mindray 迈瑞

STVi

Shear Wave Viscoelastography

Technical White Paper

Introduction

Shear wave elastography, as an emerging ultrasound imaging technology that can non-invasively and quantitatively measure tissue stiffness in vivo, has become a hot topic in ultrasound research in the past decade. Ultrasound shear wave elastography has developed from a technology of pure research purpose to a regular clinical practice, and made its way into WFUMB and EFSUMB guidelines as well. It has been applied in various fields such as the liver and breast examinations [1-3]. Mindray's shear wave elastography function has been widely used in clinical research. Studies have shown that evaluating the elasticity of breast tumor tissue and the surrounding "hard ring" tissue using Mindray's unique shell function can improve diagnostic performance for differentiating benign and malignant breast lesions, which helps avoid unnecessary biopsies and benefit the treatment and prognosis of breast cancer [4-5]. In addition, studies have shown that shear wave elasticity is more advantageous than traditional indicators in chronic liver hepatitis B fibrosis evaluation and fibrosis grading [6-7].

However, aside from elasticity, tissues are affected by viscosity as well, and the viscous properties can affect the measurement of tissue elasticity. Viscosity is a cutting-edge quantification method of tissue properties that has become a rising research interest [1-3].

In conventional shear wave elastography, the region of interest (ROI) is usually considered as a pure elastomer, where the shear wave propagation velocity is independent of the shear wave frequency. However, in actual propagation, due to the presence of tissue viscosity, the shear wave propagation velocity usually increases along with shear wave frequency. Therefore, a more complex and realistic model is needed to calculate elasticity and viscosity.

In viscoelastography, tissue viscosity is taken into consideration. By modeling the relationship between shear wave velocity and shear wave frequency in the tissue, the elasticity and viscosity of ROI can be quantified and visualized using pseudo-color encoding.

By adopting a model that is closer to real tissue, viscoelastography can provide more parameters, such as viscosity coefficient and dispersion slope, to comprehensively describe tissue properties as a complement to traditional shear wave elastography.

In early clinical validations, viscoelastography has shown huge potential and a strong correlation with tissue inflammation. It has promising applications in various areas such as liver and breast, serving as a supplement to the study of tissue mechanical properties, and has attracted widespread attention from researchers worldwide.

Based on this, the Mindray Resona A Ultrasound System is equipped with liver viscoelastography capabilities and has pioneered the superficial viscoelastography technology globally. It provides viscosity information of the ROI in addition to shear wave elasticity, enabling a more comprehensive evaluation of the mechanical characteristics of lesion sites. In the following sections, this paper will introduce the principles and clinical applications of the viscoelastography technology STVi (Sound-Touch Visco).

Viscoelastography Technology

Viscoelasticity, as the name suggests, can be divided into elasticity and viscosity, representing the solid and liquid properties of materials, respectively. Elasticity reflects the continuum mechanics of bodies that deform reversibly under stress, and the strain produced when subjected to external forces

follows Hooke's Law. For a pure elastomer, the strain generated is proportional to external force, and the strain generated is independent of the time and the deformation instantly recovers upon removal of the external forces. Viscosity reflects the magnitude of internal frictional forces in the material, and the relationship between external forces and strain follows the Newtonian Fluid Law. For a purely viscous body, the strain is proportional to the duration external forces are applied, and the deformation is not recoverable upon removal of the external forces. Human tissues possess both elastic and viscous characteristics, and actual viscoelastic materials have both solid and liquid properties, with their mechanical behavior lying between that of pure elastomers and pure viscous bodies.

Viscoelastography, based on conventional shear wave elastography, incorporates the variation of shear wave velocity with frequency, providing a more comprehensive description of tissue mechanical properties. Viscosity in tissues causes shear wave dispersion, where the shear wave propagation velocity increases with increasing shear wave frequency. The extent of shear wave dispersion can be used to measure tissue viscosity.

If the relationship between shear wave frequency and velocity is simplified as a linear model, the following equation can be obtained:

$$\mathbf{V} = \mathbf{slope} \times \mathbf{f} + \mathbf{a}$$ [8]

where **V** represents the shear wave velocity at a specific frequency in meters per second (m/s), **f** represents the specific frequency in kilohertz (kHz), and **slope** is the dispersion coefficient representing the relationship between shear wave frequency and velocity in meters per second per kilohertz (m/s/kHz).

