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Elastography and Associated Imaging Techniques

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Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.

Transient elastography (e.g., FibroScan) **may be considered medically necessary** to assess the degree of advanced liver fibrosis and cirrhosis in an individual with ANY of the following conditions:

- Hepatitis C,
- Hepatitis B,
- Chronic alcoholic liver disease, and
- All other chronic liver diseases.

Magnetic resonance elastography (MRE) OR multiparametric magnetic resonance imaging (MRI) (e.g., LiverMultiScan®) **may be considered medically necessary** for individuals with established chronic liver disease in EITHER of the following scenarios:

- Non-alcoholic fatty liver disease (NAFLD; also referred to as metabolic dysfunction-associated steatotic liver disease [MASLD]) who have at least one of the following high-risk factors for cirrhosis:
  - Advanced age (65 years old or greater),
  - Obesity (BMI 30 or higher),
  - Diabetes, and/or
  - Alanine aminotransferase (ALT) greater than twice the upper limit of normal; OR
- When transient elastography cannot be performed or is nondiagnostic.

The use of other ultrasound elastographic techniques, including but not limited to acoustic radiation force impulse imaging (e.g., Acuson S2000) or real-time tissue elastography, for the evaluation or monitoring of individuals with chronic liver disease **is considered experimental, investigational and/or unproven**.

Transient elastography, multiparametric MRI, and MRE **are considered experimental, investigational and/or unproven** for all other indications.

Policy Guidelines

None.

Description

Noninvasive techniques to monitor liver fibrosis are being investigated as alternatives to liver biopsy in patients with chronic liver disease. There are 2 options for noninvasive monitoring: 1) Multianalyte serum assays with algorithmic analysis of either direct or indirect biomarkers (not addressed in this policy); and 2) Specialized radiologic methods, including magnetic resonance elastography (MRE), multiparametric magnetic resonance imaging (MRI), transient elastography, acoustic radiation force impulse imaging, and real-time transient elastography.

Chronic Liver Disease

Hepatitis C Virus

Infection with hepatitis C virus (HCV) can lead to permanent liver damage. Prior to noninvasive testing, liver biopsy was typically recommended before the initiation of antiviral therapy. Repeat biopsies may be performed to monitor fibrosis progression. Liver biopsies are analyzed according to a histologic scoring system; the most commonly used one for HCV is the Metavir system, which scores the presence and degree of inflammatory activity and fibrosis. The fibrosis is graded from F0 to F4, with a Metavir score of F0 signifying no fibrosis and F4 signifying cirrhosis (which is defined as the presence throughout the liver of fibrous septa that subdivide the liver parenchyma into nodules, representing the final and irreversible form of the disease). The stage of fibrosis is the most important single predictor of morbidity and mortality in patients with hepatitis C. Biopsies for HCV are also evaluated according to the degree of inflammation present, referred to as the grade or activity level. For example, the Metavir

system includes scores for necroinflammatory activity ranging from A0 to A3 (A0 = no activity, A1 = minimal activity, A2 = moderate activity, A3 = severe activity).

Hepatitis B Virus

Most people who become infected with hepatitis B virus (HBV) recover fully, but a small portion develops chronic HBV, which can lead to permanent liver damage. As with HCV, identification of liver fibrosis is needed to determine timing and management of treatment, and liver biopsy is the criterion standard for staging fibrosis. The grading of fibrosis in HBV also uses the Metavir system.

Alcoholic Liver Disease

Alcoholic liver disease (ALD) is the leading cause of liver disease in most Western countries. Histologic features of ALD usually include steatosis, alcoholic steatohepatitis (ASH), hepatocyte necrosis, Mallory bodies (tangled proteins seen in degenerating hepatocytes), a large polymorphonuclear inflammatory infiltrate, and, with continued alcohol abuse, fibrosis, and possibly cirrhosis. The grading of fibrosis is similar to the scoring system used in HCV. The commonly used Laënnec scoring system uses grades 0 to 4, with 4 being cirrhosis.

Nonalcoholic Fatty Liver Disease

Nonalcoholic fatty liver disease (NAFLD) is defined as a condition that pathologically resembles ALD but occurs in patients who are not heavy users of alcohol. Moreover, NAFLD may be associated with a variety of conditions, including obesity, diabetes, and dyslipidemia. The characteristic feature of NAFLD is steatosis. At the benign end of the disease spectrum, there is usually no appreciable inflammation, hepatocyte death, or fibrosis. In contrast, nonalcoholic steatohepatitis (NASH), which shows overlapping histologic features with ALD, is an intermediate form of liver damage, and liver biopsy may show steatosis, Mallory bodies, focal inflammation, and degenerating hepatocytes. NASH can progress to fibrosis and cirrhosis. A variety of histologic scoring systems have been used to evaluate NAFLD. The NAFLD Activity Score system for NASH includes scores for steatosis (0 to 3), lobular inflammation (0 to 3), and ballooning (0 to 2). Cases with scores of 5 or greater are considered NASH, while cases with scores of 3 and 4 are considered borderline (probable or possible) NASH. The grading of fibrosis is similar to the scoring system used in hepatitis C. The commonly used Laënnec scoring system uses grades 0 to 4, with 4 being cirrhosis.

Of note, in 2023, NAFLD was renamed to metabolic dysfunction-associated steatotic liver disease (MASLD) due to concerns over exclusionary and stigmatizing language. (1) A consensus-driven process found that the new term better reflects the metabolic nature of the disease. Similarly, NASH was renamed to metabolic-dysfunction associated steatohepatitis (MASH). Additionally, a new term, metabolic and alcohol-related/associated liver disease (MetALD) was introduced to characterize disease with both metabolic dysfunction and significant alcohol intake. Due to this recent change, unless a publication specifically refers to MASLD or MASH, the abbreviations NAFLD and NASH, respectively, will continue to be used throughout this policy.

Biopsy for Chronic Liver Disease

The diagnosis of non-neoplastic liver disease is often made from needle biopsy samples. In addition to establishing a disease etiology, liver biopsy can determine the degree of inflammation present and stage the degree of fibrosis. The degree of inflammation and fibrosis may be assessed by different scoring schemes. Most of these scoring schemes grade inflammation from 0 (no or minimal inflammation) to 4 (severe) and fibrosis from 0 (no fibrosis) to 4 (cirrhosis). There are several limitations to liver biopsy, including its invasive nature, small tissue sample size, and subjective grading system. Regarding small tissue sample size, liver fibrosis can be patchy and thus missed on a biopsy sample, which includes only 0.002% of the liver tissue. A noninvasive alternative to liver biopsy would be particularly helpful, both to initially assess patients and then to monitor response to therapy. The implications of using liver biopsy as a reference standard are discussed in the Rationale.

Noninvasive Imaging Technologies

Noninvasive imaging technologies to detect liver fibrosis or cirrhosis among patients with chronic liver disease are being evaluated as alternatives to liver biopsy. The noninvasive imaging technologies include transient elastography (e.g., FibroScan), magnetic resonance elastography, acoustic radiation force impulse (ARFI) imaging (e.g., Acuson S2000), multiparametric MRI (e.g., LiverMultiScan), and real-time tissue elastography (e.g., HI VISION Preirus).

Transient Elastography

Transient elastography (FibroScan) uses a mechanical vibrator to produce mild amplitude and low-frequency (50 Hz) waves, inducing an elastic shear wave that propagates throughout the liver. Ultrasound tracks the wave, measuring its speed in kilopascals, which correlates with liver stiffness. Increases in liver fibrosis also increase liver stiffness and resistance of liver blood flow. Transient elastography does not perform as well in patients with ascites, higher body mass index, or narrow intercostal margins. Although FibroScan may be used to measure fibrosis (unlike liver biopsy), it does not provide information on necroinflammatory activity and steatosis, nor is it accurate during acute hepatitis or hepatitis exacerbations.

Acoustic Radiation Force Impulse Imaging

ARFI imaging uses an ultrasound probe to produce an acoustic “push” pulse, which generates shear waves that propagate in tissue to assess liver stiffness. ARFI elastography evaluates the wave propagation speed (measured in meters per second) to assess liver stiffness. The faster the shear wave speed, the harder the object. ARFI technologies include Virtual Touch Quantification and Siemens Acuson S2000 system. ARFI elastography can be performed at the same time as a liver sonographic evaluation, even in patients with a significant amount of ascites.

Magnetic Resonance Elastography

Magnetic resonance elastography uses a driver to generate 60-Hz mechanical waves on the patient’s chest wall. The magnetic resonance equipment creates elastograms by processing the acquired images of propagating shear waves in the liver using an inversion algorithm. These

elastograms represent the shear stiffness as a pixel value in kilopascals. Magnetic resonance elastography has several advantages over ultrasound elastography, including: 1) the ability to analyze larger liver volumes; 2) the ability to analyze liver volumes of obese patients or patients with ascites; and 3) the ability to precisely analyze viscoelasticity using a 3-dimensional displacement vector.

Real-Time Tissue Elastography

Real-time tissue elastography is a type of strain elastography that uses a combined autocorrelation method to measure tissue strain caused by manual compression or a person's heartbeat. The relative tissue strain is displayed on conventional color B mode ultrasound images in real-time. Hitachi manufactures real-time tissue elastography devices, including the HI VISION Preirus. The challenge is to identify a region of interest while avoiding areas likely to introduce artifacts, such as large blood vessels, the area near the ribs, and the surface of the liver. Areas of low strain increase as fibrosis progresses and strain distribution becomes more complex. Various subjective and quantitative methods have been developed to evaluate the results. Real-time tissue elastography can be performed in patients with ascites or inflammation. This technology does not perform as well in severely obese individuals.

Multiparametric Magnetic Resonance Imaging

Multiparametric MRI combines proton density fat-fraction, T2*, and T1 mapping. Proton density fat-fraction provides an assessment of hepatic fat content and can be used to determine the grade of liver steatosis. T1 relaxation times are used to assess increases in extracellular fluid, which correlates with the extent of fibrosis and inflammation of the liver. Hepatic iron quantification is measured through T2* relaxation times as T1 relaxation times are decreased by excess iron in the liver tissue. LiverMultiScan® uses a clinical algorithm that accounts for an iron-corrected T1 value, based on the T2* relaxation time, and proton density fat-fraction to assess the presence of fat, inflammation, and fibrosis.

Use Outside of Chronic Liver Disease

Elastography for use outside of chronic liver disease has been focused primarily on cancer diagnoses, based upon quantitative differences in the mechanical properties of normal versus malignant tissues. Cancers are usually harder than normal tissues. This difference can be measured by applying a known stressor and measuring the resulting deformation.

Regulatory Status

A number of elastography devices have received U. S. Food and Drug Administration (FDA) approval, including but not limited to the following:

- In 2008 Acuson S2000™ Virtual Touch (Siemens AG), which provides ARFI imaging, was cleared for marketing by the FDA through the 510(k) process (K072786).
- In 2009, AIXPLORER® Ultrasound System (SuperSonic Imagine), which provides shear wave elastography, was cleared for marketing by the FDA through the 510(k) process (K091970).
- In 2010, Hitachi HI VISION™ Preirus™ Diagnostic Ultrasound Scantier (Hitachi Medical Systems America), which provides real-time tissue elastography, was cleared for marketing by the FDA through the 510(k) process (K093466).

- In 2013, FibroScan® (EchoSens), which uses transient elastography, was cleared for marketing by the FDA through the 510(k) process (K123806).
- In June 2015, LiverMultiScan (Perspectum), which is a magnetic resonance diagnostic device software application, was cleared for marketing by the FDA through the 510(k) process (K143020).
- In February 2017, ElastQ Imaging shear wave elastography (Royal Phillips) was cleared for marketing by the FDA through the 510(k) process (K163120).
- In June 2019, the SureTouch Mobile Pressure Mapping System (i.e., Bexa device) (Sure, Inc.) was cleared for marketing by the FDA through the 510K process (K181672). Bexa employs high resolution elastography to produce a map of abnormal breast tissues and masses.
- In August 2021, ADVIA Centaur Enhanced Liver Fibrosis (ELF™) test (Siemens Healthcare) was cleared for marketing by the FDA through the 513(f)(2) De Novo review pathway (DEN190056). In 2018, the device had been granted a Breakthrough Device designation for predicting disease progression in patients with advanced fibrosis due to NAFLD.
- In July 2023, the ELF™ Test was granted a Breakthrough Device Designation to aid in the identification of advanced fibrosis (≥F3) and cirrhosis (F4) in patients with NAFLD.

