

Elastography in Liver evaluation

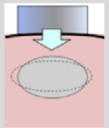
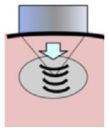
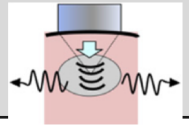
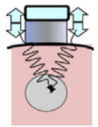
21/02/2019

Kazimierz Kukulski

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Elastography Methods

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Excitation methods \ Elastography Method	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**  Shear wave speed imaging
Controlled external vibration		Transient elastography 

Extract from: Shiina T, et al. : WFUMB Guidelines and recommendations for clinical use of ultrasound elastography: Part 1: basic principles and terminology. Ultrasound Med. Biol., 41, 2015.

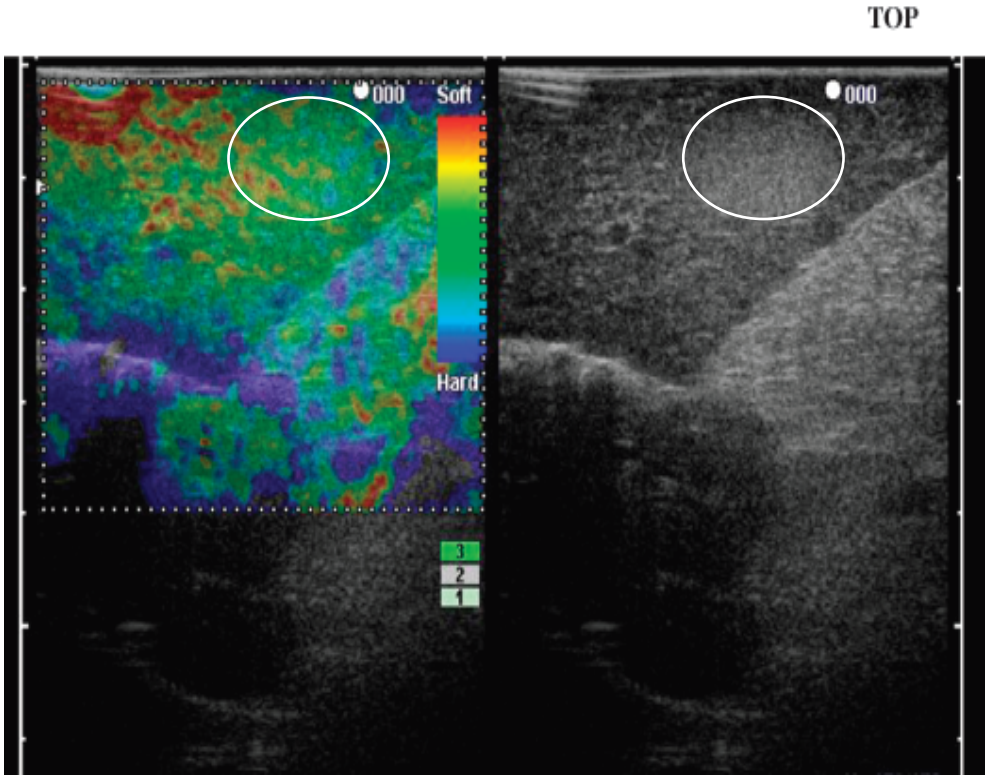


Model by: KAROUMPALIS IOANNIS M.D
CONSULTANT GASTROENTEROLOGIST
DISTRICT HOSPITAL OF ATHENS “G.GENNIMATAS”