The parameter **slope** is not viscosity itself but is correlated with viscosity.

If the relationship between shear wave propagation velocity and frequency is fitted using Voigt model, the following formula can be obtained:

$$\mathbf{V} = \sqrt{\frac{2(\mu^2+(2\pi f)^2\eta^2)}{\rho\left(\mu+\sqrt{\mu^2+(2\pi f)^2\eta^2}\right)}}$$ [8]

where **V** represents the shear wave velocity at a specific frequency, **f** represents the specific frequency, **ρ** represents tissue density, **μ** represents the elasticity value in kilopascals (kPa), and **η** represents the viscosity value in pascal-seconds (Pa·s).

Mindray's viscoelastography feature is based on shear wave elastography, which extract and calculate the shear wave velocity at different frequencies. Then, the viscosity coefficient and dispersion coefficient are calculated using viscoelasticity fitting models.

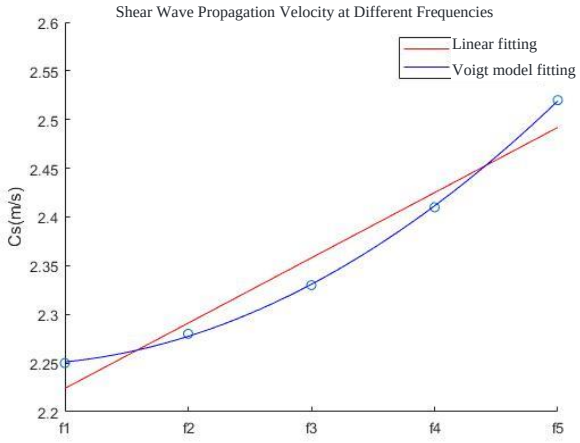

Figure 1: Viscoelasticity fitting

Viscoelastography Features

To provide users with comprehensive tissue mechanical information, Mindray's viscoelastography feature can display up to

four windows simultaneously, as shown in the following figure:

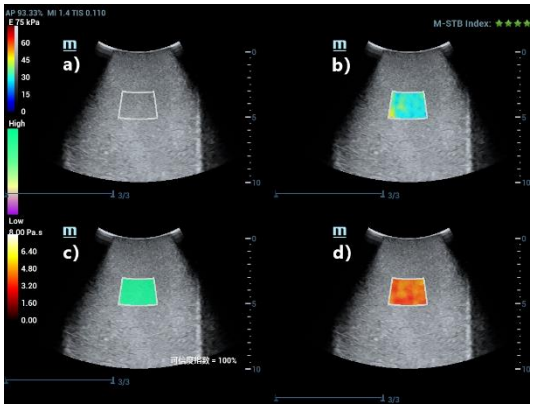

Figure 2: Display diagram - a. B-mode image; b. Shear wave elasticity image; c. Quality map; d. Viscoelasticity image

Among them, the viscoelasticity image can be switched between the viscosity image or dispersion image using a knob, providing users with more parameters for selection.

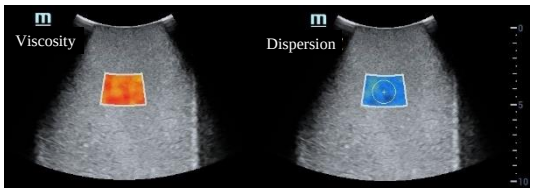

Figure 3: Comparison of viscosity image and dispersion image

In addition to an intuitive showcase of the distribution of tissue viscoelasticity through pseudo-color mapping, precise quantitative measurements of viscoelasticity values in specific ROIs can be obtained using measurement function.

Mindray's viscoelastography function provides various imaging modes that can adapt to different clinical scenarios for users to choose from.

The first mode is real-time viscoelastography. In this imaging mode, users can use B-mode image to locate the ROIs and place an ROI sampling box during the acquisition preparation stage. Once the acquisition starts, real-time updated continuous viscoelastography results can be obtained.

The second mode is high-quality viscoelastography. When it is necessary to study lesions located deeper, one single frame of high-quality viscoelasticity image with better penetration and less noise can be obtained.

The third mode is fixed ROI STVi mode, which has integrated inter-frame statistics in real-time viscoelastography. It can quickly obtain reliable results of repeated measurements in fixed locations, thereby improving efficiency.

