ViTE Visualized Transient Elastography

A New Solution to Liver Health Management

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—— A New Solution to Liver Health Management

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Preface

As an important organ of human body, liver plays an important role in vitamin metabolism, hormone metabolism, secretion of bile, detoxification, and making of coagulation factors. Severe impairment of the liver function often leads to fatal consequences to human body. Most chronic liver diseases, however, tend to be insidious and easily ignored, resulting in irreversible consequences. Therefore, the early detection of pathological changes of liver and the monitoring and management of chronic liver diseases are continuous research focuses in clinical practice.

Liver fibrosis is a pathological phenomenon of excessive deposition of fibrous connective tissue in liver caused by chronic liver damage. Hepatitis B virus, Hepatitis C virus, alcohol, fatty liver, drug-induced damage, and other factors may cause the occurrence of liver fibrosis. Considerable studies have shown that persistent liver fibrosis may develop into major diseases such as cirrhosis and liver cancer, endangering people's life [1-10]. Therefore, how to identify and correctly evaluate the stage of liver fibrosis in clinical practice in time is a key step of liver disease management.

Liver fibrosis will lead to the increase of liver stiffness. Therefore, detecting liver stiffness is an important method of evaluating liver fibrosis. In recent two decades, noninvasive testing of human tissue stiffness has gained wide attention from researchers. Different elastography technologies have been developed around the world to detect the tissue stiffness. More and more doctors have proved that ultrasound elastography has great clinical value in various applications [6-19].

The ultrasound strain elastography is capable of providing real-time strain images of a region of interest (ROI) and has been widely applied in clinical practice for decades [18-19]. The ultrasonic strain elastography is developed based on Hooke's law. Under the same pressure, hard tissue performs a smaller strain than soft tissue. After uniform pressure is imposed through a probe, the deformation distribution image of tissue can reflect the elasticity difference between different parts of tissue. However, under different pressures, even the same tissue can produce different strain results. When this technology is applied to liver, it is difficult to perform the probe pressing operation because the liver is deep from the body surface. Consequently, the depth of strain elasticity images is limited and higher requirements are raised for doctors' operation stability and patients' cooperation in breathing. In addition, the strain elasticity mainly compares the relative stiffness difference between different tissues and is very sensitive to stiffness of focal lesions. Nevertheless, liver fibrosis is a diffusion lesion without standardized contrasts of relative hardness and softness. All these restrict the application of the strain elastography in the liver sector.

The ultrasonic shear wave elastography gains more attention clinically by providing quantitative tissue stiffness measurements. The shear wave elastography mainly displays the propagation velocity of shear waves or the elastic modulus of tissue, such as Young's modulus and shear modulus. Young's modulus is the most common indicator for representing tissue stiffness. A higher Young's modulus indicates higher stiffness. For linear, elastic, and isotropic media, the reduced equation of Young's modulus is as follows:

$$E = 3G = 3\rho Cs^2$$

Where, G indicates the shear modulus, ρ indicates the tissue density, and Cs indicates the propagation velocity of shear waves. It can be inferred that shear waves propagate faster in hard tissue and more slowly in soft tissue [12-14].

Shear wave elastography can be further divided into two types based on the shear wave generation method: shear wave elastography based on acoustic radiation force and transient elastography based on external vibration.

As an important branch of shear wave elastography, transient elastography is rapidly applied and widely recognized in the clinical practice in the liver sector at home and abroad [5-10]. It utilizes a special vibrator-contained probe and contacts the human body from right intercostal space. After the vibrator produces transient vibration with a frequency of 50 Hz, the probe produces shear waves that propagate from the body surface to the liver tissue, then emits ultrasonic waves to the liver area and receives echoes. After that, the system calculates

the propagation velocity of shear waves inside the liver, so as to acquire the Young's modulus parameter of the liver [20-21]. A large number of studies suggest that the transient elasticity measurement result increases with worsening of liver fibrosis. As a non-invasive tissue elasticity diagnosis technology, transient elastography can be carried out more easily in clinical practice and is more acceptable to patients in comparison with conventional liver biopsies. Especially in the early detection of liver fibrosis, transient elastography has higher sensitivity than conventional B-mode ultrasonography.

Fatty liver is excessive fat accumulation within liver cells due to obesity, alcoholism, diabetes, and other causes. It is a common pathological change in the liver. Persistent fatty liver may lead to steatohepatitis, fibrosis, cirrhosis, and liver cancer. In recent years, the incidence of the fatty liver disease is on the rise in the world and the age of onset is getting younger, attracting extensive clinical attention [22-24]. In particular, Non-Alcoholic Fatty Liver Disease (NAFLD) has become the first chronic liver disease and the top cause for abnormal biochemical indicators of liver in health examination in China. Conventional B-mode ultrasonography mainly provides qualitative results, with low sensitivity in the diagnosis of mild fatty liver, and its specificity needs to be improved. The Magnetic Resonance Spectroscopy (1 H-MRS) and MRI Proton Density Fat Fraction (MRI-PDFF) [25] detection can obtain the fat content of liver but they are costly and cannot be popularized easily. Therefore, a convenient technique for early quantitative diagnosis of fatty liver is urgently needed in clinical practice. Therefore, in the conventional transient elastography system, in addition to detection and evaluation of liver fibrosis, a Controlled Attenuation Parameter (CAP) is provided to detect the ultrasonic attenuation in the liver to quantitatively detect and evaluate the fatty liver. It has been clinically proven that CAP can be used to detect hepatic steatosis with the fat content greater than 5% and accurately differentiate mild hepatic steatosis from moderate to severe hepatic steatosis [23-24].

