RTE Real-time Tissue Elastography

SWM Shear Wave Measurement

Elastography ATLAS

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Contents

Background of Elastography Development

Cancerous tissue becomes stiffer as the density of blood vessels and/or cells increases. This stiffening is believed to start from the early stages of development of the cancer[1]. Visualization of stiffness data, therefore, could enable early-stage differentiation of benign and malignant tissue. Elastography has been developed for non-invasive imaging of tissue elasticity (stiffness) using a diagnostic ultrasound system. The transducer is used to gently compress the tissues, and the resultant pattern of induced strain gives diagnostic information about the tissue stiffness. Hitachi was the first company to commercialize Real-time Tissue Elastography (hereafter RTE) as a method for tissue stiffness visualization. Now, RTE is clinically applied in many medical institutions.

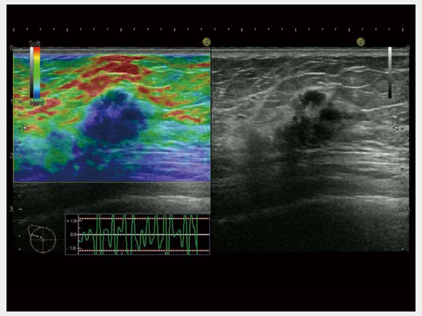


Fig. 1: Breast Elastography

1 Overview of Elastography

Methods and Principles of Elastography

The guidelines of the World Federation for Ultrasound in Medicine and Biology (hereafter WFUMB) classify Elastography methods as shown in Table 1.

Elastography methods can be classified into two main types: strain imaging and shear wave imaging.

RTE is classified as strain imaging, while Shear Wave Measurement (hereafter SWM) is classified as shear wave imaging method. The different principles are explained below.

Methods / Excitation methods	Strain imaging	Shear wave imaging
Manual compression	Strain elastography **RTE**	N/A
Acoustic radiation force impulse excitation	ARFI Imaging	Point shear wave speed measurement **SWM**

Table 1: Classification of Elastography methods

Principles of Real-time Tissue Elastography (RTE) (Strain Elastography)

Under a constant applied force, soft tissue will show significant strain while stiff tissue shows little strain (Fig. 2). These tissue characteristics can be color-coded and displayed as a strain map which can be superimposed on the corresponding B-mode image. Areas demonstrating relatively less strain (stiffer parts) in the region of interest (ROI) will be colored blue, areas demonstrating relatively more strain (softer parts) in red, with the areas of mean stiffness in green (Fig. 3).

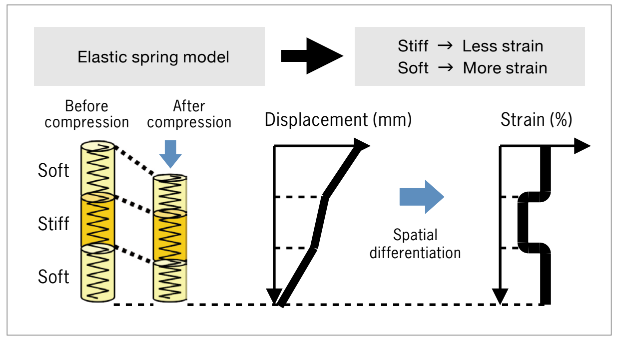


Fig. 2: Schematic showing the principles of RTE

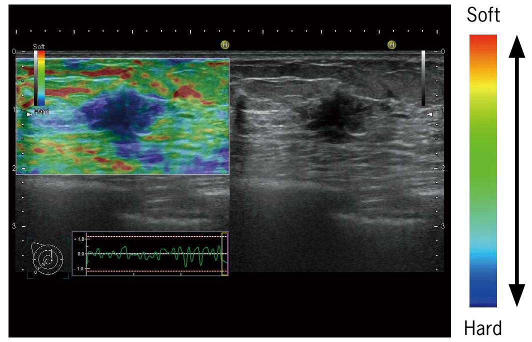


Fig. 3: Breast Elastography

Principles of Shear Wave Measurement (SWM) (Point Shear Wave Speed Measurement)

A focused ultrasound pulse is transmitted by the transducer. From the resultant displacement of the tissue, shear waves are generated and propagate off-axis. Tracking pulses are used to detect the propagation velocity of the shear wave (Vs) by measuring the difference in arrival time (time lag) between the two points a known distance apart (distance) (Fig. 4).