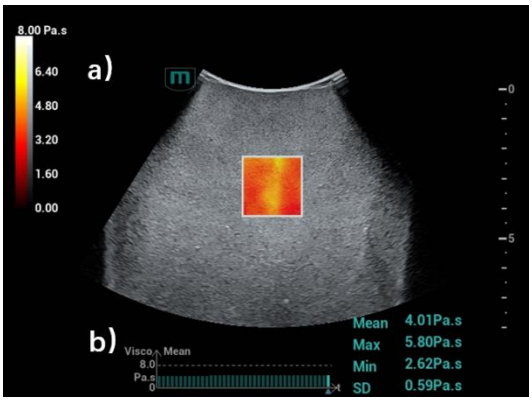

Figure 4: a. Fixed ROI acquisition example; b. Inter-frame statistics bar

Similar to shear wave elastography, viscoelastography is also highly sensitive to respiratory and motion interference during examinations, especially in liver or thyroid examinations, where patients often need to cooperate by holding their breath. To visualize the motion interference during the examination and assist doctors in judging the image acquisition quality and reliability, viscoelastography provides the Motion Stability Index (M-STB Index) function, as shown in the following figure:

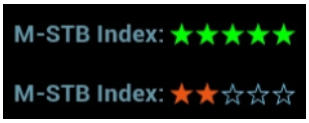

Figure 5: Motion stability - a. Minimal motion interference during acquisition, with reliable images; b. Significant motion interference during acquisition, with unreliable images

Viscoelasticity Research Tools

Various viscoelasticity measurement and quantification tools are available for users to select from and help conduct research or diagnosis according to clinical requirements. These measurement tools are convenient to use, powerful in functionality, and easy to grasp.

Where to place the ROI has always been a problem in liver elasticity acquisitions, which is greatly influenced by its distance to hepatic capsule, distribution of blood vessels, sound shadow under ribs and respiration of patient. It highly depends on the experience of doctors. The liver elasticity automatic measurement function provides two sub-functions: "Automatic ROI for Liver" and "Smart LSM", and can help users acquire liver elasticity data precisely and efficiently. The former sub-function can automatically locate appropriate ROI positions and sizes by identifying liver parenchyma during the elasticity (including viscosity) acquisition preparation stage. The latter can summarize the measurement habits of senior clinicians after elasticity acquisition, automatically place appropriate measurement circles for measurement, obtain measurement results and generate reports. By summarizing ROI selection and measurement habits of experienced clinicians, this function can assist users in clinical examinations and greatly improve efficiency.

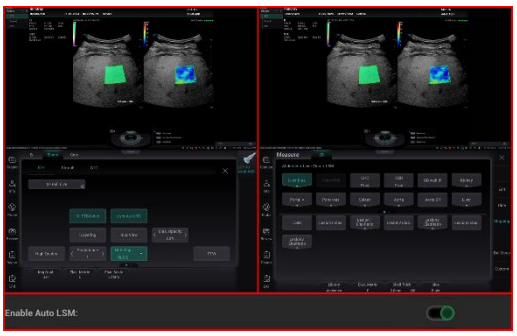

Figure 6: a. Automatic ROI selection; b. Automatic measurement; c. Automatic measurement presets

In a comparison of **38** patients and **185** sets of measurement data between two hospitals, the automatic measurement of liver fibrosis and cirrhosis using the Mindray system showed results that were comparable to manual measurements by senior clinicians, greatly improving examination efficiency without compromising diagnostic accuracy.

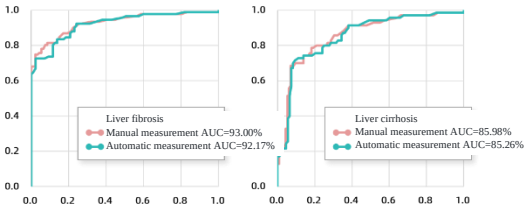

Figure 7: AUC comparison of automatic measurement and manual measurement of senior clinicians for liver fibrosis and cirrhosis

Viscoelasticity will affect the influence shear wave frequency has on shear wave velocity. Different manufacturers and platforms use different shear wave velocities in their shear wave elasticity product, making their measurements incomparable across platforms. For example, FibroScan uses 50Hz shear wave and MRE typically uses 60Hz. In commercial shear wave elasticity functions, the shear wave echo data received by the transducer are wideband. ‘Frequency’ here refers to the frequency transducers receive after shear wave

propagation, rather than the ARFI frequency of the probe. In typical tissues, shear wave propagation frequency usually ranges from 50 to 800Hz, and varies across different probes and tissues.

