

HISKY

White Paper

iLivTouch®

the complete elastography solution for chronic liver diseases

Transforming Liver Disease Management

Liver diseases pose significant global health challenges, contributing to high morbidity and mortality rates. Accurate assessment of liver stiffness and fat accumulation is essential for early diagnosis, staging, and effective management of chronic liver diseases. Traditionally, liver biopsy has been the "gold standard" for diagnosing liver conditions. However, it is invasive, costly, and limited by sampling errors, inter-observer variability, and potential complications.

To address these limitations, serological tests were introduced as non-invasive alternatives, offering insights into liver health through biochemical markers. While useful for large-scale screening, these tests lack specificity and are less reliable for fibrosis staging. Advances in medical imaging have since led to the development of non-invasive technologies, including Transient Elastography (TE), Magnetic Resonance Elastography (MRE), and Shear Wave Elastography (SWE) based on Acoustic Radiation Force Impulse (ARFI). Among these, TE has emerged as the preferred method due to its accessibility, cost-effectiveness, and ability to provide fast, reproducible results for liver stiffness evaluation.

Developed by Hisky Medical, the iLivTouch® system,, built on TE technology, offers unique advantages that set it apart from other methods. With its multi-frequency capabilities, single-probe design, and advanced algorithms, iLivTouch® provides accurate, quantitative, and real-time measurements of Liver Stiffness Measurement (LSM) and Ultrasound Attenuation Parameter (UAP), enabling comprehensive assessment of liver health.. Its adaptability across diverse patient populations and integration into clinical workflows make it a transformative tool in hepatology, empowering clinicians to improve diagnostic precision and patient outcomes. This document underscores the pivotal role of iLivTouch® in advancing liver health diagnostics and addressing the growing burden of liver diseases worldwide.

1. Background and Introduction

Liver fibrosis is a critical prognostic indicator, directly linked to global morbidity and mortality in chronic liver disease (CLD). Globally, CLD affects over 1.7 billion people, contributing to approximately 2 million deaths annually, with cirrhosis and hepatocellular carcinoma (HCC) accounting for majority of liver-related mortality[1]. The economic burden is equally staggering worldwide due to hospitalizations, transplants, and lost productivity. Early identification of fibrosis progression is pivotal to mitigating this burden, as fibrosis remains the strongest histopathologic predictor of mortality. Without intervention, fibrosis advances to cirrhosis, culminating in complications like HCC and liver failure, often necessitating transplantation[2].

The etiology of CLD varies regionally. While chronic hepatitis B (CHB) remains predominant in Asia and Africa (affecting 296 million globally), hepatitis C (HCV) is more prevalent in high-income countries, with 58 million cases worldwide[3]. However, Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has emerged as the leading driver of CLD,

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affecting 25-30% of the global population. Its progressive form, Metabolic Dysfunction-Associated SteatoHepatitis (MASH), now accounts for 20-30% of cirrhosis cases in Western countries and is rising rapidly in Asia due to obesity and diabetes epidemics[4].

Several liver conditions, such as Hepatitis B, C, and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), contribute to persistent hepatocellular injury, which leads to the development of fibrosis[5]. Although antiviral therapies have reduced HCV incidence, CHB and MASLD/MASH are projected to dominate future CLD burdens. Rising obesity, diabetes, and alcohol consumption are fueling a rapid global increase in MASLD, suggesting that cirrhosis prevalence will persist unless chronic liver diseases are diagnosed and treated timely[5]. Early diagnosis of fibrosis is therefore essential to initiate timely interventions.

Transient Elastography (TE) addresses this unmet need by non-invasively quantifying both liver fibrosis and steatosis—a key feature of MASLD/MASH. For populations at risk of viral hepatitis or metabolic liver disease, TE enables large-scale screening to detect early fibrosis (F1-F2 stages) and steatosis. In clinical practice, TE supports risk stratification, monitors treatment response (e.g., viral suppression or MASH resolution), and reduces reliance on invasive biopsies. By integrating fibrosis and steatosis assessment, TE has become indispensable for managing the dual epidemics of viral hepatitis and metabolic liver disease.

2. Elastography: What It Is, Purpose & Types

2.1. What is elastography?

Elastography is an advanced medical imaging modality that quantifies tissue stiffness, providing essential diagnostic information. The technique is built upon the principle that tissues exhibit varying degrees of stiffness based on their pathological conditions—stiffer tissues are often indicative of abnormal stage of fibrosis. That is, high elastography correspond with high stiffness or low elasticity. Unlike traditional imaging which only visualizes structural changes, elastography evaluates the mechanical properties of tissues by creating "shear waves" or tissue displacements, making elastography a powerful tool for detecting diseases such as liver fibrosis, cancer, and musculoskeletal disorders. By utilizing either ultrasound or magnetic resonance technology, elastography allows for rapid, non-invasive assessment of tissue elasticity. Its wide applicability spans several clinical fields, with hepatology, oncology, and musculoskeletal health being key areas of focus [6][7].