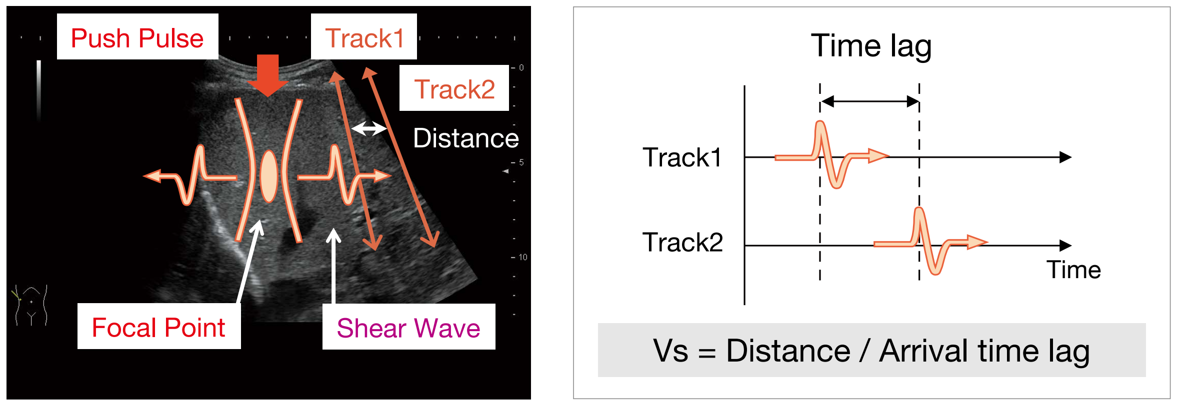


Fig. 4: Schematic showing the principles of SWM

2 Neoplastic Disease of the Breast (Workflow and Evaluation with RTE)

Clinical Benefits of Elastography [1]

It is anticipated that the use of Elastography in breast cancer screening could reduce the recall rate and improve the positive predictive value. Additionally, when used for detailed breast examination, it is expected to improve specificity. This could reduce the number of patients receiving unnecessary biopsies. In breast-conserving surgery, Elastography has been reported as an effective tool for the determination of the limit of the excision. Moreover, Elastography can be effective in the visualization and differential diagnosis of the intraductal component that often appears as a non mass-forming lesion.

Techniques Proposed by WFUMB

Guidelines for Breast Elastography were announced at the WFUMB World Congress in 2015, following the 2014 Convention of the Japan Society of Ultrasonics in Medicine (JSUM). The guideline proposes three different Elastography imaging techniques as shown in Table 2 and recommends selection of the appropriate technique according to the lesion.

Method	Technique	Depth of lesion	Size of tumor imaged
No Manual Compression	Try not to apply pressure.	In some cases (large breasts or deep lesions) Minimal vibration may be required.	
Minimal Vibration	Apply extremely fine vibration with a few cycles/second.	This method can be used for relatively shallow lesions to moderately deep lesions.	It allows elastography imaging of small targets several millimeters in size such as non-mass abnormalities.
Significant Compression	Apply fairly significant compression/release. (approximately 1-2 mm).	As long as the tumor is fairly large, adequate elastography images of lesions at most depths can be obtained.	

Table 2: Elastography techniques based on the WFUMB guideline

RTE-specific Functions Supporting Ultrasound Examination of the Breast

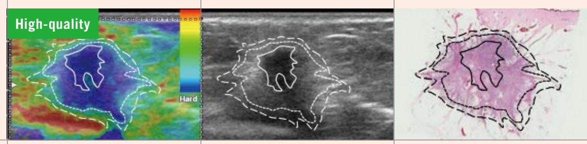
! Point

Our high-quality RTE (Fig. 5) is furnished with unique functions for efficient ultrasound examination of the breast. These enable significant improvement in workflow. In addition, they enable acquisition of objective and highly reproducible data independent of the proficiency of the examiner.

Examination workflow (Supported functions)

RTE Scan ('No Manual Compression' method) → **Frame Selection** (Auto Frame Selection) → **Strain Ratio Measurement** (Assist Strain Ratio)

Stable real-time visualization	Stable Elastography images can be obtained using any one of the three techniques proposed by WFUMB.
Single-click automatic frame selection (Auto Frame Selection)	From multiple frames obtained during RTE, the system automatically selects and displays the most appropriate frame for measurement on freeze (Fig. 6).
Single-click diagnostic support (Assist Strain Ratio)	Fat Lesion Ratio (FLR) is a semi-quantitative method for the assessment of strain. ROIs are set both in fat and in the tumor (lesion) to obtain a Strain Ratio. Assist Strain Ratio is a function that automatically sets the ROIs for FLR measurement, improving both the reproducibility and objectivity as well as reducing the time required for measurement.