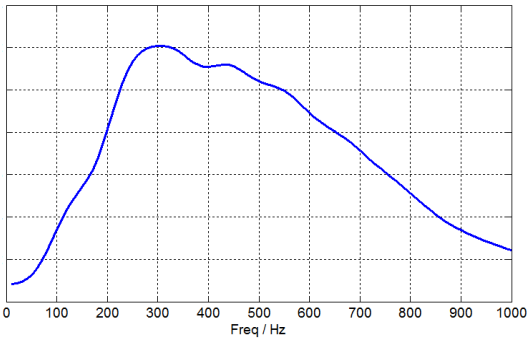

Figure 8: Frequency band of shear wave in vivo

The frequency-specified STE, as a Mindray exclusive function, can extract shear wave velocities at certain frequencies from the received wideband shear wave echo data and display them in pseudo-color mapping. Since the influence shear wave frequency has on shear wave velocity is ruled out, the elasticity obtained is ‘normalized’ and more comparable than traditional STE. The frequency-specified STE which builds on traditional elastography technologies, has its potential to deepen our knowledge on shear wave elasticity and broaden its clinical application as well as research direction.

For example, as shown in figure 9, subfigure a. shows the wideband STE result of a benign breast lesion, and subfigure b. shows the 200Hz STE result of the same lesion. The measurement and color pattern of 200Hz STE matches the pathological result better. Subfigure c. and d. are the wideband STE and 200Hz STE results of a malignant breast lesion, and 200Hz STE result matches the pathological result better as well.

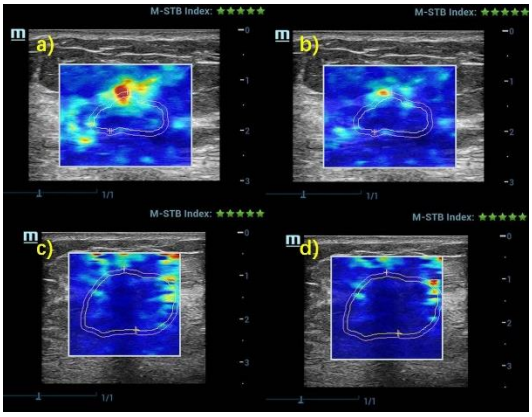

Figure 9: Case study of frequency-specified STE

In fixed ROI scenario, automatic statistical analysis of measurements within the ROI can be performed using the viscoelasticity bar function, and there are two types of statistical methods.

One is in the spatial domain, which evaluates the spatial uniformity within the local ROI. As shown in the figure, the viscoelastic fixed ROI function provides various spatial distribution statistical results within the local ROI, including mean, maximum, minimum, and standard deviation. Doctors can select different quantitative parameters for clinical research.

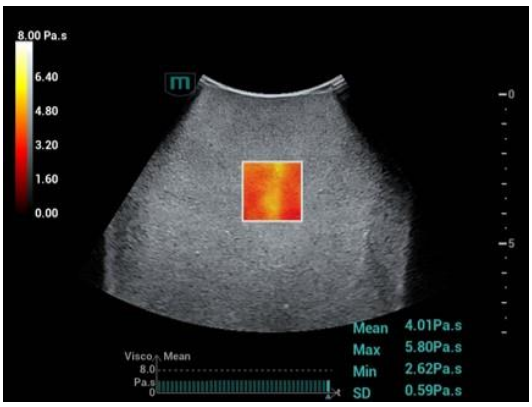

Figure 10: Spatial statistical results within the ROI

The other is in the temporal domain, which records continuous measurements of the local ROI. As shown in the figure, the viscoelastic **fixed ROI** function provides statistical results for multiple measurements, including median, interquartile range (IQR), average, standard deviation (STD), as well as IQR/Med or STD/Avg ratios representing stability between multiple results.

Figure 11: Statistical results of multiple measurements

The Multi-Parametric United Analysis feature (M-Ref. Live) can present different imaging modes and parameters selected by the user in real-time on the same screen, facilitating a comprehensive evaluation of lesions from multiple dimensions. Viscoelastography is available for combination in both breast and liver exams. For more detail, refer to the *Multi-Parametric United Analysis White Paper*.

