Breast Imaging for Screening and Diagnosing Cancer (for Louisiana Only)

Policy Number: CS010LA.~~Q~~R
Effective Date: ~~January 1, 2023~~TBD

➲ Instructions for Use

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Application

This Medical Policy only applies to the state of Louisiana.

Coverage Rationale

Note: This policy does not address **routine** preventive benefit for breast cancer screening (**using** ~~including~~ **conventional** mammography).

The following are proven and medically necessary ~~**for the following individuals**~~**:**

- **Diagnostic Breast Ultrasound**
- Digital mammography for individuals with dense breast tissue
- ~~Diagnostic Breast Ultrasound~~
- ~~Breast Magnetic Resonance Imaging (MRI)~~**Magnetic Resonance Imaging (MRI) of the breast** for individuals who are high risk for breast cancer as defined as having any of the following:
  - Prior thoracic radiation therapy between the ages 10 and 30
  - Lifetime risk estimated at greater than or equal to 20% as defined by models that are largely dependent on family history (e.g., Gail, Claus, Tyrer-Cuzick or BRCAPRO)
  - Personal history of breast cancer (not treated with bilateral mastectomy)
  - Personal history with any of the following:
    - Li-Fraumeni Syndrome (TP53 mutation)
    - Confirmed BRCA 1 or BRCA 2 gene mutations

  - Peutz-Jehgers Syndrome (STK11, LKB1 gene variations)
  - PTEN gene mutation
- Family history with any of the following:
  - At least one first-degree relative who has a BRCA1 or BRCA2 mutation
  - First-degree relative who carries a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes, or Peutz-Jehgers Syndrome)
  - At least two first-degree relatives with breast or ovarian cancer
  - One first-degree relative with bilateral breast cancer, or both breast and ovarian cancer
  - First or second-degree male relative (father, brother, uncle, grandfather) diagnosed with breast cancer

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

- Automated Breast Ultrasound system
- ~~Breast Magnetic Resonance Imaging (MRI) for individuals with dense breast tissue not accompanied by defined risk factors as described above~~
- ~~Computer-Aided Detection (CAD)~~**Computer-Aided Detection (CAD)**
- Computer-Aided Tactile Breast Imaging
- ~~Computed Tomography~~ **Computed Tomography** (CT) of the breast
- Electrical Impedance Scanning (EIS)
- Magnetic Resonance Elastography (MRE)
- **Magnetic Resonance Imaging (MRI) of the breast for individuals with dense breast tissue not accompanied by defined risk factors as described above**
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- Molecular Breast Imaging (e.g., Breast Specific Gamma Imaging, Scintimammography, Positron Emission Mammography)

Note: For breast computed tomography (CT) and 3D rendering of the breast, or additional indications for breast MRI, refer to the ~~Cardiology and Radiology Imaging Guidelines – Breast Imaging Guidelines~~Cardiology and Radiology Imaging Guidelines – **Breast Imaging Guidelines** **section of the Cardiovascular and Radiology Imaging Guidelines.**~~.~~

Definitions

Automated Breast Ultrasound (ABUS): ABUS systems are ultrasound imaging platforms that use high-frequency broadband transducers to automate the acquisition of volume data to provide two-dimensional (2D) and three-dimensional (3D) B-mode images of breast tissue. ABUS 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. (ECRI, 2021)

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, 2022)

~~**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, 2022)~~

~~**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, 2022)~~

~~**Computer-Aided Detection (CAD) 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). (ACS, 2022)~~

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, 2022)

~~**Computed Tomography (CT):** A noninvasive diagnostic imaging procedure that uses a combination of X-rays and computer technology to produce horizontal, or axial, images (often called slices) of the body. A CT scan directs multiple narrow beams of X-rays (radiation) around a specific body site that create a multi-dimensional view of a patient's body. A three-dimensional volume of the breast is reconstructed from the acquired images. It is proposed that breast CT may allow for better accuracy by reducing problems caused by overlapping tissue. (NCI, 2019)~~

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, 2022)

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, 2022)

~~**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)~~

Molecular Breast Imaging (MBI): Procedure that uses a radioactive tracer and special camera to find breast cancer. Rather than simply taking a picture of a breast, molecular breast imaging is a type of functional imaging. This means that the pictures it creates show differences in the activity of the tissue. (ACS, 2022)

Positron Emission Mammography (PEM): PEM is a new imaging modality that has higher resolution than PET-CT and can be performed on patients unable to have an MRI scan. PEM performs high- resolution metabolic imaging for breast cancer using an FDG tracer. The PEM detectors are integrated into a conventional mammography system, allowing acquisition of the emission images immediately after the mammogram. (ACS, 2022)

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 federal, state, or contractual requirements 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 Guidelines may apply.

Coding Clarification: Computer-aided detection (CAD) is included with the MRI breast CPT 77048 and 77049 procedures. If CAD is performed with these codes, there is no additional reimbursement.

CPT Code	Description
*0422T	Tactile breast imaging by computer-aided tactile sensors, unilateral or bilateral
*0633T	Computed tomography, breast, including 3D rendering, when performed, unilateral; without contrast material
*0634T	Computed tomography, breast, including 3D rendering, when performed, unilateral; with contrast material(s)
*0635T	Computed tomography, breast, including 3D rendering, when performed, unilateral; without contrast, followed by contrast material(s)
*0636T	Computed tomography, breast, including 3D rendering, when performed, bilateral; without contrast material(s)
*0637T	Computed tomography, breast, including 3D rendering, when performed, bilateral; with contrast material(s)
*0638T	Computed tomography, breast, including 3D rendering, when performed, bilateral; without contrast, followed by contrast material(s)

CPT Code	Description
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 with; 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

~~Codes labeled with an asterisk (*) are not on the state of Louisiana Fee Schedule and therefore not covered by the State of Louisiana Medicaid Program.~~

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

Codes labeled with an asterisk (*) are not on the state of Louisiana Fee Schedule and therefore may not be covered by the State of Louisiana Medicaid Program.

Description of Services

Regular screening is the most reliable method for detecting breast cancer early when treatment is the most effective. Screening recommendations vary according to breast

cancer risk, and several tools are available to approximate breast cancer risk based on various combinations of risk factors. Current methods of breast screening and diagnosis include breast self-examination, clinical breast exam, ultrasonography, mammography, and magnetic resonance imaging.

Mammography remains the generally accepted standard for breast cancer screening and diagnosis. However, efforts to provide new insights regarding the origins of breast disease and to find different approaches for addressing several key challenges in breast cancer, including detecting disease in mammographically dense tissue, distinguishing between malignant and benign lesions, and understanding the impact of neoadjuvant chemotherapies, has led to the investigation of several novel methods of breast imaging for breast cancer management.

Clinical Evidence

Automated Breast Ultrasound System (ABUS)

Clinical evidence is inconclusive to show whether automated breast ultrasound improves the detection rate of breast cancer in comparison to screening mammography and handheld ultrasound. Future research should include better-designed studies, including prospective studies and randomized controlled trials evaluating this technology.

In a Clinical Evidence Assessment, ECRI (2022) concluded that the evidence for breast ultrasound using an automated system for cancer screening in women with dense breast tissue was inconclusive due to lack of data addressing clinical utility. The evidence suggests that screening mammography plus ABUS increases breast cancer detection rate among women with dense breasts and increases recall and biopsy rates, which could increase anxiety and cost. Studies suggest similar detection rates between ABUS and HHUS; whether ABUS offers benefits over HHUS is unclear because too few data are available.

In the 2021 ECRI Clinical Evidence Assessment Report, automated breast ultrasound systems for diagnosing breast cancer found that evidence shows that ABUS is as accurate as handheld ultrasound (HHUS) for detecting breast cancer in women with palpable masses, breast cancer symptoms, or abnormalities seen on a screening mammogram. However, too few data are available to determine whether ABUS provides any benefit over HHUS in terms of accuracy or care delivery. Clinical utility studies with randomly assigned patient groups are needed to assess ABUS's potential benefits and drawbacks and should report longer-term clinical outcomes (e.g., quality of life) as well as shorter-term measures of procedure time, pain, patient satisfaction, and cost-effectiveness.

