

**Policy** # 00672

Original Effective Date: 08/01/2019 Current Effective Date: 08/14/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

# **Services Are Considered Investigational**

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers myocardial strain imaging in individuals who have exposure to medications or radiation that could result in cardiotoxicity to be **investigational.\*** 

Based on review of available data, the Company considers myocardial strain imaging in all other situations to be **investigational.\*** 

# **Background/Overview**

The term strain indicates dimensional or deformational change under force. When used in echocardiography, the term 'strain' is used to describe the magnitude of shortening, thickening, and lengthening of the myocardium through the cardiac cycle. The most frequent measure of myocardial strain is the deformation of the left ventricle in the long axis, termed global longitudinal strain. During systole, ventricular myocardial fibers shorten with movement from the base to the apex. Global longitudinal strain is used as a measure of global left ventricle function and provides a quantitative myocardial deformation analysis of each left ventricle segment. Myocardial strain imaging is intended to detect subclinical changes in left ventricle function in individuals with a preserved left ventricle ejection fraction, allowing for early detection of systolic dysfunction. Since strain imaging can identify left ventricle dysfunction earlier than standard methods, this raises the possibility of heart failure prophylaxis and primary prevention before the patient develops symptoms and irreversible myocardial dysfunction. Potential applications of speckle-tracking echocardiography are coronary artery disease, ischemic cardiomyopathy, valvular heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathies, stress cardiomyopathy, and chemotherapyrelated cardiotoxicity.

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### **Myocardial Strain Imaging**

Myocardial strain can be measured by cardiac magnetic resonance imaging (MRI), tissue Doppler imaging or by speckle-tracking echocardiography. Tissue Doppler strain imaging has been in use since the 1990s but has limitations that include angle dependency and significant noise. In 2016, Smiseth et al reported that the most widely used method of measuring myocardial strain at the present time is speckle-tracking echocardiography. In speckle-tracking echocardiography, natural acoustic markers generated by the interaction between the ultrasound beam and myocardial fibers form interference patterns (speckles). These markers are stable, and speckle-tracking echocardiography analyzes the spatial dislocation (tracking) of each point (speckle) on routine 2-dimensional sonograms. Echocardiograms are processed using specific acoustic-tracking software on dedicated workstations, with offline semiautomated analysis of myocardial strain. The 2-dimensional displacement is identified by a search with image processing algorithms for similar patterns across 2 frames. When tracked frame-to-frame, the spatiotemporal displacement of the speckles provides information about myocardial deformation across the cardiac cycle. Global longitudinal strain provides a quantitative analysis of each left ventricle segment, which is expressed as a percentage. In addition to global longitudinal strain, speckle-tracking echocardiography allows evaluation of left ventricle rotational and torsional dynamics.

# FDA or Other Governmental Regulatory Approval

# U.S. Food and Drug Administration (FDA)

A number of image analysis systems have been cleared for marketing by the U.S. FDA through the 510(k) process. Examples of these are shown in Table 1. For example, the Echolnsight software system (Epsilon Imaging) "enables the production and visualization of 2-dimensional tissue motion measurements (including tissue velocities, strains, strain rates) and cardiac structural measurement information derived from tracking speckle in tissue regions visualized in any B mode (including harmonic) imagery loops as captured by most commercial ultrasound systems" (K110447). The FDA determined that this device was substantially equivalent to existing devices (eg,syngo US Workplace, Siemens, K091286) for analysis of ultrasound imaging of the human heart.

**Table 1. Examples of Software That Have Received FDA Clearance** 

Brand Name	Manufacturer	510(k)	FDA Product	Clearance Date
		Number	Code	

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Myostrain	Myocardial Solutions	K182756	LNH	02/14/2019
Vivid	GE	K181685	IYN	10/25/2018
Aplio	Toshiba		IYN	01/11/2018
2D CARDIAC PERFORMANCE ANALYSIS	Tomtec	K120135	LLZ	04/13/2012
Echolnsight	Epsilon Imaging	K110447	LLZ	05/27/2011
Q-lab	Phillips	K023877	LLZ	12/23/2002

FDA: Food and Drug Administration.

# Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Myocardial strain refers to the deformation (shortening, lengthening, or thickening) of the myocardium through the cardiac cycle. Myocardial strain can be measured by tissue Doppler imaging or, more recently, speckle-tracking echocardiography. Speckle-tracking echocardiography uses imaging software to assess the movement of specific markers in the myocardium that are detected in standard echocardiograms. It is proposed that a reduction in myocardial strain may indicate sub-clinical impairment of the heart and can be used to inform treatment before development of symptoms and irreversible myocardial dysfunction.