After more than ten years of clinical application and study, the conventional transient elastography has exposed some limitations, and its further development is greatly challenged. Some limitations are as follows: (1) The positioning is inaccurate in blind testing. Liver is at least 2–3 cm from the body surface. The liver size and location vary with people. Especially, people with liver fibrosis or cirrhosis may have an enlarged liver or decreased liver. The conventional transient elastography utilizes only the M mode signal to judge whether the signal is aimed at the liver. Operators' proficiency can affect the measurement result accuracy. The fixed signal sampling range is not suitable for effective detection of livers with different sizes and depths. (2) The operation QC is inadequate. Liver parenchyma is surrounded by gallbladder, great vessels, gastrointestinal tract, and other tissues, which can easily interfere with the imaging. The liver position often moves when a patient breathes. The conventional transient elastography cannot guarantee the examination stability or repeatability and invalid measurement is prone to occur. (3) Repeated operations are too slow. In clinical practice, transient elastography usually needs at least 10 effective measurements for each examination. Ideally, conventional transient elastography requires that operations be performed on the probe at least 10 times repeatedly, and all measurement results can be calculated and obtained after more than 1 min, which is time-consuming and strenuous.

For these, Mindray Hepatus system is developed using a new generation of transient elastography called "ViTE visualized transient elastography". It provides a new clinical solution to liver health management.

ViTE Probe and Shear Wave

The ViTE visualized transient elastography adopted in Mindray Hepatus system is a non-invasive quantitative imaging method for visually measuring the liver tissue stiffness in a ROI in real time. The adopted innovative probe can provide real-time 2D color Doppler ultrasound images for guidance prior to elasticity measurement, to help doctors locate a ROI within the liver. It can also provide synchronous 2D color Doppler ultrasound images for tracking during real-time continuous transient elasticity measurement, to assist users in observing whether the target position changes in this process, thereby improving the examination effectiveness.

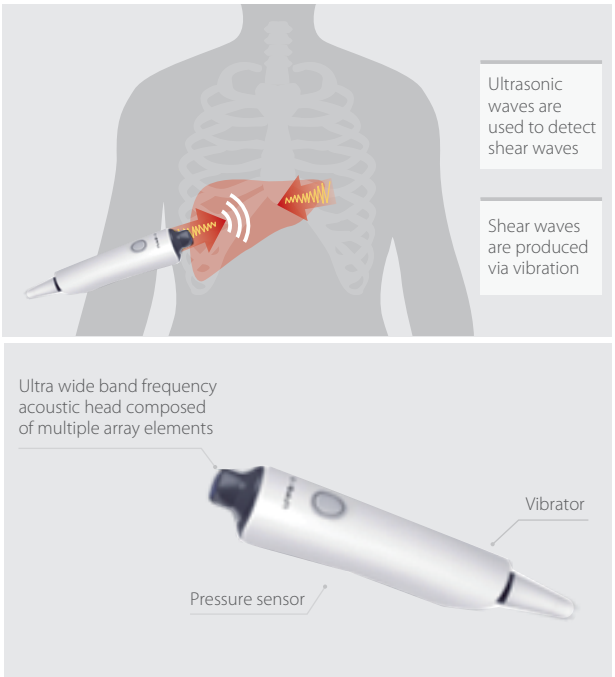


Figure 1 ViTE Probe

As shown in Figure 1, the probe used for ViTE examination consists of an acoustic head, a vibrator, a pressure sensor, and other important modules.

The acoustic head is designed with an ultra wide band

frequency and composed of dozens of ultrasonic transducer array elements. The size of the head is applicable to intercostal contact examination. In addition, the acoustic head supports ultrasonic emission focusing and scan control, which helps obtain a larger imaging field of vision. The head also implements transient elasticity detection of the liver tissue in a wider band range and routine color Doppler ultrasound imaging, such as 2D grayscale B-mode ultrasound imaging, color Doppler flow imaging, and Doppler flow speed PW imaging.

With the innovative acoustic head, users can observe real-time 2D images before ViTE measurement, and select ROI targets in the liver tissue based on image guidance for elasticity examination, as shown in Figure 2. Real-time image guidance can help users conveniently avoid gallbladder, liver capsule, fat layer, kidney, and other tissues, as well as larger blood vessels inside the liver, thereby improving the effectiveness of elasticity examination.

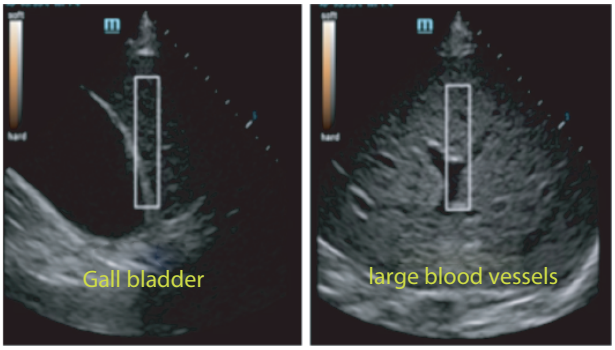
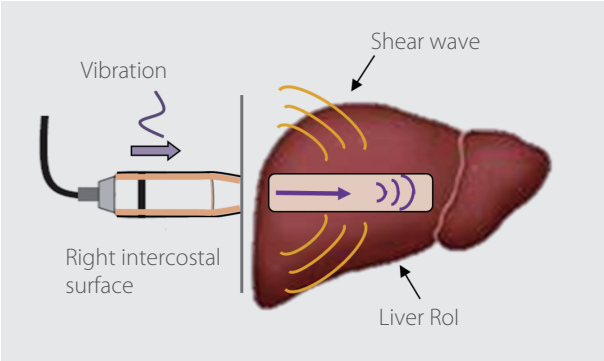


Figure 2 Image Guidance and ROI Selection

After ViTE measurement is triggered, the vibrator drives the acoustic head to perform transient vibration at a specific waveform frequency of 50 Hz (usually 20 ms sine or cosine waveform) so that shear waves are generated and propagate within the human liver. As shown in Figure 3, in the region in the axial direction of the probe, shear waves propagate from the body surface to the liver tissue and pass through the ROI. [26] Thanks to symmetry and superposition, tissue displacement caused by the shear wave propagation in the axis region is also in the axial direction. This is conducive to the tracking of shear wave propagation process by using ultrasonic waves.