In a meta-analysis of studies comparing the diagnostic performance of mammography (MG) alone versus MG combined with adjunctive imaging studies, Hadadi et al. (2021) determined that adding adjunctive modalities to MG for women with dense breasts significantly increased cancer detection rates (CDRs). The authors reviewed 41 published studies with an overall sample size of 228,508 participants that compared MG alone with MG combined with handheld ultrasound (HHUS), automated breast ultrasound (ABUS), digital breast tomosynthesis (DBT), contrast-enhanced mammography (CEM) and/or magnetic resonance imaging (MRI). Four studies (n = 23,596) compared the performance between MG and MG plus ABUS although the authors noted that none of the studies reported diagnostic accuracy for non-dense breasts. When evaluating the CDRs, the authors reported that the CDR was found to be significantly higher when using MG plus ABUS compared to MG alone and that the recall rate was approximately doubled for MG plus ABUS than for MG alone. In women with dense breasts, the authors determined that the four studies showed in increase in CDRs

ranging from 27% to 105% when ABUS was used as an adjunct to MG. Limitations noted in these studies included the fact that 2 of the 4 studies included higher proportions of women at high-risk which may have contributed to the recall rate, and that 3 of the studies had lower thresholds for recall. The authors concluded that adjunctive breast imaging modalities, including ABUS, increased cancer detection in women with dense and non-dense breasts.

A comparison study by Chen et al. (2021) was performed to evaluate the dependability of automated breast ultrasound (ABUS) compared with handheld ultrasound (HHUS) and mammography (MG) on the Breast Imaging Reporting and Data System (BI-RADS) category and size assessment of malignant breast lesions. A total of 344 confirmed malignant lesions were recruited. All participants underwent MG, HHUS, and ABUS examinations. Agreements on the BI-RADS category were evaluated. Lesion size assessed using the three methods was compared with the size of the pathological result as the control. Regarding the four major molecular subtypes, correlation coefficients between size on imaging and pathology were also evaluated. The agreement between ABUS and HHUS on the BI-RADS category was 86.63% (kappa = 0.77), whereas it was 32.22% (kappa = 0.10) between ABUS and MG. Imaging lesion size compared to pathologic lesion size was assessed correctly in 36.92%/52.91% (ABUS), 33.14%/48.84% (HHUS) and 33.44%/43.87% (MG), with the threshold of 3 mm/5 mm, respectively. The correlation coefficient of size of ABUS-Pathology (0.75, Spearman) was higher than that of the MG-Pathology (0.58, Spearman) with $p < 0.01$, but not different from that of the HHUS-Pathology (0.74, Spearman) with $p > 0.05$. The correlation coefficient of ABUS-Pathology was higher than that of MG-Pathology in the triple-negative subtype, luminal B subtype, and luminal A subtype ($p < 0.01$). The authors concluded that the agreement between ABUS and HHUS in the BI-RADS category was good, whereas that between ABUS and MG was poor. ABUS and HHUS allowed a more accurate assessment of malignant tumor size compared to MG. Limitations include single-factor analysis, retrospective observations, and a small sample size making it difficult to decide whether these conclusions can be generalized to a larger population.

A prospective observation study was completed by Gatta et al. (2021) to evaluate the performance and cancer detection rate of mammography alone or with the addition of 3D prone automated breast ultrasonography (ABUS) in women with dense breasts. The study was based on the screening of 1165 asymptomatic women with dense breasts who selected independent of risk factors. The results evaluated include the cancers detected between June 2017 and February 2019, and all surveys were subjected to a double reading. Mammography detected four cancers, while mammography combined with a prone Sofia system (3D ABUS) doubled the detection rate, with eight instances of cancer being found. The diagnostic yield difference was 3.4 per 1000. Mammography alone was subjected to a recall rate of 14.5 for 1000 women, while mammography combined with 3D prone ABUS resulted in a recall rate of 26.6 per 1000 women. An additional 12.1 recalls per 1000 women screened was observed. The authors concluded that integrating full-field digital mammography (FFDM) with 3D prone ABUS in women with high breast density increases and improves breast cancer detection rates in a significant manner, including small and invasive cancers, and it has a tolerable impact on recall rate. Moreover, 3D prone ABUS performance results are comparable with the performance results of the supine 3D ABUS system. Limitations include being a descriptive prospective mono-center study with a small sample size making it difficult to decide whether these conclusions can be generalized to a larger population. Further investigation is needed before clinical usefulness of this procedure is proven.

A prospective comparison study by Güldogan et al. (2021) was performed to compare the diagnostic performance of an automated breast ultrasound system (ABUS) with hand-held ultrasound (HHUS) in the detection and characterization of lesions regarding BI-RADS

classification in women with dense breasts. After ethical approval, from July 2017 to August 2019, 592 consecutive patients were enrolled in this prospective study. On the same day, patients underwent ABUS followed by HHUS. Three breast radiologists participated in this study. The number and type of lesions and BI-RADS categorization of both ABUS and HHUS examinations of each patient were recorded in an excel file. The level of agreement between the two ultrasound systems in terms of lesion number and BI-RADS category were analyzed statistically. ABUS and HHUS detected 1005 and 1491 cystic and 270 and 336 mass lesions in 592 patients respectively. ABUS and HHUS detected 171 and 167 positive/suspicious cases (BIRADS 0/3/4/5). Forty suspicious lesions underwent core needle biopsy whereas 11 malignant lesions were detected by both methods. The remaining lesions were followed with a mean of 31 months. The mean size of solid lesions detected by HHUS and ABUS was 7.67 mm (range 2.1-41 mm) and 7.74 mm (range 2-42 mm) respectively. The agreement for detection of cystic lesions between two methods for each breast was good (kappa: 0.61-0.62 $p < 0.001$). The agreement of two methods for solid mass lesions for each breast was moderate ($k = 0.57$-0.60 $p < 0.001$). There was good agreement between the two methods for detecting suspicious lesions (kappa = 0.66 $p < 0.001$). The authors concluded that the level of agreement of ABUS and HHUS for dichotomic assignment of BI-RADS categories was good. Although ABUS detected fewer lesions compared to HHUS, both methods detected all malignant lesions. The authors stated that ABUS is a reliable method for the detection of malignancy in dense breasts. All researchers were well experienced in HHUS, and new in interpreting ABUS images. This may have caused bias in determining the BI-RADS category of lesions for HHUS. Limitations include being a single-center study, low volume of cancer cases, and the included patients were imaged by a single radiologist.

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.~~

~~Magnetic Resonance Imaging of the Breast~~

~~Onega et al. (2022) completed a clinical trial (NCT02980848) and comparison study to examine whether preoperative magnetic resonance imaging (MRI) yields additional biopsy and cancer detection by extent of breast density. The authors followed women in the Breast Cancer Surveillance Consortium with an incident breast cancer diagnosed from 2005 to 2017. They quantified breast biopsies and cancers detected within 6 months of diagnosis by preoperative breast MRI receipt, overall and by breast density, accounting for MRI selection bias using inverse probability weighted logistic regression. Among 19,324 women with newly diagnosed breast cancer, 28% had preoperative MRI, 11% additional biopsy, and 5% additional cancer detected. Four times as many women with preoperative MRI underwent additional biopsy compared to women without MRI (22.6% v. 5.1%). Additional biopsy rates with preoperative MRI increased with increasing breast density (27.4% for extremely dense compared to 16.2% for almost entirely fatty breasts). Rates of additional cancer detection were almost four times higher for women with v. without MRI (9.9% v. 2.6%). Conditional on additional biopsy, age-adjusted rates of additional cancer detection were lowest among women with extremely dense breasts, regardless of imaging modality (with MRI: 35.0%; 95% CI 27.0-43.0%; without MRI: 45.1%; 95% CI 32.6-57.5%). The authors concluded that for women with dense breasts, preoperative MRI was associated with much higher biopsy rates, without concomitant higher cancer detection. Preoperative MRI may be considered for some women, but selecting women based on breast density is not supported by evidence. There are several limitations to this study. The authors were not able to quantify the exact sequences of additional imaging and biopsy within the preoperative window, so were unable to definitively attribute an additional biopsy to the preoperative MRI. The authors were unable to report on the effect of MRI on additional cancer detection by breast density in conjunction with other clinical characteristics, such as histology and subtype due to small numbers. Further, they were not able to assess whether the cancer was upgraded based on additional biopsies. Further investigation is needed before clinical usefulness of this procedure is proven.~~