FDA product code: IYO, LNH, QQB.

Refer to the FDA website at <http://www.accessdata.fda.gov> for the most current listing of approved devices.

Rationale

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

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

Noninvasive Testing for Chronic Liver Disease

Liver biopsy is an imperfect reference standard. There is a high rate of sampling error, which can lead to underdiagnosis of liver disease. (2, 3) These errors will bias estimates of performance characteristics of the noninvasive tests to which it is compared, and therefore such errors must be considered in appraising the body of evidence. Mehta et al. (2009) estimated that even under the best scenario where sensitivity and specificity of liver biopsy are 90%, and the prevalence of significant disease (increased liver fibrosis, scored as Metavir ≥F2) is 40%; a perfect alternative marker would have calculated the area under the receiver operating

characteristic (AUROC) curve of 0.90. (4) Therefore, the effectiveness of alternative technologies may be underestimated. In fact, when the accuracy of biopsy is presumed to be 80%, a comparative technology with an AUROC curve of 0.76 may actually have an AUROC curve of 0.93 to 0.99 for diagnosing true disease.

Due to a large number of primary studies published on this topic, this medical policy focuses on systematic reviews when available. The validation of multiple noninvasive tests is assessed individually in the following sections. Although options exist for performing systematic reviews with imperfect reference standards, (5) most available reviews did not use any correction for the imperfect reference.

The focus of this medical policy is noninvasive monitoring utilizing specialized radiologic methods, including magnetic resonance elastography, multiparametric magnetic resonance imaging (MRI), transient elastography, acoustic radiation force impulse imaging, and real-time transient elastography. This medical policy does not address multianalyte serum assays with algorithmic analysis of either direct or indirect biomarkers.

Noninvasive Imaging - Transient Elastography (Liver)

Clinical Context and Test Purpose

The purpose of noninvasive testing in individuals with chronic liver disease is to detect liver fibrosis so that individuals can avoid the potential adverse events of an invasive liver biopsy and receive appropriate treatment. The degree of liver fibrosis is an important factor in determining the appropriate approach for managing individuals with liver disease (e.g., hepatitis, alcoholic liver disease [ALD], nonalcoholic fatty liver disease [NAFLD]).

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

Populations

The relevant population of interest is individuals with chronic liver disease.

Interventions

The test being considered is transient elastography.

Comparators

The following tests and practices are currently being used to diagnose chronic liver disease: liver biopsy, other noninvasive radiologic methods, and multianalyte serum assays.

Outcomes

The general outcomes of interest are test validity, morbid events, and treatment-related morbidity. Follow-up over months to years is of interest to the relevant outcomes.

Study Selection Criteria

For the evaluation of the clinical validity of the tests within this review, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).
- Included a suitable reference standard (describe the reference standard).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

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

There is extensive literature on the use of transient elastography (e.g., FibroScan) to gauge liver fibrosis and cirrhosis. Summaries of systematic reviews are shown in Tables 1 and 2. Brener (2015) performed a health technology assessment summarizing many of the systematic reviews below. (6) The assessment focused on reviews of the diagnostic accuracy and effect on patient outcomes of transient elastography for liver fibrosis in patients with hepatitis C virus (HCV), hepatitis B virus (HBV), NAFLD, ALD, or cholestatic diseases. Fourteen systematic reviews of transient elastography with biopsy reference standard shown below were included in the Brener assessment, summarizing more than 150 primary studies. (7-20) There was variation in the underlying cause of liver disease and the cutoff values of transient elastography stiffness used to define Metavir stages in the systematic reviews. There did not appear to be a substantial difference in diagnostic accuracy for 1 disease over any other. The reviews demonstrated that transient elastography has good diagnostic accuracy compared with biopsy for the assessment of liver fibrosis and steatosis.

Crossan et al. (2015) found that FibroScan was the noninvasive liver test most assessed in validation studies across liver diseases (37 studies in HCV, 13 in HBV, 8 in NAFLD, 6 in ALD). (21) Cutoffs for positivity for fibrosis staging varied between diseases and were frequently not prespecified or validated: HCV, 5.2 to 10.1 kilopascal (kPa) in the 37 studies for Metavir stages ≥F2; HBV, 6.3 to 8.9 kPa in 13 studies for stages ≥F2; NAFLD, 7.5 to 10.4 kPa in 8 studies for stages ≥F3; ALD, 11.0 to 12.5 in 4 studies for stages ≥F3. Summary sensitivities and specificities by disease are shown in Table 2. The overall sensitivity and specificity for cirrhosis including all diseases (65 studies; cutoffs range, 9.2 to 26.5 kPa) were 89% (95% confidence interval [CI], 86% to 91%) and 89% (95% CI, 87% to 91%), respectively. The rate of uninterpretable results, when reported, with FibroScan (due to <10 valid measurements; success rate, <60%; interquartile range, >30%) was 8.5% in HCV and 9.6% in NAFLD.

Table 1. Transient Elastography Systematic Review Characteristics

Study	Dates	Studies	N	Population
Bota et al. (2013) (7)	To May 2012	13	1163	Chronic hepatitis
Cai et al. (2021) (22)	To Mar 2019	62	NR	ALD, NAFLD
Chon et al. (2012) (8)	2002 to Mar 2011	18	2772	HBV
Crossan et al. (2015) (21)	1998 to Apr 2012	66	NR	HCV, HBV, NAFLD, ALD

Friedrich-Rust et al. (2008) (9)	2002 to Apr 2007	50	11,275	All causes of liver disease
Geng et al. (2016) (23)	To Jan 2015	57	10,569	Multiple causes of liver disease
Jiang et al. (2018) (24)	To Dec 2017	11	1735	NAFLD
Kwok et al. (2014) (10)	To Jun 2013	22	1047	NAFLD
Li et al. (2016) (25)	Jan 2003 to Nov 2014	27	4386	HBV
Njei et al. (2016) (26)	To Jan 2016	6	756	HCV/HIV coinfection
Pavlov et al. (2015) (27)	To Aug 2014	14	834	ALD
Poynard et al. (2011) (12)	Feb 2001 to Dec 2010	18	2714	HBV
Shaheen et al. (2007) (13)	Jan 1997 to Oct 2006	12	1981	HCV
Shi et al. (2014) (14)	To May 2013	9	1771	All causes of steatosis
Steadman et al. (2013) (15)	2001 to Jun 2011	64	6028	HCV, HBV, NAFLD, CLD, liver transplant
Stebbing et al. (2010) (16)	NR, prior to Feb 2009	22	4625	All causes of liver disease
Talwalkar et al. (2007) (17)	To Jan 2007	9	2083	All causes of liver disease
Tsochatzis et al. (2011) (18)	To May 2009	40	7661	All causes of liver disease
Tsochatzis et al. (2014) (19)	1998 to Apr 2012	302	NR	HCV, HBV, ALD, NAFLD
Xu et al. (2015) (28)	To Dec 2013	19	3113	HBV
Xue-Ying (2019) (20)	Jan 2008 to Dec 2018	81	32,694	HBV

ALD: alcoholic liver disease; CLD: chronic liver disease; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; NAFLD: nonalcoholic fatty liver disease; NR: not reported.

Table 2. Transient Elastography Systematic Reviews Diagnostic Accuracy Results

		Significant Fibrosis (i.e., Metavir Stages F2-F4)		**Cirrhosis (i.e., Metavir Stage F4)**	
Study	**Population**	**Studies/ Sample Size**	**AUROC (95% CI) Sensitivity (95% CI) Specificity (95% CI)**	**Studies/ Sample Size**	**AUROC (95% CI) Sensitivity (95% CI) Specificity (95% CI)**
Bota et al. (2013) (7)	Multiple diseases	10/1016	0.87 (0.83 to 0.89) 78% (72% to 83%) 84% (75% to 90%)	13/1163	0.93 (0.91 to 0.95) 89% (80% to 94%) 87% (82% to 91%)

	HCV			4/NR	NR 92% (78% to 97%) 86% (82% to 90%)
Cai et al. (2021) (22)	ALD/NAFLD	40/2569	0.86 (0.83 to 0.89) 77% (73% to 81%) 82% (78% to 86%)	34/914	0.95 (0.92 to 0.96) 91% (87% to 94%) 86% (83% to 89%)
Chon et al. (2012) (8)	Chronic HBV	12/2000	0.86 (0.86 to 0.86) 74.3% (NR) 78.3% (NR)	16/2614	0.93 (0.93 to 0.93) 84.6% (NR) 81.5% (NR)
Crossan et al. (2015) (21)	HCV	37/NR	NR 79% (74% to 84%) 83% (77% to 88%)	36/NR	NR 89% (84% to 92%) 91% (89% to 93%)
	HBV	13/NR	NR 71% (62% to 78%) 84% (74% to 91%)	19/NR	NR 86% (79% to 91%) 85% (78% to 89%)
	NAFLD			4/NR	NR 96% (83% to 99%) 89% (85% to 92%)
	ALD	1/NR	NR 81% (70% to 88%) 92% (76% to 98%)	4/NR	NR 87% (64% to 96%) 82% (67% to 91%)
Friedrich-Rust et al. (2008) (9)	Multiple diseases	25/3685	0.84 (0.82 to 0.86) NR NR	25/4557	0.94 (0.93 to 0.95) NR NR
	HCV	NR	0.84 (0.80 to 0.86) NR NR		
Geng et al. (2016) (23)	Multiple diseases				0.93 (NR) 81% (79% to 83%) 88% (87% to 89%)
Jiang et al. (2018) (24)	NAFLD	10/NR	0.85 (0.82 to 0.88) 77% (70% to 84%) 80% (74% to 84%)	11/NR	0.96 (0.93 to 0.97) 90% (73% to 97%) 91% (87% to 94%)
Kwok et al. (2014) (10)	NAFLD	7/800	0.83 (0.79 to 0.87) 0.79 (0.72 to 0.84) 0.75 (0.71 to 0.79)	57/ 10,569	0.96 (0.94 to 0.99) 92% (82% to 97%) 92% (86% to 98%)
Li et al. (2016) (25)	HBV	19/NR	0.88 (0.85 to 0.91) 81% (76% to 85%) 82% (71% to 87%)	24/NR	0.93 (0.91 to 0.95) 86% (82% to 90%) 88% (84% to 90%)
Njei et al. (2016) (26)	HCV/HIV	6/756	NR 97% (82% to 91%) 64% (45% to 79%)	6/756	NR 90% (74% to 91%) 87% (80% to 92%)