	RTE image	B-mode image	histology
	The dark blue core	Central area of low echogenicity	Area of dense cancer cells with advanced fibrosis
	Blue gradation to the lesion boundary	Hyperechoic image towards the lesion boundary	Mixed area of cancer cells, fibrosis, inflamed cells, and fat tissue
	Peripheral green colored area (excluding the surrounding red area)	Hyperechoic lesion boundary with gradual shift to fat	Mix of cancer cells and fat

Fig. 5: High-quality RTE and B-mode image compared with pathological tissue.
RTE image reflects the morphological information shown in pathological tissue.

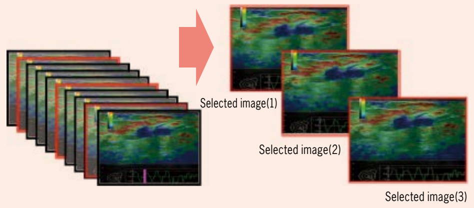


Fig. 6: Schematic of Auto Frame Selection function

Courtesy of: Dr. Maki Kuwayama, Department of Radiological Technology, TOYOTA-KAI Medical Corporation KARIYA TOYOTA General Hospital

Differentiation Between Benign and Malignant Breast Tumors

Elasticity Score (Tsukuba Elasticity Score)

The areas showing reduced or no strain in the tumor (blue) using RTE were compared to the hypoechoic area in the B-mode image and scored using five different categories. Fig. 7 shows the comparison results.

SCORE 1	Strain is seen throughout the hypoechoic area. (The entire lesion is coded in green, similar to the surrounding normal mammary gland.)
SCORE 2	Part of the hypoechoic area shows no strain. (The lesion is seen as a mosaic pattern of green and blue.)
SCORE 3	No strain is seen at the core of the hypoechoic area, but strain is seen at the rim. (The lesion core is blue and the rim is green.)
SCORE 4	No strain is seen within the hypoechoic area. (The whole lesion is coded blue.)
SCORE 5	No strain is seen in the hypoechoic area nor in the surrounding area. (The lesion and the surrounding area are blue.)

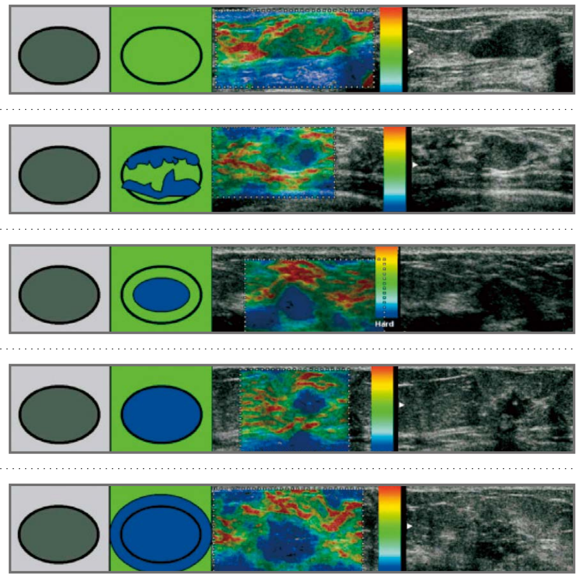


Fig. 7: Elasticity Score (Tsukuba Elasticity Score)
Radiology: Volume 239:Number2-May,2006

FLR (Fat Lesion Ratio)

The FLR is the ratio of the mean strain in the target to that of the adjacent fat. This semi-quantitative measurement gives a numerical value that assesses the stiffness of the target area relative to the fat (Fig. 8). This method can be used for both large tumors but also for a stiffness assessment of non mass-forming tumors[1]. The WFUMB Guideline includes references to cutoff values[2].

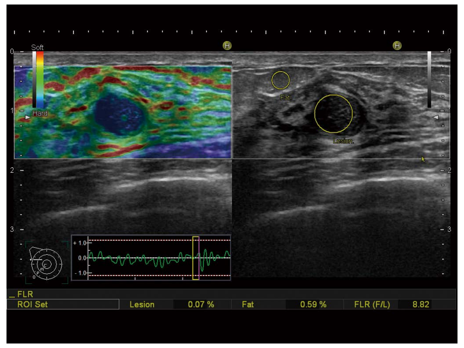


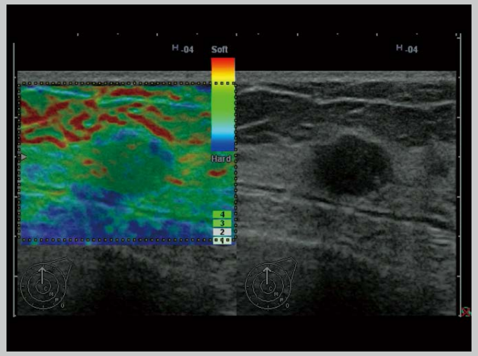
Fig. 8: FLR measurement
Courtesy of: Dr. Kazutaka Nakajima, General Surgery, Kawasaki Medical School