Types of Shear Wave Elastography[1] used for Liver Assessment							
Illustration	Type	Commercial Vendors	Force	Property Assessed	Tissue Volume	Qualitative or Quantitative	Mode of Imaging
	Transient Elastography (TE)	Hisky Medical Echosens	Body Surface-to-Liver, Mechanically Induced (50Hz) Pulse	Axial Shear Wave Speed (SWS)[2]	3 cc	Quantitative (Median of 10 measurements of the ROI Average)	A TM E B[3]
	Point Shear Wave Elastography (pSWE)	Siemens Philips Fujifilm Canon	Ultrasound Induced, Focused Radiation Force Impulse	Deep Lateral SWS	< 1 cc	Quantitative (Average of ROI)	E B
	2D-SWE	GE	Ultrasound Induced, Multiple Radiation Force Simultaneous Impulses	Deep Lateral SWS	< 2 cc	Quantitative	E B
	3D-SWE	SuperSonic Imagine	Ultrasound Induced, R Radiation Force Focused over Multiple Depths	Deep Conical SWS	< 2 cc	Quantitative	E B
	S-WAVE	Sonic Incytes	Body Surface-to-Liver, Mechanically Induced Continuous Pulsing	SWS	100 cc	Quantitative (Median of 5 ROI Averages)	B

1. Displacement and strain elastography (e.g. Acoustic Radiation Force Impulse or ARFI) omitted.
2. SWS converted to shear modulus using Young's modulus formula. TE measures SWS without an image.
3. Available on select models only.

2.2. What are the types of elastography?

Elastography encompasses several distinct methods, each utilizing different methodologies to evaluate tissue elasticity and enhance diagnostic accuracy.

Strain Elastography (SE) is one of the earliest forms of elastography and is used on conventional ultrasound systems; it utilizes manual compression or physiological movements to assess tissue stiffness. SE is predominantly used in superficial organs like the breast, thyroid, and prostate, where compression can be applied more easily. Although it offers qualitative data, the accuracy of SE is highly operator-dependent, and its use is generally limited to evaluating superficial structures[6].

Shear Wave Elastography (SWE) based on Acoustic Radiation Force Impulse (ARFI) technology is a cutting-edge ultrasound technique that induces shear waves in tissues using focused acoustic pulses. These waves propagate at speeds that correlate directly with tissue stiffness, with faster wave velocities indicating stiffer tissues. SWE provides real-time, two-dimensional elastograms, offering quantitative and high-resolution measurements of tissue stiffness. This technology can be used for liver fibrosis assessment and has

applications in oncology, where it aids in distinguishing benign from malignant tumors. However, its accuracy may be influenced by patient factors, such as body habitus or inflammation. Operator expertise ensures optimal reliability and diagnostic value[6].

Transient Elastography (TE) is a non-invasive imaging technique that measures tissue stiffness by generating shear waves through a mechanical "push" delivered to the skin surface. The shear waves propagate through the tissue, and their velocity is measured to determine stiffness—faster wave speeds indicate greater stiffness. The technology produces a quantitative measurement of liver stiffness, offering reliable insights into the progression of liver fibrosis.TE is widely used in hepatology for the diagnosis and management of chronic liver diseases. It is highly effective for staging liver fibrosis and detecting cirrhosis, making it a valuable tool in guiding treatment decisions. One of the key advantages of TE is its speed and reproducibility, with results generated in minutes. It is non-invasive, painless, and easy to perform, requiring minimal patient preparation. These features make TE a preferred method for routine liver disease monitoring and large-scale population health screenings[6].

Magnetic Resonance Elastography (MRE) combines MRI technology with external mechanical vibrations to produce highly detailed maps of tissue stiffness. Unlike ultrasound-based methods, MRE provides a more comprehensive view of stiffness in deeper tissues, including the liver, brain, and muscles. MRE is highly accurate and can assess larger areas of tissue, making it the "gold standard" for liver fibrosis evaluation. However, its cost and limited availability due to specialized equipment restrict its widespread use in routine clinical settings[6].

2.3. Using elastography for liver stiffness assessment

Elastography has emerged as a valuable non-invasive alternative to liver biopsy for assessing liver stiffness and evaluating fibrosis in chronic liver diseases. Accurate staging of fibrosis is crucial in guiding clinical decisions, such as initiating antiviral treatment, as it significantly impacts prognosis and patient management. Although liver biopsy remains the "gold standard" for fibrosis assessment, it is invasive, with a risk of serious complications in up to 1% of cases. Additionally, biopsy is subject to sampling error and variability in interpretation, as it assesses only a very small portion of the liver, approximately 1/50,000 of the total liver volume[7]. Furthermore, the invasive nature and associated risks make liver biopsy unsuitable for longitudinal monitoring. Repeated biopsies to track disease progression or treatment response are clinically impractical, exposing patients to cumulative risks and potential inconsistencies due to sampling variability across different time points. Given these limitations, non-invasive ultrasound elastography methods offer a safer, more feasible option for evaluating liver fibrosis and enable dynamic, repeatable assessments during follow-up.