Pavlov et al. (2015) (27)	ALD	7/338	NR 94% (86% to 97%) 89% (76% to 95%)	7/330	NR 95% (87% to 98%) 71% (56% to 82%)
Poynard et al. (2011) (12)	HBV	4/NR	0.84 (0.78 to 0.89) NR NR	NR	0.93 (0.87 to 0.99) NR NR
Shaheen et al. (2007) (13)	HCV	4/NR	0.84 (0.78 to 0.89) NR NR	NR	0.93 (0.87 to 0.99) NR NR
Shi et al. (2014) (14)	No summary statistics reported. Concluded that transient elastography controlled attenuation parameter has good sensitivity and specificity for diagnosing steatosis, but it has limited utility.				
Steadman et al. (2013) (15)	Multiple diseases	45/NR	0.88 (0.84 to 0.90) 80% (76% to 83%) 81% (77% to 85%)	49/NR	0.94 (0.91 to 0.96) 86% (82% to 89%) 89% (87% to 91%)
	HBV	5/710	0.81 (0.78 to 0.84) 77% (68% to 84%) 72% (55% to 85%)	8/1092	0.86 (0.82 to 0.89) 67% (57% to 75%) 87% (83% to 91%)
	HCV	13/2732	0.89 (0.86 to 0.91) 76% (61% to 86%) 86% (77% to 92%)	12/2887	0.94 (0.92 to 0.96) 85% (77% to 91%) 91% (87% to 93%)
	NAFLD	5/630	0.78 (0.74 to 0.82) 77% (70% to 83%) 75% (70% to 79%)	4/469	0.96 (0.94 to 0.97) 92% (77% to 98%) 95% (88% to 98%)
Stebbing et al. (2010) (16)	Multiple diseases	17/3066	NR 72% (71% to 72%) 82% (82% to 83%)	17/4052	NR 84% (84% to 85%) 95% (94% to 95%)
Talwalkar et al. (2007) (17)	Multiple diseases	7/>1100	0.87 (0.83 to 0.91) 70% (67% to 73%) 84% (80% to 88%)	9/2083	0.96 (0.94 to 0.98) 87% (84% to 90%) 91% (89% to 92%)
Tsochatzis et al. (2011) (18)	Multiple diseases	31/5919	NR 79% (74% to 82%) 78% (72% to 83%)	30/6530	NR 83% (79% to 86%) 89% (87% to 91%)
	HCV	14/NR	NR 78% (71% to 84%) 80% (71% to 86%)	11/NR	NR 83% (77% to 88%) 90% (87% to 93%)
	HBV	4/NR	NR 84% (67% to 93%) 78% (68% to 85%)	6/NR	NR 80% (61% to 91%) 86% (82% to 94%)
Tsochatzis et al. (2014) (19)	HCV	37/NR	0.87 (0.83 to 0.90) 79% (74% to 84%) 83% (77% to 88%)	36/NR	0.96 (0.94 to 0.97) 89% (84% to 92%) 91% (89% to 93%)
	HBV	13/NR	0.83 (0.76 to 0.90)	13/NR	0.92 (0.89 to 0.96)

			71% (62% to 78%) 84% (74% to 91%)		86% (79% to 91%) 85% (78% to 89%)
	NAFLD			4/NR	0.96 (0.94 to 0.99) 96% (83% to 99%) 89% (85% to 92%)
	ALD			6/NR	0.90 (0.87 to 0.94) 86% (76% to 92%) 83% (74% to 89%)
Xu et al. (2015) (28)	HBV	14/2318	0.82 (0.78 to 0.86) NR NR	18/2996	0.91 (0.89 to 0.93) NR NR
Xue-Ying et al. (2019) (20)	HBV	29/5035	0.83 (0.80 to 0.86) 72% (68% to 76%) 82% (77% to 86%)	NR/NR	NR NR NR

ALD: alcoholic liver disease; AUROC: area under the receiver operating characteristic curve; CI: confidence interval; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; NAFLD: nonalcoholic fatty liver disease; NR: not reported.

Clinically Useful

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

Direct Evidence

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

There are currently no published studies that directly demonstrate the effect of transient elastography (e.g., FibroScan) on patient outcomes.

FibroScan is used extensively in practice to make management decisions. In addition, FibroScan was used as an alternative to biopsy to diagnose fibrosis or cirrhosis to establish trial eligibility in several trials (ION-1, -3; VALENCE; ASTRAL-2, -3, -4) that confirmed the efficacy of HCV treatments. (29-34) For example, in the VALENCE trial, cirrhosis could be defined by liver biopsy or a confirmatory FibroTest or FibroScan result at 12.5 kPa or greater. In VALENCE, FibroScan was used to determine cirrhosis in 74% of the participants. In a retrospective, multicenter analysis of 7256 chronic HCV patients by Abdel Alem et al. (2019), both transient elastography and FIB-4 were found to be predictors of treatment failure to sofosbuvir-based treatment regimens with an NPV of 95%. (35)

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Section Summary: Noninvasive Imaging - Transient Elastography (Liver)

For individuals who have chronic liver disease who receive transient elastography (e.g., FibroScan), the evidence includes many systematic reviews of more than 50 observational studies (>10,000 patients). Transient elastography has been studied in populations with viral hepatitis, NAFLD, and ALD. There are varying cutoffs for positivity. Failures of the test are not uncommon, particularly for those with high body mass index, but these failures often went undetected in analyses of the validation studies. Given these limitations and the imperfect reference standard, it can be difficult to interpret performance characteristics. However, for the purposes of deciding whether a patient has severe fibrosis or cirrhosis, the FibroScan results provide data sufficiently useful to determine therapy. In fact, FibroScan has been used as an alternative to biopsy to establish eligibility regarding the presence of fibrosis or cirrhosis in the participants of several RCTs. These trials showed the efficacy of HCV treatments, which in turn demonstrated that the test can identify patients who would benefit from therapy.

Noninvasive Imaging: Multiparametric Magnetic Resonance Imaging (Liver)

Clinical Context and Test Purpose

The purpose of noninvasive testing in individuals with chronic liver disease is to detect liver fibrosis so that individuals can avoid the potential adverse events of an invasive liver biopsy and receive appropriate treatment. The degree of liver fibrosis is an important factor in determining the appropriate approach for managing individuals with liver disease (e.g., hepatitis, ALD, NAFLD).

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

Populations

The relevant population of interest is individuals with chronic liver disease.

Interventions

The test being considered is multiparametric MRI (e.g., LiverMultiScan).

Comparators

The following tests and practices are currently being used to diagnose chronic liver disease: liver biopsy, other noninvasive radiologic methods, and multianalyte serum assays.

Outcomes

The general outcomes of interest are test validity, morbid events, and treatment-related morbidity. Follow-up over months to years is of interest to the relevant outcomes.

Study Selection Criteria

For the evaluation of the clinical validity of the tests within this review, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).

- Included a suitable reference standard (describe the reference standard).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

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

Azizi et al. (2024) published a systematic review comparing the diagnostic accuracy of MRI proton density fat fraction with liver biopsy. (36) Tables 3 and 4 summarize study characteristics and results, respectively. Authors concluded that MRI Proton Density Fat Fraction has high diagnostic accuracy, though its accuracy slightly declines as the severity of hepatic steatosis increases.

Table 3. Magnetic Resonance Imaging Systematic Review Characteristics

Study	Dates	Studies	N (Range)	Population	Index tests	Reference Standard
Azizi et al. (2024) (36)	Until January 2024	22	2844 (19 to 497)	Patients with MASLD and hepatic steatosis	MRI-PDFF	Histology

MASLD: metabolic dysfunction-associated steatotic liver disease; MRI: magnetic resonance imaging; PDFF: proton density fat-fraction.

Table 4. Magnetic Resonance Imaging Systematic Review Results

Index Test	Steatosis		
Azizi et al. (2024) (36)	**AUC** **Sensitivity** **Specificity**		
	Grade ≥1	Grade ≥2	Grade 3
Total studies (n)	17 (2454)	16 (1726)	12 (1469)
Index Test Threshold	5.7	NR	NR
MRI-PDFF	0.97 0.93 0.93	0.91 0.79 0.90	0.91 0.76 0.89

AUC: area under the curve; MRI: magnetic resonance imaging; NR: not reported; PDFF: proton density fat-fraction.

Tables 5 and 6a/6b summarize studies that have evaluated the diagnostic accuracy of multiparametric MRI, which incorporates assessment of proton density fat-fraction, T_2*, and T_1 mapping to characterize liver fat, iron, fibrosis, and inflammation. Generally, technical failures were less common with MRI than transient elastography. (37-39)

Table 5. Characteristics of Studies Assessing the Diagnostic Accuracy of Multiparametric Magnetic Resonance Imaging

Study	Population	Design	Index Test(s)	Reference Standard	Timing of Reference and Index Tests
Beyer at al. (2021) (37)	N=580 patients with suspected NAFLD/NASH	Retrospective evaluation of patients from 2 clinical trials	MRI PDFF (LMS-IDEAL)* CAP (FibroScan)	Liver biopsy	Not reported
Imajo et al. (2021) (38)	N=145 patients with suspected NASH	Prospective, observational	MRI liver fat* MRI cT_1 measurements* MRI cT_1 + PDFF* MRE VCTE-LSM (FibroScan) CAP (FibroScan) 2D-SWE	Liver biopsy	All performed at first clinical visit
McDonald et al. (2018) (39)	N=149 patients with known or suspected liver disease	Prospective, validation cohort	MRI cT_1* ELF test TE (FibroScan)	Liver biopsy	Liver biopsy performed within 2 weeks of noninvasive assessments

*Measurements obtained with LiverMultiscan protocol.
2D-SWE: 2-dimensional shear-wave elastography; CAP: controlled attenuation parameter; ELF: Enhanced Liver Fibrosis; LMS-IDEAL: LiverMultiScan-Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation; MRE: magnetic resonance elastography; MRI: magnetic resonance imaging; NAFLD: non-alcoholic fatty liver disease; NASH: non-alcoholic steatohepatitis; PDFF: proton density fat-fraction; TE: transient elastography; VCTE-LSM: vibration-controlled transient elastography-liver stiffness measure.

Table 6a. Results of Studies Assessing the Diagnostic Accuracy of Multiparametric Magnetic Resonance Imaging

		Significant Fibrosis		
Study	**Population**	**Test**	**AUROC (95% CI) Sensitivity Specificity**	
Beyer at al. (2021) (37)	Suspected NAFLD/NASH			
			Stage ≥2	

Imajo et al. (2021) (38)	Suspected NASH	MRE	0.92 (0.87 to 0.97) NR NR	
		VCTE-LSM	0.88 (0.81 to 0.95) NR NR	
		2D-SWE	0.87 (0.76 to 0.99) NR NR	
		MRI cT_1^*	0.62 (0.49 to 0.74) NR NR	
			Stage ≥3	*Stage ≥5*
McDonald et al. (2018) (39)	Known or suspected liver disease (unselected)	MRI cT_1^*	0.72 (0.63 to 0.80) 88% 51%	0.72 (0.64 to 0.81) 71% 64%
		ELF test	0.70 (0.61 to 0.78) 49% 77%	0.68 (0.57 to 0.79) 19% 91%
		TE	0.84 (0.76 to 0.91) NR NR	0.86 (0.79 to 0.93) NR NR

*Measurements obtained with LiverMultiscan protocol.
2D-SWE: 2-dimensional shear-wave elastography; AUROC: area under the receiver operating characteristic curve; CI: confidence interval; ELF: Enhanced Liver Fibrosis; MRE: magnetic resonance elastography; MRI: magnetic resonance imaging; NAFLD: non-alcoholic fatty liver disease; NASH: non-alcoholic steatohepatitis; NR: not reported; TE: transient elastography; VCTE-LSM: vibration-controlled transient elastography-liver stiffness measure.