~~A systematic review by Zeng et al. (2021) was performed to review the published literature to explore the effect of supplemental screening (MRI or breast ultrasound) compared to mammography alone on cancer detection and interval cancer rates. A further aim was to identify specific groups where supplemental screening is most effective at reducing the interval cancer rate (ICR). This study reviewed the evidence evaluating the effect of supplemental imaging on ICR in women undergoing screening mammography. This~~

~~systematic review included studies that reported both cancer detection rate (CDR) and ICR in women undergoing screening mammography alone compared to those undergoing screening mammography with supplemental imaging. Five studies (3 randomized trials) were eligible. These reported on 142,153 women undergoing mammography screening alone or mammography with supplemental imaging (3 ultrasound and 2 MRI studies). Two studies included a general screening population and 3 included special populations (young, high genetic risk and/or dense breasts). The incremental CDR for supplemental MRI was 14.2 to 16.5/1000 screens and for ultrasound was 0 to 4.4/1000 screens. Effect on ICR was variable but evidence of a reduced ICR was more consistent for studies using supplemental MRI (ICR 0.3 to 0.8 per 1000 screens) than those using ultrasound (ICR 0.49 to 1.9 per 1000 screens). The higher CDR and lower ICR with supplemental screening were associated with higher recall and biopsy rates particularly with supplemental MRI (9.5% 15.9%, up to 69/1000 screens). The authors concluded that cancers detected with supplemental imaging modalities were generally smaller and earlier stage. Mammography with supplemental MRI or ultrasound increases detection of cancers (versus mammography only) in some sub-groups but also increases recall and biopsy rates and may have a relatively modest effect in reducing ICR. Limitations include a small number of studies and the heterogeneity of the studies.~~

~~Clinical Practice Guidelines~~

~~American Cancer Society (ACS)~~

~~The ACS guideline on breast cancer and early detection (2022) specifically recommended against annual MRI screening in women at less than a 15% lifetime risk of breast cancer. The available data for MRI imaging is inconclusive for its use for routine screening in women who are not at high risk.~~

~~American College of Obstetricians and Gynecologists (ACOG)~~

~~In 2020 ACOG reaffirmed their recommendation for 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. ACOG also recommends that health care providers comply with state laws that may require disclosure to women of their breast density as recorded in a mammogram report.~~

~~American College of Radiology (ACR)~~

~~The American College of Radiology Appropriateness Criteria for Breast Cancer Screening (2017) considers MRI for screening high risk women including women with a BRCA gene mutation and their untested first degree relatives, women with a history of chest irradiation between 10 to 30 years of age, and women with 20% or greater lifetime risk of breast cancer usually appropriate.~~

~~American Society of Breast Surgeons (ASBrS)~~

~~A consensus guideline by the American Society of Breast Surgeons on diagnostic and screening magnetic resonance imaging of the breast (2017) also supports the use of MRI as a screening technique in women. The guideline particularly supports women age 25 or older with a BRCA gene mutation, women with other germline mutations known to predispose to a high risk of breast cancer, women with a history of chest irradiation, and women with a~~

~~20% 25% or greater estimated lifetime risk of breast cancer based on models primarily based on family history.~~

~~European Society of Breast Imaging (EUSOBI)~~

~~Breast density is an independent risk factor for the development of breast cancer and also decreases the sensitivity of mammography for screening. Consequently, women with extremely dense breasts face an increased risk of late diagnosis of breast cancer. These women are, therefore, underserved with current mammographic screening programs. The results of recent studies reporting on contrast-enhanced breast MRI as a screening method in women with extremely dense breasts provide compelling evidence that this approach can enable an important reduction in breast cancer mortality for these women and is cost-effective. Because there is now a valid option to improve breast cancer screening, the EUSOBI recommends that women should be informed about their breast density. EUSOBI thus calls on all providers of mammography screening to share density information with the women being screened. Considering the available evidence, in women aged 50 to 70 years with extremely dense breasts, the EUSOBI now recommends offering screening breast MRI every 2 to 4 years. The EUSOBI acknowledges that it may currently not be possible to offer breast MRI immediately and everywhere and underscores that quality assurance procedures need to be established but urges radiological societies and policymakers to act on this now. Since the wishes and values of individual women differ, in screening the principles of shared decision making should be embraced. Women should be counselled on the benefits and risks of mammography and MRI based screening, so that they can make an informed choice about their preferred screening method (2022).~~

Computer-Aided Detection (CAD) ~~with MRI of the Breast~~

Clinical evidence has not yet shown that CAD improves patient outcomes or lowers breast cancer mortality when added to mammography screening, MRI of the breast, or ultrasonography~~aphy~~. Future research should include better-designed studies, including prospective studies and randomized controlled trials evaluating CAD with these ~~is~~ technologies ~~y in large numbers of screening ultrasounds~~.

Park (2022) conducted a retrospective study to evaluate cancer size measurement by CAD and radiologist on breast MRI relative to histopathology and to determine clinicopathologic and MRI factors that may affect measurements. A total of 208 preoperative MRI of breast cancers taken between January 2017 and March 2021 met inclusion criteria. Correlation between CAD-generated size and pathologic size as well as that between radiologist-measured size and pathologic size were evaluated. A classification of size discrepancies was placed into accurate and inaccurate groups. For both CAD and radiologist, clinicopathologic and imaging factors were compared between accurate and inaccurate groups. The results of the study showed the mean sizes as predicted by CAD, radiologist and pathology were 2.66 ± 1.68 cm, 2.54 ± 1.68 cm, and 2.30 ± 1.61 cm, with significant difference ($p < 0.001$). Correlation coefficients of cancer size measurement by radiologist and CAD in reference to pathology were 0.898 and 0.823. Radiologist's measurement was more accurate than CAD, with statistical significance ($p < 0.001$). CAD-generated measurement was significantly more inaccurate for cancers of larger pathologic size (>2 cm), in the presence of an extensive intraductal component (EIC), with positive progesterone receptor (PR), and of non-mass enhancement. Radiologist-measured size was significantly more inaccurate for cancers in presence of an in situ component, EIC, positive human epidermal growth factor receptor 2 (HER2), and non-mass enhancement. The author concluded comparison of breast cancer size measurement between CAD and pathology, and between a radiologist and pathology, showed very strong correlations. Radiologist-measured tumor size was more accurate than CAD-generated size.

Cancer size measured by radiologist and CAD on MRI can be inaccurate for cancers with EIC and of the non-mass enhancement type. Limitations in the study include a lack of multicentric cancers, interobserver variability and a retrospective study design.

~~The Blue Cross and Blue Shield Association 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).~~

~~Clinical Practice Guidelines~~

~~American College of Radiology (ACR)~~

~~In 2017, the ACR revised the practice parameter for performing and interpreting magnetic resonance imaging. The use of computer aided detection (CAD)/computer aided evaluation (CAE) with breast MRI is not specifically recommended or addressed.~~

~~National Comprehensive Cancer Network (NCCN)~~

~~The NCCN guidelines for Breast Cancer Screening and Diagnosis (2021) does not address the use of computer aided detection (CAD)/computer aided evaluation (CAE) for breast MRI testing.~~

~~Computer-Aided Detection in Mammography Screening~~

A retrospective mammography review was performed by Park et al. (2022) to investigate whether artificial-intelligence-based, computer-aided diagnosis (AI-CAD) could facilitate the detection of missed cancer on digital mammography. A total of 204 women diagnosed with breast cancer with diagnostic (present) and prior mammograms between 2018 and 2020 were included in this study. Two breast radiologists reviewed the mammographic features and classified them into true negative, minimal sign or missed cancer. They analyzed the AI-CAD results with an abnormality score and assessed whether the AI-CAD correctly localized the known cancer sites. Of the 204 cases, 137 were classified as true negative, 33 as minimal signs, and 34 as missed cancer. The sensitivity, specificity and diagnostic accuracy of AI-CAD were 84.7%, 91.5% and 86.3% on diagnostic mammogram and 67.2%, 91.2% and 83.38% on prior mammogram, respectively. The authors concluded that AI-CAD correctly localized 27 cases from 34 missed cancers on prior mammograms. The findings in the preceding mammography of AI-CAD-detected missed cancer were common in the order of calcifications, focal asymmetry and asymmetry. Asymmetry was the most common finding among the seven cases, which could not be detected by AI-CAD in the missed cases (5/7). The assistance of AI-CAD can be helpful in the early detection of breast cancer in mammography screenings. Limitations to this study include a small number of patients with biopsy-proven malignancy with selection bias. Only one AI-CAD software was used for analysis. In addition, it is still difficult to determine the extent to which the suspicious findings detected by the AI-CAD in prior mammograms will lead to early cancer detection in actual practice. Additionally, false positive findings can affect the radiologist's judgment and lead to an increase in recall rate. Further research with randomized controlled trials is needed to validate these findings.

