to detect a non-mass lesion was lower than the ability to detect a mass-type lesion for both the ABVS and handheld US. It was concluded that for a second-look US examination subsequent to preoperative breast MRI in patients with breast cancer, the ABVS is a more efficient modality than handheld US for preoperative evaluations. However, both techniques have limitations in detecting non mass lesions. This study is limited to a small sample size.

Prosch et al. (2011) conducted a prospective diagnostic study. The study examined 148 breasts of 76 patients with handheld ultrasound (US) and ABUS. The ABUS data were evaluated separately by two investigators. The inter-observer agreement for the breast imaging reporting and data system (BI-RADS) classification among the two observers using ABUS was high, the agreement with handheld US was moderate. The sensitivity in the detection of breast cancer was 87.5% for handheld US and 75% for the ABUS evaluation by observer 1. The sensitivity was 87.5% for the ABUS evaluation and 83% for mammography by observer 2. The authors concluded that ABUS examinations focusing on the BIRADS classification have low inter-observer variability, compared to handheld US.

An extensive literature search was conducted. All of the studies found were small sample size, case, comparative, and retrospective in nature. The results presented in the majority of the study abstracts report overall favorable results when using three-dimensional automated breast ultrasound. The main limitation in the studies that have been conducted is that they included a higher proportion of malignant lesions or breast masses than would be found in the

screening population. Larger scale research will be needed to be conducted to determine its role in breast cancer screening.

### **Magnetic Resonance Elastography of the Breast**

Although there are ongoing studies and clinical trials, there continues to be a lack of strong high quality evidence in the peer-reviewed medical literature to support the safety and efficacy of MRE. When used in conjunction with conventional ultrasound, breast elastography appears to be promising in assisting to differentiate potentially benign from malignant lesions, however, large prospective clinical trials addressing appropriate patient selection, diagnostic parameters, and practical application of this technique are necessary prior to widespread clinical use.

A prospective study by Siegmann et al. (2010) evaluated the value of adding magnetic resonance elastography (MRE) to contrast-enhanced MR imaging (MRI) for evaluating breast lesions in 57 patients. The sensitivity of MRI was 97.3% whereas specificity was 55%. If contrast-enhanced MRI was combined with  $\alpha 0$  (indicator of tissue stiffness), the diagnostic accuracy could be significantly increased. The authors concluded that combining MRE with MRI increase the diagnostic performance of breast MRI; however, larger studies are needed to validate the results and to identify the patients best suited for a combined procedure.

### **Breast Specific Gamma Imaging (BSGI) (also known as Scintimammography)**

Limited evidence on the diagnostic accuracy of BSGI reports that the test has a relatively high sensitivity and specificity for detecting malignancy. However, the evidence does not establish that BSGI improves outcomes when used as an adjunct to mammography for breast cancer screening. In the available studies, the negative predictive value of BSGI has not been high enough to preclude biopsy in patients with inconclusive mammograms. In addition, the evidence is not sufficient to conclude that BSGI is better than MRI for this purpose. Larger, higher-quality studies are required to determine whether BSGI has a useful role as an adjunct to mammography.

Guo et al (2016). In a 2016 systematic review and meta-analysis, the authors sought to establish if Tc-99m sestamibi scintimammography is useful in the prediction of neoadjuvant chemotherapy responses in breast cancer. Electronic database were searched for relevant publications in English, and fourteen studies, for a total of 503 individuals, fulfilled the inclusion criteria. The results indicated that Tc-99m MIBI scintimammography had acceptable sensitivity in the prediction of neoadjuvant chemotherapy response in breast cancer; however, its relatively low specificity showed that a combination of other imaging modalities would still be needed. Subgroup analysis indicated that performing early mid-treatment Tc-99m MIBI scintimammography (using the reduction rate of one or two cycles or within the first half-courses of chemotherapy compared with the baseline) was better than carrying out later (after three or more courses) or post-treatment scintimammography in the prediction of neoadjuvant chemotherapy response.