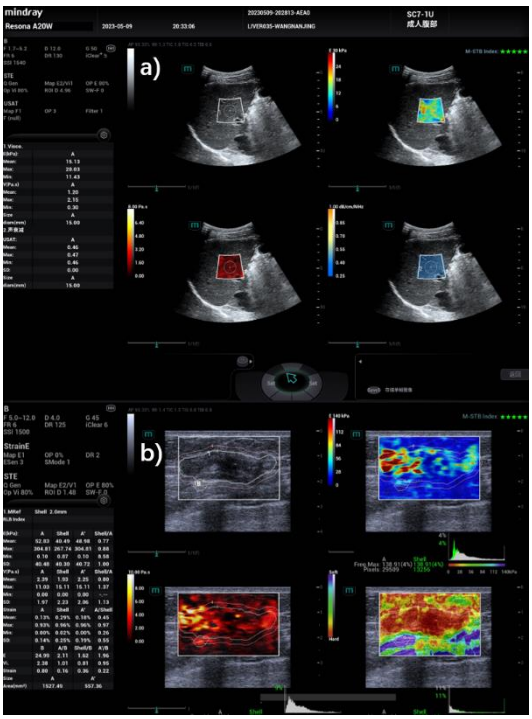

Figure 12: Multi-Parametric United Analysis - a. Liver M-Ref, combining STE + STVi + USAT; b. Breast M-Ref, combining STE + STVi + Strain E

Case Study - Breast Application

Doctors conducted clinical research using Mindray's viscoelastography function on over 400 cases of breast patients, with a benign-to-malignant ratio close to 1:1. The research results showed that viscoelastography can effectively differentiate benign and malignant breast lesions and can serve as complement to diagnosis of shear wave elastography.

As shown in the figure, there is a significant difference in the maximum of dispersion coefficient among benign and malignant breast lesions. In benign lesions, the mean value of the dispersion coefficient is 11.22 m/s/kHz, while in malignant lesions, the value reaches 17.35 m/s/kHz.

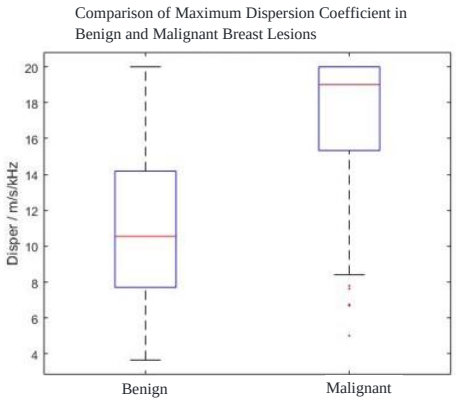

Figure 13: Comparison of maximum dispersion coefficient in benign and malignant breast lesions

In addition to quantitatively assessing the viscoelasticity values of lesions, qualitative analysis of lesions can also be performed based on the color map. In malignant tumors, the surrounding tissues exhibit high viscoelasticity. Figure 14 shows a typical case of a malignant tumor, where the surrounding infiltrated area has high viscoelasticity values. From the figure, it can be observed that the area with high viscoelasticity values is larger than the area of the lesion displayed in B-mode and STE image, forming a ‘high-viscosity rim’ feature.

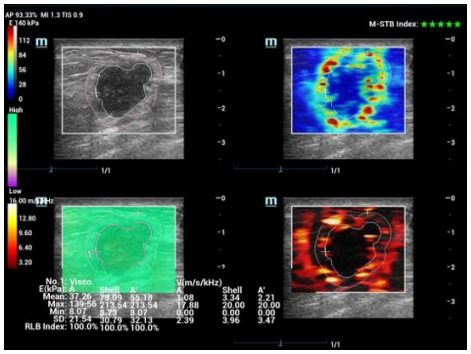

Figure 14: A typical viscoelasticity image of a malignant tumor

It is worth mentioning that in some malignant cases, the dispersion values may be high while the elasticity values are low, as shown in Figure 15. The existence of such cases indicates that viscoelastography plays a complementary role to shear wave elastography in the diagnosis of benign and malignant breast lesions.