Elastography techniques, including Transient Elastography (TE),point Shear Wave Elastography (pSWE), and 2D-SWE, are widely used for liver fibrosis assessment. TE remains the EFSUMB-recommended first-line modality due to its standardized cut-offs validated across etiologies (viral hepatitis, MASLD, etc.) and operator-independent design. EASL/ALEH guidelines prioritize TE for cirrhosis screening in MASLD, where its high negative predictive value (NPV > 95%) optimizes early detection[7]. While pSWE and 2D-SWE enable real-time B-mode guidance, EFSUMB notes critical limitations: system-specific cut-offs and operator-dependent reproducibility. TE's workflow efficiency and guideline endorsement solidify its role in population-level liver disease management[7].

3. The Principles of Transient Elastography and Ultrasound Attenuation for Liver Assessment

Transient elastography technology, along with cancer saliva detection and nerve regenerator, was rated as one of the 20 biotechnology breakthroughs that changed medicine by the American magazine "Popular Mechanics"[8].

Transient Elastography uses a dedicated probe to emit a fixed low-frequency shear wave to implement instantaneous active excitation on liver tissue, while emitting a high-frequency signal to "track" the propagation of the shear wave in the liver and calculate the propagation speed (shear wave speed or SWS). Using Young's modulus, SWS is converted in units of kilopascals (kPa) to quantify the stiffness value of the liver. At the same time, by tracking the attenuation of the high-frequency signal during the propagation of the liver and by combining the fat attenuation model embedded in the system, an algorithm is used to derive the signal attenuation coefficient of the liver. From this, the quantitative results of fatty degeneration of the liver are derived.

Various systems from different manufacturers employ distinct types of probes. **The iLivTouch® system developed by Hisky utilizes a single probe suitable for all patient body sizes.** The iLivTouch® system's single-probe design offers several significant advantages. It simplifies operation by eliminating the need for probe changes, enhancing user experience and efficiency. The versatile probe accommodates a wide range of detection needs, covering various tissue depths and patient profiles, including different body types and conditions. This design reduces costs by avoiding the need to purchase and maintain multiple probes, making it more economical for healthcare providers. Equipped with advanced wide-band technology and advanced algorithms, the single probe delivers precise measurements of liver stiffness and fat attenuation parameters at varying depths. This streamlined approach ensures consistent, accurate results while saving time and improving diagnostic efficiency, making iLivTouch® an ideal choice for clinical diagnostics and health screening.

3.1. Hisky iLivTouch® Transient Elastography Technology

3.1.1. Overview of iLivTouch® Transient Elastography Technology

Developed by Hisky, the iLivTouch® Transient Elastography Technology represents a quantitative elastography method, internationally patented for the non-invasive assessment of liver stiffness through shear wave velocity measurement. By tracking the propagation of a mechanically induced 50 Hz shear wave, iLivTouch® Transient Elastography quantitatively evaluates the stiffness of liver tissue, offering a robust alternative to traditional liver fibrosis assessment methods. This technique provides clinicians with quantitative data on liver elasticity, supporting both initial diagnostic evaluations and longitudinal monitoring of liver health.



Figure 1 iLivTouch® with two forms of presentation,the portable and the mobile cart version. Note the included ultrasound probe and the unique fibrosis scanning probe[6].

3.1.2. Mechanisms of Shear Wave Generation

The shear wave generation process within iLivTouch® Transient Elastography Technology utilizes a pressure/force sensor integrated into the probe that continuously tracks and calibrates the movement of a controlled, reciprocating piston mechanism. The probeprovides single shear wave pulse with specific frequency of 50Hz for measurements and estimates of tissue stiffness. The resulting shear wave propagates through the liver tissue. This deliberate design ensures that the shear wave's propagation is accurately captured as it dissipates through the liver, yielding a highly reliable stiffness profile.



Figure 2 System Interface of iLivTouch®

3.1.3. Multi-Frequency Tracking and Depth-Resolved Analysis

A defining feature of iLivTouch® Transient Elastography Technology is its multi-frequency tracking capability, which facilitates real-time monitoring of shear wave propagation at varying depths within the liver tissue. Leveraging a spectrum of carefully calibrated frequencies, iLivTouch® Transient Elastography can assess tissue response across various depths beneath the skin, with each frequency tuned to optimize detection at specific depths. This multi-frequency tracking, coupled with sophisticated algorithms, enables iLivTouch® Transient Elastography to capture motion dynamics more accurately than conventional ultrasound devices, which are unable to track shear waves. Additionally, the iLivTouch® Transient Elastography platform's adaptability across a range of patient profiles reduces the need for multiple probe types, providing comprehensive, depth-resolved assessments without the need for alternate hardware configurations.

3.1.4. Static Force Sensing and Transmission Control

The iLivTouch® Transient Elastography Technology probe is equipped with static force sensor designed to ensure that sufficient, yet controlled, pressure is applied real-time during the measurement process. By signaling when the applied force is either insufficient or excessive, this system maintains optimal contact between the probe and the skin, ensuring efficient transmission of mechanical vibrations into the liver tissue. This careful control over static force is critical, as tissue stiffness measurements can be affected by external pressure variations. Through the inclusion of this sensor, iLivTouch® Transient Elastography enhances the consistency and reliability of its liver stiffness assessments by reducing artifacts induced by non-standardized pressure.