Table 6b. Results of Studies Assessing the Diagnostic Accuracy of Multiparametric Magnetic Resonance Imaging

		Steatosis				**Advanced NASH (NAS ≥4 and ≥F2)**	
Study	**Population**	**Test**	**AUROC (95% CI) Sensitivity Specificity**			**Test**	**AUROC (95% CI) Sensitivity Specificity**
			Grade ≥1	Grade ≥2	Grade ≥3		

Beyer at al. (2021) (37)	Suspected NAFLD/NASH	MRI PDFF (LMS-IDEAL)*	1.0 (0.99 to 1.00) 99% 100%	0.77 (0.73 to 0.82) 72% 72%	0.81 (0.76 to 0.87) 68% 81%		
		CAP (FibroScan)	0.95 (0.91 to 0.99) 89% 100%	0.60 (0.55 to 0.65) 78% 41%	0.63 (0.57 to 0.70) 61% 59%		
Imajo et al. (2021) (38)	Suspected NASH	MRI liver fat*	0.92 (0.87 to 0.98) NR NR	0.86 (0.80 to 0.93) NR NR		MRI cT_1*	0.74 (0.66 to 0.82) NR NR
		CAP (FibroScan)	0.75 (0.58 to 0.92) NR NR	0.68 (0.59 to 0.78) NR NR		MRI liver fat*	0.71 (0.63 to 0.80) NR NR
						MRE	0.66 (0.57 to 0.75) NR NR
						VCTE-LSM	0.64 (0.54 to 0.74) NR NR

*Measurements obtained with LiverMultiscan protocol.
AUROC: area under the receiver operating characteristic curve; CAP: controlled attenuation parameter; CI: confidence interval; LMS-IDEAL: LiverMultiScan-Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation; MRE: magnetic resonance elastography; MRI: magnetic resonance imaging; NAFLD: non-alcoholic fatty liver disease; NASH: non-alcoholic steatohepatitis; NR: not reported; PDFF: proton density fat-fraction; VCTE-LSM: vibration-controlled transient elastography-liver stiffness measure.

Jayaswal et al. (2020) compared the prognostic value of MRI cT1 measurements, transient elastography, and multianalyte serum assays in a cohort of 197 patients with compensated chronic liver disease. (40) Patients who were referred for a clinically indicated liver biopsy, or with a known diagnosis of liver cirrhosis, were eligible. At baseline, patients underwent multiparametric MRI scans, transient elastography, and blood tests. Additionally, all patients received a liver biopsy and had their fibrosis rated on the Ishak scale; results of the biopsies informed clinical care. The most common underlying disease states were NAFLD (n=85, 43%), viral hepatitis (n=50, 25%), and ALD (n=22, 11%). The primary endpoint was a composite of

ascites, variceal bleeding, hepatic encephalopathy, hepatocellular carcinoma, liver transplantation and mortality. Binary cutoff values were predefined. Patients were followed for a median of 43 months. Over this period, 14 new clinical events were recorded, including 11 deaths. The prognostic value of the noninvasive testing is summarized in Table 5. Technical failures were also reported (e.g., poor quality scan); reliable measurements were obtained in 182 of 197 (92%) patients for multiparametric MRI and in 121 of 160 (76%) patients for transient elastography (transient elastography was additionally not attempted in 37 patients). The study was limited by having variable follow-up periods and the effect of patients being censored at different time points was not taken into account, so sensitivities, specificities, PPVs and NPVs should be interpreted cautiously. The CI for the survival analysis were wide likely due to the relatively small number of new clinical events observed.

Table 7. Survival Analysis and Performance in Identifying Development of a New Clinical Event[a]

Test, Binary Cutoff	Cox Regression Analysis, HR (95% CI)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Liver cT_1 >825 ms	9.91 (1.287 to 76.24)	92.3	47.3	11.9	98.8
Transient elastography >8 kPa	7.79 (0.974 to 62.3)	88.9	51.8	12.9	98.3
FIB-4 >1.45	4.11 (0.91 to 18.56)	84.6	47.7	10.9	97.6
APRI >1	2.645 (0.886 to 7.9)	46.2	79.2	14.3	95.1
AST/ALT >1	6.093 (1.673 to 22.19)	76.9	65.6	14.3	97.4
Ishak >F4 (liver biopsy)	12.64 (2.8 to 57.08)	84.6	73.9	20.4	98.4

[a] Composite of ascites, variceal bleeding, hepatic encephalopathy, HCC, liver transplantation, and mortality.

ALT: alanine aminotransferase; APRI: AST-to-platelet ratio; AST: aspartate aminotransferase; CI: confidence interval; FIB-4: fibrosis-4 index; HR: hazard ratio; kPa: kilopascal; ms: millisecond(s).

Pavlides et al. (2016) evaluated whether data obtained from multiparametric MRI was predictive of all-cause mortality and liver-related clinical events. (41) Patients who were referred for a clinically indicated liver biopsy, or with a diagnosis of liver cirrhosis on MRI scan, were eligible. Liver-related clinical events were defined as liver-related death, hepatocellular carcinoma, and new hepatic decompensation (i.e., clinically evident ascites, variceal bleeding, and hepatic encephalopathy). Patients received multiparametric MRI and liver cT_1 values were mapped into a Liver Inflammation and Fibrosis (LIF) score. One hundred twenty-three patients were recruited to the study; 6 were excluded due to claustrophobia or incomplete MRI data. Of the 117 patients who had complete MRI data, follow-up data were available for 112; the study

reported outcomes on these 112 patients. The most common underlying disease states were NAFLD (35%), viral hepatitis (30%), and ALD (10%). Over a median follow-up time of 27 months, 10 patients had a liver-related clinical event and 6 patients died. No patients who had a LIF <2 (no or mild liver disease) developed a clinical event. Ten of 56 (18%) patients with a LIF ≥2 (moderate or severe liver disease) experienced a clinical event. A study limitation is the use of LIF scores, which are no longer used in clinical practice. The authors further described the study as a small proof of principle study.

Clinically Useful

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

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs. The primary benefit of multiparametric MRI for chronic liver disease is the ability to avoid liver biopsy in patients without significant fibrosis. There are currently no such published studies to demonstrate the effect on patient outcomes.

Multiparametric MRI has been used as an alternative to biopsy for measuring fibrosis or cirrhosis in clinical trials. Phase 2 clinical trials have used multiparametric MRI to measure therapeutic efficacy of an investigational treatments for NASH (42) and NAFLD. (43)

The utility of multiparametric MRI to provide clinically useful information on the presence and extent of liver fibrosis and inflammation has been evaluated in smaller prospective studies. Specifically, it has been evaluated in the setting of biochemical remission in liver diseases where noninvasive testing for continued disease activity could further aid in direct management of patients as a prognostic marker of future liver-related complications. Quantitative multiparametric MRI has been used to measure disease burden after treatment in patients with chronic HCV (44) and autoimmune hepatitis. (45-48)

Section Summary: Multiparametric Magnetic Resonance Imaging

For individuals who have chronic liver disease who receive multiparametric MRI, the evidence includes several prospective and retrospective observational studies. Multiparametric MRI (e.g., LiverMultiScan) has been studied in mixed populations, including NAFLD, viral hepatitis, and ALD. Quantitative MRI provides various measures assessing both liver fat content and fibrosis and inflammation. Various cutoffs have been utilized for positivity. Generally, multiparametric MRI performed similarly to transient elastography, and fewer technical failures of multiparametric MRI were reported. The prognostic ability of quantitative MRI to predict liver-related clinical events has been evaluated in 2 studies; both reported positive correlations with wide CIs. Additionally, multiparametric MRI has been used to measure the presence of fibrosis or cirrhosis in the patients who have achieved biochemical remission after treatment in small prospective studies.

Noninvasive Imaging – Magnetic Resonance Elastography (MRE) (Liver)

Clinical Context and Test Purpose

The purpose of noninvasive testing in individuals with chronic liver disease is to detect liver fibrosis so that individuals can avoid the potential adverse events of an invasive liver biopsy and receive appropriate treatment. The degree of liver fibrosis is an important factor in determining the appropriate approach for managing individuals with liver disease (e.g., hepatitis, ALD, NAFLD).

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

Populations

The relevant population of interest is individuals with chronic liver disease.

Interventions

The test being considered is MRE.

Comparators

The following tests and practices are currently being used to diagnose chronic liver disease: liver biopsy, other noninvasive radiologic methods, and multianalyte serum assays.

Outcomes

The general outcomes of interest are test validity, morbid events, and treatment-related morbidity. Follow-up over months to years is of interest to the relevant outcomes.

Study Selection Criteria

For the evaluation of the clinical validity of the tests within this policy, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).
- Included a suitable reference standard (describe the reference standard).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

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

Tables 8 and 9 summarize the characteristics and results of systematic reviews that have assessed the diagnostic accuracy of MRE. MRE has been studied primarily in hepatitis and NAFLD.

Table 8. Characteristics of Systematic Reviews Assessing Magnetic Resonance Elastography

Study	Dates	Studies	N	Population

Crossan et al. (2015) (21)	1998 to Apr 2012	3	NR	Chronic liver disease
Guo et al. (2015) (49)	To Jun 2013	11	982	Multiple diseases
Singh et al. (2015) (54)	2003 to Sept 2013	12	697	Chronic liver disease
Singh et al. (2016) (55)	To Oct 2014	9	232	NAFLD
Xiao et al. (2017) (56)	To 2016	5	628	NAFLD

NAFLD: nonalcoholic fatty liver disease; NR: not reported.

Table 9. Results of Systematic Reviews Assessing the Diagnostic Accuracy of Magnetic Resonance Elastography

		Significant Fibrosis (i.e., Stages F2-F4)		Cirrhosis (i.e., Stage F4)	
Study	**Population**	**Studies/ Sample Size**	**AUROC (95% CI) Sensitivity (95% CI) Specificity (95% CI)**	**Studies/ Sample Size**	**AUROC (95% CI) Sensitivity (95% CI) Specificity (95% CI)**
Crossan et al. (2015) (21)	Chronic liver disease	3/NR	NR 94% (13% to 100%) 92% (72% to 98%)		
Guo et al. (2015) (49)	Multiple diseases	9/NR	NR 87% (84% to 90%) 94% (91% to 97%)		NR 93% (88% to 96%) 91% (88% to 93%)
Singh et al. (2015) (54)	Chronic hepatitis	12/697	0.84 (0.76 to 0.92) 73% (NR) 79% (NR)	12/697	0.92 (0.90 to 0.94) 91% (NR) 81% (NR)
Singh et al. (2016) (55)	NAFLD	9/232	0.87 (0.82 to 0.93) 79% (76% to 90%) 81% (72% to 91%)	9/232	0.91 (0.76 to 0.95) 88% (82% to 100%) 87% (77% to 97%)
Xiao et al. (2017) (56)	NAFLD	3/384	0.88 (0.83 to 0.92) 73.2% (65.7% to 87.3%) 90.7% (85.0% to 95.7%)	3/384	0.92 (0.80-1.00) 86.6% (80.0% to 90.9%) 93.4% (91.4% to 94.5%)

AUROC: area under the receiver operating characteristic curve; CI: confidence interval; NAFLD: nonalcoholic fatty liver disease; NR: not reported.

Clinically Useful

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

Direct Evidence

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

There are currently no published studies that directly demonstrate the effect of MRE on patient outcomes.

Section Summary: Noninvasive Imaging – MRE (Liver)
MRE has a high success rate and is highly reproducible across operators and time. The diagnostic accuracy also appears to be high. In particular, MRE has high diagnostic accuracy for the detection of fibrosis in NAFLD, independent of body mass index and degree of inflammation.

Noninvasive Imaging – Acoustic Radiation Force Impulse (ARFI) Imaging (Liver)
Clinical Context and Test Purpose
The purpose of noninvasive testing in individuals with chronic liver disease is to detect liver fibrosis so that individuals can avoid the potential adverse events of an invasive liver biopsy and receive appropriate treatment. The degree of liver fibrosis is an important factor in determining the appropriate approach for managing individuals with liver disease (e.g., hepatitis, ALD, NAFLD).

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

Populations
The relevant population of interest is individuals with chronic liver disease.

Interventions
The test being considered is ARFI imaging.

Comparators
The following tests and practices are currently being used to diagnose chronic liver disease: liver biopsy, other noninvasive radiologic methods, and multianalyte serum assays.

Outcomes
The general outcomes of interest are test validity, morbid events, and treatment-related morbidity. Follow-up over months to years is of interest to the relevant outcomes.

Study Selection Criteria
For the evaluation of the clinical validity of the tests within this review, studies that meet the following eligibility criteria were considered:
- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).
- Included a suitable reference standard (describe the reference standard).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

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

Tables 10 and 11 summarize the characteristics and results of systematic reviews that have assessed the diagnostic accuracy of ARFI imaging.