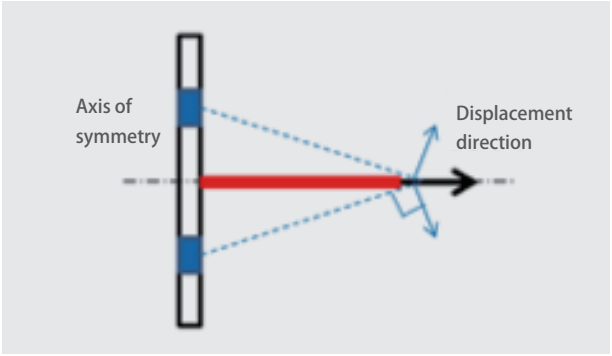


Figure 3 Shear Waves Generated due to External Vibration

The system rapidly transmits ultrasonic waves at a rate of up to 8.5 kHz to a ROI and receives echo signals, to accurately track the propagation process of shear waves at every moment. The tracking process usually lasts about 100 ms in order to obtain the shear wave propagation signal in the sufficient depth range. See Figure 4.

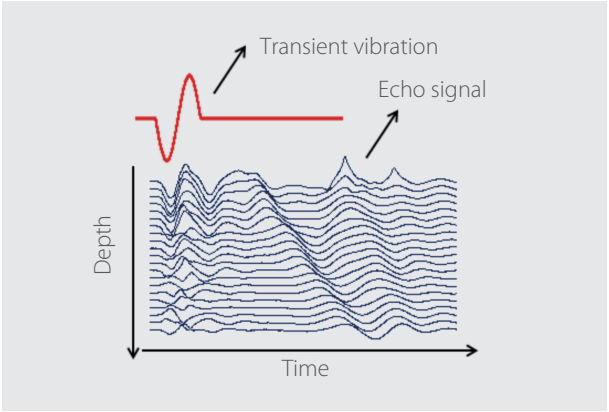


Figure 4 Tracking of Shear Wave Propagation by Using Ultrasonic Signals

By detecting tissue displacement changes caused by shear wave propagation in a ROI at every moment, the system can obtain the shear wave propagation path map, as shown in Figure 5. The system also calculates the propagation velocity of shear waves and then figures out the Young's modulus of the tissue to reflect the liver stiffness. The human liver tissue can approximate to a linear, elastic, and isotropic medium. The calculation formula of Young's modulus is as follows:

$$E = 3\rho C_s^2$$

Where, ρ indicates the tissue density, which approximates to the water density, that is, ρ = 1000 kg/m³. Cs indicates the propagation velocity of shear waves.

The shear wave propagation path map intuitively shows the shear wave depth at different moments. Liver fibrosis is a diffuse lesion. The propagation velocity of shear waves on the

liver tissue is relatively uniform. It can be seen that the propagation path of shear waves is usually linear and the propagation velocity corresponds to the slope of the propagation path. From the propagation path map, users can also obtain a lot of information for judging the quality of elasticity examination. For example, a short propagation path indicates that the penetration depth of shear waves is insufficient. Poor linearity of the propagation path indicates that the ROI is not uniform or the elasticity calculation result may be inaccurate. A messy propagation path map or lack of obvious path indicates that the shear waves do not propagate well and the measurement is invalid. In this case, it is necessary to re-adjust the probe position, angle or ROI for measurement again.

Users can also directly observe strain images of tissue at each depth at different moments, as shown in Figure 5(b).Compared with the shear wave propagation path map, a strain image contains more complex information such as the probe vibration, aftermath interference, and reflected wave.

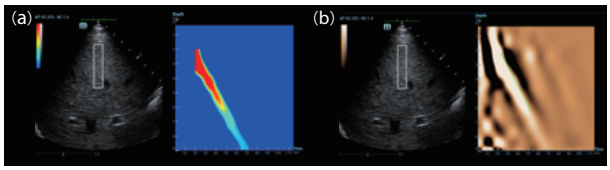


Figure 5 Shear Wave Propagation Path Map

The pressure sensor is another highlight of the ViTE probe compared with conventional ultrasonic probes. It is mainly used to reflect the pressure in real time when the probe is in contact with human body. In the transient elasticity examination, the overtight pressure will reduce the vibration amplitude and affect the shear wave strength and penetration depth. If the pressure is too low, the probe may come away from the body after vibration, or the contact position or angle of the probe may change due to instable probe holding, affecting the elasticity examination effect. The system sets an appropriate pressure range in advance and gives prompts in real time through the LED indicator on the probe and the image display screen. Orange indicates abnormal pressure while green indicates appropriate pressure, as shown in Figure 6. If the probe pressure is abnormal, the elasticity data collection cannot be triggered. The dual-prompt design ensures that users are alerted in time regardless of whether they focus on the probe or the image screen during their operations.

Figure 6 Probe LED Indicator for Pressure Indication (Green: Appropriate Pressure; Orange: Abnormal Pressure)

In order to reduce the fatigue caused by holding the probe for a long time, the ViTE probe adopts an innovative ergonomic design, as shown in Figure 7. The probe weighs less than 290 g and the holding diameter is smaller than 40 mm. The light and slim probe has a frosted and slinky surface, which is convenient for holding and pushing the probe. The overall body sealing design is easy for daily cleaning and disinfection.

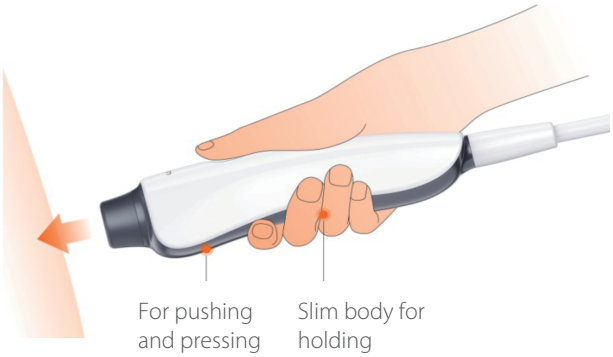


Figure 7 Appearance of the ViTE Probe

The ViTE probe is an important device for generating and detecting shear waves. Shear waves are the signal source for transient elasticity detection and have a key influence on the performance of transient elastography. In order to ensure the accuracy and repeatability of transient elasticity detection, the ViTE probe is designed with multiple innovative technologies, such as the high-precision vibration guidance design, high-sensitivity sensing design, and high-reliability acoustic head design. The performance has passed 1.2 million pressing tests, 4.5 million vibration tests, and 3.5 billion transmitting and receiving tests in terms of stability. In addition, the dynamic wide-band acoustic head using multiple array elements enables the ViTE probe to support three examination modes: adult abdomen examination, difficulty abdomen examination, and pediatric abdomen examination. The probe provides ultrasonic waves of different frequencies to meet requirements for the penetration depth and resolution of different somatotypes.