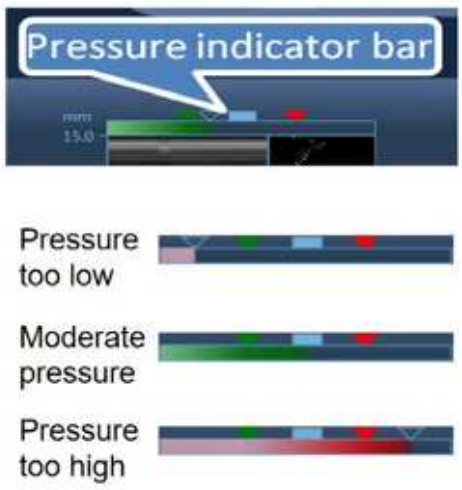


Figure 3 Pressure sensing function of iLivTouch®

3.2. Determination of liver stiffness measurement (LSM) value

Low-frequency shear waves are used to actively excite the liver tissue instantaneously, and high-frequency signals are sent to track the propagation of shear waves in the liver. Combined with the liver histological model, a quantitative liver tissue stiffness value is given to evaluate the degree of fibrosis.

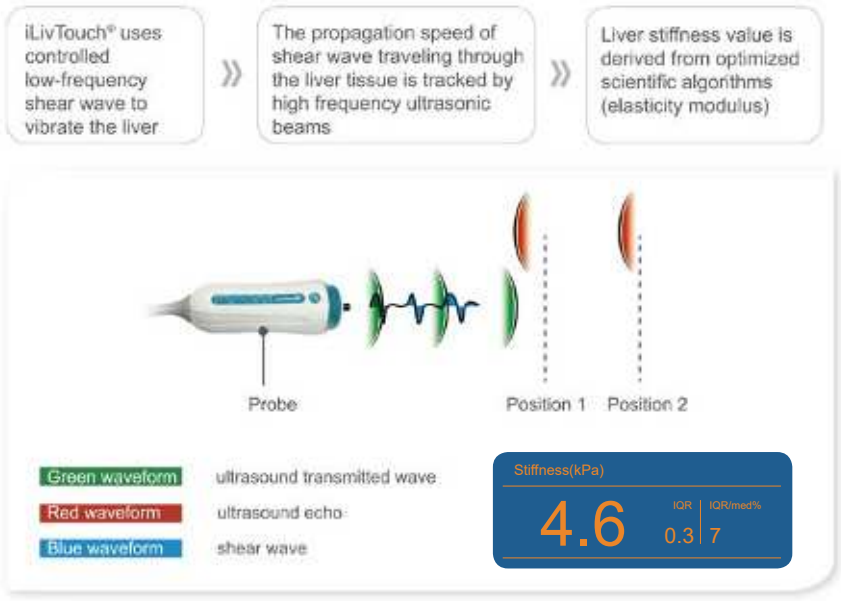


Figure 4 Illustration of liver stiffness measurement

3.3. Determination of ultrasound attenuation parameter (UAP) value

Fatty liver cells are enriched with fat droplets, which have a significant effect on ultrasound signal scattering. By tracking the energy attenuation of ultrasound signals during propagation in liver tissue, the fat ultrasound attenuation parameter, a quantitative detection result of fatty liver, is given to evaluate the degree of liver steatosis.

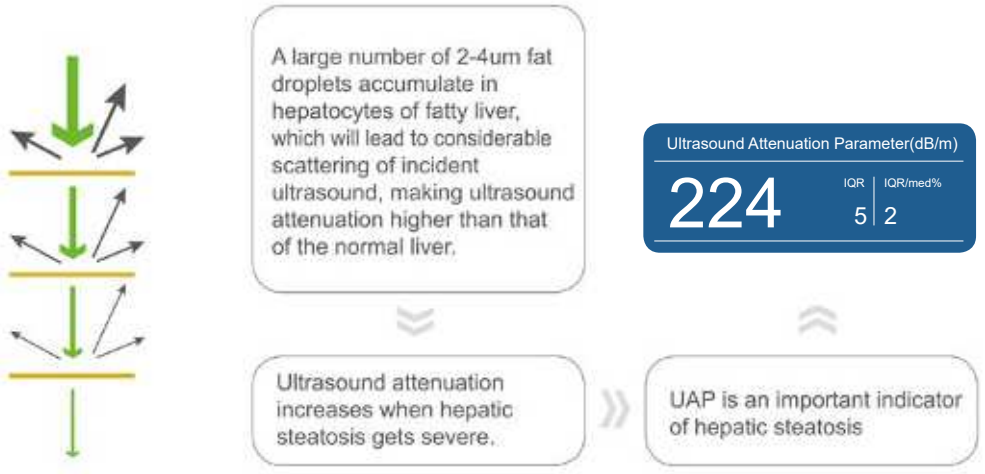


Figure 5 Illustration of ultrasound attenuation parameter measurement

Study of iLivTouch® UAP	Comparative method	No.of patients	Cut-off values for each degree of steatosis (dB/m)		
			S≥1	S≥2	S≥3
Deng et al. (2016)	Liver biopsy	254	230.6	246.9	261.1
Hou etal. (2022)	Standardultrasound	3770	257.2	286.2	315
Mu et al. (2023)	MRI-PDFF	275	259	274	295
Qiao et al. (2020)	Liver biopsy	130	276	288	293
Qu et al. (2021)	Liver biopsy	237	244	269	296
Yu et al. (2021)	CAP	85	278	305	307
Zhu et al. (2021)	Liver biopsy	497	295	314	324