Clinical Images

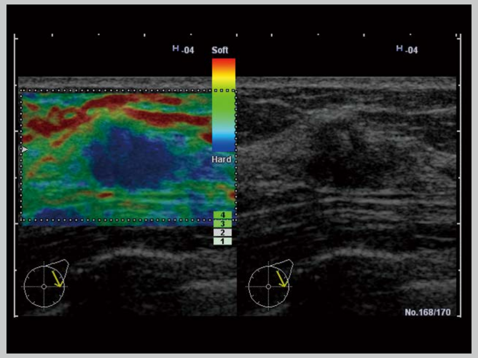
Mass-forming Lesions

The entire fibroadenoma appears green (soft lesion), while the invasive ductal carcinoma is coded blue (stiff tumor).

Fibroadenoma



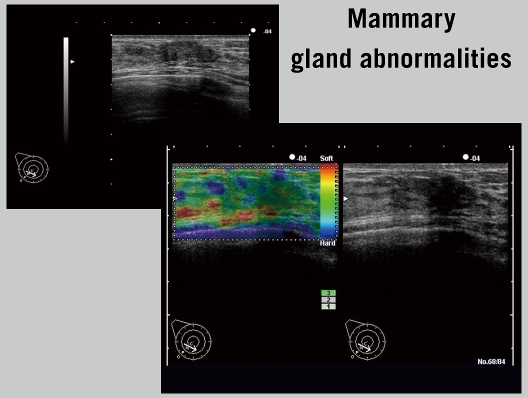
Invasive ductal carcinoma



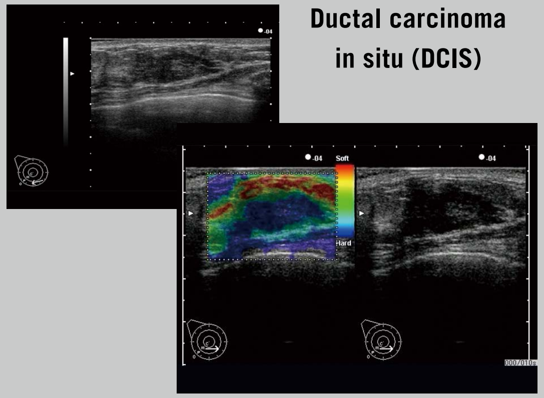
Courtesy of: Dr. Ako Ito, Department of Surgery, Hitachi, Ltd. Hitachi General Hospital

Non Mass-forming Lesions

Mammary gland abnormalities



Ductal carcinoma in situ (DCIS)

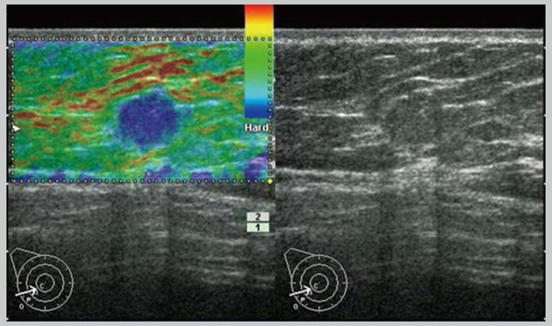


Courtesy of: Dr. Ako Ito, Department of Surgery, Hitachi, Ltd. Hitachi General Hospital

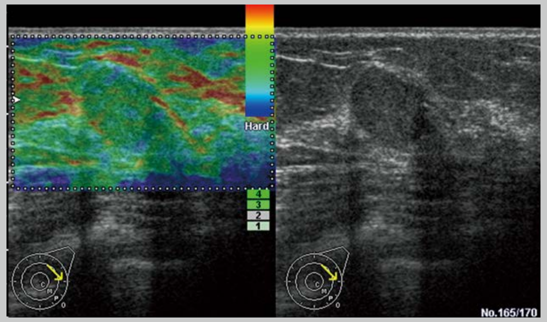
Mucinous Cancer vs. Fibroadenoma

Both tumors have similar appearances on B-mode, smooth with a well-defined boundary, but display different stiffness with RTE.

