

# Current ultrasound-related strategies for assessing liver fibrosis in chronic liver disease

Li-Yun Xue<sup>1</sup>, Hong Ding<sup>2</sup>

<sup>1</sup>Department of Ultrasound, Zhongshan Hospital, Fudan University, Shanghai 200032, China;

<sup>2</sup>Department of Ultrasound, Huashan Hospital, Fudan University, Shanghai 200040, China.

*To the Editor:* Liver fibrosis is a consequence of several chronic liver diseases (CLDs). Accurate assessment of fibrosis severity is important for the management of patients with CLDs. Liver biopsy is the reference standard to follow fibrosis progression, but it is limited by its invasiveness, sampling error, and the intra- and interobserver variability. Therefore, developing non-invasive methods is essential for liver fibrosis assessment.

Conventional ultrasound (US) can provide some diagnostic information, but this modality is subjective and insensitive in early stages of fibrosis. The most widely studied non-invasive technique assesses liver stiffness, mainly with US-based shear wave elastography including transient elastography (TE), point shear wave elastography (pSWE), and two-dimensional shear wave elastography (2D-SWE). Meanwhile, computer-aided quantitative techniques have been used to support radiological image analysis.

SWE techniques are based on the generation of shear waves by an external or internal mechanical push. In TE, a piston-mounted transducer induces a mechanical externally controlled vibration to the skin, generating an elastic shear wave that propagates through the liver. Pulse-echo US acquisitions are used to measure shear wave velocity, which is directly proportional to tissue stiffness. TE is used most widely. Its value for evaluating liver fibrosis stage in patients with CLDs has been proved; however, TE has limitations. No real-time imaging is used, and the lack of gray-scale images introduces the potential for errors in adequate region of interest (ROI) selection.<sup>[1]</sup>

pSWE is used in the acoustic radiation force impulse imaging (ARFI) system and the elastography point quantification (ElastPQ) system, both of which can be implemented with conventional US devices using modified US probes. In pSWE, shear waves are generated in a small ROI (approximately 1 cm<sup>3</sup>) of the liver by applying a

high-frequency (up to 600 Hz) ARFI pulse. Monitoring shear wave-mediated displacement of liver tissue caused by the shear waves is achieved with B-mode imaging.<sup>[2]</sup>

The clinical application of ARFI with virtual touch tissue quantification (VTQ) technology has been validated through the comparison with TE, and both techniques have high predictive accuracy for detecting cirrhosis, with the area under the receiver operating characteristic curve >90%.<sup>[3]</sup> ARFI has several potential advantages over TE: it can be performed on a standard US machine, and it may be more applicable for assessing complications such as ascites, and more regions can be examined and managed by the operator<sup>[4]</sup> [Table 1].

ElastPQ is another shear wave elastography method that uses ARFI technology. As it is integrated into a conventional US machine, the liver stiffness measurements are easily available after selecting the ROI on abdominal US.

In TE or ARFI methods, a single shear wave is temporarily emitted at a single frequency. In the SuperSonic ShearWave Imagine Aixplorer<sup>TM</sup>, the transducer emits a plurality of pulse wave beams at increasing depths, with a wide frequency band ranging from 60 to 600 Hz. By superimposing a real-time color mapping of the elasticity encoded pixel-by-pixel over the standard B-mode image, 2D-SWE enables quantitative imaging of the tissue elasticity by placing an ROI within the color mapping.

2D-SWE has good to excellent accuracy for diagnosing advanced fibrosis and cirrhosis, with most assessments performed in viral hepatitis patients.<sup>[5]</sup> Portal hypertension is one of the most important clinical consequences of patients with CLDs and can be accurately evaluated by 2D-SWE.<sup>[6]</sup>

Considering the good diagnostic performances of these methods, the European Federation of Societies for

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**Correspondence to:** Hong Ding, Department of Ultrasound, Huashan Hospital, Fudan University, Shanghai 200040, China  
E-Mail: ding\_hong@fudan.edu.cn

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**Table 1: Comparison of different types of shear wave elastography.**

Shear wave elastography	Manufactures	Excitation methods	Units of measurements	Advantages and limitations
TE	Echosens	Mechanically induced impulse at tissue surface; a single shear wave is emitted temporarily at a single frequency.	kPa	No gray-scale ultrasound guidance.
ARFI quantification (VTQ)	Siemens Hitachi-Aloka	Ultrasound induced focused radiation force impulse at depth; a single shear wave is emitted temporarily at a single frequency.	m/s	It can be guided by conventional gray image.
ElastPQ	Philips	Ultrasound induced focused radiation force impulse at depth; a single shear wave is emitted temporarily at a single frequency.	kPa	It can be guided by conventional gray image.
2D-SWE	SuperSonic Imagine	Ultrasound induced focus swept over depth faster than shear wave speed to create a Mach cone; transducer emits a plurality of pulse wave beams at increasing depths, with a wide frequency band.	kPa and m/s	It can be guided by conventional gray image; generating a real-time color mapping.

TE: Transient elastography; ARFI: Acoustic radiation force impulse; VTQ: Virtual touch tissue quantification; ElastPQ: Elastography point quantification; 2D-SWE: Two-dimensional shear wave elastography.

Ultrasound in Medicine and Biology guidelines<sup>[7]</sup> recommend that TE, ARFI, and 2D-SWE techniques can be used as first-line tools for assessing the severity of liver fibrosis in patients with chronic hepatitis C, and they perform best for ruling out cirrhosis. pSWE as demonstrated with VTQ and 2D-SWE are useful for identifying cirrhosis in patients with chronic hepatitis B.

In recent years, computer-aided quantitative techniques have been successfully used to support human decision making in radiological image analysis. In traditional machine learning methods, there are various methods for calculating features, but the completeness of the feature extraction cannot be guaranteed, and these methods are susceptible to image distortion.<sup>[8]</sup>

Deep learning, a branch of machine learning, can directly process and automatically learn mid-level and high-level abstract features acquired from raw data of medical images.<sup>[8,9]</sup> Convolutional neural network is a type of discriminative deep architecture that includes several modules, each of which generally consists of a convolutional layer, a pooling layer, and a fully connected layer. Deep learning methods applying during 2D-SWE analysis reportedly have excellent performance for fibrosis staging.<sup>[10]</sup>

Deep learning models need large, labeled training datasets to achieve excellent learning performance, which is a challenge in current US image analyses. One pathway to address this issue is using transfer learning to improve the performance by transferring knowledge from other domains to the medical US domain.<sup>[8]</sup> It is reported that liver fibrosis can be staged by transfer learning models based on the combination of grayscale and 2D-SWE images with excellent performance.<sup>[11]</sup> The value of transfer learning in assessing liver fibrosis has great

potential but requires further exploration in large-scale studies.

In conclusion, SWE has played a crucial role in assessing liver fibrosis. Emerging computer-aided quantitative techniques for analyzing US images are increasingly used, especially deep learning. With the growing use of artificial intelligence systems, computer-aided quantitative techniques will be the focus of future research.

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### Conflicts of interest

None.

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