Table 1 UAP values in the most representative publications [1]

4. Transient Elastography (TE) vs. Other Liver Disease Detection Methods

4.1. Liver biopsy

Liver biopsy is currently regarded as the clinical "gold standard" for diagnosing liver fibrosis and steatosis. This procedure involves histopathological examination of liver tissue to confirm diagnoses, assess the degree of inflammation and fibrosis, and evaluate the efficacy of treatments. It employs a rapid puncture method using negative pressure aspiration to extract a small tissue sample, which is then analyzed under a microscope.

However, liver biopsy is invasive and requires hospitalization, anesthesia, and pre-procedural tests, including liver biochemical and coagulation assessments. Patients must also be educated on precautions, such as breathing techniques to mitigate anxiety. Post-procedure, they require 24 hours of bed rest and monitoring of vital signs. This entire process can be time-consuming and costly, with complications occurring in 1%-3% of patients. Pain is reported by 20%-30%, while the risk of bleeding is about 0.3%, and the mortality rate stands at 0.03%.

Due to its invasive nature, many patients are reluctant to undergo the procedure, which limits its widespread application. Additionally, individuals can typically have only one biopsy per year, complicating effective follow-up care. The biopsy sample, usually weighing 0.02-0.03g, represents only a minute fraction of the liver (around 1/50,000th of its total volume). While sampling from diffuse diseases like fatty liver or hepatitis may provide an accurate overall assessment, structural diseases like cirrhosis can lead to incomplete samples. In cases of liver fibrosis and cirrhosis, sampling errors can result in an underestimation of the condition in 15%-30% of cases due to their heterogeneous distribution throughout the liver.

LB is considered as the gold standard for diagnosing liver fibrosis, but sampling errors and both intra- and inter-observer agreement on biopsy samples may lead to poor reproducibility for many liver biopsies, and the procedure is invasive and expensive (A1).

— Asian-Pacific Association for the Study of the Liver (APASL) consensus guidelines on invasive and non-invasive assessment of hepatic fibrosis: a 2016 update.

Non-invasive TE testing for liver fibrosis and steatosis is painless, non-invasive, and does not require hospitalization, saving time for both physicians and nursing staff. Current studies have not reported adverse reactions or complications, and patients find it easy to understand and accept. Each non-invasive test provides a sample with a diameter of 1cm and length of 4cm, offering a sample size 100 times larger than that of a liver biopsy.

4.2. Serological testing

Various fibrosis markers and biochemical scoring systems, such as the FIB-4, FibroTest, and APRI, have been developed to assess liver fibrosis. These methods require blood sampling and laboratory analysis, with costs ranging from $20 to $40 per test and results available in 3-5 days. Key biomarkers for liver fibrosis include type III procollagen (PCIII), type IV

collagen (IVC), serum hyaluronic acid (HA), and laminin (LN). While these markers relate to the synthesis and degradation of extracellular matrix proteins associated with fibrosis, they lack specificity and can be elevated in other organ conditions and in older populations. Moreover, they reflect dynamic physiological processes rather than providing a quantitative measure of liver fibrosis. Biochemical scoring systems offer comprehensive assessments of hematological indicators but are indirectly related to liver fibrosis and aim to correlate with liver biopsy results through statistical methods.

Current assessment methods have limitations, as they are often restricted to specific liver diseases like hepatitis C. Furthermore, many therapeutic drugs can alter hematological parameters, making these scores unsuitable for monitoring patients during treatment. This underscores the need for more reliable assessment tools in liver disease management.

The results of serological fibrosis markers can only indicate abnormalities in ECM metabolism but cannot quantify the extent of deposited liver fibrosis.

Serum biomarkers of fibrosis are well validated in patients with chronic viral hepatitis (with more evidence for HCV than for HBV and HIV/HCV coinfection). They are less well validated in NAFLD and not validated in other chronic liver diseases (A1).

— EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis 2015

Non-invasive TE tests for liver fibrosis and steatosis measure objective physical parameters directly related to the liver without being affected by factors outside the liver. These tests are suitable for all patients with chronic liver disease, including those undergoing treatment. Additionally, TE tests provide immediate results, whereas hematological markers may take several days.

4.3. Color Doppler and B-mode Ultrasound

Non-invasive testing for liver fibrosis and steatosis using TE significantly differs from conventional color Doppler and B-mode ultrasound diagnostics. One major distinction is that standard ultrasound utilize ultrasonic frequency above 2 MHz for imaging, while transient elastography uses a vibration frequency of 50 Hz to measure the elasticity of tissue.
Additionally, the types of probes vary. Color Doppler and B-mode ultrasounds use curvilinear ultrasound probes, whereas the non-invasive TE system can incorporates both an ultrasound probe and a specialized elastography probe for assessing liver stiffness.