Table 10. Characteristics of Systematic Reviews Assessing Acoustic Radiation Force Impulse Imaging

Study	Dates	Studies	N	Population
Bota et al. (2013) (7)	To May 2012	6	518	Chronic hepatitis
Crossan et al. (2015) (21)	1998 to Apr 2012	4	NR	HCV
Guo et al. (2015) (49)	To Jun 2013	15	2128	Multiple diseases
Hu et al. (2017) (50)	To Jul 2014	7	723	NAFLD
Lin et al. (2020) (51)	To Apr 2019	29	NR	Non-viral liver disease
Jiang et al. (2018) (24)	To Dec 2017	9	982	NAFLD
Liu et al. (2015) (52)	To Apr 2016	23	2691	HBV or HCV
Nierhoff et al. (2013) (53)	2007 to Feb 2012	36	3951	Multiple diseases

HBV: hepatitis B virus; HCV: hepatitis C virus; NAFLD: nonalcoholic fatty liver disease; NR: not reported.

Table 11. Results of Systematic Reviews Assessing the Diagnostic Accuracy of Acoustic Radiation Force Impulse Imaging

		Significant Fibrosis (i.e., Stages F2-F4)		Cirrhosis (i.e., Stage F4)	
Study	**Population**	**Studies/ Sample Size**	**AUROC (95% CI) Sensitivity (95% CI) Specificity (95% CI)**	**Studies/ Sample Size**	**AUROC (95% CI) Sensitivity (95% CI) Specificity (95% CI)**
Bota et al. (2013) (7)	Chronic hepatitis	6/518	0.88 (0.83 to 0.93) NR NR		0.92 (0.87 to 0.98) NR NR
Crossan et al. (2015) (21)	HCV	4/NR	NR 85% (69% to 94%) 89% (72% to 97%)		
Guo et al. (2015) (49)	Multiple diseases	13/NR	NR 76% (73% to 78%) 80% (77% to 83%)	14/NR	NR 88% (84% to 91%) 80% (81% to 84%)
Hu et al. (2017) (50)	HBV, HCV	15/NR	88% (85% to 91%) 75% (69% to 78%) 85% (81% to 89%)		
Jiang et al. (2018) (24)	NAFLD	6/NR	0.86 (0.83 to 0.89) 70% (59% to 79%) 84% (79% to 88%)	7/NR	0.95 (0.93 to 0.97) 89% (60% to 98%) 91% (82% to 95%)

Liu et al. (2015) (52)	NAFLD	7/723	NR 80% (76% to 84%) 85% (81% to 89%)		
Lin et al. (2020) (51)	Non-viral liver disease	23/NR	0.87 (0.83 to 0.89) 79% (73% TO 83%) 81% (75% TO 86%)	14/NR	0.94 (0.92 to 0.96) 89% (79% TO 95%) 89% (85% TO 92%)
Nierhoff et al. (2013) (53)	Multiple diseases	26/NR	0.83 (0.80 to 0.86) NR NR	27/NR	0.91 (0.89 to 0.93) NR NR

AUROC: area under the receiver operating characteristic curve; CI: confidence interval; HBV: hepatitis B virus; HCV: hepatitis C virus; NAFLD: nonalcoholic fatty liver disease; NR: not reported.

A 5-year observational study by Kluppel et al. (2024) compared the prognostic value of ARFI elastography, the FIB-4 score, and liver biopsy. (57) AFRI was significantly better than FIB-4 at predicting liver-related death within 5 years (p=.02), but it did not differ significantly from biopsy (p=.83). For predicting liver decompensation or variceal bleeding, AFRI outperformed both biopsy (p=.02) and FIB-4 (p=.003). However, there was no significant difference between AFRI and biopsy (p=.33) or FIB-4 (p=.14) in predicting hepatocellular carcinoma.

Clinically Useful

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

Direct Evidence

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

There are currently no published studies that directly demonstrate the effect of ARFI imaging on patient outcomes.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of ARFI imaging has not been established, a chain of evidence supporting the clinical utility of this test for this population cannot be constructed.

Section Summary: Noninvasive Imaging – Acoustic Radiation Force Impulse Imaging (Liver)

The use of ARFI imaging has been evaluated in viral hepatitis and NAFLD. Moreover, many have noted that ARFI imaging has potential advantages over FibroScan. ARFI can be implemented on a standard ultrasound machine, may be more applicable for assessing complications such as ascites and may be more applicable in obese patients. ARFI imaging appears to

have similar diagnostic accuracy to FibroScan, but there are fewer data available on performance characteristics. Validation studies have used varying cutoffs for positivity.

Noninvasive Imaging – Real-Time Tissue Elastography (RTE) (Liver)

Clinical Context and Test Purpose

The purpose of noninvasive testing in individuals with chronic liver disease is to detect liver fibrosis so that individuals can avoid the potential adverse events of an invasive liver biopsy and receive appropriate treatment. The degree of liver fibrosis is an important factor in determining the appropriate approach for managing individuals with liver disease (e.g., hepatitis, ALD, NAFLD).

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

Populations

The relevant population of interest is individuals with chronic liver disease.

Interventions

The test being considered is RTE.

Comparators

The following tests and practices are currently being used to diagnose chronic liver disease: liver biopsy, other noninvasive radiologic methods, and multianalyte serum assays.

Outcomes

The general outcomes of interest are test validity, morbid events, and treatment-related morbidity. Follow-up over months to years is of interest to the relevant outcomes.

Study Selection Criteria

For the evaluation of the clinical validity of the tests within this review, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores).
- Included a suitable reference standard (describe the reference standard).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

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

Kobayashi et al. (2015) published the results of a meta-analysis assessing RTE for staging liver fibrosis. (58) The authors selected 15 studies (N=1626) published through December 2013, including patients with multiple liver diseases and healthy adults. A bivariate random-effects model was used to estimate summary sensitivity and specificity. The summary AUROC,

sensitivity, and specificity were 0.69, 79% (95% CI, 75% to 83%), and 76% (95% CI, 68% to 82%) for detection of significant fibrosis (stage ≥F2), and 0.72, 74% (95% CI, 63% to 82%), and 84% (95% CI, 79% to 88%) for detection of cirrhosis, respectively. Reviewers found evidence of heterogeneity due to differences in study populations, scoring methods, and cutoffs for positivity. They also found evidence of publication bias based on funnel plot asymmetry.

Hong et al. (2014) reported on the results of a meta-analysis evaluating RTE for staging fibrosis in multiple diseases. (59) Thirteen studies (N=1347) published between April 2000 and April 2014 that used a liver biopsy or transient elastography as the reference standard were included. Different quantitative methods were used to measure liver stiffness in the included studies: Liver Fibrosis Index (LFI), Elasticity Index, elastic ratio 1 (ER1), and elastic ratio 2 (ER2). For predicting significant fibrosis (stage ≥ F2), the pooled sensitivities for LFI and ER1 were 78% (95% CI, 70% to 84%) and 86% (95% CI, 80% to 90%), respectively. The specificities were 63% (95% CI, 46% to 78%) and 89% (95% CI, 83% to 94%) and the AUROCs were 0.79 (95% CI, 0.75 to 0.82) and 0.94 (95% CI, 0.92 to 0.96), respectively. For predicting cirrhosis (stage F4), the pooled sensitivities of LFI, ER1, and ER2 were 79% (95% CI, 61% to 91%), 96% (95% CI, 87% to 99%), and 79% (95% CI, 61% to 91%), respectively. The specificities were 88% (95% CI, 81% to 93%) for LFI, 89% (95% CI, 83% to 93%) for ER1, and 88% (95% CI, 81% to 93%) for ER2, and the AUROCs were 0.85 (95% CI, 0.81 to 0.87), 0.93 (95% CI, 0.94 to 0.98), and 0.92 (95% CI, not reported), respectively. Pooled estimates for Elasticity Index were not performed due to insufficient data.

Clinically Useful

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

Direct Evidence

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

There are currently no published studies that directly demonstrate the effect of RTE on patient outcomes.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of RTE has not been established, a chain of evidence supporting the clinical utility of this test for this population cannot be constructed.

Section Summary: Noninvasive Imaging – Real-Time Tissue Elastography (Liver)

RTE has been evaluated in multiple diseases with varying scoring methods and cutoffs. Although data are limited, the accuracy of RTE appears to be similar to FibroScan for the evaluation of significant liver fibrosis, but less accurate for the evaluation of cirrhosis. However, there was evidence of publication bias in the systematic review and the diagnostic accuracy may be overestimated.

Noninvasive Imaging – Elastography (Other than Liver)

Elastography-based imaging techniques have received substantial attention in recent years for non-invasive assessment of tissue mechanical properties. While ultrasound elastography has shown promising results for non-invasive assessment of liver fibrosis, new applications in other organs are emerging, including but not limited to, thyroid, breast, and prostate. (60)

Thyroid

Yang et al. (2020) conducted a retrospective analysis that compared the diagnostic parameters of ultrasound elastography and fine-needle aspiration cytology for the differential diagnosis of thyroid nodules, using surgical pathology as the reference standard. (61) In total, 205 patients with abnormal thyroid function test results underwent ultrasound-guided fine-needle aspiration cytology on the basis of the American College of Radiology Thyroid Imaging-Reporting and Data System classification and strain ultrasound elastography according to the ASTERIA criteria. Histopathological examination of the surgical specimens was performed according to the 2017 World Health Organization classification system. Moreover, a beneficial score analysis for each modality was conducted. Of 265 nodules, 212 measured ≥1 cm. The strain index value increased from benign to malignant nodules, and the presence of autoimmune thyroid diseases did not affect the results (p>0.05 for all categories). The sensitivities of histopathological examination, ultrasound elastography, and fine-needle aspiration cytology for detection of nodules measuring ≥1 cm were 1, 1, and 0.97, respectively. The working area for detecting nodule(s) in a single image was similar between strain ultrasound elastography and fine-needle aspiration cytology for highly and moderately suspicious nodules. However, for mildly suspicious, unsuspicious, and benign nodules, the working area for detecting nodule(s) in a single image was higher in strain ultrasound elastography than in fine-needle aspiration cytology. The study had several limitations: 1) It was retrospective in nature, and a dynamic study was not performed, 2) All patients presented with nodules measuring >1 cm, however thyroid papillary carcinoma can measure <1 cm, 3) Only a small proportion of patients presented with malignant nodules, 4) The cutoff strain index values for the differential diagnosis of thyroid nodules were not evaluated, and these values are operator dependent, and 5) Fine-needle aspiration cytology was performed only once in all patients. The authors concluded that strain ultrasound elastography for highly suspicious and moderately suspicious nodules facilitated the detection of mildly suspicious nodules, but not suspicious and benign nodules. Thus, it may be a more accurate and reliable alternative for the differential diagnosis of thyroid nodules than fine-needle aspiration cytology. However, a higher number of patients with calcified nodules are required to assess the hypothesis. Additionally, ultrasound elastography is a good auxiliary method to identify whether a nodule is a thyroid papillary carcinoma. Other types of malignant tumors, which may not be stiff, can develop in

the thyroid. However, the significance of ultrasound elastography in identifying non-stiff malignant tumors is unclear.