Brem et al (2016). The authors conducted this retrospective review to determine the incremental increase in breast cancer detection when BSGI is used as an adjunct to mammography in women at increased risk for breast cancer. 849 patients undergoing BSGI from April 2010 through January 2014 were retrospectively reviewed. Eligible patients were identified as women at increased risk for breast cancer and whose most recent mammogram was benign. Examinations exhibiting focally increased radiotracer uptake were considered positive. Incremental increase in cancer detection was calculated as the percentage of mammographically occult BSGI-detected breast cancer and the number of mammographically occult breast cancers detected per 1,000 women screened. Reviewed for this study were patients in whom 14 BSGI examinations detected mammographically occult breast cancer. Patients ranged in age from 26 to 83 with a mean age of 57. Eleven of 14 cancers were detected in women with dense breasts. The addition of BSGI to the annual breast screen of asymptomatic women at increased risk for breast cancer yields 16.5 cancers per 1,000 women screened. When high-risk lesions and cancers were combined, BSGI detected 33.0 high-risk lesions and cancers per 1,000 women screened. The authors concluded that BSGI is a reliable adjunct modality to screening mammography that increases breast cancer detection by 1.7% (14/849) in women at increased risk for breast cancer, comparable to results reported for breast MRI. BSGI is beneficial in breast cancer detection in women at increased risk, particularly in those with dense breasts. Limitation of this study is retrospective study design.

In the 2013 ECRI Evidence Report, Noninvasive Diagnostic Tests for Breast Abnormalities found that only women with a pre-scintimammography suspicion of malignancy of 5 percent or less will have their post-scintimammography suspicion of malignancy change sufficiently to suggest that a change in patient management may be appropriate.

An Archived 2015 Hayes report evaluating breast-specific gamma imaging (BSGI) found that the available evidence does not provide conclusive evidence that breast-specific gamma imaging can be relied on rather than biopsy, US, or MRI in women who have suspicious breast lesions on mammograms. In several of the reviewed studies, BSGI detected some cancerous lesions that were not detected by mammography; however, these studies did not report whether the increased detection corresponded to a statistically significant increase in the sensitivity of BSGI compared with mammography. In the studies that provided data on patient management, BSGI was not rigorously compared with MRI or US to determine whether it was more effective. Only two studies reported the statistical significance of

results, both of which indicated that BSGI was more specific than MRI. Although further studies may indicate that breast-specific gamma imaging has greater sensitivity than ultrasonography and MRI, breast-specific gamma imaging has the disadvantage that it exposes the patient to radiation. In addition, unlike biopsy, breast-specific gamma imaging does not provide a definitive diagnosis since it incorrectly indicates that 15% to 40% of benign lesions are cancerous. The quality of the evidence is low due to the predominately retrospective study design, small sample sizes, and, in some cases, lack of statistical analysis of results. Additional studies are needed to determine the place in therapy of BSGI versus the alternatives.

Weigert et al reported data from a retrospective multicenter patient registry. This study analyzed 1042 patients drawn from 2004 patients in the registry. Women included in the study had BSGI imaging, pathologic diagnosis by biopsy, and at least six months follow-up. BSGI had been recommended for patients with at least two of the following indications: equivocal or negative mammogram/ultrasound and an unresolved clinical concern; personal history of breast cancer or current cancer diagnosis; palpable masses negative on mammogram or ultrasound; radiodense breast tissue; or high risk for breast cancer. In this population, BSGI had a reported sensitivity of 91%, specificity of 77%, positive predictive value of 57%, and NPV of 96%. In 139 patients who had a suspicious lesion on mammography, BSGI imaging was negative in 21 cases, 13 of which were true negatives and eight of which were false negatives. The mix of indications in this study makes it difficult to generalize the results or to determine whether the performance of BSGI varies by indication.