The principles behind these technologies also differ. Color Doppler and B-mode ultrasound analyze tissue conditions by detecting scattering, reflection, refraction, and attenuation of ultrasound waves, along with the Doppler effect. In contrast, non-invasive TE testing measures liver tissue stiffness by assessing the speed of elastography wave propagation.

Moreover, the results produced are different. Ultrasound generates tissue images, while transient elastography provides specific values for tissue stiffness (in kPa) and fat attenuation (in dB/m). In terms of assessment sensitivity, ultrasound is highly responsive to morphological changes but may lack sensitivity in early liver fibrosis stages where changes are minimal. It can only roughly categorize liver

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fat content and is dependent on the operator's skill. Conversely, non-invasive TE testing offers quantifiable values for liver fibrosis and steatosis, allowing for early detection and easier follow-up.

Finally, non-invasive TE testing takes only 2 minutes, compared to the 15-20 minutes typically required for ultrasound examinations.

Conventional ultrasound cannot be used for the diagnosis of hepatic fibrosis (B2).

— Asian-Pacific Association for the Study of the Liver (APASL) consensus guidelines on invasive and non-invasive assessment of hepatic fibrosis: a 2016 update.

4.4. MRE

Magnetic Resonance Elastography (MRE) is an MRI-based method that visualizes the movement of acoustic shear waves within the liver. By applying mathematical algorithms, MRE generates cross-sectional images that illustrate the magnitude of the liver tissue's complex shear modulus. Research indicates that MRE is highly effective in diagnosing fibrosis in patients with MASLD and maintains accuracy and reliability in individuals with obesity[9].

MRE, while non-invasive, is a longer procedure, as it requires a full MRI scan, typically taking 15-30 minutes. Patients must also lie still inside the MRI machine, which can be uncomfortable for some. Many obese patients and patients with implantable devices may not be suitable for MRI.

MRE is more expensive and requires MRI equipment, which is not as readily available as the portable TE devices. MRE's cost and limited availability make it less accessible for routine screening[9].

Transient Elastography is a quicker and more affordable procedure, typically taking only a few minutes, and is less demanding for the patient. It can be performed without extensive preparation, making it more practical for routine monitoring.

4.5. 2D-SWE/3D-SWE

2D-SWE and 3D-SWE are non-invasive techniques developed for the evaluation of Liver Stiffness (LS) using the. Acoustic Radiation Force Impulse (ARFI) technique. These technologies interrogate the tissue at several points; they display a qualitative color-coded elasticity map (elastogram), usually superimposed on the conventional B-mode ultrasound image, and it additionally allows for quantitative measurement by placing a smaller region of interest (ROI) inside the color map. The result of a measurement is usually displayed as the mean and standard deviation, either in m/s or kPa[1].

However, these techniques do not control the frequency of shear wave. They cannot generate shear waves of fixed frequency or

direction. Shear wave frequencies generated from different tissues are different and the speed is also different, which will affect the measurement result.

Limited by the principles of ultrasonic power safety, the acoustic radiation force produces a single point push, which is weaker than mechanical push., There may be calculation errors and the accuracy may be reduced, especially in deep tissue.

There is also a lack of unified cut-off values for liver fibrosis staging, and results from different US elastography systems are not interchangeable. Moreover, research and publications supporting ARFI/SWE in liver disease are limited compared to TE, with EASL-ALEH Clinical Practice Guidelines assigning a lower grading of recommendation (B1/B2) compared to TE[10].

Transient Elastography (TE) provides a more standardized, reproducible, and validated method for liver stiffness assessment. TE generates a mechanical push that creates shear waves of fixed frequency, ensuring consistent and accurate measurements across tissue depths. It offers well-established cut-off values for liver fibrosis staging, enabling reliable comparisons and clinical application. Supported by extensive research and global guidelines such as those from AASLD, APASL, EASL and ALEH, TE is recognized as the preferred technique for non-invasive liver fibrosis assessment, with higher recommendation levels (A1) and broader clinical acceptance. Its reliability, accessibility, and integration into routine clinical workflows make it the "gold standard" in hepatology diagnostics.

4.6. MRI-PDFF (for steatosis)

MRI-PDFF (Proton Density Fat Fraction) is a quantitative imaging biomarker that measures the proportion of fat protons relative to total protons in the liver, offering a precise estimate of liver fat content. This technique is based on the unique properties of protons in water and fat molecules, which resonate at slightly different frequencies when subjected to a magnetic field in MRI [11].

This method has become a "gold standard" for diagnosing and monitoring steatosis due to its ability to provide a more detailed and reliable measurement. MRI-PDFF is highly sensitive and specific, allowing clinicians to detect even small changes in liver fat content, making it ideal for both early diagnosis and evaluating the effectiveness of treatment over time [11].

Although MRI-PDFF is highly effective, it has some limitations that may restrict its widespread use. These include its higher cost and limited availability compared to ultrasound-based techniques like transient elastography, which are more commonly used in clinical practice. Additionally, MRI-PDFF is sensitive to patient movement, such as breathing, which can compromise image quality and accuracy, similar to other MRI-based methods.