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### **Summary of Evidence**

For individuals who have exposure to medications or radiation that could result in cardiotoxicity who receive myocardial strain imaging, the evidence includes systematic reviews of observational studies and a randomized controlled trial (RCT). Relevant outcomes include symptoms, morbid events, quality of life, treatment-related mortality, and treatment-related morbidity. A systematic review of 13 studies with 384 individuals treated for cancer suggests that myocardial strain imaging with tissue Doppler imaging or speckle-tracking echocardiography may be able to identify changes in myocardial deformation that precede changes in left ventricle ejection fraction. Although myocardial strain imaging may detect sub-clinical myocardial changes, the value of these changes in predicting clinical outcomes or guiding therapy is uncertain. In the SUCCOUR RCT, left ventricle surveillance with global longitudinal strain was associated with an increased use of cardioprotective therapy and a lower incidence of cancer-therapy-related cardiac dysfunction as compared to left ventricular ejection fraction surveillance. However, no difference in the primary endpoint of final left ventricular ejection fraction at 1-year follow-up was observed between the groups and interpretation of findings was limited by important design and relevance limitations. At 3-year follow-up, despite the increase in the use of cardioprotective therapies in the global longitudinal strain-guided group, there were minimal differences in the change in left ventricular ejection fraction between groups. Additional studies are indicated to better define the threshold for cardioprotective therapy and assess whether a global longitudinal strain-guided approach to cardioprotective therapy reduces the long-term risk of heart failure and improves clinical outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

# **Supplemental Information**

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

#### **Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

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### American College of Cardiology et al

In 2019, the American College of Cardiology, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons published appropriate use criteria for multimodality imaging in the assessment of cardiac structure and function in nonvalvular heart disease (Table 2).

Using a modified Delphi approach, the panel rated indications as "appropriate", "may be appropriate", and "not appropriate". The specific studies that formed the basis of the American College of Cardiology guidelines are not cited; however, they note that they used American College of Cardiology/American Heart Association clinical practice guidelines whenever possible.

Of 81 indications considered for strain rate imaging, the panel rated only 4 as "appropriate" (Table 2). Three of the 4 concerned evaluation (initial or follow-up) in individuals prior to and following exposure to potentially cardiotoxic agents. The other indication was follow-up testing to clarify initial diagnostic testing for individuals with suspected hypertrophic cardiomyopathy. The guidelines did not separate out imaging with speckle tracking and tissue Doppler and did not make recommendations related to the comparative effectiveness of these imaging modalities.

The panel rated 14 other indications "may be appropriate" (Table 2). According to the panel, interventions in this category should be performed depending on individual clinical patient circumstances and patient and provider preferences, including shared decision making.

Table 2. Summary of American College of Cardiology Appropriate Use Criteria for Myocardial Strain Imaging

Clinical Scenario and Indication	
Initial evaluation in an asymptomatic patient:	
- Initial evaluation prior to exposure to medications/radiation that could result in cardiotoxicity/heart failure	Appropriate
- Initial cardiac evaluation of a known systemic, congenital, or acquired disease that could be associated with structural heart disease	May be appropriate

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Clinical Scenario and Indication	Rating
- Screening evaluation for structure and function in first-degree relatives of a patient with an inherited cardiomyopathy	May be appropriate
- Preparticipation assessment of an asymptomatic athlete with 1 or more of the following: abnormal examination, abnormal ECG, or definite (or high suspicion for) family history of inheritable heart disease)	May be appropriate
Initial evaluation of a patient with clinical signs and/or symptoms of heart disease:	
- Initial evaluation when symptoms or signs suggest heart disease	May be appropriate
- Arrhythmias or conduction disorders: Newly diagnosed LBBB; Nonsustained VT	May be appropriate
- Palpitations/presyncope/syncope: Clinical symptoms or signs consistent with a cardiac diagnosis known to cause presyncope/syncope (including but not limited to hypertrophic cardiomyopathy and heart failure)	May be appropriate
- Respiratory failure/exertional shortness of breath: Exertional shortness of breath/dyspnea or hypoxemia of uncertain etiology	May be appropriate
- HF/cardiomyopathy: Initial evaluation of known or suspected HF (systolic or diastolic) based on symptoms, signs, or abnormal test results to assess systolic or diastolic function and to assess for possible etiology (CAD, valvular disease); Suspected inherited or acquired cardiomyopathy (eg, restrictive, infiltrative, dilated, hypertrophic)	May be appropriate
- Device therapy: Known implanted pacing/ICD/CRT device with symptoms possibly due to suboptimal device settings	May be appropriate
- Cardiac transplantation: Monitoring for rejection or coronary arteriopathy in a cardiac transplant recipient	May be appropriate
- Other: Suspected pericardial diseases	May be appropriate