Mucinous cancer



Fibroadenoma



Courtesy of: Dr. Eriko Tono, Department of Radiology, Faculty of Medicine, Univ. of Tsukuba

3 Diffuse Liver Disease

(Liver Fibrosis Assessment by Combined Use of RTE and SWM)

Clinical Benefits of Elastography[3]

In the diagnosis and treatment of diffuse liver disease, it is extremely important to determine which patients are suitable for antiviral therapies, predict their curative effects, and correctly diagnose the degree of liver fibrosis. Though regarded as the gold standard for diagnosis, a liver biopsy is an invasive examination and therefore cannot be repeated frequently. Ultrasound Elastography has been reported as an effective method for evaluating the level of fibrosis non-invasively in all diffuse liver diseases and could provide an alternative to liver biopsy.

Features of Each Method

For liver fibrosis assessment, the following two Elastography methods can be used: assessment with RTE and the Liver Fibrosis Index (LF Index), and shear wave speed measurement with SWM. The features and an evaluation of these two methods follows:

Features of Liver Fibrosis Assessment Using RTE

Point

(1) Provides an accurate measurement of the degree of liver fibrosis.

Assessment with RTE (LF Index) is known to be unaffected by inflammation, congestion, or jaundice.[4]

(2) Allows measurement in patients with ascites.

(3) Assessment can be made with a standard convex transducer.

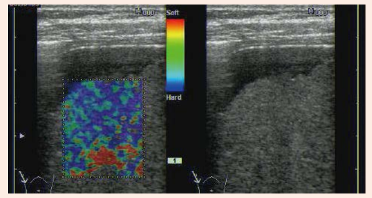


Fig. 9: Data acquisition from patients with ascites

<Imaging Method>

With the transducer placed in a right intercostal space (around S5/S8) between the anterior and mid axillary line, scanning is performed to obtain a RTE image of the liver using heart beat-induced strain (Fig.10).

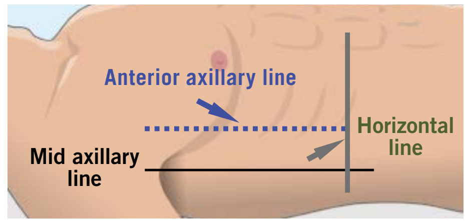


Fig. 10: Schematic image of reference line for imaging

<Assessment with RTE> - Comparison with the New Inuyama Classification -

As liver fibrosis develops in patients with hepatitis, the tissue shows local variations in stiffness. The stiffer regions (blue areas) increase in number and size, and the RTE image takes on a mottled appearance.[5] Hepatitis staging is diagnosed using an invasive biopsy, but RTE allows a non-invasive assessment that can be used frequently in follow-up observation and treatments.

Fig. 11 shows RTE images paired with a pathological tissue specimen for each fibrosis stage as classified using the New Inuyama Classification (Table 3).

Stage of fibrosis	F0: No fibrosis F1: Periportal fibrosis F2: Bridging fibrosis F3: Bridging fibrosis with lobular distortion F4: Hepatic cirrhosis
Stage	

Table 3: New Inuyama Classification

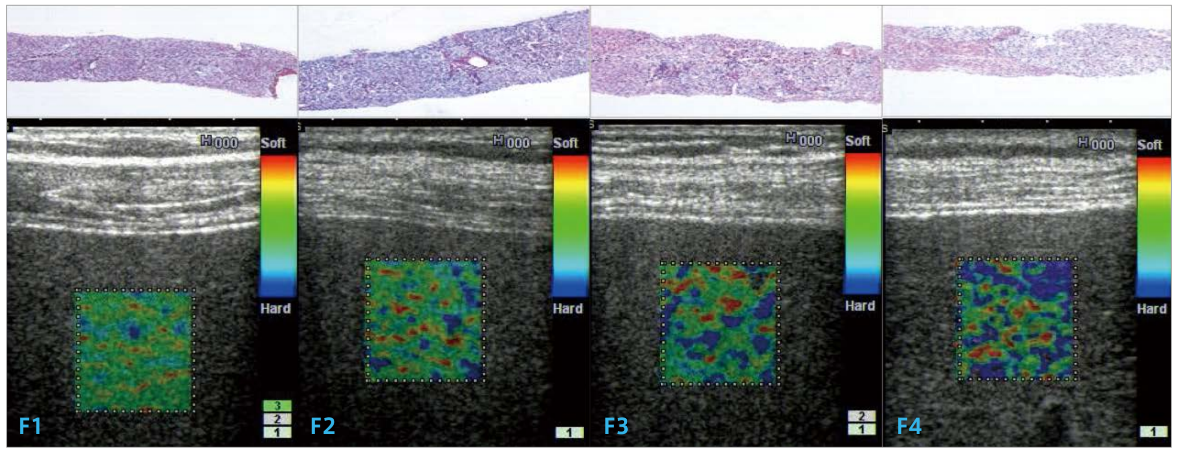


Fig. 11: Comparison of liver RTE images with New Inuyama Classification stages

Courtesy of: Dr. Kenji Fujimoto, Minami Wakayama Medical Center

<RTE-specific Functions for Liver Fibrosis Assessment>

Point

Liver Fibrosis Index (LF Index) measurement

The LF Index is a unique measurement for liver fibrosis assessment. From an analysis of the RTE image pattern of the liver with hepatitis C, the hepatitis stage can be estimated as an LF Index value (Fig. 12). The formula is calculated based on a multiple regression analysis with nine different feature values as independent variables, and histopathological fibrosis diagnosis F stages as dependent variables. The LF Index correctly reflects the degree of liver fibrosis without influence from inflammation, jaundice, and so on.