~~Computer-Aided Detection for Ultrasound~~

~~Clinical evidence has not yet shown that CAD improves patient outcomes or lowers breast cancer mortality when added to ultrasonography. Future research should include better-~~

~~designed studies, including prospective studies and randomized controlled trials evaluating this technology in large numbers of screening ultrasounds.~~

In a secondary analysis of data from a prospective study, Dahlblom et al. (2021) examine how an artificial intelligence (AI) system performs at digital mammography (DM) from a screening population with ground truth defined by digital breast tomosynthesis (DBT), and whether AI could detect breast cancers at DM that had originally only been detected at DBT. In this secondary analysis of data from a prospective study, DM examinations from 14,768 women (mean age, 57 years), examined with both DM and DBT with independent double reading in the Malmö Breast Tomosynthesis Screening Trial (MBTST) (ClinicalTrials.gov: NCT01091545; data collection, 2010-2015), were analyzed with an AI system. Of 136 screening-detected cancers, 95 cancers were detected at DM and 41 cancers were detected only at DBT. The system identifies suspicious areas in the image, scored 1-100, and provides a risk score of 1 to 10 for the whole examination. A cancer was defined as AI detected if the cancer lesion was correctly localized and scored at least 62 (threshold determined by the AI system developers), therefore resulting in the highest examination risk score of 10. Data were analyzed with descriptive statistics, and detection performance was analyzed with receiver operating characteristics. The highest examination risk score was assigned to 10% (1493 of 14 786) of the examinations. With 90.8% specificity, the AI system detected 75% (71 of 95) of the DM-detected cancers and 44% (18 of 41) of cancers at DM that had originally been detected only at DBT. The majority were invasive cancers (17 of 18). The authors concluded that almost half of the additional DBT-only screening-detected cancers in the MBTST were detected at DM with AI. AI did not reach double reading performance; however, if combined with double reading, AI has the potential to achieve a substantial portion of the benefit of DBT screening. As this retrospective study is based on radiologist readings without AI, the authors state it was not possible to study how the sensitivity and number of false-positive recalls would be affected by integrated AI and radiologists' readings in a real-world screening situation. The results here thus establish a current maximum additional cancer detection potential; however, further studies are needed to explore the clinical potential of AI.

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.

~~***Clinical Practice Guidelines***~~

~~***Clinical Practice Guidelines***~~

~~American College of Radiology (ACR)~~
~~In 2017, the ACR revised the practice parameter for performing and interpreting magnetic resonance imaging. The use of computer aided detection (CAD)/computer aided evaluation (CAE) with breast MRI is not specifically recommended or addressed.~~

~~National Comprehensive Cancer Network (NCCN)~~

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~~American College of Radiology (ACR, 2018)~~

~~In 2018, the ACR revised the practice parameter for the performance of screening and diagnostic mammography to state "Double reading and computer-aided detection (CAD) may slightly increase the sensitivity of mammographic interpretation and may be used. However, this sensitivity is usually at the expense of decreased specificity with increased recall and biopsy rates."~~

~~**Computed Tomography of the Breast**~~

~~The current evidence consists of very low quality, uncontrolled studies for computed tomography of the breast. The impact of this device on patient outcomes has not been determined. Future research should include better designed studies, including comparative, prospective and randomized controlled trials evaluating this technology.~~

~~Komolafe et al. (2022) performed a systematic review and meta-analysis to evaluate the comparison of diagnostic accuracy of cone beam breast computed tomography (CBBCT) and digital breast tomosynthesis (DBT) to characterize breast cancers. Two independent reviewers identified screening on diagnostic studies from 1 January 2015 to 30 December 2021, with at least reported sensitivity and specificity for both CBBCT (n = 5) and DBT (n = 17). A univariate pooled meta-analysis was performed using the random effects model to estimate the sensitivity and specificity while other diagnostic parameters like the area under the ROC curve (AUC), positive likelihood ratio (LR +), and negative likelihood ratio (LR -) were estimated using the bivariate model. The pooled sensitivity specificity, LR + and LR - and AUC at 95% confidence interval are 86.7% (80.3 91.2), 87.0% (79.9 91.8), 6.28 (4.40 8.96), 0.17 (0.12 0.25) and 0.925 for the 17 included studies in DBT arm, respectively, while 83.7% (54.6 95.7), 71.3% (47.5 87.2), 2.71 (1.39 5.29), 0.20 (0.04-1.05), and 0.831 are the pooled sensitivity specificity, LR + and LR - and AUC for the five studies in the CBBCT arm, respectively. The authors concluded that Our study demonstrates that DBT shows improved diagnostic performance over CBBCT regarding all estimated diagnostic parameters, with the statistical improvement in the AUC of DBT over CBBCT. The CBBCT might be a useful modality for breast cancer detection, thus we recommend more prospective studies on CBBCT application. There are limitations to the studies reviewed. The result of both arms was not extracted from the same studies and compared with a different cohort introducing potential bias. The sample size of the CBBCT arm is one-third of that of the DBT arm, thus the CBBCT result is underrepresented. In addition, there are no large multicenter prospective or clinical trial studies available. The findings of this study need to be validated by well-designed studies. Further investigation is needed before clinical usefulness of this procedure is proven.~~

~~In the 2020 ECRI Clinical Evidence Assessment Report, Breast Computed Tomography for Breast Cancer Screening found limited information to support the use of this technology~~

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~~Uhlig (2019) published a systematic review of the diagnostic accuracy of cone beam breast CT. A total of 362 studies were screened, of which 6 with 559 patients were included. All studies were conducted between 2015 and 2018 and evaluated female participants. Five studies included non-contrast cone beam breast computed tomography (NC-CBBCT) and three included contrast-enhanced cone beam breast computed tomography (CE-CBBCT). Overall, the study quality was high, except for one study of NC-CBBCT which was presented as a conferenced abstract and was given a lower rating due to lack of complete study design and conduct details. There was high between-study heterogeneity among the NC-CBBCT studies (I2 = 98.4%, 95% CI 80.6 to 94.2%. Using NC-CBBCT, pooled sensitivity was 0.789 (95% CI 0.66 to 0.89) and pooled specificity was 0.697 (95% CI 0.471 to 0.851). The NC-CBBCT partial area under the curve (AUC), calculated from only regions with reported study specificities and standardized to the whole space, was 0.817. There was no statistically significant heterogeneity among the three studies that evaluated CE-CBBCT (I2 = 57.3, 95% CI 0 to 84.1%,). Protocols for administration of iodinated intravenous contrast media were different in each study. The pooled sensitivity was 0.899 (95% CI 0.785 to 0.956) and the pooled specificity was 0.788 (95% CI 0.709 to 0.85). The CE-CBBCT partial AUC for was 0.869. The evidence available for CBBCT tends to show superior diagnostic performance for CE-CBBCT over NC-CBBCT regarding sensitivity, specificity and partial area under the curve (AUC). Diagnostic accuracy of CE-CBBCT was numerically comparable to that of breast MRI with meta-analyses reporting sensitivity of 0.9 and specificity of 0.72. The authors conclude that the results are encouraging but that additional "further large-scale, prospective studies and long-term follow-up studies are required.~~

Computer-Aided Tactile Breast Imaging

The current evidence consists of very low-quality, uncontrolled studies of the diagnostic efficacy for either tactile breast imaging device. The impact of these devices on patient outcomes has not been determined. There is significant potential for bias in these studies that could result in hyper-inflated estimates of diagnostic accuracy of tactile breast imaging relative to other screening modalities. Limitations to the research include insufficient reporting of the referral process and work-up prior to tactile breast imaging, lack of randomization, unclear blinding, and inconsistent application of the gold standard. Future research should include better-designed studies, including comparative, prospective and randomized controlled trials evaluating this technology.