Hepatus Integrated Design

Apart from the ViTE probe, Mindray Hepatus system creatively integrates vibration control, ultrasonic emission and receiving control, sensor control functions. In this way, the system supports flexible switching between image guidance in the acquisition preparation state and probe vibration & shear wave signal tracking in the acquisition measurement state, and implements synchronous image detection in multiple continuous elasticity measurements. The integrated design also brings other benefits. For example, apart from transient elasticity detection, the ViTE probe allows users to complete various imaging operations required for routine ultrasonic examination without switching the probe, for example, 2D grayscale

B-mode ultrasound imaging, color Doppler flow imaging, and Doppler flow speed PW imaging, thereby greatly increasing clinical convenience. In addition, the integrated design effectively reduces the machine volume while ensuring high-performance imaging, providing great convenience in clinical use. Thanks to the integrated design, the ViTE function can be used alone and flexibly compatible with other ultrasonic platforms. While using the ViTE function, users can also use abdominal angiography, 2D shear wave elastography, sound speed measurement in the liver, and other advanced ultrasonic functions. Multiple probes are available. They can be used for multi-dimensional joint diagnosis or contrast study of the liver fibrosis progression, and comprehensive screening of other liver diseases such as liver cancer and portal hypertension. Mindray provides two high-end ViTE models and configurations for user selection, as shown in Figure 8.

Figure 8 Mindray Hepatus Non-invasive Liver Diagnostic ultrasound system

Steatosis Analysis Parameter LiSA

When ultrasonic waves propagate in the medium, the sound energy is reduced continuously due to absorption, reflection and other causes. The sound attenuation of soft tissue increases with tissue thickness, and the sound attenuation is also affected by the ultrasonic frequency. A higher frequency indicates faster attenuation. Studies have shown that fatty liver can cause faster attenuation of ultrasonic waves in the liver. Therefore, detecting parameters related to acoustic attenuation for the liver has become a quantitative method of evaluating the fatty liver severity. For example, the Controlled Attenuation Parameter (CAP)(unit: dB/m) commonly used in clinical practice can reflect the attenuation of ultrasonic waves of a certain frequency along with the propagation depth in the liver. More severe fatty liver indicates a larger CAP value [27–29]. However, the ultrasonic signal used for CAP calculation is only the one-dimensional ultrasonic echo signal from part of the liver. When the target tissue position changes, the measurement result stability will be affected.

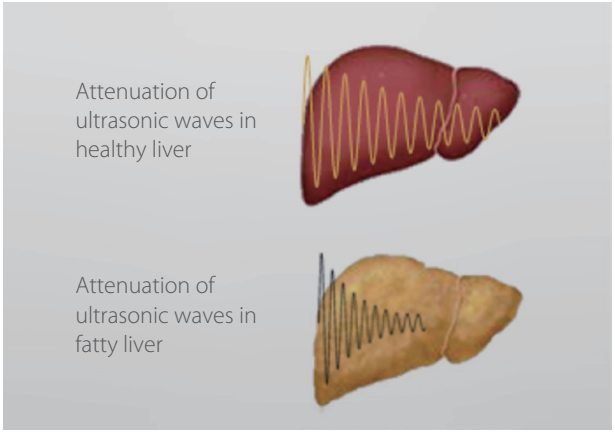


Figure 9 Impact of Fatty Liver on Ultrasonic Wave Attenuation

Mindray Hepatus platform provides an innovative Liver Ultra-Sound Attenuation (LiSA) parameter. With this parameter, the system not only provides visualized images to guide accurate positioning of liver targets before measurement, but also obtains 2D echo signals of the liver tissue in a wide range, to comprehensively calculate acoustic attenuation parameters, as shown in Figure 10. In the CAP measurement, the system mainly extracts liver tissue echo signals at different depths in the central axis direction of the probe to calculate the average attenuation parameter. In the LiSA measurement, the system adopts a wider sampling range and the calculation amount is larger. The system can calculate the average attenuation parameter of the ultrasonic waves along with the depth in the 2D area of the liver tissue, improving the stability and accuracy of sound attenuation measurement. Both LiSA results and elasticity results can be displayed during ViTE measurement, as shown in Figure 11.

Similar to CAP results, LiSA results also correspond to the acoustic attenuation parameter of 3.5 MHz ultrasonic waves. Therefore, the unit dB/m of LiSA can also be converted into another common unit dB/cm/MHz used in the acoustic field according to doctors' needs, to facilitate the contrast study of different acoustic attenuation results.