$$\text{LF Index}=-0.00897\times\text{MEAN}-0.00502\times\text{SD}+0.0232\times\text{\%AREA}+0.0253\times\text{COMP}+0.775\times\text{SKEW}-0.281\times\text{KURT}+2.08\times\text{ENT}+3.04\times\text{IDM}+40.0\times\text{ASM}-5.54$$

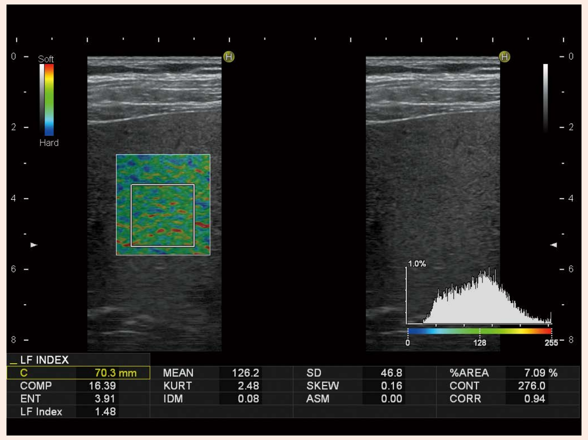


Fig. 12: LF Index clinical image

Correlation between liver biopsy histology F stages and LF Index values

A LF Index validation study of 245 cases of chronic hepatitis B, C and hepatic cirrhosis was conducted and revealed significant differences between F1 and F2, F1 and F3, F1 and F4, F2 and F4, and F3 and F4. The RTE LF Index highly correlates with the stage of hepatic fibrosis and is effective for evaluation before and after treatment (Fig. 13).

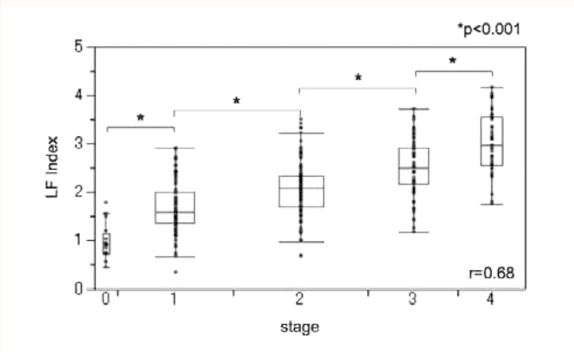


Fig. 13: Correlation between liver fibrosis F stages and LF Index values

Fujimoto K, et al. Non-invasive evaluation method of the liver fibrosis using Real-time tissue elastography~ Usefulness of judgment liver fibrosis stage by Liver fibrosis index(LF index). Kanzo,51:539-541,2010

Compatibility with convex transducers

Convex transducers support RTE and hence enable RTE to be performed immediately as an extension of the conventional routine ultrasound examination. They provide a wide field of view for visualization making it easy to direct the imaging towards the heart. This results in RTE images with high reproducibility. In addition, convex transducers offer good penetration and can reduce the incidence of poor imaging in conventionally difficult-to-image cases, such as patients with fatty liver disease (Fig. 14).

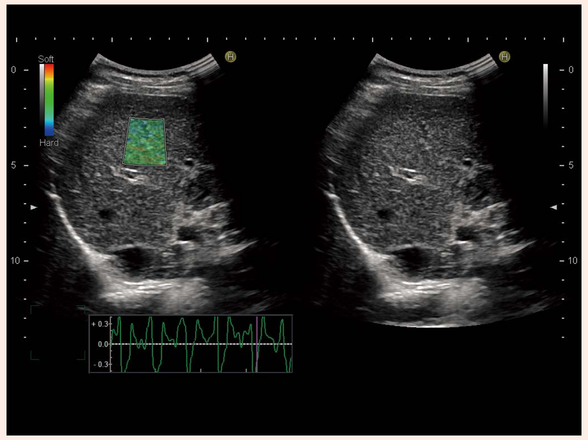


Fig. 14: Elastography taken using a convex transducer

SWM-specific Functions for Liver Fibrosis Assessment

It has been reported that liver fibrosis assessment using shear wave speed measurement methods can ascertain the degree of fibrosis as well as that of inflammation, because the degree of inflammation, congestion, and jaundice affects the measurement results.