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.

Computed Tomography of the Breast

There is a very low-quality body of evidence consisting of uncontrolled studies for computed tomography of the breast, which is insufficient to draw conclusions regarding evidence and patient outcomes.

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Electrical Impedance Scanning (EIS)

There is a lack of evidence in the published literature to show that electrical impedance scanning for the detection and classification of breast lesions can predict clinical events, alter treatment or is effective as or more effective than currently used methods. Additional well-designed studies are needed to determine whether or not EIS is effective as an adjunct to mammography or provides a positive clinical benefit and outcome.

In a 2022 systematic review and meta-analysis, Rezanejad Gatabi et al. sought to evaluate the accuracy of the electrical impedance tomography (EIT) technique for breast cancer diagnosis. A total of 12 selected studies met inclusion criteria and included data for 5487 patients with breast cancer. The findings revealed EIT had a higher diagnostic accuracy (sensitivity and specificity of 75.88% and 82.04%, respectively). The pooled diagnostic odds ratio was 14.37 and the pooled effect of accuracy was 0.79 with 95% CI. The authors concluded that EIT can be used as a useful method alongside mammography. EIT sensitivity could not be compared with the sensitivity of MRI, but in terms of specificity, it can be considered as a new method that probably can get more attention. Furthermore, large-scale studies will be needed to support the evidence. Limitations include heterogeneity in the study, insufficient information and unclear mean age in different groups and unable to analyze patients histopathology. (Author Stojadinovic 2006 which was previously cited in this policy, is included in this systematic review.)

Impedance measuring acquisition systems focused on breast tumor detection, as well as image processing techniques for 3D imaging, are examined in this systematic review by Gómez-Cortés (2022) to define potential opportunity areas for future research. The description of reported works using electrical impedance tomography (EIT)-based techniques and methodologies for 3D bioimpedance imaging of breast tissues with tumors is presented. The review is based on searching and analyzing related works reported in the most important research databases and is structured according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) parameters and statements. Nineteen papers reporting breast tumor detection and location using EIT were systematically selected and analyzed in this review. Clinical trials in the experimental stage did not produce results in most of analyzed proposals (about 80%), wherein statistical criteria comparison was not possible, such as specificity, sensitivity and predictive values. The authors concluded that a 3D representation of bioimpedance is a potential tool for medical applications in malignant breast tumors detection being

capable to estimate an ap-proximate the tumor volume and geometric location, in contrast with a tumor area computing capacity, but not the tumor extension depth, in a 2D representation. Clinical trials are required to consider statistical parameters in the comparison of the proposed systems. Only 20% of the reviewed articles concluded in clinical trials, this limitation does not allow comparative studies with other breast tumor detection methods. Further investigation is needed before clinical usefulness of this procedure is proven.

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.

~~In 2006, Stojadinovic et al. conducted a follow-up study. The results were reported for 1,361 consecutively enrolled asymptomatic women ages 30-39 years (used to measure specificity), and 189 women ages 30-45 years who had a suspicious breast abnormality and were referred for biopsy (used to measure sensitivity). (14) The researchers assumed that none of the women in the first group had breast cancer and, consequently, that any positive EIS results were false positives; no follow-up data were collected on these women. In the second group of women with breast abnormalities, 59.3% were aged 40-45. The specificity in the first group was 95% (assuming all positive results were incorrect); the specificity in the second group among women with benign breast disease was 80.7%. The sensitivity in the second group was 38%, but it ranged from 29% among women aged 30-39 to 42% among women aged 40-45. The authors concluded that the relative probability that a woman with a positive EIS result currently has breast cancer is 7.68 and that about one cancer would be detected for every 77 women referred for follow-up. This study has a number of limitations, including the assumption that none of the women in the specificity arm had cancer (the authors argue that this assumption is likely to have little impact on the overall results given the low prevalence of cancer in this population); the age difference between the two groups (and the difference in sensitivity by age, although whether or not this is statistically significant is not reported), and the measurement of sensitivity and specificity in two different populations. The authors themselves conclude that the results are encouraging but that "further large-scale, long-term follow-up studies are required and underway in the intended use populations.~~

~~***Clinical Practice Guidelines***~~

~~National Comprehensive Cancer Network (NCCN)~~

~~The 2021 NCCN Clinical Practice Guideline for Breast Cancer Screening and Diagnosis does not mention EIS as a diagnostic tool in the diagnosis or management of breast tumors.~~

Magnetic Resonance Elastography of the Breast (MRE)

Researchers have tested the feasibility of breast elastography and the results confirm the hypothesis that breast elastography can quantitatively depict the elastic properties of breast tissues and reveal high shear elasticity in known breast tumors. However, the clinical benefits of elastography imaging are still under evaluation and no clinical diagnosis can be made other than being able to tell whether or not a structure inside the patient is stiffer than another one. Further research is needed to evaluate the potential clinical applications of breast elastography, such as detecting breast carcinoma and characterizing suspicious breast lesions.

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 α0 (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.

Magnetic Resonance Imaging of the Breast

More robust data are needed to refine the role of magnetic resonance imaging in breast cancer screening, including its use for individuals with dense breast tissue and no high risk factors for breast cancer.

Onega et al. (2022) completed a clinical trial (NCT02980848) and comparison study to examine whether preoperative magnetic resonance imaging (MRI) yields additional biopsy and cancer detection by extent of breast density. The authors followed women in the Breast Cancer Surveillance Consortium with an incident breast cancer diagnosed from 2005 to 2017. They quantified breast biopsies and cancers detected within 6 months of diagnosis by preoperative breast MRI receipt, overall and by breast density, accounting for MRI selection bias using inverse probability weighted logistic regression. Among 19,324 women with newly diagnosed breast cancer, 28% had preoperative MRI, 11% additional biopsy, and 5% additional cancer detected. Four times as many women with preoperative MRI underwent additional biopsy compared to women without MRI (22.6% v. 5.1%). Additional biopsy rates with preoperative MRI increased with increasing breast density (27.4% for extremely dense compared to 16.2% for almost entirely fatty breasts). Rates of additional cancer detection were almost four times higher for women with v. without MRI (9.9% v. 2.6%). Conditional on additional biopsy, age-adjusted rates of additional cancer detection were lowest among women with extremely dense breasts, regardless of imaging modality (with MRI: 35.0%; 95% CI 27.0–43.0%; without MRI: 45.1%; 95% CI 32.6–57.5%). The authors concluded that for women with dense breasts, preoperative MRI was associated with much higher biopsy rates, without concomitant higher cancer detection. Preoperative MRI may be considered for some women, but selecting women based on breast density is not supported by evidence. There are several limitations to this study. The authors were not able to quantify the exact sequences of additional imaging and biopsy within the preoperative window, so were unable to definitively attribute an additional biopsy to the

preoperative MRI. The authors were unable to report on the effect of MRI on additional cancer detection by breast density in conjunction with other clinical characteristics, such as histology and subtype due to small numbers. Further, they were not able to assess whether the cancer was upgraded based on additional biopsies. Further investigation is needed before clinical usefulness of this procedure is proven.