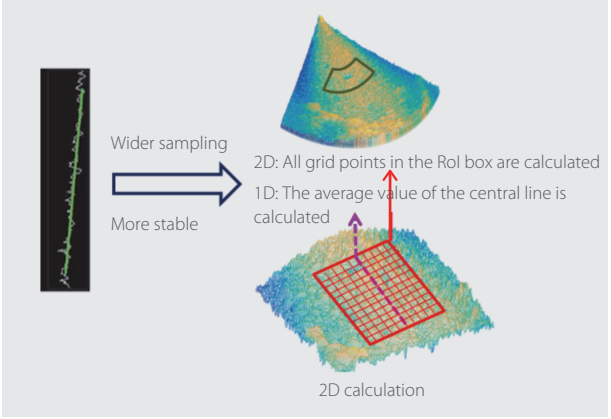


Figure 10 A Larger Range of Liver Tissue Attenuation in the LiSA Calculation

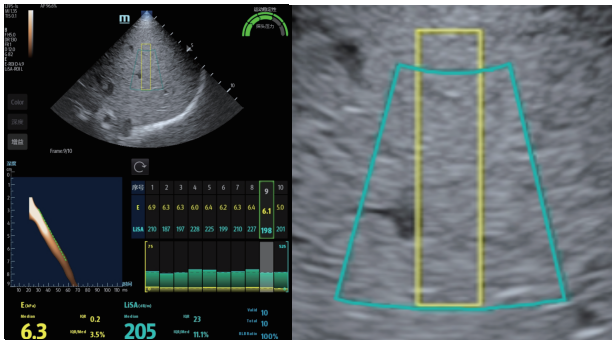


Figure 11 Simultaneous Measurement and Display of LiSA and Elasticity Results

Features of ViTE Imaging

The visualized transient elastography of Hepatus creatively uses two operation states to assist in regulating clinical operations.

One is ViTE acquisition preparation state, in which user operations prior to acquisition are regulated. In the acquisition preparation state, users can observe 2D B-mode ultrasound images or color Doppler flow images in real time, so as to select appropriate ROIs. Pressure is provided in real time to assist users in adjusting the probe contact force, so that the best shear wave propagates into human body. In addition, the ViTE technology provides Mindray unique motion stability indication (M-STB) for detecting the image stability, which is particularly important in liver examination. Patients' breathing usually causes a change in the liver position. Therefore, in the liver examination, it is usually necessary for patients to hold their breath to maintain the stability of the examined area. The sliding and rotation of the probe can also cause the change in the examination position in the clinical examination, affecting the measurement stability. M-STB can effectively help doctors monitor the motion stability in real time. As shown in Figure 12, the M-STB indication is displayed in orange when the motion interference is severe, and in green when the motion interference is low or does not exist.

In a word, the ViTE technology guides positioning by using visualized images before measurement, and provides the quality control index (probe pressure index & motion stability index), to better regulate the clinical operations.

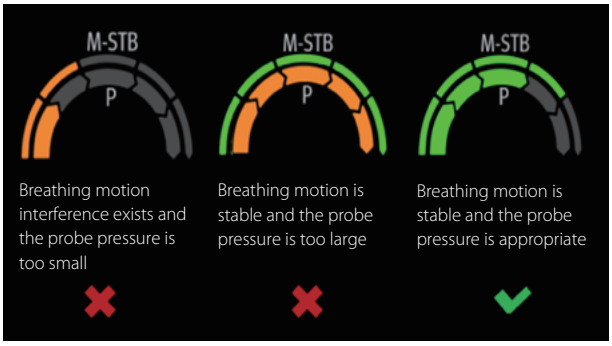


Figure 12 Quality control index

The other is ViTE acquisition measurement state, in which the probe vibration is controlled to produce shear waves and the shear wave propagation process is detected so that elasticity results are calculated. In routine transient elasticity examination, it is usually required to obtain at least 10 effective results and calculate the median as the final output result, in an effort to improve accuracy and repeatability. Doctors need to repeat operations multiple times. Mindray ViTE technology ensures that consecutive 10 elasticity measurement results can be obtained in real time after the measurement is triggered once. The high-performance tissue displacement detection algorithm [30] and shear wave velocity and elasticity calculation algorithm are used to shorten the time of multiple elasticity detection processes to 7s. Multiple continuous measurement processes are accompanied with multiple continuous probe vibrations. The system provides multiple continuous measurement count options. Doctors can select a required option based on their operation stability and patients' ability in holding their breath.

ViTE also provides an intelligent acquisition measurement mode, Q-Scan intelligent acquisition. It not only provides super fast detection speed, but also intelligently identifies the validity of result of each elasticity measurement in the acquisition measurement process, and automatically supplement measurements. As shown in Figure 13, an invalid measurement occurs in the continuous detection process (the result is invalid in the ninth measurement and "XX" is displayed). After intelligently identifying the invalid measurement, the system automatically completes the 11th supplementary measurement, thereby obtaining 10 effective measurement results quickly. Doctors need to keep the probe stable during measurement.

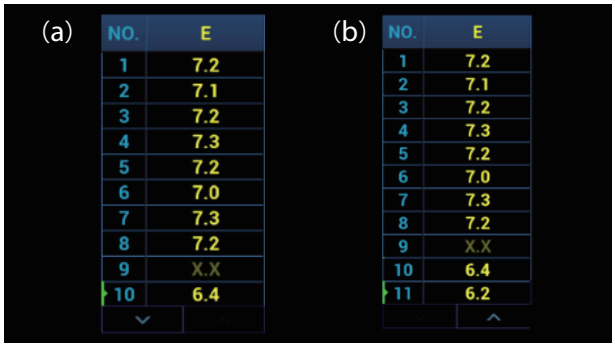


Figure 13Q-Scan Intelligent Acquisition(a) The measurement count is the same as user settings. (b) Q-Scan: The system automatically supplements measurement in the case of invalid measurement.

Each measurement result of ViTE is displayed in the list box. The system automatically calculates and displays statistical results, such as the median, Interquartile Range (IQR), and IQR/median, as shown in Figure 14. The median is output as the final measurement result. IQR/median helps judge the stability among multiple measurement results, and a smaller value indicates better stability. The system also provides a trend statistics image area, in which users can judge stability of measurement values intuitively.