In contrast, using Transient Elastography (TE) is often preferable for routine clinical practice. TE is more accessible, cost-effective, and less affected by patient motion, offering reliable results with minimal patient preparation. It has become the "gold standard" for liver stiffness measurement, providing fast and reproducible assessments that can be easily integrated into clinical workflows, particularly for large-scale screenings and monitoring chronic liver diseases.

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5. Clinical Recommendations of Transient Elastography (TE)

At present, TE has been widely used such as liver diseases screening in the public, high-risk groups early prevention, diagnosis of suspected patients, monitoring and follow-up of patients with liver diseases, and the evaluation of curative effect, involving the department of hepatology, infectious disease, gastroenterology, physical examination, ultrasound, endocrinology, hepatobiliary surgery, etc. Global experts and scholars have published about **120 TE related guidelines and consensus statements.**

1) 2024-AASLD Practice Guideline on imaging-based non-invasive liver disease assessments of hepatic fibrosis and steatosis[12]

There is considerable experience with the use of TE-Liver Stiffness Measurements (LSM) in HCV and HBV, with substantial reliability for discriminating between significant fibrosis (F2-4), advanced fibrosis (F3-4),and cirrhosis (F4). TE-LSM predicted cirrhosis more accurately than ELF and FibroTest in treatment-naive patients with HBV. TE-LSM outperformed APRI and FIB-4 for detection of advanced fibrosis in HBV/HIV co-infected adults on combined antiretroviral therapy.

2) 2024-AASLD Practice Guideline on non-invasive liver disease assessments of portal hypertension[13]

In a meta-analysis examining the diagnostic performance of TE-LSM for CSPH, there was high correlation between TE-LSM and HVPG (pooled correlation coefficient = 0.78, 95% CI 0.74-0.82). It is notable that TE-LSM performs better for detection of CSPH than do blood-based tests.

3) 2024-EASL position paper on clinical follow-up after HCV cure[14]

This has been shown in studies in which risk assessment of HCC was evaluated by transient elastography.

4) 2024-EASL-EASD-EASO Clinical Practice Guidelines on the management of MetabolicDysfunction-associated Steatotic Liver Disease (MASLD)[15]

A stepwise approach using blood-based scores (such as FIB-4) and, sequentially, imaging techniques (such as transient elastography) is suitable to rule-out/in advanced fibrosis, which is predictive of liver-related outcomes. Several observational studies showed that LSM had good accuracy for liver-related events, liver-related and overall mortality.

5) 2023-EASL Clinical Practice Guidelines on the management of liver diseases in pregnancy[16]

All women should be screened for alcohol use in pregnancy. Investigations should not only include serum liver tests but also a test to detect liver fibrosis (e.g. transient elastography) since advanced liver fibrosis may present with normal serum liver tests (ALD fibrosis/cirrhosis).

6) 2022-AACE&AASLD-American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD)[17]

Transient elastography (TE) and/or MRI-based techniques can be used as screening tools for NAFLD, NASH, and fibrosis. Clinicians should consider persons belonging to the "high-risk" groups who have an indeterminate or high FIB-4 score for further workup with an LSM (transient elastography) or ELF test, as available.

7) 2022-EASL-Baveno VII-Renewing consensus in portal hypertension[18]

LSM values by transient elastography (TE) <10 kPa in the absence of other known clinical/imaging signs rule out cACLD; values between 10 and 15 kPa are suggestive of cACLD; values > 15 kPa are highly suggestive of cACLD.(B.1) (Changed) Patients with chronic liver disease and an LSM < 10 kPa by TE have a negligible 3-year risk of decompensation and liver-related death. (A.1) (New)

8) 2021-EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis-2021 update[19]

TE is the most widely validated and available. TE using the appropriate probe and the other ultrasound-based measurements have an applicability of > 95%, provide results in real time and only take a few minutes to be performed. TE has excellent diagnostic accuracy for advanced fibrosis, with AUROCs above 0.90.

6. Clinical Applications of iLivTouch®

The following diseases can be screened, diagnosed, monitored and followed up with iLivTouch®: viral hepatitis, Metabolic dysfunction-associated (non-alcoholic) fatty liver disease, biliary tract disease, alcoholic liver disease, drug-induced liver injury, autoimmune liver disease, cirrhosis and its complications, liver cancer, etc. Global experts and scholars have published iLivTouch® related scientific research results in various fields, with a total of more than **320 publications**.

1) 2023-Prevalence of Liver Steatosis and Fibrosis in the General Population and Various High-Risk Populations: A Nationwide Study With 5.7 Million Adults in China-Gastroenterology-IF = 29.4[20]

This study has been one of the first attempts to comprehensively understand the epidemiology of liver steatosis and fibrosis assessed by iLivTouch® (Hisky Medical) in the general population and in various high-risk sub populations based on such a large population sample. In the general population, the prevalence of liver steatosis was 44.39% , with a significantly higher prevalence in men than in women, and in the northern region than in the southern region of China. The findings of this study highlight that fatty liver and liver fibrosis should be included in disease management programs as targets for screening and regular monitoring in high-risk populations, especially in those with diabetes.