A systematic review by Zeng et al. (2021) was performed to review the published literature to explore the effect of supplemental screening (MRI or breast ultrasound) compared to mammography alone on cancer detection and interval cancer rates. A further aim was to identify specific groups where supplemental screening is most effective at reducing the interval cancer rate (ICR). This study reviewed the evidence evaluating the effect of supplemental imaging on ICR in women undergoing screening mammography. This systematic review included studies that reported both cancer detection rate (CDR) and ICR in women undergoing screening mammography alone compared to those undergoing screening mammography with supplemental imaging. Five studies (3 randomized trials) were eligible. These reported on 142,153 women undergoing mammography screening alone or mammography with supplemental imaging (3 ultrasound and 2 MRI studies). Two studies included a general screening population and 3 included special populations (young, high genetic risk and/or dense breasts). The incremental CDR for supplemental MRI was 14.2 to 16.5/1000 screens and for ultrasound was 0 to 4.4/1000 screens. Effect on ICR was variable but evidence of a reduced ICR was more consistent for studies using supplemental MRI (ICR 0.3 to 0.8 per 1000 screens) than those using ultrasound (ICR 0.49 to 1.9 per 1000 screens). The higher CDR and lower ICR with supplemental screening were associated with higher recall and biopsy rates particularly with supplemental MRI (9.5%-15.9%, up to 69/1000 screens). The authors concluded that cancers detected with supplemental imaging modalities were generally smaller and earlier stage. Mammography with supplemental MRI or ultrasound increases detection of cancers (versus mammography only) in some sub-groups but also increases recall and biopsy rates and may have a relatively modest effect in reducing ICR. Limitations include a small number of studies and the heterogeneity of the studies.

~~Clinical Practice Guidelines~~

~~American Cancer Society (ACS)~~

~~The ACS guideline on breast cancer and early detection (2022) specifically recommended against annual MRI screening in women at less than a 15% lifetime risk of breast cancer. The available data for MRI imaging is inconclusive for its use for routine screening in women who are not at high risk.~~

~~American College of Obstetricians and Gynecologists (ACOG)~~

~~In 2020 ACOG reaffirmed their recommendation for 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. ACOG also recommends that health care providers comply with state laws that may require disclosure to women of their breast density as recorded in a mammogram report.~~

~~American College of Radiology (ACR)~~

~~The American College of Radiology Appropriateness Criteria for Breast Cancer Screening (2017) considers MRI for screening high-risk women including women with a BRCA gene mutation and their untested first-degree relatives, women with a history of chest irradiation between 10 to 30 years of age, and women with 20% or greater lifetime risk of breast cancer usually appropriate.~~

~~American Society of Breast Surgeons (ASBrS)~~

~~A consensus guideline by the American Society of Breast Surgeons on diagnostic and screening magnetic resonance imaging of the breast (2017) also supports the use of MRI as a screening technique in women. The guideline particularly supports women age 25 or older with a BRCA gene mutation, women with other germline mutations known to predispose to a high risk of breast cancer, women with a history of chest irradiation, and women with a 20%-25% or greater estimated lifetime risk of breast cancer based on models primarily based on family history.~~

~~European Society of Breast Imaging (EUSOBI)~~

~~Breast density is an independent risk factor for the development of breast cancer and also decreases the sensitivity of mammography for screening. Consequently, women with extremely dense breasts face an increased risk of late diagnosis of breast cancer. These women are, therefore, underserved with current mammographic screening programs. The results of recent studies reporting on contrast-enhanced breast MRI as a screening method in women with extremely dense breasts provide compelling evidence that this approach can enable an important reduction in breast cancer mortality for these women and is cost-effective. Because there is now a valid option to improve breast cancer screening, the EUSOBI recommends that women should be informed about their breast density. EUSOBI thus calls on all providers of mammography screening to share density information with the women being screened. Considering the available evidence, in women aged 50 to 70 years with extremely dense breasts, the EUSOBI now recommends offering screening breast MRI every 2 to 4 years. The EUSOBI acknowledges that it may currently not be possible to offer breast MRI immediately and everywhere and underscores that quality assurance procedures need to be established but urges radiological societies and policymakers to act on this now. Since the wishes and values of individual women differ, in screening the principles of shared decision-making should be embraced. Women should be counselled on the benefits and risks of mammography and MRI-based screening, so that they can make an informed choice about their preferred screening method (2022).~~

Molecular Imaging

The published literature on molecular breast imaging is limited by a number of factors. The studies include populations that usually do not represent those encountered in clinical practice and that have mixed indications. There are methodologic limitations in the available studies, which have been judged to have medium to high risk of bias, and they lack information on the impact on therapeutic efficacy. Limited evidence on the diagnostic accuracy of molecular imaging reports that these tests have a relatively high sensitivity and specificity for detecting malignancy. However, the evidence does not establish that this imaging improves outcomes when used as an adjunct to mammography for breast cancer screening. Larger, higher-quality studies are required to determine whether molecular imaging has a useful role as an adjunct to mammography.

De Feo et al. (2022) conducted a systematic review to assess if breast-specific gamma imaging (BSGI) is a more valuable choice in detecting breast malignant lesions compared

to morphological counterparts such mammography (MMG), ultrasound (US), and magnetic resonance imaging in terms of specificity, sensibility and positive and negative predictive value. A total of 15 studies compared BSGI with MMG, US, and MRI. BSGI sensitivity was similar to MRI, but specificity was higher. Specificity was always higher than MMG and US. BSGI had higher positive predictive value and negative predicative value. When used for the evaluation of a suspected breast lesion, the overall sensitivity was better than the examined overall sensitivity when BSGI was excluded. Risk of bias and applicability concerns domain showed mainly low risk of bias. The authors concluded BSGI is a valuable imaging modality with similar sensitivity to MRI but higher specificity, although at the cost of higher radiation burden. (Authors Kim 2012 and Cho 2016 which were previously cited in this policy, are included in this systematic review.)

~~Guo et al (2016). In~~ a 2016 systematic review and meta-analysis, **Guo et al., .** ~~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.

~~A 2013 TEC Assessment by the Blue Cross Blue Shield Association evaluated the use of BSGI, or scintimammography with breast-specific gamma camera as a diagnostic modality for~~

~~screening to detect breast tumors and concluded that there is no evidence of improved health outcomes.~~

~~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.~~

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. (Liberman et al., 2003)

Clinical Practice Guidelines

American Cancer Society (ACS)

The ACS recommendation for breast cancer early detection and diagnosis states that breast ultrasound is useful for looking at some breast changes, such as lumps (especially those that can be felt but not seen on a mammogram). Ultrasound can be especially helpful in women with dense breast tissue, which can make it hard to see abnormal areas on mammograms. It also can be used to get a better look at a suspicious area that was seen on a mammogram. Ultrasound is useful because it can often tell the difference between fluid-filled masses like cysts and solid masses (ACS, 2022).

The ACS guidelines for breast cancer screening states scintimammography, positron emission tomography, and electrical impedance imaging, have received FDA approval as diagnostic adjuncts to mammography. None of these new technologies has successfully undergone clinical testing that would justify its use in screening for breast cancer (ACS, 2003; updated 2015).

The ACS guideline on breast cancer screening for women at average risk specifically recommends against annual MRI screening in women at less than a 15% lifetime risk of breast cancer (ACS, 2007; updated 2015).

American College of Obstetricians and Gynecologists (ACOG)

In 2020 ACOG reaffirmed their recommendation for 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. ACOG also recommends that health care providers comply with state laws that may require disclosure to women of their breast density as recorded in a mammogram report.

American College of Radiology (ACR)

The ACR practice parameter for the performance of screening and diagnostic mammography states the following:

- **Double reading and CAD may be used but may slightly increase the sensitivity of mammographic interpretation.**
- **This sensitivity is usually at the expense of decreased specificity with increased recall and biopsy rates (ACR, 2018).**

The ACR appropriateness criteria for breast cancer screening considers MRI for screening high-risk women including women with a BRCA gene mutation and their untested first-degree relatives, women with a history of chest irradiation between 10 to 30 years of age, and women with 20% or greater lifetime risk of breast cancer usually appropriate (Mainiero, 2017).

According to practice parameter for the performance of molecular breast imaging (MBI) using a dedicated gamma camera ~~(2017)~~, there is insufficient evidence to support the use of breast specific gamma imaging (BSGI). Also, the relatively high radiation dose currently associated with BSGI/MBI has prompted the ~~American College of Radiology~~ACR to recommend against the use for screening (ACR, 2017).