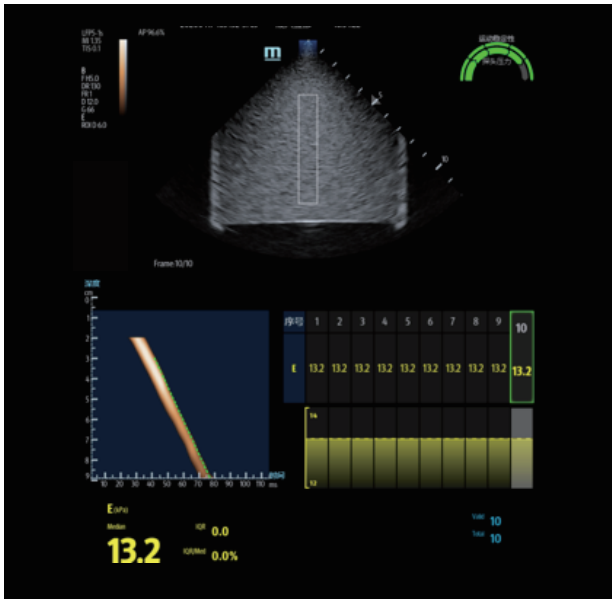


Figure 14 Elasticity Measurement Results and Trend Statistics Diagram

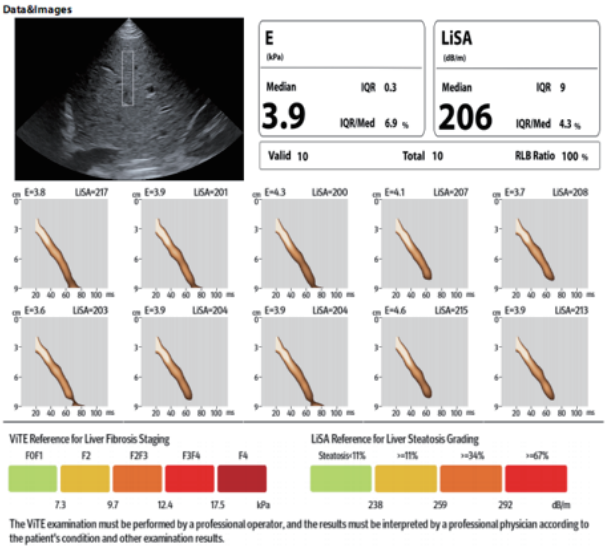


Figure 15 ViTE Examination Report

In each elasticity detection, apart from elasticity measurement results and shear wave path map, Mindray Hepatus system also generates a synchronous 2D grayscale or color flow image, and provides the pressure of the probe in contact with the human body before the elasticity acquisition, which is valuable information. After acquisition, users can browse 2D images, pressure prompts, shear wave path map, and elasticity results obtained from each acquisition, so as to judge whether the current examination is valid and whether re-measurement is required.

Measurement results and images of ViTE can be recorded in the examination report. As shown in Figure 15, the report summarizes some conclusions and suggestions from current domestic and overseas clinical studies on the evaluation of transient elasticity for liver fibrosis staging and the evaluation of acoustic attenuation parameter grading of fatty liver [27, 31-33]. These clinical studies take pathological biopsy results as the golden standard and elaborate the auxiliary diagnostic performance of transient elasticity measurement, acoustic attenuation parameter measurement, and other technologies in the liver health assessment. For example, in most cases with no or mild liver fibrosis, the transient elasticity measurement result (E) is smaller than 7.3 kPa. If the transient elasticity measurement result (E) is greater than 9.7 kPa, the possibility of severe liver fibrosis is high. If the transient elasticity measurement result (E) is greater than 12.4 kPa or even greater than 17.5 kPa, the possibility of cirrhosis is high. The criteria for liver fibrosis progression may vary with the causes. Liver congestion, higher transaminase level, higher bilirubin level, high BMI, food intake, and other factors can also affect the elasticity measurement results [34]. Doctors can provide comprehensive diagnostic suggestions based on patients' various clinical indicators or multi-dimensional examination results.

In addition to the ViTE probe, Mindray Hepatus is equipped with a unique high-resolution convex array probe. The probe is capable of providing excellent color Doppler ultrasound imaging of abdomen for users and comprehensively evaluating the liver morphology and hemodynamics, thereby helping with clinical diagnosis. As shown in Figure 16, doctors can conduct liver biopsies under the ultrasound guidance, or screen patients for ascites and evaluate hemodynamics.

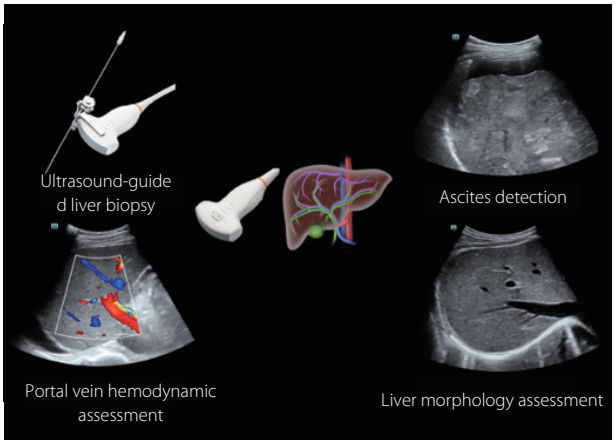


Figure 16Convex Array Probe Equipped to Provide Comprehensive Color Doppler Ultrasound Imaging

Case Study — Application in Liver Fibrosis

In the infection center of a famous hospital in Shanghai, doctors used Mindray ViTE function to conduct a preliminary clinical study on more than 300 cases of patients with liver diseases. The pathological analysis results of liver biopsies are used as the golden standard and the diagnosis performance of the staging of ViTE liver fibrosis is evaluated in detail. The study suggests that ViTE has great clinical diagnosis value in assisting with the non-invasive diagnosis of early liver cirrhosis and the identification of liver fibrosis staging.

The ViTE examination of liver is generally carried out from the right intercostal space. The ViTE measured values often fluctuate slightly due to the probe contact surface position, patients' breathing motion, and other factors. Therefore, it is generally recommended in clinical practice that at least 10 effective measurement results be selected and the Median of statistical results be used as the final measurement result, to enhance the ViTE measurement accuracy and repeatability of liver. If multiple measured values fluctuate greatly, for example, IQR/Median is greater than 30%, the current measurement is considered invalid.

In this clinical study, clinical operation requirements in guides related to liver fibrosis diagnosis are referenced and B-mode ultrasound images are used to guide accurate positioning of liver tissue. The selected ROI is 40 mm in height and 8 mm in width, and the continuous scan mode of 10 measurements triggered once is adopted to obtain elasticity results. In the pathological examination, the liver fibrosis staging results are evaluated according to the Scheuer scoring system.