Kim (2012) evaluated the adjunctive benefits of BSGI versus MRI in breast cancer patients with dense breasts. This study included a total of 66 patients with dense breasts (breast density greater than 50%) and already biopsy-confirmed breast cancer. All of the patients underwent BSGI and MRI as part of an adjunct modality before the initial therapy. Of 66 patients, the 97 undetermined breast lesions were newly detected and correlated with the biopsy results. Twenty-six of the 97 breast lesions proved to be malignant tumors; the remaining 71 lesions were diagnosed as benign tumors. The sensitivity and specificity of BSGI were 88.8% and 90.1% respectively, while the sensitivity and specificity of MRI were 92.3% and 39.4%, respectively. MRI detected 43 false-positive breast lesions, 37 (86.0%) of which were correctly diagnosed as benign lesions using BSGI. In 12 malignant lesions less than 1 cm, the sensitivities of BSGI and MR imaging were 83.3% and 91.7% respectively. The author concluded that BSGI showed an equivocal sensitivity and a high specificity compared to MRI in the diagnosis of breast lesions. In addition, BSGI had a good sensitivity in discriminating breast cancers less than or equal to 1 cm. The results of this study suggested that BSGI could play a crucial role as an adjunctive imaging modality which can be used to evaluate breast cancer patients with dense breasts. The study was limited by small sample size; larger prospective studies are needed to determine the true sensitivity and specificity of BSGI.

Based on 44 studies of scintimammography, an analysis found that for non-palpable lesions, the specificity of scintimammography was 39.2% (at a fixed 95% sensitivity). At the mean threshold of the included studies, the sensitivity was 68.7% and specificity was 84.8%. The analysis also found that in women with non-palpable lesions, the negative likelihood ratio of scintimammography was 0.41 (i.e., if a woman with a non-palpable lesion is diagnosed as having no cancer by scintimammography, her chance of having breast cancer drops from 20% to 9.3%). (AHRQ, 2006)

A meta-analysis of scintimammography included 5,473 patients from studies performed since 1997. The overall sensitivity was 85% and the specificity was 84% for single-site trial studies, and for multi-center trial studies the overall sensitivity was 85% and the specificity was 83%. (Hussain and Buscombe, 2006) Another meta-analysis evaluating scintimammography included 5,340 patients from studies published between January 1967 and December 1999. The aggregated summary estimates of sensitivity and specificity for scintimammography were 85.2% and 86.6% respectively. The authors concluded that scintimammography may be used effectively as an adjunct to mammography when additional information is required to reach a definitive diagnosis. The authors also indicated that the role of scintimammography should be assessed on the basis of large, multi-center studies. (Lieberman et al., 2003)

### **Professional Societies/Organizations**

#### **American Cancer Society (ACS)**

According to the 2016 ACS guidelines, routine breast cancer screening with scintimammography is not recommended.

#### **American College of Radiology (ACR) and the Society for Pediatric Radiology (SPR)**

According to the 2015 joint ACR-SPR Practice Parameter for the Performance of Tumor Scintigraphy (with gamma cameras): There is insufficient evidence to support the use of breast specific gamma imaging (BSGI) for breast cancer screening, and is not indicated for screening in their present form. However, scintimammography may be useful in selected patients (e.g., breast cancer screening in selected patients, evaluation of indeterminate breast abnormalities, initial staging, and recurrence detection).

## **Society of Nuclear Medicine and Molecular Imaging (SNMMI) (formerly Society of Nuclear Medicine)**

SNM published an updated 2012 procedure standards for breast scintigraphy with breast-specific gamma cameras that indicate that further study is needed to determine the population and usefulness most likely to benefit from this procedure. This guideline lists potential indications and cites references for each indication but does not provide a systemic review of the literature, including assessment of study quality. The guideline is based on consensus, and most of it is devoted to procedures and specifications of the examination, documentation and recording, quality control and radiation safety.

## **Electrical Impedance Scanning (EIS)**

Experimental studies have shown that significant changes occur in the electrical properties of breast cancer tissue compared to the surrounding normal tissue. This phenomenon motivated studies on cancer detection using electrical impedance techniques. However, the separation of malignant tumors from benign lesions based on impedance measurements needs further investigation. There is insufficient evidence in the published peer-reviewed scientific literature to support the diagnostic utility of electrical impedance scanning (EIS) of the breast of the breast. The incremental diagnostic value of these alternative breast imaging procedures as an adjunct to mammography has not yet been established, and the impact of the use of these systems on meaningful health outcomes remains unknown.