American Society of Breast Surgeons (ASBrS)

A consensus guideline by the American Society of Breast Surgeons on diagnostic and screening magnetic resonance imaging of the breast (2017) also supports the use of MRI as a screening technique in women. The guideline particularly supports women age 25 or older with a BRCA gene mutation, women with other germline mutations known to predispose to a high risk of breast cancer, women with a history of chest irradiation, and women with a 20%-25% or greater estimated lifetime risk of breast cancer based on models primarily based on family history.

~~American Cancer Society (ACS)~~

~~According to ACS guidelines, routine breast cancer screening with scintimammography is not recommended. In their 2022 update on the section 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.~~

~~American College of Obstetricians and Gynecologists (ACOG)~~

~~The American College of Obstetricians and Gynecologists (2017) updated its 2011 practice bulletin on breast cancer screening in average-risk women. There was no discussion or recommendation for scintimammography or any other gamma imaging techniques for routine screening.~~

~~American College of Radiology (ACR)~~

~~According to practice parameter for the performance of molecular breast imaging (MBI) using a dedicated gamma camera (2017), there is insufficient evidence to support the use of breast specific gamma imaging (BSGI). Also, the relatively high radiation dose currently associated with BSGI/MBI has prompted the American College of Radiology to recommend against the use for screening.~~

European Society of Breast Imaging (EUSOBI)

Breast density is an independent risk factor for the development of breast cancer and also decreases the sensitivity of mammography for screening. Consequently, women with extremely dense breasts face an increased risk of late diagnosis of breast cancer. These women are, therefore, underserved with current mammographic screening programs. The results of recent studies reporting on contrast-enhanced breast MRI as a screening method in women with extremely dense breasts provide compelling evidence that this approach can enable an important reduction in breast cancer mortality for these women and is cost-effective. Because there is now a valid option to improve breast cancer screening, the EUSOBI recommends that women should be informed about their breast density. EUSOBI thus calls on all providers of mammography screening to share density information with the women being screened. Considering the available evidence, in women aged 50 to 70 years with extremely dense breasts, the EUSOBI now recommends offering screening breast MRI every 2 to 4 years. The EUSOBI acknowledges that it may currently not be possible to offer breast MRI immediately and everywhere and underscores that quality assurance procedures need to be established but urges radiological societies and policymakers to act on this now. Since the wishes and values of individual women differ, in screening the principles of shared decision-making should be embraced. Women should be counselled on the benefits and risks of mammography and MRI-based screening, so that they can make an informed choice about their preferred screening method (2022).

National Comprehensive Cancer Network (NCCN)

The 2021 NCCN Clinical Practice Guideline for Breast Cancer Screening and Diagnosis states, "current evidence does not support the routine use of molecular imaging (e.g. breast-specific gamma imaging, sestamibi scan, or positron emission mammography) as screening procedures, but there is emerging evidence that these tests may improve detection of early breast cancers among women with mammographically dense breasts. However, the whole-body effective radiation dose with these tests is substantially higher than that of mammography."

~~Society of Breast Imaging (SBI)~~

~~In the 2018 revised SBI Position Statement entitled 'Use of Alternative Imaging Approaches to Detection of Breast Cancer' states that the following: Molecular Breast Imaging (MBI) is not recommended for screening surveillance in any higher-risk population.~~

Society of Breast Imaging (SBI)/American College of Radiology (ACR)

The SBI and ACR recommendation (2010) for breast cancer screening with breast ultrasound state the following:

- **Can be considered in high-risk women for whom magnetic resonance imaging (MRI) screening may be appropriate but who cannot have MRI for any reason**
- **Can be considered in women with dense breast tissue as an adjunct to mammography (Lee, 2010).**

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

SNM published a Procedure Standard (2010) 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.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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.

Automated Breast Ultrasound System (ABUS)

Automated breast (or whole breast) ultrasound devices are regulated by the FDA as Class III devices. Refer to the following website for more information on devices used for automated breast ultrasound systems (search by product name in device name section or Product Code ITX): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April ~~June~~ 25~~1~~, 2023~~2~~)

~~Magnetic Resonance Elastography of the Breast~~

~~Refer to 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/pmn.cfm. (Accessed June 1, 2022)~~

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/pmn.cfm.

(Accessed **April 25** ~~June 1~~, 2023~~2~~)

Computer-Aided Detection for MRI of the Breast

Refer to 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/pmn.cfm. (Accessed April ~~June~~ 25~~1~~, 2023~~2~~)

Computer-Aided Detection for Ultrasound

Refer to 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/pmn.cfm. (Accessed April~~June~~ 25~~1~~, 2023~~2~~)

Computed Tomography of the Breast

Refer to the following website for more information on devices used for computed tomography of the breast (search by product name JAK in device name section): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April~~June~~ 25~~1~~, 2023~~2~~)

~~Automated Breast Ultrasound System (ABUS)~~

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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. Refer to 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/pmn.cfm. (Accessed **April**~~June~~ **25**~~1~~, 2023~~2~~)~~.~~

~~Computer-Aided Detection for MRI of the Breast~~

~~Refer to 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/pmn.cfm. (Accessed June 1, 2022)~~

~~Computer-Aided Detection for Ultrasound~~

~~Refer to 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/pmn.cfm. (Accessed June 1, 2022)~~

~~**Computed Tomography of the Breast**~~

~~Refer to the following website for more information on devices used for computed tomography of the breast (search by product name JAK in device name section): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.~~

~~**(Accessed June 1, 2022)**~~**Magnetic Resonance Elastography of the Breast**

**Refer to 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/pmn.cfm. (Accessed April~~~~June~~ ~~1~~25, 2023~~2~~)

References

American Cancer Society (ACS). Breast Cancer Early Detection and Diagnosis. Revised January 14, 2022.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Gynecology. Breast cancer risk assessment screening in average-risk women Practice Bulletin 179. 2017.

American College of Obstetricians and Gynecologists (ACOG). Management of women with dense breasts diagnosed by mammography. Reaffirmed 2020.

~~American College of Radiology (ACR) Appropriateness criteria: Breast cancer screening. Updated 2017.~~

~~American College of Radiology (ACR) Practice parameter for performing and interpreting magnetic resonance imaging(MRI). Updated 2017.~~

American College of Radiology (ACR) Practice parameter for the performance of molecular breast imaging (MBI) using a dedicated gamma camera. 2017.

American College of Radiology (ACR) Practice parameter for the performance of screening and diagnostic mammography. **2014;** Revised 2018.

American Society of Breast Surgeons (ASBS). Consensus guideline on diagnostic and screening magnetic resonance imaging of the breast. 2017.

~~Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). TEC Special Report: screening asymptomatic women with dense breasts and normal mammograms for breast cancer. TEC Assessments 2013.~~

~~Blue Cross Blue Shield Association (BCBSA) Technology Evaluation Center. Computer-aided detection of malignancy with magnetic resonance imaging of the breast. June 2006c.~~

Brem RF, Ruda RC, Yang JL, et al. Breast-specific γ-imaging for the detection of mammographically occult breast cancer in women at increased risk. J Nucl Med. 2016 May;57(5):678-84.

Chen H, Han M, Jing H, et al. Dependability of automated breast ultrasound (ABUS) in assessing breast imaging reporting and data system (BI-RADS) category and size of malignant breast lesions compared with handheld ultrasound (HHUS) and mammography (MG). Int J Gen Med. 2021 Dec 1;14:9193-9202.

Cho KR, Seo BK, Woo OH, et al. Breast cancer detection in a screening population: Comparison of digital mammography, computer-aided detection applied to digital mammography and breast ultrasound. J Breast Cancer. 2016 Sep; 19(3):316-323.

Dahlblom V, Andersson I, Lång K, et al. Artificial intelligence detection of missed cancers at digital mammography that were detected at digital breast tomosynthesis. Radiol Artif Intell. 2021 Sep 1;3(6):e200299.

De Feo MS, Sidrak MMA, Conte M, et al. Breast-Specific Gamma Imaging: an added value in the diagnosis of breast cancer, a systematic review. Cancers (Basel). 2022 Sep 23;14(19):4619.

ECRI. Automated breast ultrasound systems for diagnosing breast cancer. Plymouth Meeting (PA): ECRI; 2021 Jul. (Clinical Evidence Assessment).