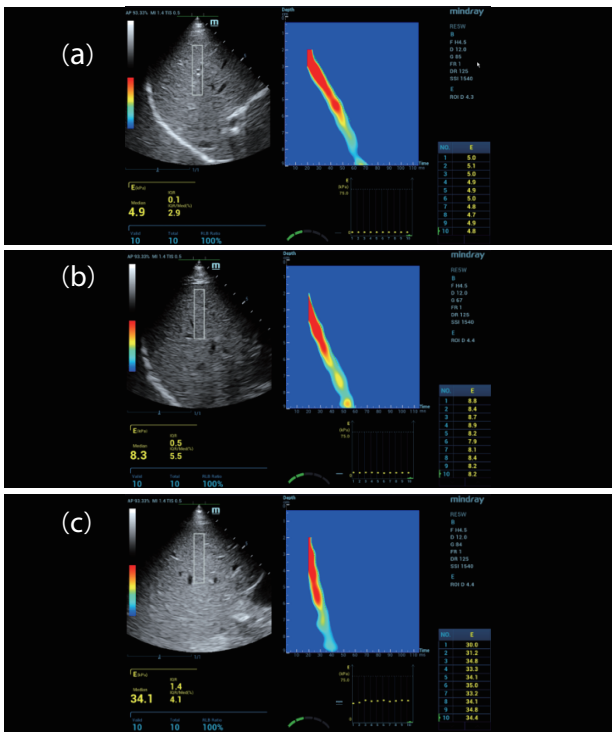


Figure 17 ViTE Images of Liver Fibrosis of Different Severity (a) No Liver Fibrosis (b) Significant Liver Fibrosis (c) Cirrhosis

Figure 17 shows the typical ViTE examination results of patients without liver fibrosis, patients with significant liver fibrosis, and patients with cirrhosis. It can be seen that, with the worsening of liver fibrosis, the ViTE shear wave propagation path becomes steep obviously, the propagation speed increases, and the elasticity measurement results rise accordingly.

Results obtained by Mindray Hepatus in this study show that only a small proportion of patients with cirrhosis have lower stability of multiple measured values, with a slight increase in IQR/Median, as shown in Figure 18. The shear wave path map shows that the propagation path linearity decreases accordingly. Invalid measurements are more likely to occur on cirrhosis patients with higher liver stiffness, as shown in Figure 19.

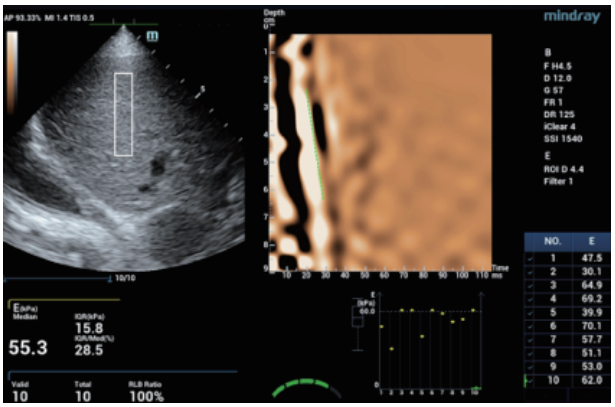


Figure 18 Lower Stability of Measured Values for a Small Proportion of Cases with Cirrhosis

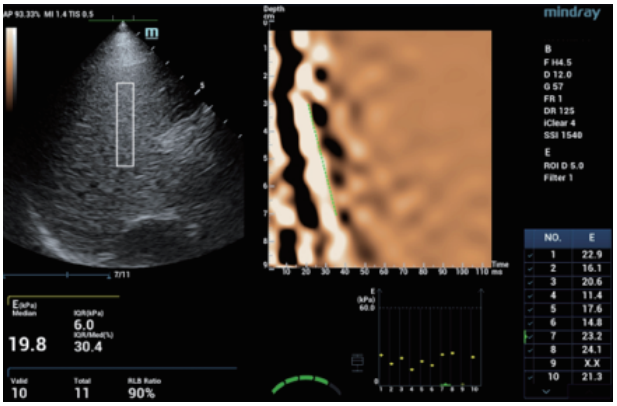


Figure 19 Invalid Measurements Occurring on a Small Proportion of Cases with Cirrhosis

The clinical study also finds that the penetration depth of shear waves generated using the ViTE technology exceeds 75 mm and even reaches 90 mm in most cases. Therefore, the ViTE technology is suitable for the examination of patients with different somatotypes (such as slim patients, tall patients, and obese patients).

Take patients with hepatitis B as an example. Liver biopsies were conducted on 83 patients with hepatitis B in this study, including 25 patients with no liver fibrosis (S0) or with only mild

liver fibrosis (S1), 43 patients with significant liver fibrosis (S2), 9 patients with advanced liver fibrosis (S3), and 6 patients with cirrhosis (S4). Figure 20 shows the statistics on ViTE Young's modulus of preceding cases in terms of Scheuer staging criteria [35] for different pathological results. It can be seen that there are obvious differences between the measurement results of different stages of liver fibrosis and the Young's modulus measured values increase with the progression of liver fibrosis. Use the demarcation of >= S4, >= S3, and <= S2 as an example, The Area Under Receiver Operating Characteristic Curve (AUROC) can be up to 0.97, 0.93, and 0.83 respectively, indicating high consistency between results obtained using the ViTE technology and pathological results of liver biopsies.

In a word, the ViTE technology can effectively help differentiate different degrees of liver fibrosis progression in clinical practice, and identify early liver fibrosis and early cirrhosis in time. As a non-invasive quantitative diagnosis technology, ViTE brings a new experience of visualization, fast detection, and high safety. It is more acceptable to patients and doctors can regulate operations more easily.