In a multicenter RCT performed at 18 secondary and tertiary hospitals across England between February 2015 and September 2018, Mehanna et al. (2024) compared the efficacy of ultrasound (US) elastography-guided fine-needle aspiration cytology (FNAC) versus US-guided FNAC in reducing nondiagnostic rates for thyroid nodules. (62) Eligible adults with single or multiple thyroid nodules who had not previously undergone FNAC were randomized (1:1 ratio) to US elastography FNAC (intervention) or conventional US FNAC (control). The primary outcome was the proportion of patients who have a nondiagnostic cytologic Thy1 (British Thyroid Association system) result following the first FNAC. A total of 982 participants (mean age, 51.3 years ± 15 [SD] [IQR, 39–63]; male-to-female ratio, 1:4) were randomized. Of the 493 participants who underwent US elastography, 467 (94.7%) were examined with strain US elastography. There was no difference between the two arms in the nondiagnostic (Thy1) rate following the first FNAC (19% vs 16%; risk difference [RD], 0.03 [95% CI: −0.01, 0.07]; P=.11) or in the median time to reach the final definitive diagnosis (3.3 months [IQR, 1.5–6.4] for US elastography FNAC vs 3.4 months [IQR, 1.5–6.2] for US FNAC). All sensitivity analyses supported the primary analysis. Fewer participants in the US elastography FNAC arm underwent diagnostic hemithyroidectomy than in the US FNAC arm (183 of 493 [37%] vs 196 of 489 [40%]), but this was not statistically significant (adjusted RD, 0.02 [95% CI: −0.06, 0.01]; P=0.15). There was no evidence of a difference in malignancy rates between the two arms: 70 of 493 (14%) in US elastography FNAC arm versus 79 of 489 (16%) in US FNAC arm (P=.39). There was also no difference in the rate of benign histologic findings between the groups (RD, −0.01 [95% CI: −0.04, 0.03]; P=.7). Researchers determined that strain US elastography does not appear to have additional benefit over conventional US FNAC in the diagnosis of malignancy in thyroid nodules.

Breast

In 2017, Blank and colleagues published a systematic review and meta-analysis. (63) The authors reported measured elasticities of benign and malignant breast pathologies from SWE, quantitatively confirmed the effect of the selected ROI on these measures and tested the hypothesis that a metric of heterogeneity based on the mean and maximum elasticity can improve specificity of diagnosis. The elasticity of benign, malignant and specific pathologic states were reported from 22 publications encompassing 2,989 patients, identified from a structured search of literature from May to September 2015. A total of 12 articles were included in a meta-analysis that grouped results by the method of ROI selection to discriminate between different pathologies. These researchers observed a significant correlation between the method of selection of ROI for malignant mean ($p<0.001$) and maximum ($p=0.027$) elasticity, but no correlation with benign measures. They defined a quantitative heterogeneity parameter, the "stiffness gradient", computed from the mean and maximum measured elasticity. The stiffness gradient outperformed the current standard maximum elasticity metric in stratifying malignancy risk by a margin of 15% for the partial ROI, and 42% for the maximized ROI. An anecdotal example of improved differentiation using the stiffness gradient on pathology-specific lesions was also provided. The authors concluded that these results

quantitatively indicated that the method of ROI selection in SWE not only has a significant impact on the resulting mean reported elasticity of a lesion but may provide some insight into lesion heterogeneity. They stated that these findings suggested that further exploration of quantitative heterogeneity is needed to improve the specificity of diagnosis.

Park et al. (2017) investigated factors related to false shear wave elastography (SWE) results for breast non-mass lesions (NMLs) detected by B-mode US. (64) This retrospective study enrolled 152 NMLs detected by B-mode US and later pathologically confirmed (79 malignant, 73 benign). All lesions underwent B-mode US and SWE. Quantitative (mean elasticity [E_{mean}]) and qualitative (maximum stiffness color) SWE parameters were assessed, and 'E_{mean} > 85.1 kPa' or 'stiff color (green to red)' determined malignancy. Final SWE results were matched to pathology results. Multivariate logistic regression analysis identified factors associated with false SWE results for diagnosis of breast NMLs. Associated calcifications (E_{mean}: odds ratio [OR]=7.60, P<0.01; maximum stiffness color: OR=6.30, P=0.02), in situ cancer compared to invasive cancer (maximum stiffness color: OR=5.29, P = 0.02), and lesion size (E_{mean}: OR=0.90, P<0.01; maximum stiffness color: OR=0.91, P=0.01) were significantly associated with false negative SWE results for malignant NMLs. Distance from the nipple (E_{mean}: OR=0.84, P=0.03; maximum stiffness color: OR=0.93, P=0.04) was significantly associated with false positive SWE results for benign NMLs. The authors concluded that the presence of associated calcifications, absence of the invasive component, and smaller lesion size for malignant NMLs and shorter distance from the nipple for benign NMLs are factors significantly associated with false SWE results.

Choi et al. (2019) compared the diagnostic performance of B-mode ultrasound, SWE, and combined B-mode ultrasound and SWE in small breast lesions (≤ 2 cm), and evaluated the factors associated with false SWE results. (65) A total of 428 small breast lesions (≤ 2 cm) of 415 consecutive patients between August 2013 and February 2017 were included. The diagnostic performance of each set was evaluated using the area under the receiver operating characteristic curve (AUC) analysis. Histologic diagnosis was used as reference standard. Multivariate logistic regression analyses identified the factors associated with false SWE results. Of 428 lesions, 142 (33.2%) were malignant and 286 (66.8%) were benign. The AUC of the combined modality was higher than that of B-mode ultrasound (0.792 *vs* 0.572, p<0.001) and that of SWE was higher than that of B-mode ultrasound (0.718 *vs* 0.572, p<0.001). Multivariate analysis showed that the smaller lesion size and *in situ* cancer were associated with false negative, and patient's age, high-risk lesion, shorter distance from the skin or chest wall, and deeper breast thickness were associated with false positive (all p<0.05). The authors concluded that the addition of SWE to B-mode ultrasound could improve the diagnostic performance in ≤ 2 cm lesions. However, ultrasound lesion size, pathology, and lesion location are likely to affect the SWE value and result in false results.

In a single center study, Shahzad et al. (2022) sought to determine the role of strain elastography (SE) and SWE in differentiating benign and malignant breast tissue. (66) One hundred breast lesions from 95 consecutive patients referred for ultrasonography followed by biopsy or surgical excisions were examined with B-mode ultrasonography and by both strain and shear wave elastography. The mean (SD) strain elastography ratio in the overall patient

population was 4.1 (2.0). Cutoff for benign vs. malignant lesions was 2.86 on the ROC curve. The AUC was 0.911 (95% CI; 0.835-0.988: SE, 0.039) with a sensitivity of 95.8% and a specificity of 89.3%. For the SWE kPa values, the ROC curve showed the AUC was 0.929 (95% CI, 0.870-0.988; SE: 0.030, *P*<.001). Assigning 45.3 as a cut off value provided a sensitivity of 95.8% with a specificity of 85.7%; the positive predictive value was 94.5% and the negative predictive value was 89.6%. The Breast Imaging Reporting and Data System (BI-RADS) category alone was able to differentiate between benign and malignant lesions with a sensitivity of 91.7% and a specificity 100% keeping the cut off value between 4a and 4b. The area under the ROC curve was 0.979. Combining the three (BI-RADS + SE + SWE) distinguished benign vs. malignant lesions with a sensitivity up to 100% and specificity up to 96.3%. Authors concluded that combining SE and SWE as a complementary tool with conventional B-mode ultrasonography has a significant potential for better characterization of solid breast lesions and decreasing unnecessary biopsies of BI-RADS IVa lesions.

Pillai et al. (2022) assessed the diagnostic accuracy of 2-D SWE for differentiating benign and malignant breast lesions in women with abnormal findings on mammography. (67) Included in this review are studies of diagnostic accuracy published before June 2021 using 2-D SWE to evaluate female breast lesions. Included studies were required to include at least 50 lesions, report quantitative shear-wave speed (SWS) thresholds, and include a reference standard of either biopsy or 2-year stability. Included studies used the mean, maximum, minimum, or SD of SWS for classification. A systematic search of PubMed, Scopus, Embase, Ovid-MEDLINE, the Cochrane Library, and Web of Science was performed. Bias and applicability of the studies were assessed using Quality Assessment of Diagnostic Accuracy Studies 2. A hierarchical summary receiver operating characteristic model was used to arrive at the summary statistics. Eighty-seven prospective and retrospective studies were included, encompassing 17,810 women (mean age 42.3 ± 10.4 years) with 19,043 lesions (7,623 malignant). Summary sensitivities and specificities, respectively, were 0.86 (95% CI, 0.83-0.88) and 0.87 (95% CI, 0.84-0.88) for mean SWS, 0.83 (95% CI, 0.80-0.85) and 0.88 (95% CI, 0.86-0.90) for the maximum, 0.86 (95% CI, 0.74-0.93) and 0.81 (95% CI, 0.69-0.89) for the minimum, and 0.82 (95% CI, 0.77-0.86) and 0.88 (95% CI, 0.85-0.91) for the SD. Alternatively, the areas under the receiver operating characteristic curve were 0.93 (95% CI, 0.91-0.94), 0.92 (95% CI, 0.90-0.94), 0.90 (95% CI, 0.82-0.96), and 0.92 (95% CI, 0.88-0.94), respectively. Reviewers concluded that this review demonstrates the discriminative power of SWE in the diagnosis of breast cancer. Using the resulting likelihood ratios, SWE may prove beneficial in downgrading BI-RADS® 4a or upgrading BI-RADS 3 lesions. However, current society guidelines do not provide definitive recommendations regarding the use of SWE and its counterpart strain elastography (SE). Comparison with our results suggests that SE alone or a combination of SE and SWE may provide better diagnostic performance than SWE alone and serve as an adjunct to current diagnostic techniques.

To reduce the number of biopsies performed on benign breast lesions categorized as BI-RADS 4–5, Xu et al. (2024) investigated the diagnostic performance of combined two-dimensional and three-dimensional shear wave elastography (2D + 3D SWE) with standard breast US for the BI-RADS assessment of breast lesions. (68) A total of 897 breast lesions, categorized as BI-RADS 3–5, were subjected to standard breast US and supplemented by 2D SWE only and 2D + 3D SWE

analysis. Based on the malignancy rate of less than 2% for BI-RADS 3, lesions assessed by standard breast US were reclassified with SWE assessment. After standard breast US evaluation, 268 (46.1%) participants underwent benign biopsies in BI-RADS 4–5 lesions. By using separated cutoffs for upstaging BI-RADS 3 at 120 kPa and downstaging BI-RADS 4a at 90 kPa in 2D + 3D SWE reclassification, 123 (21.2%) participants underwent benign biopsy, resulting in a 54.1% reduction (123 versus 268). However, after 2D + 3D SWE reclassification at separated cutoffs, nine malignancies were missed in BI-RADS 3 category including three invasive ductal/lobular carcinomas (IDC/ILC), three ductal carcinomas in situ (DCIS), two papillary carcinomas, and one tubular carcinoma. Additionally, in comparison with reclassifying BI-RADS 4a lesions with an independent cutoff and reclassifying BI-RADS 3 and 4a lesions with separated cutoffs, reclassification of BI-RADS 4b, 4c, and 5 with SWE provided no benefit on reduction of benign biopsies, suggesting that women with breast lesions in BI-RADS 4b, 4c, and 5 were unlikely to benefit from this approach. Authors note that this study illustrated that higher SWE values of lesion resulted in higher possibility of malignancy. Nevertheless, a few low SWE cancers with low SWE values will be missed. This study detected 36 cancers with a value of less than 90 kPa in 2D + 3D SWE, and 25% (9/36) of them were missed after reclassification. The pathologic types of missed cancers did not fit very well with previous reports that DCIS and papillary cancers had relatively low values on elastography. Future research may explore the potential relationships between subtypes of breast cancers and elastography characterizations.