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2) 2024-Prognostic significance of liver stiffness in patients with primary biliary cholangitis: validation of Baveno VII criteria-Hepatology International-IF = 6.6[21]

LSM and ΔLSM/ΔT were independent risk factors for liver decompensation, liver transplantation, or liver-related death (primary outcomes, $p < 0.001$, both). LSM can be used to monitor disease progression and predict long-term prognosis in patients with PBC.

3) 2022-A novel quantitative ultrasound technique for identifying non-alcoholic steatohepatitis-Liver Int-IF = 6.7[22]

A total of 259 Chinese individuals with biopsy-proven non-alcoholic fatty liver disease (NAFLD) were enrolled in the study. The histological spectrum of NAFLD was classified according to the NASH clinical research network scoring system. Radio frequency (RF) data from iLivTouch®, was acquired for further QUS analysis. The QUS score, which was developed from QUS, provides a novel, non-invasive and practical way for identifying NASH.

4) 2022-A cross-sectional study of alcohol consumption and alcoholic liver disease in Beijing: based on 74,998 community residents-BMC Public Health-IF = 4.5[23]

Compared with other cities or regions in China, the level of alcohol consumption in Beijing is at an upper middle level. But the ALD prevalence is low likely because ethanol intake is relatively low. Our analysis revealed that heavy drinking is a major risk factor for ALD development, those with liver steatosis (FibroTouch UAP ≥ 240 dB/m) or liver fibrosis (iLivTouch LSM ≥ 12.96 kPa).

5) 2022-Remnant Lipoprotein Cholesterol as a Factor Related to Adult Fatty Liver Disease-The Journal of Clinical Endocrinology & Metabolism-IF = 5.8[24]

RLP-C has a strong positive correlation with FLD occurrence and FLD severity. We stratified the severity of FLD according to fatty ultrasound attenuation parameter: normal; mild; moderate; severe. These results may help clinicians identify and implement interventions in individuals with high FLD risk and reduce FLD prevalence.

6) 2021-Switching from entecavir to tenofovir alafenamide for chronic hepatitis B patients with low-level viraemia-Hepatology International-IF = 6.6[25]

Patients were assessed by physical examinations, blood tests (virological, biochemical parameters) and liver stiffness measurements (LSM) at baseline, week 12 and week 24 respectively. For ETV-treated patients with LLV, switching to TAF is safe enough and superior compared with continuing ETV mono therapy regarding both virological and biochemical benefits.

7) 2019-Comparison of FibroTouch® and FibroScan® for staging fibrosis in chronic liver disease Single-center prospective study-Digestive and Liver Disease-IF = 4.5[26]

The FibroTouch® is a valuable diagnostic tool for diagnosing liver fibrosis with good diagnostic accuracy which was comparable with that of the FibroScan®, but superior to that of the APRI and FIB-4.

Note: FibroTouch® is the former brand name of the iLivTouch® non-invasive liver detection system.

7. Closing Remarks

Among diagnostic approaches for liver fibrosis and steatosis, TE is widely used for its simplicity, speed, and reproducibility. Serological tests, such as fibrosis markers and biochemical scoring systems, provide indirect assessments and are suitable for large-scale screening but lack the specificity needed for accurate staging, especially in heterogeneous liver conditions. Liver biopsy, though considered the "gold standard" for fibrosis staging, is invasive, costly, and prone to sampling errors. Color Doppler and B-mode Ultrasound are effective for anatomical imaging but do not offer quantitative data for fibrosis and steatosis evaluation. MRE excels in accuracy for advanced cases but is limited by cost and accessibility. 2D-SWE and 3D-SWE offer real-time elastograms and broader imaging capabilities, but their performance depends on operator skill and calibration.

Hisky's iLivTouch® system addresses the limitations of these methods with its non-invasive, highly adaptable design. It delivers precise, quantitative, and real-time measurements of Liver Stiffness Measurement (LSM) and Ultrasound Attenuation Parameter (UAP) using advanced algorithms and multi-frequency technology. Unlike other systems, it does not require multiple probes, offering consistent results across different tissue depths. By integrating the strengths of various methods, iLivTouch® provides an efficient, patient-friendly, and highly accurate solution for diagnosing and managing liver diseases.Key advantages of iLivTouch® include:

- Precision-Driven Diagnosis – Provides quantitative fibrosis (LSM) and steatosis (UAP) staging, enabling data-driven treatment decisions.
- Streamlined Clinical Workflow – Delivers results within minutes per scan and requires minimal operator training, reducing patient wait times largely in high-volume settings.
- Patient-Friendly Design – Non-invasive and painless procedure reduces patient anxiety and enhances compliance.
- Comprehensive Applicability – A single probe supports all body types and clinical needs, from screening in primary care to disease monitoring and post-treatment tracking.
- Evidence-Based Validation – Supported by extensive clinical studies and international guidelines (e.g., AASLD, EASL), ensuring diagnostic reliability.

By integrating the strengths of various methods while overcoming their limitations, iLivTouch® establishes a new standard for efficient, patient-centric liver disease management, ultimately improving diagnostic accuracy and therapeutic outcomes.

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