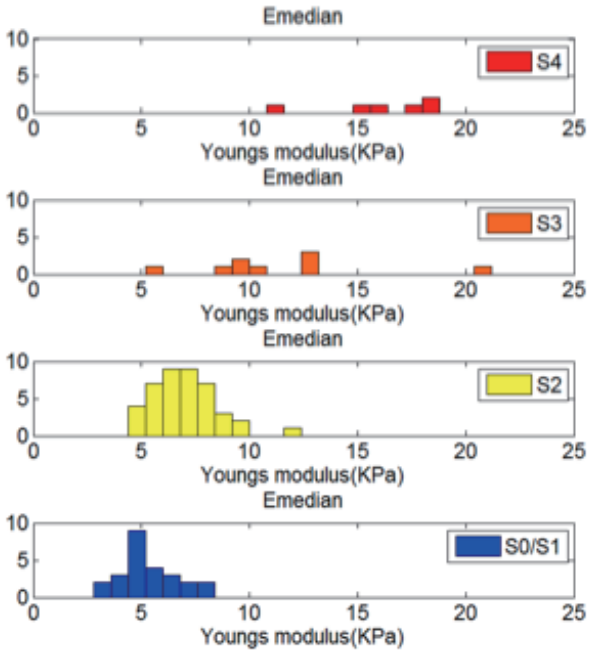


Figure 20 Distribution of Young's Modulus Values at Different Stages of Liver Fibrosis — HBV Cases

Case Study — Application in Fatty Liver

In the infection center of a famous hospital in Shenzhen, doctors used Mindray ViTE function to conduct a preliminary clinical study on 58 cases of patients with liver diseases. Operations were performed by skillful doctors according to specifications.

After the liver targets are positioned accurately in a visualized manner, the LiSA results and conventional CAP results were obtained for comparison. Ten valid measurements were obtained for each case. The results show that LiSA has great clinical diagnostic value in assisting with the non-invasive quantitative diagnosis of fatty liver. The LiSA results are highly consistent with CAP results and the stability of measured values is significantly improved, as shown in Figure 21 and Figure 22. The IQR/Median values calculated using multiple LiSA measurement values is relatively lower. The visualized operation experience effectively enhances doctors' confidence in diagnosis. It is found clinically that the measured LiSA value increases with the worsening of fatty liver, as shown in Figure 23.

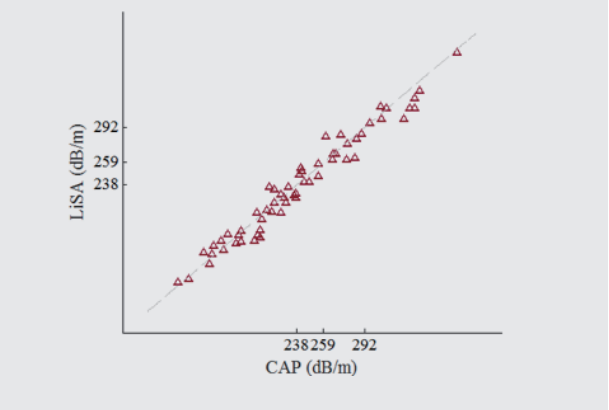


Figure21 Consistency Comparison Between LiSA and CAP Results

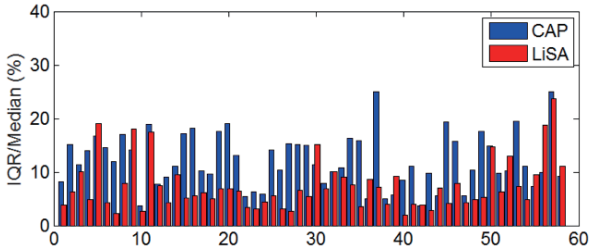


Figure22 Stability Comparison Between LiSA and CAP Measured Values

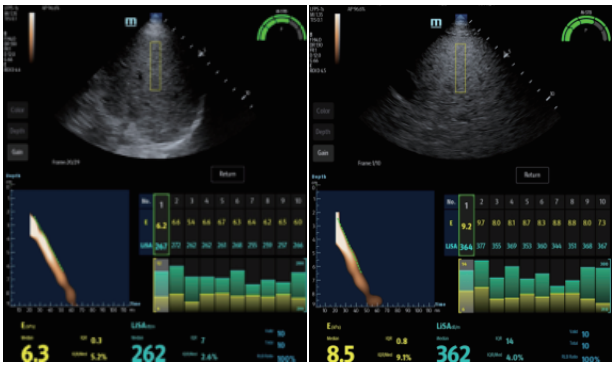


Figure23 Increase of the LiSA Measured Value with Worsening of Fatty Liver

Conclusion

Mindray ViTE visualized transient elastography provides a novel method for assisting with clinical quantitative evaluation of liver fibrosis progression and fatty liver severity. It serves as a new solution to liver health management.

The Hepatus integrated system adopts the innovative probe design. The ViTE visualized transient elastography can provide real-time 2D images to guide accurate positioning of liver target areas prior to examination. The system provides both motion interference and pressure prompts to ensure that high-quality shear waves are produced for propagation. The Hepatus rapidly detects shear wave signals in ROIs at a rate of up to 8.5 kHz to accurately capture the shear wave propagation process, effectively improving the accuracy and stability of measurement results. The system also shortens multiple times of clinical examination and calculation within 7s, greatly boosting the clinical operation convenience.

In this preliminary clinical study, although the clinical sample size is not huge, the study results strongly demonstrate the reliability and effectiveness of ViTE technology in the evaluation of liver fibrosis and fatty liver. Visualized image-guided positioning, motion interference prompt, and pressure prompt also bring potential study value to the regulation of clinical operations.

At present, many hospitals are using ViTE visualized transient elastography to conduct more extensive clinical studies with a larger sample size. Some studies have shown that the ViTE technology presents excellent sensitivity and specificity in the auxiliary diagnosis of liver fibrosis [36]. In addition, different pathogenic causes, biochemical indicators, clinical intervention, and other factors may also have a certain impact on transient elastographic measured values. We are in the hope of providing more accurate and detailed reference indicator suggestions for clinical diagnosis in the future, to better assist clinical diagnosis.

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