Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 7/1/22**
(See policy history boxes for previous effective dates)

Title: Breast Elastography – Ultrasound or Magnetic Resonance

Description/Background

In the United States, about 1 in 8 women will develop invasive breast cancer over the course of her lifetime. In 2022, is it estimated that there will be over 280,000 new cases of invasive breast cancer diagnosed in women and over 2,600 new cases of invasive breast cancer in men.[1] In 2021 breast cancer became the most common cancer globally.[1] Mammography remains the generally accepted standard diagnostic test for breast cancer screening and diagnosis. The incidence of breast cancer has led to research on new diagnostic imaging techniques for early diagnosis.

Elasticity is the property of a substance to be deformed in response to an external force and to resume its original size and shape when the force is removed. In evaluation of superficial tissue such as skin, breast or prostate, manual palpation can distinguish normal tissue from stiffer tissue. Elastography is a noninvasive technique that evaluates the elastic properties, or stiffness of tissues, and its application for diagnosing breast cancer is based on the principle that malignant tissue is less elastic than normal, healthy breast tissue. Elastography has been investigated as an additive technique to increase the specificity of ultrasound and magnetic resonance imaging. Other emerging applications include breast, thyroid, prostate, kidney and lymph nodes.[2]

Ultrasound elastography, also known as sonoelastography, is a noninvasive imaging technique that can be used to determine relative tissue stiffness. There are 2 main types of ultrasound elastography, strain and shear wave. Strain elastography uses a static force and is a qualitative technique of compression that provides information on the relative stiffness between one tissue and another. Shear wave elastography utilizes a dynamic force and is a quantitative method that provides an estimated value of the stiffness. The process involves comparing a normal ultrasound image to one in which the suspect area is compressed. In strain elastography, an ultrasound transducer generally provides the force. In shear wave elastography, a handheld probe that combines an ultrasound transducer with a mechanical vibrator is used. Sonographic

measurements are made based on movement of the tissue in response to the compression and decompression waves. Generally, USE is considered to provide complementary information to conventional US. This technology has been widely utilized in staging hepatic fibrosis.[3,4,5]

Magnetic resonance elastography is the 3-dimensional analysis of wave propagation and tissue deformation. The technique uses standard MRI equipment with some modifications. The main steps involved in MRE include generating mechanical waves in soft tissues, acquiring MR images of the propagation of the induced shear waves and processing the images of the shear waves to a quantitative map of tissue stiffness, the elastogram. Currently, MRE's principal application is for staging hepatic fibrosis.[6]

Regulatory Status

The SonixTouch Ultrasound System (Richmond, British Columbia) was given 501(k) approval by the FDA in 2008 as a multi-purpose mobile, software controlled diagnostic ultrasound system with on-screen thermal and mechanical indices related to potential bio-effect mechanisms. The elastography imaging mode is similar to the Siemens S2000 Elasticity imaging mode implementation (also called eSie Touch Elasticity Imaging).[7]

Acuson S1000, S2000, S3000 Ultrasound System with eSie™ Touch elasticity imaging (Siemens Medical Solutions USA, Inc., Buffalo, MN) received FDA 501(k) approval in 2014.[8]

Other manufacturers with ultrasound elastography implementations include Easote, Hitachi, GE, Philips, Toshiba and Samsung.

MRE was classified by the FDA as a Class I device, cleared through the premarket 510(k) mechanism. MRE produces an acoustic frequency vibration and then uses MRI for the measurement of displacement caused by vibrations leading to measurements of stiffness. MRE was patented by the Mayo Foundation; the Mayo Foundation founded Resoundant. GE, Siemens and Phillips licensed the MRE technology from Resoundant.[8]

Philips Medical Systems (The Netherlands) was given 510(k) approval by the FDA in 2014 MR Elastography software option for magnetic resonance diagnostic device.[9,10]

Medical Policy Statement

Breast elastography by either ultrasound or magnetic resonance is considered experimental / investigational. There is insufficient evidence of the effectiveness of elastography in the screening or diagnosis of breast cancer.

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

NA

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

Established codes:

N/A

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

76391 76981 76982 76983

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Ultrasound Elastography

Sigrist et al (2017)[2] reported on a review of the principles and concepts of ultrasound elastography (USE), including summaries of studies assessing malignancy of masses in the liver, breast, thyroid, kidney, prostate and lymph nodes. Several studies evaluated whether the addition of shear wave imaging can improve the performance of B-mode US in assessing breast malignancy. In the review, specific studies highlighted included:

> Feldmann et al (2015) used qualitative and quantitative 2 dimensional shear wave elastography (2D-SWE) parameters in addition to B-mode US to differentiate between malignant and benign breast lesions in 82 patients. They showed that using benign shear wave imaging signs to selectively downgrade B-mode US classified BI-RADS 4a (low suspicion for malignancy) and BI-RADS 4b (intermediate suspicion for malignancy) lesions improved specificity of US (13% to 51%) without loss in sensitivity (100%).
>
> Berg et al (2012) performed a study with 958 women with breast lesions showing that shear wave imaging improved the specificity of B-mode US (61.1% to 78.5%).