In a prospective, multi-center study, Wang et al (2010) reported the sensitivity and specificity for the combination of EIS and ultrasound in identifying breast cancer and calculated the relative risk of breast cancer in young women. The young women (583 cases) scheduled for mammary biopsy underwent EIS and ultrasound, respectively. EIS and ultrasound results were compared with final histopathology results. Of the 583 cases, 143 were diagnosed with breast cancer. The relative probability of breast cancer for the young women was detected by EIS, ultrasound, and the combination method. The authors concluded that the combination of EIS and ultrasound is likely to become an applicable method for early detection of breast cancer in young women.

A prospective, multicenter clinical trial by Stojadinovic et al. (2005) evaluated EIS in 1,103 women. Twenty-nine cancers with a mean tumor size 1.7 cm were confirmed thru biopsy. Electrical impedance scanning had 17% sensitivity, 90% specificity, and a negative predictive value (NPV) of 98%. Statistically significant increases in specificity were observed for women who were premenopausal and women who were not using hormone replacement therapy. False-positive rates were increased in postmenopausal women and those taking exogenous hormones. While the authors concluded that EIS appears promising for early detection of breast cancer, the increased false positive rates in postmenopausal women and those taking exogenous hormones is concerning.

## ***Professional Societies/Organizations***

### **American Cancer Society (ACS)**

In a 2016 update on experimental breast imaging, the ACS states that while this test is approved by the Food and Drug Administration (FDA) to help classify tumors found on mammograms, at this time there hasn't been enough clinical testing to use it in breast cancer screening.

### **Society of Breast Imaging (SBI)**

In the 2013 SBI Position Statement entitled 'Use of Alternative Imaging Approaches to Detection of Breast Cancer' states that the following: "Often predicated on the increased vascularity associated with cancer, techniques to detect increased heat production, oxygen consumption, electrical impedance, light absorption, microwave transmission, and nitrous oxide production have indicated changes in the breast containing cancer that may assist in detection or diagnosis. While many of these approaches have received FDA approval for safety, such techniques remain either experimental or investigational, given the lack of standard techniques that can be uniformly applied and paucity of sufficient research to substantiate reliability of results. None of these tests have been shown to reduce mortality among tested women in randomized controlled trials." Mammography provides the only examination satisfying both the benchmarks for screening and diagnosis based on objective and randomized clinical trials.

### **Computer-Aided Detection with MRI of the Breast**

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). The use of CAD may also reduce the time needed to interpret breast MRI images, which currently takes much longer than reading mammograms.

DeMartini et al. (2005) performed a study to determine the utility of CADStream applied to breast MRI in 15 newly diagnosed breast cancer patients (16 lesions) undergoing neoadjuvant chemotherapy. Prior to chemotherapy, all tumors demonstrated CAD-assessed significant enhancement. Following chemotherapy, 7/16 tumors showed no residual significant enhancement, but all had residual disease at pathology. The authors concluded that CAD may be helpful in assessing changes in MRI enhancement profiles of tumors following chemotherapy. However, CAD-assessed

significant enhancement following chemotherapy can be falsely negative for residual malignancy, and CAD tumor sizes are less accurate than those measured by the radiologist in predicting size of residual malignancy. CAD may complement but should not replace the radiologist's assessment of tumors in this patient population.

Currently, there are a few retrospectively designed studies which do not establish the accuracy or clinical utility of CAD systems. Additional well-designed prospective trials are needed to establish what if any impact CAD systems may have on long-term breast cancer survival rates.

### ***Professional Societies/Technology Assessments***

#### **American College of Radiology (ACR) Practice Guideline for the Performance of Magnetic Resonance Imaging-Guided Breast Interventional Procedures**

In 2016, the American College of Radiology (ACR) amended the 2014 practice parameter for the use of MRI-Guided Breast Interventional Procedures. The use of computer aided detection (CAD)/computer aided evaluation (CAE) with breast MRI is not specifically recommended or addressed.