<Shear Wave Measurement (SWM)>

Once the ROI is placed at the measurement site in the liver parenchyma, the measured value will appear in approximately two seconds.

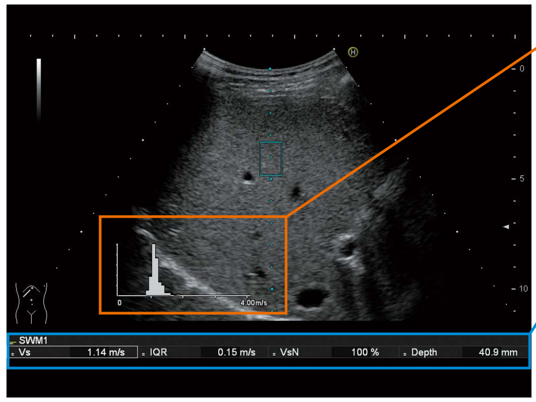
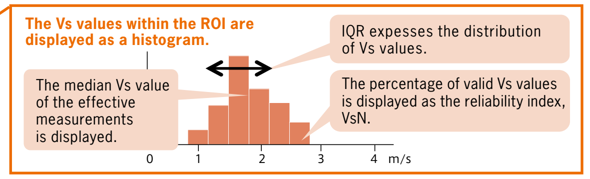


Fig. 15(a) Shows an example of the SWM screen and measurement results.



*Availability of histogram display differs with the ultrasound system.

Fig. 15 (b): Schematic of histogram of Vs values

Item	Unit	Contents
Vs	m/s	Propagation velocity of shear wave (Median of multiple Vs measurements)
IQR	m/s	Interquartile range of Vs values (±25% of the median)
VsN	**%**	**Vs measurement efficacy rate**
Depth	mm	Depth of ROI center

Table 4: Summary of SWM results

<Features of SWM>

Point

(1) Measurement without time lag

A fast, single-click measurement. Automatic image recording.

(2) Automatic multiple measurements for reliability.

Multiple values, m x n, are calculated by transmitting n pulses for each measurement as shown in Fig. 16. The median of the effective values is calculated and displayed as the Vs value.

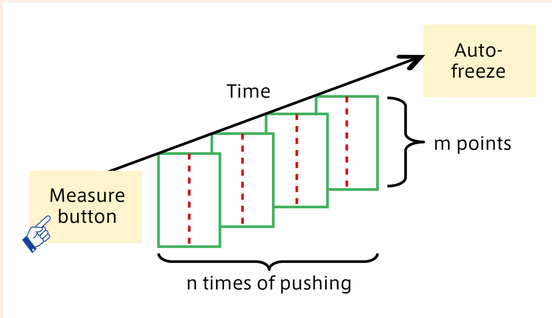


Fig. 16: Schematic of automatic multiple measurements

(3) Evaluation of the measurement reliability using VsN

The measurement of the true shear wave propagation velocity in tissue can be affected by breathing or other body movements from the patient, or lack of steadiness of the examiner's hand. In such cases, it may be difficult to determine the reliability of the measurement based only on the value of the shear wave propagation velocity (Vs). The reliability indicator (VsN) shows the ratio of effective values from the total number acquired with each measurement. This function allows the user to determine the reliability of the measurement.

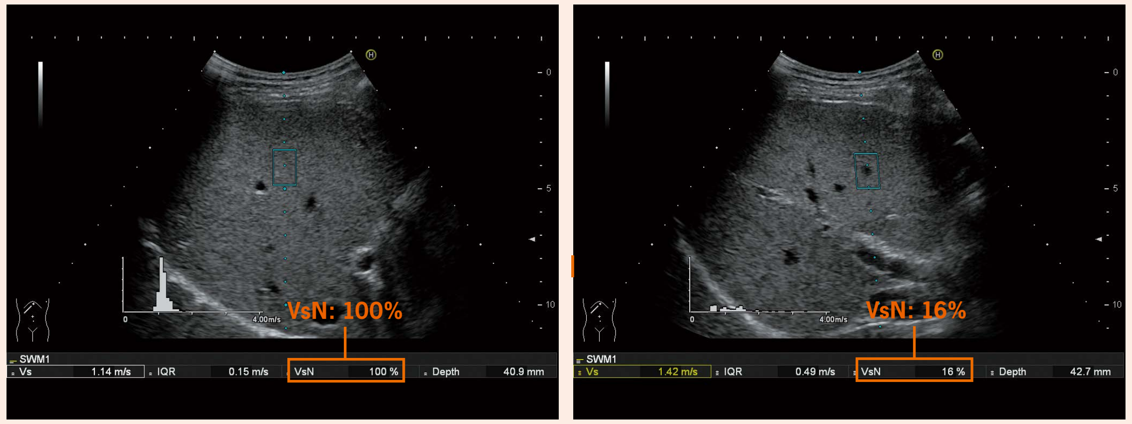


Fig. 17: Reliability index (VsN) display

Clinical Case : Combinational Elastography[6]