Prostate

In a preliminary study, Dai et al. (2020) explored the correlation between SWE and grade group (GG) of prostate cancer (PCa). (69) This retrospective study involved prostate-specific antigen elevated patients with elevated prostate-specific antigen levels who underwent SWE before transrectal ultrasound-guided needle biopsy. A total of 49 PCa lesions were reviewed after radical prostatectomy; 3-7 regions of interest were placed within the cancerous area on axial view compared with the tumor foci outlined on the slides by pathologist. The maximum SWE value was measured, quantitative SWE parameters (E_{max}, E_{mean}, E_{min} and standard deviation [SD]) were recorded and correlated with GG and then parameters were compared between indolent (≤2) and aggressive (≥3) GGs. The diagnostic value of each parameter was compared with the receiver operating characteristic curve. Forty-nine PCa foci were divided into two groups on the basis of their GGs. All SWE parameters exhibited a significant linear trend with GG. The area under the receiver operating characteristic curve (AUC) was 0.816 for E_{max}; with a cutoff point of 84 kPa, sensitivity and specificity were 81.3% and 82.4% to differentiate low and high GGs in PCa. The AUC was 0.776 for E_{mean}; with a cutoff point of 71 kPa, sensitivity and specificity were 78.1% and 76.5%. For E_{min}, the AUC was 0.739; with a cutoff point of 60 kPa, sensitivity and specificity were 68.8% and 70.6%. For SD, the AUC was 0.681; with a cutoff point of 8.3 kPa, sensitivity and specificity were 46.9% and 94.1%. There were no significant differences between the four SWE parameters ($p < 0.05$ for all). SWE features were correlated with GGs, and this correlation may have excellent diagnostic performance in predicting high GG in PCa.

In a systematic review, Anbarasan et al. (2021) evaluated SWE for the detection of PCa and compared diagnostic estimates between studies reporting the detection of all PCa and clinically

significant PCa (csPCa). (70) Sixteen studies including 2277 patients were included for review. Nine studies evaluated SWE for the detection of PCa using systematic biopsy as a reference standard at the per-sample level, with a pooled sensitivity and specificity of 0.85 (95% CI = 0.74-0.92) and 0.85 (95% CI = 0.75-0.91), respectively. Five studies evaluated SWE for the detection of PCa using histopathology of radical prostatectomy (RP) specimens as the reference standard, with a pooled sensitivity and specificity of 0.71 (95% CI = 0.55-0.83) and 0.74 (95% CI = 0.42-0.92), respectively. Sub-group analysis revealed a higher pooled sensitivity (0.77 vs. 0.62) and specificity (0.84 vs. 0.53) for detection of csPCa compared to all PCa among studies using RP specimens as the reference standard. Reviewers concluded that while an attractive strategy, the SWE role for the diagnosis of csPCa in the context of novel ultrasound techniques and the emerging "magnetic resonance pathway" needs to be evaluated further.

Almalki et al. (2024) aimed to examine the validity and reproducibility of strain elastography (SE) for detecting PCa in patients with elevated prostate-specific antigen (PSA) levels. (71) The study included 107 males with elevated PSA levels. All eligible patients underwent transrectal ultrasound (TRUS) with real-time elastography (RTE) to detect suspicious lesions. Two readers independently evaluated the lesions and assigned a strain ratio and elastography score to each lesion. Histopathology was used as a reference standard to estimate the validity of RTE in predicting malignant lesions. An intraclass correlation (ICC) was performed to detect reliability of the strain ratios and elastography scores. TRUS-guided biopsy detected malignancies in 64 (59.8%) patients. TRUS with RTE revealed 122 lesions. The strain ratio index (SRI) cut-off values to diagnose malignancy were 4.05 and 4.35, with sensitivity, specificity, and accuracy of 94.7%, 91.3%, and 93.4%, respectively. An elastography score > 3 was the best cut-off value for detecting malignancy. According to readers, the sensitivity, specificity, and accuracy were 91.3–94.7%, 89.5–93.4%, and 91.3–90.9%, respectively. Excellent inter-reader agreement was recorded for SRI and elastography scores, with ICC of 0.937 and 0.800, respectively. The current study reported a statistically significant association between elastography scores assessed by both readers and histopathology results. Benign lesions had lower elastography scores, whereas malignant lesions had higher scores. The study had some limitations: 1) It was a single-center study, indicating the need for prospective multicenter studies to generalize results; 2) The high prevalence of malignant lesions may have skewed the accuracy of the parameter calculation; 3) Multiparametric-MRI was not used for comparison with SE. In a clinical setting, confirming the diagnosis and reducing unnecessary biopsies using SE in conjunction with multiparametric-MRI is recommended. However, as previously mentioned, SE can be a valuable, non-invasive, rapid tool in low- and middle-income countries or low-resource settings where multiparametric-MRI might be unavailable. With highly experienced operators, SE can predict malignant lesions with a higher diagnostic performance.

Practice Guidelines and Position Statements

Nonalcoholic Fatty Liver Disease

American Gastroenterological Association et al.

In 2018, the practice guidelines on the diagnosis and management of nonalcoholic fatty liver disease (NAFLD), developed by the American Gastroenterological Association (AGA), the American Association for the Study of Liver Diseases, and the American College of

Gastroenterology, stated that “NFS [NAFLD fibrosis score] or FIB-4 [Fibrosis-4] index are clinically useful tools for identifying NAFLD patients with a higher likelihood of having bridging fibrosis (stage 3) or cirrhosis (stage 4).” (72) This guideline also cited vibration-controlled transient elastography (VCTE) and magnetic resonance elastography (MRE) as “clinically useful tools for identifying advanced fibrosis in patients with NAFLD.”

A 2022 consensus-based clinical care pathway was published by the AGA on risk stratification and management of NAFLD, including some recommendations regarding the use of non-invasive testing for individuals with chronic liver disease. (73) Among individuals with increased risk of NAFLD or nonalcoholic steatohepatitis (NASH)-related fibrosis (i.e., individuals with type-2 diabetes, ≥2 metabolic risk factors, or an incidental finding of hepatic steatosis or elevated aminotransferases), assessment with a nonproprietary fibrosis scoring system such as FIB-4 is recommended, although aspartate transaminase to platelet ratio index can be used in lieu of FIB-4 scoring. Depending on the fibrosis score, imaging-based testing for liver stiffness may be warranted with transient elastography (FibroScan), although bidimensional shear wave elastography or point shear wave elastography are also imaging options included in the clinical care pathway.

In 2023, the AGA published an expert review on the role of noninvasive tests [NITs] in the evaluation and management of NAFLD. (74) The following practice advice statements were made.

- "A Fibrosis 4 Index score [FIB-4] <1.3 is associated with strong negative predictive value for advanced hepatic fibrosis and may be useful for exclusion of advanced hepatic fibrosis in patients with NAFLD.
- A combination of 2 or more NITs combining serum biomarkers and/or imaging-based biomarkers is preferred for staging and risk stratification of patients with NAFLD whose Fibrosis 4 Index score [FIB-4] is >1.3.
- Use of NITs in accordance with manufacturer’s specifications can minimize risk of discordant results and adverse events.
- NITs should be interpreted with context and consideration of pertinent clinical data...to optimize positive predictive value in the identification of patients with advanced fibrosis.
- Liver biopsy should be considered for patients with NIT results that are indeterminate or discordant; conflict with other clinical, laboratory, or radiologic findings; or when alternative etiologies for liver disease are suspected.
- Serial longitudinal monitoring using NITs for assessment of disease progression or regression may inform clinical management.
- Patients with NAFLD and NITs results suggestive of advanced fibrosis or cirrhosis should be considered for surveillance of liver complications. Patients with NAFLD and NITs suggestive of advanced hepatic fibrosis should be monitored with serial liver stiffness measurement; vibration controlled transient elastography; or magnetic resonance elastography, given its correlation with clinically significant portal hypertension and clinical decompensation."

American Association for the Study of Liver Diseases

A 2023 updated practice guidance issued by the AASLD included the following guidance statements on the use of noninvasive techniques for diagnosis and management of NAFLD and hepatic steatosis. (75)

- All patients with hepatic steatosis or clinically suspected NAFLD based on the presence of obesity and metabolic risk factors should undergo primary risk assessment with FIB-4
- In patients with pre-DM [diabetes mellitus], T2DM, or 2 or more metabolic risk factors (or imaging evidence of hepatic steatosis), primary risk assessment with FIB-4 should be repeated every 1–2 years
- Although standard ultrasound can detect hepatic steatosis, it is not recommended as a tool to identify hepatic steatosis due to low sensitivity across the NAFLD spectrum
- CAP [controlled attenuation parameter] as a point-of-care technique may be used to identify steatosis. MRI-PDFF [proton density fat fraction] can additionally quantify steatosis
- If FIB-4 is ≥ 1.3, VCTE, MRE, or ELF [Enhanced Liver Fibrosis] may be used to exclude advanced fibrosis
- Improvement in ALT or reduction in liver fat content by imaging in response to an intervention can be used as a surrogate for histological improvement in disease activity

A 2024 publication from the AASLD describes the impact of new nomenclature on the AASLD practice guidance on NAFLD and hepatic steatosis described above. (76) Briefly, available data suggest a near complete overlap (99%) between the metabolic dysfunction-associated steatotic liver disease (MASLD)-defined population and the historical NAFLD-defined population. Therefore, all recommendations on the clinical assessment and management of NAFLD AND NASH can be applied to patients with MASLD, and metabolic dysfunction associated steatohepatitis (MASH). Additionally, data from biomarker validation studies among patients with NAFLD and NASH are applicable to patients with MASLD and MASH, respectively, until further guidance.

A 2022 joint clinical practice guideline issued by the American Association of Clinical Endocrinology and AASLD included the following recommendations on the use of noninvasive techniques for diagnosis of NAFLD with clinically significant fibrosis (stage F2 to F4) (77):

- Clinicians should use liver fibrosis prediction calculations to assess the risk of NAFLD with liver fibrosis. The preferred noninvasive initial test is the FIB-4 (Grade B, Level 2 evidence)
- High-risk individuals with indeterminate or high FIB-4 score for further workup with an transient elastography or enhanced liver fibrosis test, as available (Grade B, Level 2 evidence)
- Clinicians should prefer the use of transient elastography as best validated to identify advanced disease and predict liver-related outcomes. Alternative imaging approaches may be considered, including shear wave elastography (less well validated) and/or magnetic resonance elastography (most accurate but with a high cost and limited availability; best if ordered by liver specialist for selected cases) (Grade B, Level 2 evidence).

In 2024, the AASLD published guidelines focused on imaging-based noninvasive liver disease assessment (NILDA) of hepatic fibrosis and steatosis. (78) Recommendations are provided in Table 12 and include guidance for individuals with various etiologies of chronic liver disease,

including hepatocellular (hepatitis C virus [HCV], HCV/HIV, hepatitis B virus [HBV], HCV/HBV, HBV/HIV, NAFLD, alcohol-associated liver disease [ALD]) and cholestatic disorders (primary sclerosing cholangitis [PSC], primary biliary cholangitis [PBC]).