#### **Blue Cross Blue Shield Association (BCBSA) Technology Evaluation Center (TEC)**

The Blue Cross Blue Shield Association (BCBSA) Technology Evaluation Center (TEC) completed a technology assessment in 2006 for CAD with MRI and concluded that there is insufficient evidence to assess whether the use of CAD systems would maintain or increase the sensitivity, specificity, and recall rates of MRI of the breast. Given the inability to evaluate these intermediate outcomes, it is not possible to assess the impact of CAD on health outcomes such as treatment success among breast cancer patients or survival. (BCBSA, 2006c)

#### **National Comprehensive Cancer Network (NCCN)**

Invasive Breast Cancer Version (2017) and Breast Cancer Screening and Diagnosis (2017) Does not address the use of computer aided detection (CAD)/computer aided evaluation (CAE) for breast MRI testing.

#### **Computer-Aided Detection for Ultrasound**

Very few studies were identified that evaluated CAD for detection and diagnosis of breast cancer. Prospective studies are needed to confirm that CAD systems improve diagnostic performance for radiologists interpreting breast ultrasound images, and that any improvement in diagnostic performance results in a clinical benefit, such as appropriately selecting patients for biopsy or for clinical follow-up.

Cho et al (2016) conducted a retrospective study to compare the detection of breast cancer using full-field digital mammography (FFDM), FFDM with computer-aided detection (FFDM+CAD), ultrasound (US), and FFDM+CAD plus US (FFDM+CAD+US), and to investigate the factors affecting cancer detection. This study was conducted from 2008 to 2012, and 48,251 women underwent FFDM and US for cancer screening. The clinical and pathological data was reviewed to investigate factors affecting cancer detection, and used generalized estimation equations to compare the cancer detectability of different imaging modalities. The results of this study showed the detectability of breast cancer by US or FFDM+CAD+US to be superior to that of FFDM or FFDM+ CAD. However, cancer detectability was not significantly different between FFDM versus FFDM+CAD and US alone versus FFDM+CAD+US. The tumor size influenced cancer detectability by all imaging modalities. In FFDM and FFDM+CAD, the non-detecting group consisted of younger patients and patients with a denser breast composition. In breast US, carcinoma *in situ* was more frequent in the non-detecting group. The authors concluded that for breast cancer screening, breast US alone is satisfactory for all age groups, although FFDM+ CAD+US is the perfect screening method. Patient age, breast composition, and pathological tumor size and type may influence cancer detection during screening. The study is also limited by small sample size, retrospective and non-blinded study design.

### ***Professional Societies***

#### **American College of Radiology (ACR)**

The ACR Practice Guideline for the performance of screening and diagnostic mammography (2014) states "Double reading and computer-aided detection (CAD) may slightly increase the sensitivity of mammographic interpretation, and may be used. However, this sensitivity is at the expense of decreased specificity with increased recall and biopsy rates.

#### **Computer-Aided Tactile Breast Imaging**

Comprehensive literature review of Hayes, ECRI, AHRQ, MCG, NICE, and Cochrane did not produce detailed comprehensive information regarding this technology. Controlled trials are needed to demonstrate that use of computer aided tactile breast imaging results in improved clinical outcomes.

Tasoulis et al. (2014) unnecessary referrals of patients with breast lumps represent a significant issue, since only a few patients actually have lumps when examined by a breast specialist. Tactile imaging (TI) is a novel modality in breast diagnostics armamentarium. The aim of this study was to assess TI's diagnostic performance and compare it to



clinical breast examination (CBE). This is a prospective, blinded, comparative study of 276 consecutive patients. All patients underwent conventional imaging and tissue sampling if either a radiological or a palpable abnormality was present. Sensitivity, specificity and positive and negative predictive values for CBE and TI were calculated. Radiological findings and final diagnosis based on histology and/or cytology were used as reference standards. Receiver operator characteristic (ROC) curve analysis was also performed for each method. Sensitivity and specificity of TI in detecting radiologically proven abnormalities were 85.5% and 35%, respectively. CBE's sensitivity was 80.3% and specificity 76%. In detecting a histopathological entity according to histology/cytology, sensitivity was 88.2% for TI and 81.6% for CBE. Specificity was 38.5% and 85.7% for TI and CBE, respectively. These results suggest a trend towards higher sensitivity of TI compared to CBE but significantly lower specificity. Subgroup analysis revealed superior sensitivity of TI in detecting a histological entity in pre-menopausal women. However, CBE's overall performance was superior compared to TI's according to ROC curve analysis. Although further research is necessary, the use of TI by the primary care physician as a selection tool for referring patients to a breast specialist should be considered especially in pre-menopausal women.