The reviewers concluded that if a lesion classified as BI-RADS 4a has benign shear wave imaging features, it can be downgraded to BI-RADS 3 (probably benign), warranting follow-up rather than biopsy. The reviewers concluded that the technique shows promise to improve patient management and reduce unnecessary biopsies, but additional studies are warranted for further validation.

Sadigh et al (2013)[11] conducted an individual patient data meta-analysis comparing the diagnostic performance of ultrasound elastography (USE) versus B-mode ultrasound (USB) across size ranges of breast masses. Included studies were published between January 2008 and February 2011 in peer-reviewed journals. Information on 1,332 patients and 1,412 breast masses was included in the review. For breast masses <10 mm (n=543; 121 malignant), the sensitivity/specificity of USE and USB were 76% / 93% and 95% / 68%, respectively. For

masses 10-19 mm of size (n=528; 247 malignant), sensitivity/specificity of USE and USB were 82% / 90% and 95% / 67%, respectively. For masses >19 mm of size (n=325; 162 malignant), sensitivity/specificity of USE and USB were 74% / 94% and 97% / 55%, respectively. The reviewers' concluded that regardless of the mass size, USE has higher specificity and lower sensitivity compared to USB in characterizing breast masses.

Limitations of breast USE have been consistently identified in the literature include: elastogram color coding and scoring are not standardized, occasionally a malignant lesion may appear soft in SWI, it is difficult to characterize heterogeneous lesions with mixed benign (cystic) and malignant (necrotic) features, some benign lesions may also be stiff, and masses in the posterior breast are difficult to assess due to tissue attenuation.

Magnetic Resonance Elastography

Lorenzen et al (2002)[12] reported on a study of MRE and diagnosis of breast lesions involving 20 patients (15 with malignant tumors and 5 with benign tumors) and 15 healthy volunteers. Malignant invasive breast tumors documented the highest values of elasticity with a median of 15.9 kPa and a wide range of stiffnesses between 8 and 28 kPa. In contrast, benign breast lesions represented low values of elasticity, which were significantly different from malignant breast tumors (median elasticity: 7.0 kPa; $p = 0.0012$). This was comparable to the stiffest tissue areas in healthy volunteers (median elasticity 7.0 kPa), whereas breast parenchyma (median: 2.5 kPa) and fatty breast tissue (median: 1.7 kPa) showed the lowest values of elasticity. Two invasive ductal carcinomas had elasticity values of 8 kPa and two stiff parenchyma areas in healthy volunteers had elasticities of 13 and 15 kPa. These lesions could not be differentiated by their elasticity. The authors concluded that MRE is a promising new imaging modality with the capability to assess the viscoelastic properties of breast tumors and the surrounding tissues. They noted that an obvious limitation of the overlap in the elasticity ranges of soft malignant tumors and stiff benign lesions.

Siegmann et al (2010)[13] assessed the additional value of MRE to contrast-enhanced MR (ce MRI) for the characterization of breast lesion. Suspected breast lesions in 57 patients were examined by both methodologies. All lesions were classified into BI-RADS categories. Viscoelastic parameters were calculated. Histology of the lesions was correlated with BI-RADS and viscoelastic properties. The positive predictive value (PPV) for malignancy, and the sensitivity and specificity of ce MRI were calculated. The lesions (mean size 27.6 mm) were malignant in 64.9% (n=37) of cases. The PPV for malignancy was significantly ($p < 0.0001$) dependent on BI-RADS classification. The sensitivity of ce MRI for breast cancer detection was 97.3% (36/37), whereas specificity was 55% (11/20). If ce MRI was combined with the viscoelastic parameters calculated by MRE, the diagnostic accuracy could be significantly increased ($p < 0.05$; AUC(ce MRI) = 0.93, AUC(combined) = 0.96). The authors concluded that the combination of MRE and ce MRI could increase the diagnostic performance of breast MRI. They stated that further investigations of larger cohorts and smaller lesions (in particular those only visible on MRI) are necessary to validate these results.

Early studies suggest that MRE shows promise in differentiating benign from malignant tumors in a variety of organ systems, however an overlap in stiffness is a limiting factor and prospective studies involving larger numbers of patients are required for validation.[6]

SUPPLEMENTAL INFORMATION

World Federation of Ultrasound in Medicine and Biology, 2015[14]

Guidelines and Recommendations for Clinical Use of Ultrasound Elastography: Part 2: Breast

"Elastography is a complimentary technique to B-mode imaging. Elastography (SE or SWE) should be performed and interpreted along with standard B-mode imaging."

