Transient Elastography White Paper

Clinical Applications of Ultrasound-Based Elastography in Chronic Liver Disease

mindray
NORTH AMERICA

Introduction

Chronic liver disease is the progressive deterioration of liver function through a process of inflammation, destruction, and regeneration of liver tissue, leading to fibrosis and cirrhosis.

Chronic liver disease is a worldwide problem, caused by a wide range of factors, including obesity, alcoholism, and diabetes. Fibrosis, or the increasing deposition of fibrous tissue within the liver, may lead to scarring and liver dysfunction and the development of cirrhosis. This, in turn, may result in portal hypertension, hepatic insufficiency, and hepatocellular carcinoma.

Patients with high levels of liver fibrosis (F3–F4) are at risk for clinical complications, including ascites, variceal hemorrhage, and hepatic encephalopathy. The stage of liver fibrosis is important to determine prognosis, for surveillance, for treatment planning, and to determine the potential for reversibility.[1]

According to the Center for Disease Control (CDC), chronic liver disease is one of the top 15 causes of death in the United States. Approximately 4.5 million adults In the U.S. have chronic liver disease and cirrhosis, which is 1.8 percent of the adult population. There were 54,803 deaths from chronic liver disease and cirrhosis in 2023.[2]

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly referred to as non-alcoholic fatty liver disease (NAFLD), is currently the most common chronic liver disease worldwide and the global prevalence of MASLD increased from 25.3% in 1990-2006 to 38.0% in 2016-2019.[3]

Need for Accurate, Non-Invasive Diagnostic Tool

Severe liver dysfunction is often fatal. However, chronic liver diseases are frequently asymptomatic, resulting in long-term and often irreversible damage. As a result, the early detection of liver diseases, and staging and surveillance of chronic liver disorders is critical.

Clinical guidelines recommend the use of noninvasive tests for the detection and staging of liver fibrosis. Liver function blood tests are used to help screen for liver disease and monitor treatment and disease progression. While biopsy is the gold standard for staging fibrosis, it is invasive and subject to sampling errors and potential severe complications in up to one percent of cases. However, histologic examination of liver specimens does provide information on inflammation that cannot currently be evaluated with ultrasound.[4,5]

An accurate non-invasive quantitative method that can visualize liver structure and provide two-dimensional ultrasound attenuation data is urgently needed in clinical routine.

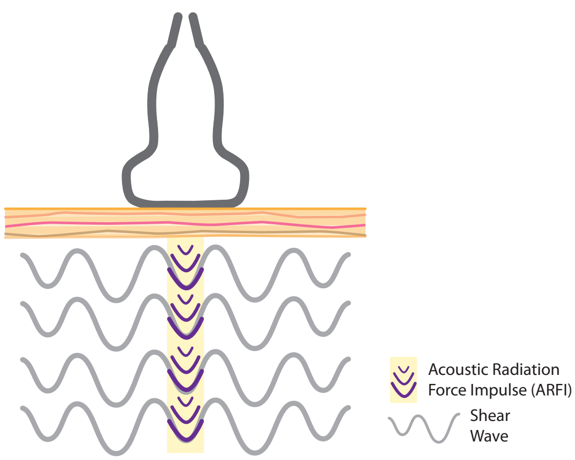
Elastography in Clinical Practice

Elastography is an imaging technique that quantifies the elasticity, or stiffness of tissue. This is the tendency of tissue to resist deformation with an applied force, or to resume its original shape after removal of the force.[6] While elastography can be used to image the breast, thyroid, and other tissues in the body, it is commonly used to evaluate chronic liver disease. Patients may be referred to elastography for one of the following:

- Bloodwork for liver function is outside of normal
- Known steatosis that is believed to have progressed to fibrosis
- Known liver disease, where needle biopsy is contraindicated
- Follow up exams to monitor progression of disease

Scar tissue, or fibrosis, is known to differ mechanically from surrounding healthy tissues. Liver stiffness, associated with fibrosis, can be measured by assessing physical properties of tissue and the extent of tissue deformation induced by an applied force, i.e., the speed of mechanical waves through tissue. Pathologic, or fibrotic tissue, is usually stiffer than healthy tissue, resulting in higher values.

The use of shear wave elastography (SWE) for the noninvasive assessment of liver fibrosis has grown rapidly since its introduction, and substantial new information regarding disease-specific liver stiffness is now available in the literature. The "Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement," published in 2020, reviewed the recommended procedure for acquiring stiffness measurements. According to the authors, there has been substantial improvement in the acoustic radiation force impulse (ARFI) technology — most notably, the addition of a quality assessment of the shear wave propagation.[7]



Evolution of Elastography

Clinicians have used palpation to evaluate tissue stiffness for hundreds of years, but the modern concept of elastography was introduced when researchers recorded skin vibration waves in the 1950s.[8]

Elastography-based imaging techniques take advantage of changed tissue elasticity in various pathologies to yield qualitative and quantitative information that can be used for diagnostic purposes.