Table 12. AASLD Recommendations for Imaging-based Noninvasive Liver Disease Assessment

Recommendation	SOR	QOE
In adults with chronic HCV, chronic HBV, and NAFLD, AASLD recommends using imaging-based NILDA tests to detect significant fibrosis (F2-4), advanced fibrosis (F3-4), and cirrhosis (F4)	Strong	Moderate
In adults with ALD or chronic cholestatic liver disease, AASLD suggests using imaging-based NILDA tests to detect advanced fibrosis (F3-4) and cirrhosis (F4)	Conditional	Low
In adults with CLD, AASLD recommends utilizing either US-based elastography methods or MRE to stage fibrosis. Depending on local availability and expertise, it is reasonable to perform MRE as an investigation when concomitant cross-sectional imaging is needed or for patients in whom the accuracy of US-based elastography might be compromised	Ungraded	Ungraded
In adults with CLD, AASLD suggests imaging-based NILDA be incorporated into the initial fibrosis staging process because it is more accurate than blood-based NILDA	Conditional	Low
In adults with CLD undergoing initial fibrosis staging, AASLD suggests combining blood-based and imaging-based NILDA, particularly for the detection of significant fibrosis (F2-4) and advanced fibrosis (F3-4)	Conditional	Low
AASLD suggests against the use of imaging-based NILDA as a standalone test to assess regression or progression of liver fibrosis	Ungraded	Ungraded
AASLD suggests interpreting a longitudinal decrease or increase in liver stiffness within an individualized clinical context that considers the effect of NILDA modifiers and other supportive evidence of improving or worsening clinical course	Ungraded	Ungraded
In patients with treated HBV and HCV, AASLD suggests using the LSM obtained prior to the start of antiviral therapy as the most accurate longitudinal NILDA parameter for the effect of prognostication, given the limited amount of evidence associating LSM with clinical outcomes once viral suppression or eradication is achieved	Ungraded	Ungraded
In adults, TE-CAP has good diagnostic accuracy to grade steatosis and can be used in clinical practice	Ungraded	Ungraded
In adults, imaging-based NILDA, specifically TE-CAP and MRI-PDFF or MRS, are superior to blood-based NILDA tests and should be used in the assessment of hepatic steatosis where available	Ungraded	Ungraded

In the pediatric population, there is insufficient evidence to recommend a single imaging-based NILDA over another to assess liver fibrosis or steatosis	Ungraded	Ungraded
Recognizing that liver histology is an imperfect reference standard, prior to considering a liver biopsy to assess fibrosis staging in patients with CLD, AASLD recommends using blood and imaging-based NILDA as the initial tests to detect significant (F2-4) to advanced fibrosis (F3-4) and cirrhosis (F4)	Ungraded	Ungraded

AASLD: American Association for the Study of Liver Diseases; ALD: alcohol-associated liver disease; CLD: chronic liver disease; HBV: hepatitis C virus; HCV: hepatitis C virus; MRE: magnetic resonance elastography; MRI-PDFF: magnetic resonance imaging proton density fat fraction; MRS: magnetic resonance spectroscopy; NILDA: noninvasive liver disease assessment; QOE: quality of evidence; SOR: strength of recommendation; TE-CAP: transient elastography with controlled attenuation parameter; US: ultrasound

National Institute for Health and Care Excellence

In 2016, the NICE published guidance on the assessment and management of NAFLD. (79) The guidance did not reference elastography.

American Gastroenterological Association Institute

In 2017, the American Gastroenterological Association Institute published guidelines on the role of elastography in chronic liver disease. The guidelines indicate that in adults with NAFLD, magnetic resonance-guided elastography has little or no increased diagnostic accuracy for identifying cirrhosis compared with VCTE in patients who have cirrhosis and has higher diagnostic accuracy than VCTE in patients who do not have cirrhosis (very low quality of evidence). (80)

Hepatitis B and C Viruses

National Institute for Health and Care Excellence (NICE)

In 2017, the NICE published updated guidance on the management and treatment of patients with hepatitis B virus. (81) The guidance recommends offering transient elastography as the initial test for liver disease in adults diagnosed with chronic hepatitis B, to inform the antiviral treatment decision (Table 13).

Table 13. Antiviral Treatment Recommendations by Transient Elasticity Score

Transient Elasticity Score	Antiviral Treatment
>11 kPa	Offer antiviral treatment
6 to 10 kPa	Offer liver biopsy to confirm fibrosis level prior to offering antiviral treatment
<6 kPa plus abnormal ALT	Offer liver biopsy to confirm fibrosis level prior to offering antiviral treatment
<6 kPa plus normal ALT	Do not offer antiviral treatment

ALT: alanine aminotransferase; kPa: kilopascal.

American Association for the Study of Liver Diseases (AASLD) / Infectious Disease Society of America (IDSA)
In 2020, the AASLD/ISDA guidelines for testing, managing, and treating hepatitis C virus (HCV) recommended that, for counseling and pretreatment assessment purposes, the following should be completed:

"Evaluation for advanced fibrosis using noninvasive markers and/or elastography, and rarely liver biopsy, is recommended for all persons with HCV infection to facilitate decision making regarding HCV treatment strategy and determine the need for initiating additional measures for the management of cirrhosis (e.g., hepatocellular carcinoma screening). Rating: Class I, Level A [evidence and/or general agreement; data derived from multiple randomized trials, or meta-analyses]" (82)

The guidelines noted that there are several noninvasive tests to stage the degree of fibrosis in patients with HCV. Tests included indirect serum biomarkers, direct serum biomarkers, and VCTE. The guidelines asserted that no single method is recognized to have high accuracy alone and careful interpretation of these tests is required.

A 2023 update of this guideline includes noninvasive liver markers such as HCV FibroSure, FIB-4, and FibroScan in their simplified treatment algorithm for HCV. (83) Specific recommendations for a preferred noninvasive testing strategy are not provided.

American Gastroenterological Association Institute
In 2017, guidelines published by the American College of Gastroenterology Institute on the role of elastography in chronic liver disease indicated that, in adults with chronic hepatitis B virus and chronic HCV, VCTE has superior diagnostic performance for diagnosing cirrhosis when compared to the APRI and FIB-4 tests (moderate quality of evidence for HCV, low quality of evidence for hepatitis B virus). (80) In addition, the guidelines state that, in adults with HCV, magnetic resonance-guided elastography has little or no increased diagnostic accuracy for identifying cirrhosis compared with VCTE in patients who have cirrhosis and has lower diagnostic accuracy than VCTE in patients who do not have cirrhosis (very low quality of evidence).

<u>Chronic Liver Disease</u>
American College of Radiology (ACR)
In 2020, the ACR appropriateness criteria rated ultrasound shear wave elastography as an 8 (usually appropriate) for the diagnosis of liver fibrosis in patients with chronic liver disease. (84) The criteria noted that high-quality data can be difficult to obtain in obese patients, and assessments of liver stiffness can be confounded by parenchyma, edema, inflammation, and cholestasis.

U.S. Preventive Services Task Force Recommendations
A 2020 U.S. Preventive Services Task Force Recommendation Statement for HCV screening notes that a diagnostic evaluation for fibrosis stage or cirrhosis with a noninvasive test reduces

the risk for harm compared to a liver biopsy. (85) This statement does not give preference to a specific noninvasive test.

Conditions Outside of the Liver

National Comprehensive Cancer Network (NCCN)

The NCCN guideline for thyroid carcinoma states FNA is the procedure of choice for evaluation of suspicious thyroid nodules. (86)

The NCCN practice guideline for breast cancer screening does not indicate elastography as a diagnostic modality. (87)

The NCCN guideline for prostate cancer does not mention elastography. (88)

Summary of Evidence

For individuals who have chronic liver disease who receive transient elastography, the evidence includes many systematic reviews of more than 50 observational studies (>10,000 patients). Relevant outcomes are test accuracy and validity, morbid events, and treatment-related morbidity. Transient elastography (FibroScan) has been studied in populations with viral hepatitis, nonalcoholic fatty liver disease (NALFD), and alcoholic liver disease (ALD). There are varying cutoffs for positivity. Failures of the test are not uncommon, particularly for those with high body mass index, but these failures often went undetected in analyses of the validation studies. Given these limitations and the imperfect reference standard, it can be difficult to interpret performance characteristics. However, for the purposes of deciding whether a patient has severe fibrosis or cirrhosis, the FibroScan results provide data sufficiently useful to determine therapy. In fact, FibroScan has been used as an alternative to biopsy to establish eligibility regarding the presence of fibrosis or cirrhosis in the participants of several randomized controlled trials (RCTs). These trials showed the efficacy of hepatitis C virus (HCV) treatments, which in turn demonstrated that the test could identify patients who would benefit from therapy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic liver disease who receive multiparametric magnetic resonance imaging (MRI), the evidence includes several prospective and retrospective observational studies. Multiparametric MRI (e.g., LiverMultiScan) has been studied in mixed populations, including NAFLD, viral hepatitis, and ALD. Quantitative MRI provides various measures to assess liver fat content, fibrosis and inflammation. Multiparametric MRI performed similarly to transient elastography, and fewer technical failures of multiparametric MRI were reported. The prognostic ability of quantitative MRI to predict liver-related clinical events has been evaluated in 2 studies. Both studies reported positive correlations. Multiparametric MRI has been used to measure the presence of fibrosis or cirrhosis in patients who have achieved biochemical remission after treatment in small prospective studies. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic liver disease who receive other noninvasive radiologic methods for liver fibrosis measurement, the evidence includes systematic reviews of observational studies and a comparative study with 5-year follow up. Relevant outcomes are test accuracy and validity, morbid events, and treatment-related morbidity. Other radiologic methods (e.g., magnetic resonance elastograpy [MRE], real-time transient elastography, acoustic radiation force impulse imaging [ARFI]) may have similar performance for detecting significant fibrosis or cirrhosis. In the comparative study, ARFI elastography was found to be at least as effective as liver histology in predicting liver-related survival and was superior to both histology and the FIB-4 score in predicting certain liver-related complications. Studies have frequently included varying cutoffs not prespecified or validated. Given these limitations and the imperfect reference standard, it is difficult to interpret performance characteristics. There is no direct evidence that other noninvasive radiologic methods improve health outcomes; further, it is not possible to construct a chain of evidence for clinical utility due to the lack of sufficient evidence on clinical validity. The evidence is insufficient to determine the effects of the technology on health outcomes. However, the American Gastroenterological Association recommendation regarding monitoring with serial liver stiffness measurement in individuals with NAFLD and noninvasive test results suggestive of advanced fibrosis or cirrhosis, includes either transient elastography or MRE.

Minimal studies were identified for the use any elastography radiologic methods (e.g., magnetic resonance elastography, real-time transient elastography, acoustic radiation force impulse imaging, transient elastography) outside of the liver. Small cohorts were noted, and some research appears promising for elastography as a potential diagnostic tool for staging of breast and thyroid nodules, although research is still in the initial stages. Large scientifically controlled studies are needed in order to validate the diagnostic performance compared to other diagnostic tests currently available (i.e., biopsy). The evidence is insufficient to determine the effects of the technology on health outcomes.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	76391, 76981, 76982, 76983, 91200, 0422T, 0648T, 0649T
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
12/31/2025	Document became inactive.
06/01/2025	Document updated with literature review. The following change was made to coverage: Added multiparametric MRI to EIU statement for all other indications. Added references 1, 36, 57, 62, 68, 71, 74, 76, 78, and 83; others updated.
10/15/2024	Reviewed. No changes.
02/01/2024	Document updated with literature review. Coverage unchanged. Add/updated references 1, 68, 69, 74, 76, 79, and 82-84.
01/15/2023	Document updated with literature review. The following changes were made to Coverage: 1) Modified conditional coverage for magnetic resonance elastography to include multiparametric magnetic resonance imaging for individuals with established chronic liver disease to include when transient elastography cannot be performed or is nondiagnostic; and 2) Added "the evaluation or monitoring of patients with chronic liver disease" to experimental, investigational and/or unproven statement for other ultrasound elastographic techniques. Added/updated the following references: 1-4, 21, 35-46, 68, and 70-72, and 76-79. Title changed from "Elastography".
12/01/2021	Reviewed. No changes.
01/01/2021	Document updated with literature review. The following change was made to Coverage: Changed "vibration-controlled transient elastography" to "transient elastography" to reflect the current nomenclature in the scientific literature. Added/updated the following references: 20, 23-39, 41-43, 46, 49, 54-57, 59-62, and 65.
06/15/2019	Reviewed. No changes.
06/01/2018	Document updated with literature review. The following changes were made to Coverage: 1) Reworded medical necessity statement on transient elastography; 2) Added conditional coverage for magnetic resonance elastography; 3) Split the experimental/investigational/unproven statement into two separate statements, one to address when the conditional criteria for vibration-controlled transient elastography and magnetic resonance

	elastography is not met, and the other to address other indications and types of elastography. References 20-24, 26-43, 49, 57-59 added.
12/01/2016	Reviewed. No changes.
03/01/2015	Document update with literature review. The following was added to coverage: Transient elastography (e.g., FibroScan) once every six months may be medically necessary to assess the degree of liver fibrosis and cirrhosis in an individual with chronic liver disease, when a liver biopsy has not been performed within six months. Entire document revised.
01/01/2014	New medical document. Elastography, by any method, is considered experimental, investigational, and/or unproven.