Non-invasive Diagnosis of Liver Clinical Condition by Real-time Tissue Elastography and Shear Wave Measurement : Get More Accessible by One Probe

Norihisa Yada, Masatoshi Kudo, Department of Gastroenterology and Hepatology, Faculty of Medicine, Kinki University

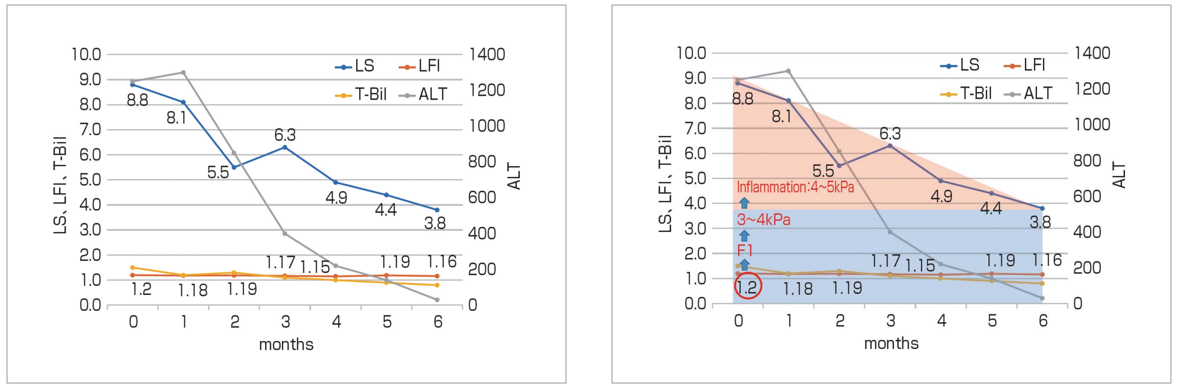
Combinational Elastography

Vs values measured with SWM vary significantly under the influence of not only fibrosis but also inflammation, jaundice or congestion. On the other hand, changes in the relative strain in chronic liver disease examined by RTE reflects only the progression of liver fibrosis and the measurement is seldom affected by these factors. Therefore, the level of inflammation, jaundice and congestion can be estimated by simultaneously performing Shear Wave Measurement and Real-time Tissue Elastography (Combinational Elastography) and analyzing the difference in the data obtained from these 2 techniques. This interpretation method is described using the case of a 27-year old male suffering from acute hepatitis B.

Clinical Case

Mild enlargement of the liver and a small volume of ascites were found in B-mode examination, and the ALT was increased to 1290IU. Jaundice and congestion were not found. LFI (LF Index) was 1.2 before treatment, equivalent to an estimated fibrosis stage of F1. With shear wave imaging, on the other hand, liver stiffness by FibroScan was 8.8kPa, which is equivalent to F3. The divergence is most probably due to the influence of inflammation because the patient had no jaundice or congestion. We may consider that, assuming F1 is in the approximate range of 3 to 4kPa, that 3 to 4 out of the 8.8kPa before treatment is accounted for by the influence of fibrosis and the remaining 4 to 5kPa reflects the influence of inflammation. Actually, liver stiffness gradually decreased with decreasing ALT and recovered to 3.8kPa after 6 weeks. The divergence between the shear wave and strain imaging results had also disappeared (Fig. 18).

Fig. 18: Treatment Course and Interpretation in an Example Case



ALT improved quickly as a result of treatment.
Likewise, liver stiffness also improved.
T-Bil and LFI remained at the same level throughout treatment.

Blue-shaded area is considered to reflect fibrosis
and the red-shaded area inflammation

Summary

Combinational Elastography using the Vs measurement obtained by SWM, with evaluation using RTE at the same time is useful for correctly assessing the clinical condition of the liver. Development of the SWM technique and RTE with a convex transducer has made it possible to perform Combinational Elastography in series following the normal ultrasound examination, using the one transducer. Non-invasive diagnosis of liver disease has become more easily accessible using ultrasound Elastography.

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