ACR BI-RADS® Atlas Fifth Edition, 2013[15]

Ultrasound Lexicon, "Associated features" includes elasticity assessment (soft, intermediate, hard).

Ongoing and Unpublished Clinical Trials

A search of clinicaltrials.gov identified the following ongoing or unpublished trials.

Table 1. Summary of Key Trials

NCT number	Trial Name	Planned Enrollment	Completion Date
Recruiting			
NCT04397029	Assessing the Sensitivity of "SureTouch™" in Identifying Clinically Significant Masses in Women Undergoing Diagnostic and Screening (US)	195	6/2024
NCT03487471	Comparison of Real-time and Shear Wave Elastography (Elasto) (Switzerland)	98	6/2021
NCT03887598	Application of Ultrasound Artificial Intelligence and Elastography in Differential Diagnosis of Breast Nodules (China)	2000	2/2020
NCT02388230	Quantification of Breast RadioTherapy Associated Late Toxicity Using Novel UltraSound Techniques (QuaRTUS) (UK)	64	12/2020
Active, Not Recruiting			
Completed			
NCT02701348	Radiological and Biological Tumoural and Peri-tumoural Factors in Neoadjuvant Endocrine-treated Breast Cancers (CARONET) (UK)	40	5/2022
NCT03851497	Application of Deep-learning and Ultrasound Elastography in Opportunistic Screening of Breast Cancer (China)	2244	1/2021
NCT02834494	Assessment of Response to Neo-adjuvant Chemotherapy for Patients With a Locally Advanced Breast Cancer with 3D Elastography (Shear Wave) (NEO-ELASTO) (France)	140	9/2020 (no results)
NCT02638935	Evaluation of Virtual Touch Tissue Imaging Quantification (VTIQ-2D-SWE) in the Assessment of BI-RADS® 3 and 4 Lesions	1304	3/2019 (no results)
NCT03276845	Multiparametric High-resolution Ultrasound of the Breast (Austria)	214	9/2017 (no results)
NCT01963624	Combined Elastography and Color Doppler Ultrasonography for Breast Screening With Ultrasound (Korea)	1241	1/2016 (no results)
NCT02226081	ShearWave™ Elastography of Breast Lesions in Chinese Patients (China)	2273	6/2015 (no results)
NCT01737970	A Study to Correlate Ultrasound Elastography with Histopathology to Monitor the Response of Locally Advanced Breast Cancer to Neoadjuvant Chemotherapy (UK)	10	7/2014
NCT01531036	3D Breast Ultrasound Elastography in Patients Under Neoadjuvant Chemotherapy (France)	33	11/2012 (no results)
NCT00716482	Ultrasound Elastography of Breast Lesions	1681	6/2010

Government Regulations

National:

No NCD on this topic.

Local:

No LCD on this topic.

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

Related Policies

Noninvasive Techniques for the Evaluation and Monitoring of Patients With Chronic Liver Disease

References

1. U.S. Breast Cancer Statistics, https://www.breastcancer.org/symptoms/understand_bc/statistics Accessed 2/28/22.
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3. Dietrich CF, et al. Strain elastography – how to do it. Ultrasound Int Open. 2017; 3: E137-E149.
4. Imtiaz, S. Breast elastography: a new paradigm in diagnostic breast imaging. Applied Radiology. March 2018. https://appliedradiology.com/articles/breast-elastography-a-new-paradigm-in-diagnostic-breast-imaging Accessed 2/28/22.
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6. Low G, et al. General review of magnetic resonance elastography. World Journal of Radiology. 2016 January 28; 8(1): 59-72.
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8. U.S. Food and Drug Administration, Acuson 510(k) Summary, K142876 https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K142876 Accessed 2/28/22.
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11. Sadigh G et al. Impact of breast mass size on accuracy of ultrasound elastography vs conventional B-mode ultrasound: a meta-analysis of individual participants. European Radiology. (2013) 23:1006-1014.
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13. Siegmann KC et al. Diagnostic value of MR elastography in addition to contrast-enhanced MR imaging of the breast-initial clinical results. Eur Radiol. 2010; 20: 318-325.
14. Barr RG et al. WFUMB Guidelines and Recommendations for Clinical Use of Ultrasound Elastography: Part 2: Breast. Ultrasound in Med & Biol. Vol. 41, No. 5, pp. 1148-1160, 2015.
15. American College of Radiology. ACR Bi-®RADS Atlas 5th Edition. https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Bi-Rads Accessed 2/28/22.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 2/28/22, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/1/19	4/16/19		Joint policy established
7/1/20	4/14/20		Routine maintenance
7/1/21	4/20/21		Routine maintenance
7/1/22	4/19/22		Routine maintenance

Next Review Date: 2nd Qtr, 2023

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: BREAST ELASTOGRAPHY – ULTRASOUND OR MAGNETIC RESONANCE

I. Coverage Determination:

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

II. Administrative Guidelines:

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