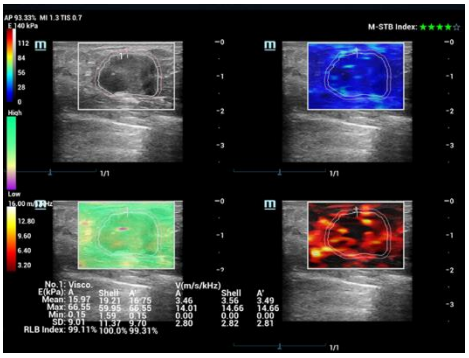

Figure 15: Example of a malignant tumor with low shear wave elasticity values and high viscoelasticity values

Case Study - Liver Application

In a well-known liver disease hospital in Shanghai, doctors conducted a preliminary clinical research on over 100 patients using Mindray's viscoelastography function. The research results showed significant differences in viscoelasticity values among different grades of liver inflammation. The following figure shows the distribution of average viscosity coefficient values for different inflammation grades. The results indicate that the average viscosity coefficient increases with the severity of inflammation, and the differences are statistically significant.

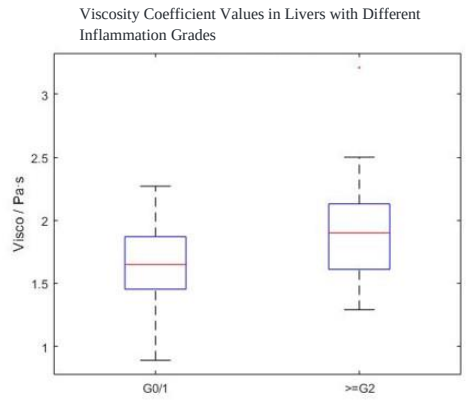

Figure 16: Increase in average viscosity coefficient with the severity of liver inflammation

It is worth mentioning that in the clinical practice of assessing liver fibrosis using shear wave elastography, it is often found that liver inflammation, especially when liver ALT level is higher than 5 times normal, elastography results will increase, resulting in false positive when evaluating liver fibrosis. The same phenomenon is also reported in WFUMB liver US guideline in 2015 and WFUMB US elastography guideline in 2018.

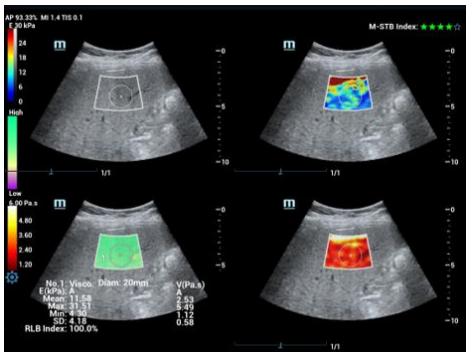

Figure 17: Example of a liver case with elevated shear wave elasticity values due to liver inflammation

As shown in Figure 17, in this G2 inflammation case proven by liver puncture, the elasticity measurement (11.58kPa) is way higher than it should be considering its fibrosis grading (F1), which indicates the influence of inflammation on the evaluation of liver fibrosis. Therefore, not only can viscosity work as an indicator of liver inflammation, it can also serve as a quality control in liver elastography examinations. When viscosity measurement is higher than normal, the influence of inflammation should be taken into consideration in liver elastography practice.

Conclusion

Mindray's viscoelastography function, STVi, as a supplement to shear wave elastography, implements a new tissue mechanical parameter that provides a more comprehensive understanding of lesion properties. Three different image modes, namely, real-time viscoelastography mode, single-frame high-quality viscoelastography mode, and fixed ROI imaging mode can adapt to different clinical scenarios based on different clinical requirements. Motion stability and quality maps serve as quality control measures to ensure the quality of acquisitions. At the same time, Mindray's viscoelastography function provides diverse and comprehensive research tools to help users conduct detailed studies on lesion pathological properties.

In early clinical practice, viscoelastography function has shown promising results in various applications such as breast and liver diagnosis, demonstrating its research and clinical value.

Furthermore, viscoelastography can be part of multi-parametric united analysis function, enabling joint diagnosis with other functions, providing a multi-dimensional evaluation of lesions and assisting users in making more comprehensive diagnoses and research.

Currently, multiple hospitals are conducting clinical research with larger sample sizes using viscoelastography technology. We hope to provide more accurate and detailed clinical

reference indicators in the future to better assist clinical diagnosis.

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