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Clinical Scenario and Indication	Rating
Sequential or follow-up testing to clarify initial diagnostic testing:	
- Evaluation of suspected hypertrophic cardiomyopathy	
- Re-evaluation (1 y) in a patient previously or currently undergoing therapy with potentially cardiotoxic agents	
- Periodic reevaluation in a patient undergoing therapy with cardiotoxic agents and worsening symptoms	Appropriate
- Pulmonary hypertension in the absence of severe valvular disease	May be appropriate
- Comprehensive further evaluation of undefined cardiomyopathy	May be appropriate
- Evaluation of suspected cardiac amyloidosis	May be appropriate
Sequential or follow-up testing: new or worsening symptoms or to guide therapy	
Re-evaluation of known structural heart disease with change in clinical status or cardiac examination or to guide therapy	May be appropriate
Re-evaluation of known cardiomyopathy with a change in clinical status or cardiac examination or to guide therapy	
Re-evaluation of known HF (systolic or diastolic) with a change in clinical status or cardiac examination without a clear precipitating change in medication or diet	
Re-evaluation for CRT device optimization in a patient with worsening HF	May be appropriate

CAD: coronary artery disease; CRT: cardiac resynchronization therapy: ECG: electrocardiogram; HF: heart failure; ICD: implantable cardioverter-defibrillator; LBBB: left bundle branch block; VT: ventricular tachycardia.

Source: Adapted from Doherty et al (2019).

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### **American Society of Clinical Oncology**

In 2017, the American Society of Clinical Oncology noted that measurement of strain has been demonstrated to have some diagnostic and prognostic use in individuals with cancer receiving cardiotoxic therapies but that there have been no studies demonstrating that early intervention based on changes in strain alone can result in changes in risk and improved outcomes.<sup>9,</sup> The American Society of Clinical Oncology also notes that screening for asymptomatic cardiac dysfunction using advanced imaging could lead to added distress in cancer survivors.

#### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

## **Medicare National Coverage**

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

### **Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this review are listed in Table 3

**Table 3. Summary of Key Trials** 

Study	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04547465	2D Speckle-tracking Echocardiography in Chemotherapy-induced Cardiomyopathy with Cardiovascular Risk Factors	300	Jun 2023 (recruiting)
NCT04429633	Strain-based vs. Left Ventricular Ejection Fraction-based Cardiotoxicity Prevention Strategy in Individuals With Breast Cancer Who Treated With Adjuvant Trastuzumab	136	Jul 2023 (recruiting)
Unpublished			

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Study	Trial Name	Planned Enrollment	Completion Date
NCT02605512	Early Detection and Prediction of Cardiotoxicity in Radiotherapy-treated Breast Cancer Individuals (BACCARAT)	120	Sep 2020 (unknown)
NCT02286908	Global Strain and Mechanical Dispersion May Predict Death and Ventricular Arrhythmias Better Than Ejection Fraction	3100	Dec 2021 (unknown)
NCT03297346	Early Detection of Cardiovascular Changes After Radiotherapy for Breast Cancer (EARLY-HEART)	250	May 2021 (unknown)

NCT: national clinical trial.

# References

- 1. Smiseth OA, Torp H, Opdahl A, et al. Myocardial strain imaging: how useful is it in clinical decision making?. Eur Heart J. Apr 14 2016; 37(15): 1196-207. PMID 26508168
- 2. Doherty JU, Kort S, Mehran R, et al. ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR/STS 2019 Appropriate Use Criteria for Multimodality Imaging in the Assessment of Cardiac Structure and Function in Nonvalvular Heart Disease: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons. J Am Soc Echocardiogr. May 2019; 32(5): 553-579. PMID 30744922
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- 4. Yingchoncharoen T, Agarwal S, Popović ZB, et al. Normal ranges of left ventricular strain: a meta-analysis. J Am Soc Echocardiogr. Feb 2013; 26(2): 185-91. PMID 23218891
- 5. Thavendiranathan P, Poulin F, Lim KD, et al. Use of myocardial strain imaging by echocardiography for the early detection of cardiotoxicity in patients during and after cancer

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- 6. Thavendiranathan P, Negishi T, Somerset E, et al. Strain-Guided Management of Potentially Cardiotoxic Cancer Therapy. J Am Coll Cardiol. Feb 02 2021; 77(4): 392-401. PMID 33220426
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- 9. Armenian SH, Lacchetti C, Lenihan D. Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline Summary. J Oncol Pract. Apr 2017; 13(4): 270-275. PMID 27922796

# **Policy History**

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Original Effective	ve Date: 08/01/2019
Current Effective	e Date: 08/14/2023
05/02/2019	Medical Policy Committee review
05/15/2019	Medical Policy Implementation Committee approval. New policy.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Investigational policy statement
	added to address cardiotoxicity.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. No change to coverage.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. No change to coverage.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. No change to coverage.
Next Scheduled	Review Date: 07/2024

# **Coding**

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology ( $CPT^{\otimes}$ ), copyright 2022

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by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	93356
HCPCS	C9762, C9763
ICD-10 Diagnosis	All related diagnoses

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

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whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  - 1. Consultation with technology evaluation center(s);
  - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  - 3. Reference to federal regulations.

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**NOTICE:** If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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