ECRI. Breast ultrasound using an automated system for cancer screening in women with dense breast tissue. Plymouth Meeting (PA): ECRI; 2022 Jul. (Clinical Evidence Assessment).

ECRI. Noninvasive Diagnostic Tests for Breast Abnormalities. Plymouth Meeting (PA): ECRI; 2006 Mar; updated 2013 Jan. (Evidence Report).

Gatta G, Cappabianca S, La Forgia D, et al. Second-generation 3D automated breast ultrasonography (prone ABUS) for dense breast cancer screening integrated to mammography: effectiveness, performance and detection rates. J Pers Med. 2021 Aug 31;11(9):875.

Gómez-Cortés JC, Díaz-Carmona JJ, Padilla-Medina JA, et al. Electrical impedance tomography technical contributions for detection and 3D geometric localization of breast tumors: a systematic review. Micromachines (Basel). 2022 Mar 23;13(4):496.

Guo C, Zhang C, Liu J, et al. Is Tc-99m sestamibi scintimammography useful in the prediction of neoadjuvant chemotherapy responses in breast cancer? A systematic review and meta-analysis. Nucl Med Commun. 2016 Jul;37(7):675-88.

Güldogan N, Yılmaz E, Arslan A, et al. Comparison of 3D-automated breast ultrasound with handheld breast ultrasound regarding detection and BI-RADS characterization of lesions in dense breasts: a study of 592 cases. Acad Radiol. 2021 Dec 23:S1076-6332(21)00561-4.

Hadadi I, Rae W, Clarke J, et al. Diagnostic performance of adjunctive imaging modalities compared to mammography alone in women with non-dense and dense breasts: A systematic review and meta-analysis. Clin Breast Cancer. 2021 Aug;21(4):278-291.

Hellgren R, Dickman P, Leifland K, et al. Comparison of handheld ultrasound and automated breast ultrasound in women recalled after mammography screening. Acta Radiol. 2017 May; 58(5):515-520.

Hussain R, Buscombe JR. A meta-analysis of scintimammography: an evidence-based approach to its clinical utility. Nucl Med Commun. 2006 Jul;27(7):589-94.

Kim BS. Usefulness of breast-specific gamma imaging as an adjunct modality in breast cancer patients with dense breast: A comparative study with MRI. Ann Nucl Med. 2012;26(2):131-137.

Kim Y, Kang BJ, Kim SH, et al. Prospective study comparing two second-look ultrasound techniques: Handheld ultrasound and an automated breast volume scanner. J Ultrasound Med. 2016 Oct; 35(10):2103-12.

Komolafe TE, Zhang C, Olagbaju OA, et al. Comparison of diagnostic test accuracy of cone-beam breast computed tomography and digital breast tomosynthesis for breast cancer: a systematic review and meta-analysis approach. Sensors (Basel). 2022 May 9;22(9):3594.

Lee CH, Dershaw DD, Kopans D, et al. Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. J Am Coll Radiol. 2010 Jan;7(1):18-27.

Liberman M, Sampalis F, Mulder DS, et al. Breast cancer diagnosis by scintimammography: a meta-analysis and review of the literature. Breast Cancer Res Treat. 2003b Jul;80(1):115-26.

Mainiero MB, Moy L, Baron P, et al. ACR Appropriateness Criteria® Breast Cancer Screening. J Am Coll Radiol. 2017 Nov;14(11S):S383-S390.

Mann RM, Athanasiou A, Baltzer PAT, et al. Breast cancer screening in women with extremely dense breasts recommendations of the European Society of Breast Imaging (EUSOBI). Eur Radiol. 2022 Jun;32(6):4036-4045.

National Cancer IInstitute (NCI) Computed tomography (CT) scans and cancer. August 2019.

National Comprehensive Cancer Network (NCCN) Clinical practice guidelines in oncology: Breast cancer. Revised v3.2022.

National Comprehensive Cancer Network (NCCN) Clinical practice guidelines in oncology: genetic/~~famililial~~ **familial** high-risk assessment: breast ovarian, and pancreatic.v2.2021.

National Comprehensive Cancer Network (NCCN) Clinical practice guidelines in oncology: Breast cancer screening and diagnosis. May 2021.

Oeffinger KC, Fontham ET, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. JAMA. 2015 Oct 20;314(15):1599-614.

Onega T, Zhu W, Kerlikowske K, et al. Preoperative MRI in breast cancer: effect of breast density on biopsy rate and yield. Breast Cancer Res Treat. 2022 Jan;191(1):177-190.

Park GE, Kang BJ, Kim SH, et al. Retrospective review of missed cancer detection and its mammography findings with artificial-intelligence-based, computer-aided diagnosis. Diagnostics (Basel). 2022 Feb 2;12(2):387.

Park JY. Evaluation of Breast Cancer Size Measurement by Computer-Aided Diagnosis (CAD) and a Radiologist on Breast MRI. J Clin Med. 2022 Feb 22;11(5):1172.

Prosch et al. Automated breast ultrasound vs. handheld ultrasound: BI-RADS classification, duration of the examination and patient comfort. European Journal of Ultrasound 2011; 32(05): 504 – 510.

Rezanejad Gatabi Z, Mirhoseini M, Khajeali N, et al. The accuracy of electrical impedance tomography for breast cancer detection: a systematic review and meta-analysis. Breast J. 2022 May 26;2022:8565490.

Siegmann KC, Xydeas T, Sinkus R, et al. Diagnostic value of MR elastography in addition to contrast-enhanced MR imaging of the breast-initial clinical results. Eur Radiol. 2010 Feb;20(2):318-25.

~~Society of Breast Imaging (SBI). Position Statement. Use of alternative imaging approaches to detection of breast cancer. Updated 2018.~~

Society of Nuclear Medicine and Molecular Imaging (SNMMI) Procedure guideline for breast scintigraphy with breast-specific gamma cameras.V1. June 2010.

Stojadinovic A, Nissan A, Gallimidi Z, et al. Electrical impedance scanning for the early detection of breast cancer in young women: preliminary results of a multicenter prospective clinical trial. J Clin Oncol. 2005 Apr 20;23(12**):2703-15.**

Stojadinovic A., Moskovitz O., Gallimidi Z. et al. Prospective study of electrical impedance scanning for identifying young women at risk of breast cancer. Breast Cancer Res Treat. 2006; 97(2):179-89.

Tasoulis MK, Zacharioudakis KE, Dimopoulos NG, Hadjiminas DJ. Diagnostic accuracy of tactile imaging in selecting patients with palpable breast abnormalities: a prospective comparative study. Breast Cancer Res Treat. 2014.

Uhlig J, Uhlig, A, Biggemann, L. et al. Diagnostic accuracy of cone-beam breast computed tomography: a systematic review and diagnostic meta-analysis. Eur Radiol 29, 1194–1202 (2019).

Wang T, Wang K, Yao Q, et al. Prospective study on combination of electrical impedance scanning and ultrasound in estimating risk of development of breast cancer in young women. Cancer Invest. 2010;28(3):295-303.

Weigert JM, Bertrand ML, Lanzkowsky L et al. Results of a multicenter patient registry to determine the clinical impact of breast-specific gamma imaging, a molecular breast imaging technique. AJR Am J Roentgenol 2012; 198(1):W69-75.

Zeng A, Brennan ME, Young S, et al. The effect of supplemental imaging on interval cancer rates in mammography screening: systematic review. Clin Breast Cancer. 2022 Apr;22(3):212-222.

Policy History/Revision Information

Date	Summary of Changes
TBD	**Coverage Rationale** • Replaced language indicating "this policy does not address preventive benefit for breast cancer screening (*including* mammography)" with "this policy does not address *routine* preventive benefit for breast cancer screening (*using conventional* mammography)" **Definitions** • Removed definition of: ○ Breast Ultrasound • Computer-Aided Detection (CAD) for Ultrasound ○ Computer-Aided Detection (CAD) with MRI of the Breast • Computed Tomography (CT) ○ Magnetic Resonance Imaging (MRI) **Applicable Codes** • Added notation to indicate HCPCS code S8080 is not on the State of Louisiana Fee Schedule and therefore may not be covered by the State of Louisiana Medicaid Program **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS010LA.Q

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual

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