In 1983, Eisenscher et al studied induced quasistatic compression by applying a vibration source to liver tissue and using M-mode ultrasound to measure wave propagation. This technique is similar to modern one-dimensional transient elastography.[9]

The development of shear wave elastography was initiated with the 1987 study of the propagation of shear waves through tissues after application of a continuous low-frequency vibration.[10] Quasistatic elastography was developed in the early 1990s by Ophir et al[11] and in 1998, Sarvazyan et al proposed shear wave elastography as a new elastographic method.[12]

The first ultrasound-based elastography system was commercially introduced in 2003 and there are now a number of novel systems available for measuring liver stiffness.

Elastography Technologies

Ultrasound Elastography is a non-invasive, low-cost imaging technique that quantitatively estimates tissue stiffness and aids in chronic liver disease diagnosis. Ultrasound-based methods are of particular interest due to a number of inherent advantages, such as wide availability, mobility and relative low cost compared to other modalities.

Multiple variations of elastography are commercially available. In general, these can be classified as strain imaging methods that use compression stimuli, and shear wave imaging that use ultrasound-generated pulses to generate shear wave stimuli. Strain elastography is a qualitative technique that provides information on the relative stiffness between one tissue and another. While widely utilized for various elastography exams, strain imaging is not a utilized method for the liver.[13] As a result, strain imaging is not included in this paper.

Shear wave elastography provides a quantitative value of tissue stiffness. Each technique has advantages and they are often complimentary to each other in clinical practice.[14] There are three primary methods of Shear Wave Elastography: Transient Elastography, Point Shear Wave Elastography, and 2D Shear Wave Elastography.

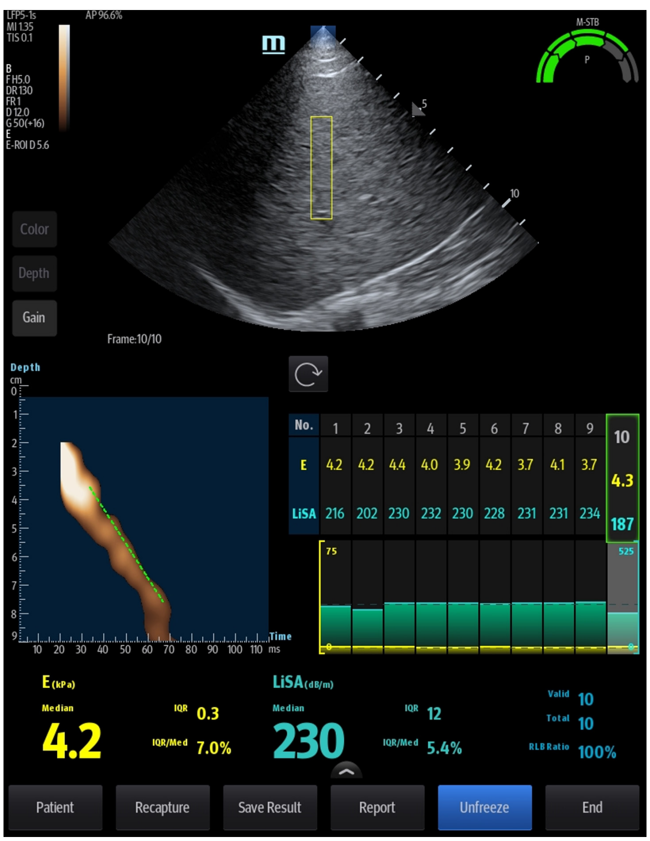
All methods are used to monitor disease progression. Ultrasound-based elastography may also reduce the need for further invasive tests and repeated biopsies, while providing valuable information regarding patient response. Multiple clinical trials have demonstrated the clinical performance of elastography in quantitative measurements of stiffness for chronic liver disease stage assessment.