## U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Mammographic x-ray systems are classified as Class II devices. The FDA regulates the marketing of mammography devices and regulates the use of such devices via the Mammography Quality Standards Act (MQSA). The FDA has granted pre-market approval to several digital mammography systems (product code MUE) for breast cancer screening and diagnosis.

### **Magnetic Resonance Elastography of the Breast**

Please see the following website for more information on devices used for elastography of the breast (search by product name LNH in device name section): <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>.

### **Breast Specific Gamma Imaging (BSGI)**

BSGI for diagnosing breast cancer is a procedure and, therefore, is not subject to FDA regulation. However, the equipment used to conduct BSGI is subject to FDA regulation. The cameras used during BSGI are considered Class I radiologic devices. A scintillation (gamma) camera is a device intended to image the distribution of radionuclides in the body by means of a photon radiation detector.

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>.

### **Automated Breast Ultrasound System (ABUS)**

Automated breast (or whole breast) ultrasound devices are regulated by the FDA as Class III devices. Please see the following website for more information on devices used for Automated Breast Ultrasound Systems (search by product name in device name section): <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>.

### **Electrical Impedance Scanning**

These devices are approved as an adjunct to mammography in patients whose lesions are American College of Radiology (ACR) Breast Imaging-Reporting and Data System (BI-RADS) category III (probably benign) or IV (suspicious abnormality), based on mammography. Please see the following website for more information on devices used for Electrical Impedance Scanning (search by product name in device name section):

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>.

### **Computer-Aided Detection for MRI of the Breast**

Please see the following website for more information on devices used for Computer-Aided Detection for MRI of the Breast (search by product name in device name section):

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>.

### **Computer-Aided Detection for Ultrasound**

Please see the following website for more information on devices used for Computer-Aided Detection for Ultrasound (search by product names MYN and LLZ in device name section):

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnmn.cfm>.

(Accessed March 13, 2018)

## CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare covers screening and diagnostic mammography when criteria are met. See the [NCD for Mammograms \(220.4\)](#) and the [NCD for FDG PET for Breast Cancer \(220.6.10\)](#). Medicare does not have NCDs for the following: Digital Mammography, Breast Magnetic Resonance Imaging (MRI), Digital Breast Tomosynthesis (3-D Mammography), Magnetic Resonance Elastography of the Breast, Breast Specific Gamma Imaging (Scintimammography), Electrical

Impedance Scanning (EIS), Computer Aided Detection for MRI of the Breast, Breast Ultrasound, Computer Aided Detection for Ultrasound, Computer Aided Tactile Breast Imaging and Automated Breast Ultrasound.

Local Coverage Determinations (LCDs) exist; see the following LCDs: [Breast Imaging: Breast Echography \(Sonography\)/Breast MRI/Ductography](#), [Breast Imaging Mammography/Breast Echography \(Sonography\)/Breast MRI/Ductography](#), [3D Interpretation and Reporting of Imaging Studies](#), [Screening and Diagnostic Mammography, Noncovered Services, Category III CPT® Codes](#), [Non-Covered Category III CPT Codes](#), and [Services That Are Not Reasonable and Necessary](#).

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**POLICY HISTORY/REVISION INFORMATION**

Date	Action/Description
01/01/2019	<ul style="list-style-type: none"> <li>• Reorganized policy template:               <ul style="list-style-type: none"> <li>○ Simplified and relocated <i>Instructions for Use</i></li> <li>○ Removed <i>Benefit Considerations</i> section</li> </ul> </li> <li>• Simplified coverage rationale (no change to guidelines)</li> <li>• Updated list of applicable CPT codes to reflect annual code edits:               <ul style="list-style-type: none"> <li>○ Added 76391, 77046, 77047, 77048, and 77049</li> <li>○ Removed 0159T, 0346T, 77058, and 77059</li> </ul> </li> <li>• Archived previous policy version 2018T0375V</li> </ul>

**INSTRUCTIONS FOR USE**

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.