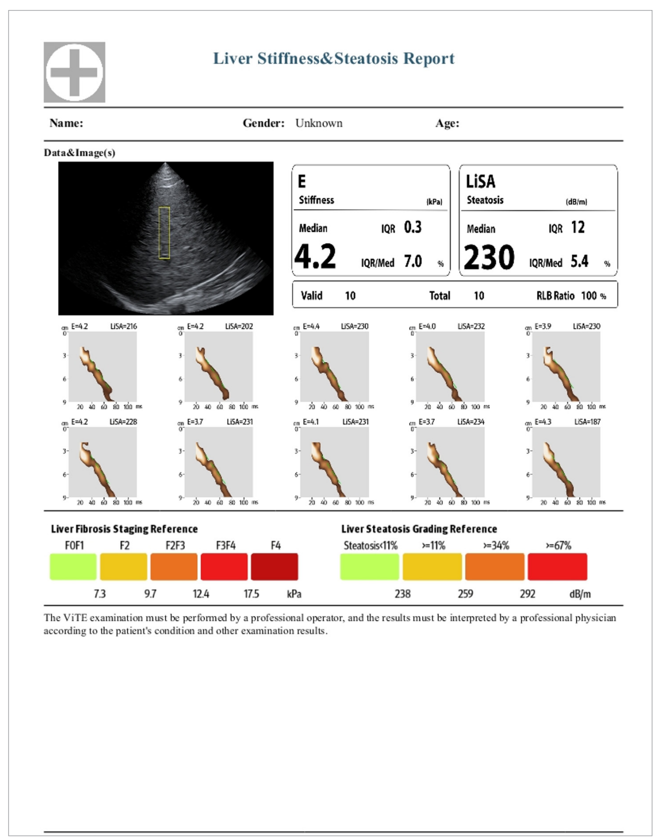
Transient Elastography

Transient elastography offers a quantitative evaluation of liver stiffness and is widely used by hepatologists and other physician practices to assess steatosis and fibrosis of liver.

Transient elastography uses a mechanical pulse generated by an external probe. For one-dimensional transient elastography, an ultrasound transducer is mounted on the axis of a vibrator and transmits low-frequency (50-Hz) vibrations. This generates an elastic shear wave that propagates through the underlying tissues. Pulse-echo ultrasound acquisitions measure the velocity of propagation of the shear wave, which is directly proportional to the tissue stiffness. Transient Elastography is an ultrasound-based technique that can be used with or without direct B-mode image guidance.

The technique is similar to shear wave elastography, in that the elastic modulus is generated from shear wave velocity. Transient Elastography is an ultrasound-based technique that can be used with or without direct B-mode image guidance. However, this external pulse calculates liver stiffness differently than that from an ARFI.





Transient elastography measures liver stiffness in a volume that approximates a cylinder 1 cm wide and 4 cm long, and between 25 mm and 65 mm below the skin surface. This volume is approximately 100 times larger than a biopsy sample, making it more representative of hepatic parenchyma. To achieve a valid evaluation of liver stiffness, at least 10 successful measurements must be acquired within a defined ROI.

Studies have shown that liver stiffness values from Transient Elastography correlate with histopathologic fibrosis stages in CLD patients. Clinicians use Transient Elastography to diagnose cirrhosis (F4 fibrosis) and to help distinguish significant (≥ F2) from non-significant (F0 and F1) fibrosis. Distinguishing between individual fibrosis stages is not well validated.

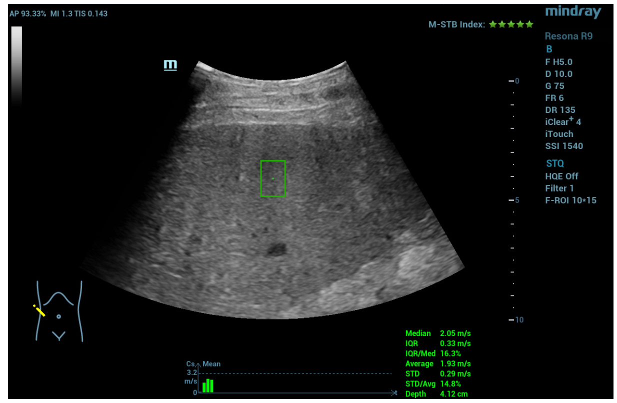
Shear Wave Elastography

Introduced in the early 2000s and gaining significant clinical traction for use in assessment of liver fibrosis between 2005-2008, multi-dimensional SWE utilizes focused ultrasound beams at different depths to create a conical shear wave front. The ROI of supersonic shear wave imaging is fan shaped and larger than other methods (as large as 50 mm × 50 mm). Real-time imaging is used to measure the velocity of this shear wave front and generate quantitative elastograms that provide a comprehensive map of tissue stiffness in the liver.

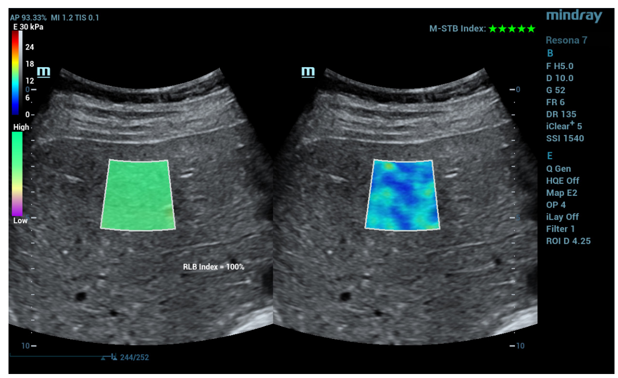
Shear Wave Elastography has gained more attention in recent years, providing quantitative stiffness measurements by displaying the shear wave propagation speed or the tissue mechanical modulus, such as shear modulus, and Young's modulus, which is most often used to quantify the stiffness.

Shear wave elastography displays a real-time stiffness image within the ROI. When tissue is displaced posteriorly by focused ultrasound beams from the probe, the restorative force of the tissue propagates laterally, generating shear waves. Focused ultrasound pulses are used to generate a transverse wave (shear wave) at specific depths within the liver, as selected by the operator. Multiple shear waves will be generated in different positions in turn to form a full image.

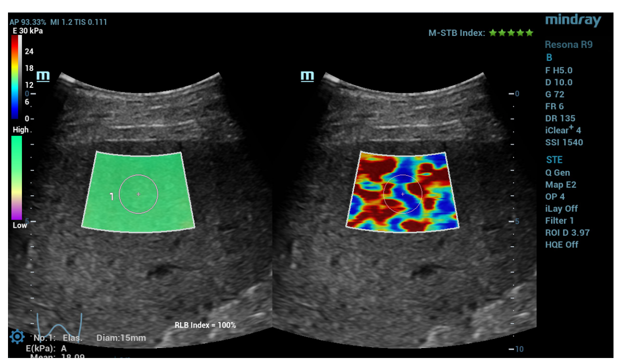
Shear waves displace tissue in a single focus with point SWE and in multiple foci with multi-dimensional (2D SWE and 3D SWE). In both methods, SWE can be performed on a conventional ultrasound system using a standard ultrasound probe.



Point Shear Wave



2D Shear Wave Elastography Normal Liver



2D Shear Wave Elastography Diseased Liver

Tracking ultrasound pulses measure the velocity of the shear waves as they travel through the liver parenchyma. The propagation speeds are calculated using Young's modulus of elasticity, defined as the ratio of stress to strain along an axis. The results are either directly reported or converted to Young's modulus E and reported to provide a quantitative estimate of tissue elasticity. Modern ultrasound equipment may provide on screen metrics to ensure the acquisition is optimal, such as Motion Stability Index to indicate motion in data capture and Reliability Index to verify the interrogated tissue is homogenous with no interfering vessels.

In liver applications, the operator can use B-mode ultrasound to directly visualize the liver to select a uniform area of liver parenchyma without large vessels or dilated bile ducts. Unlike Transient Elastography where the shear waves are produced by excitation at the body surface, SWE produces shear waves which originate locally inside the liver, reducing the impact of obesity on the accuracy of the exam.

Mean Lesion Off

STE-Fixed	E Mean(kPa)	Cs Mean(m/s)	Depth(cm)	Size (cm x cm)	HQE	Calc
1	7.00	1.52	4.08	1.0x1.0	Off	✓
2	7.08	1.52	4.08	1.0x1.0	Off	✓
3	7.16	1.53	4.08	1.0x1.0	Off	✓
4	7.25	1.54	4.08	1.0x1.0	Off	✓
5	8.67	1.67	4.08	1.0x1.0	Off	✓
6	8.60	1.66	4.08	1.0x1.0	Off	✓
7	8.53	1.66	4.08	1.0x1.0	Off	✓
8	8.47	1.65	4.08	1.0x1.0	Off	✓

Overall Statistics

	Median	IQR	IQR/Median	Average	STD	STD/Average
E Mean(kPa)	7.86	1.40	17.9%	7.84	0.73	9.3%
Cs Mean(m/s)	1.60	0.13	8.1%	1.59	0.07	4.2%

Sample Elastography Report

Conclusion

Chronic liver disease is a worldwide problem and the global prevalence of MASLD has increased significantly over the past 20 years. An accurate quantitative method that can provide visible liver structure and two-dimensional ultrasound attenuation data is urgently needed in clinical routine.

Ultrasound Elastography is a non-invasive, low-cost imaging technique that quantitatively estimates tissue stiffness and may reduce the need for further invasive tests and repeated biopsies, while providing valuable information regarding patient response and disease progression.

Recent advancements, such as the development of advanced ultrasound elastography techniques, including ultrasound B-Mode guidance, 2D elastographic color-map visualization and measurement quality criteria, will continue to expand the clinical utility and impact of elastography.

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