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Haemangioma; type A

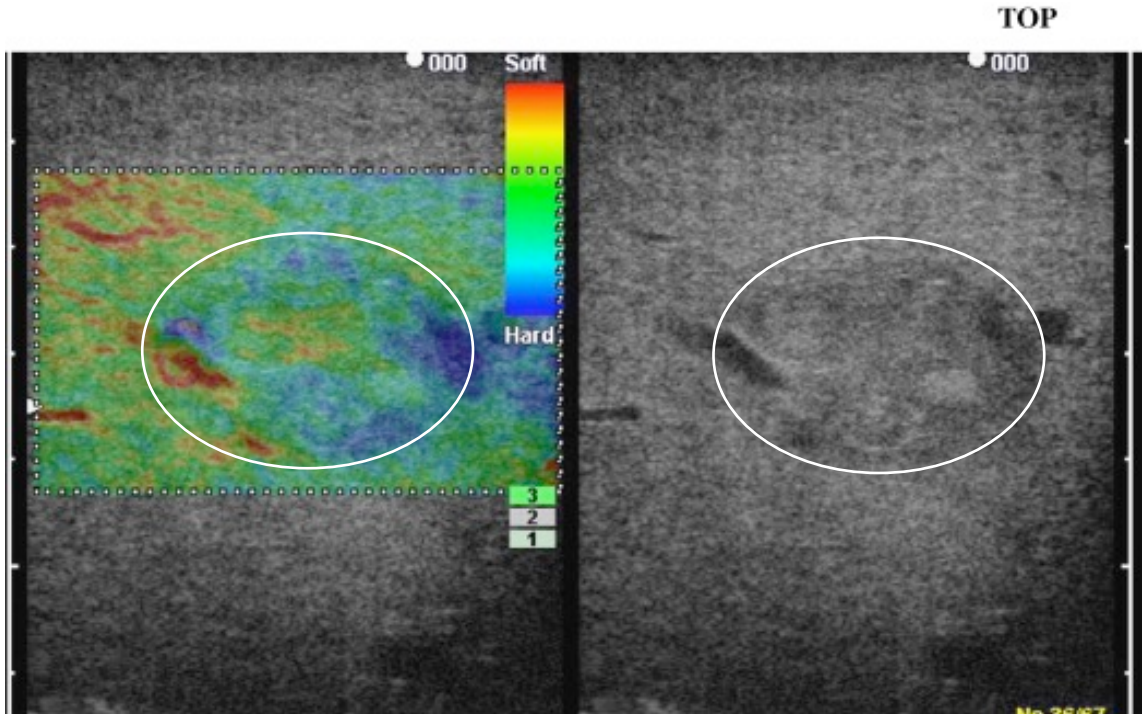
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HCC; 1cm; type B

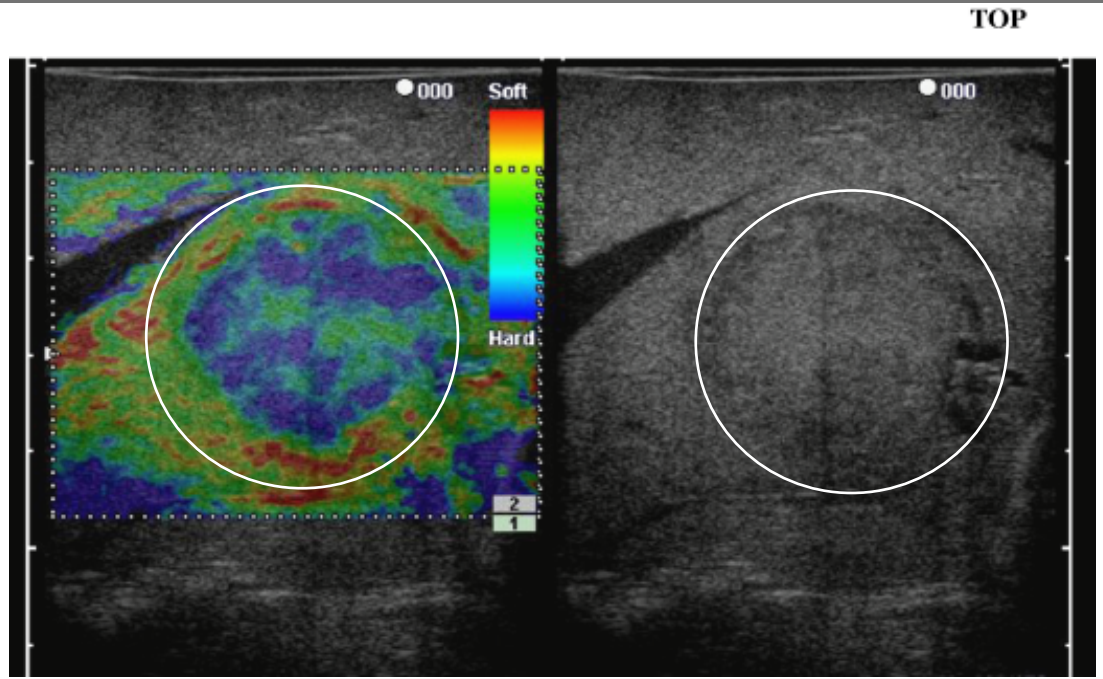
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Rectal adenocarcinoma, 12mm, type C

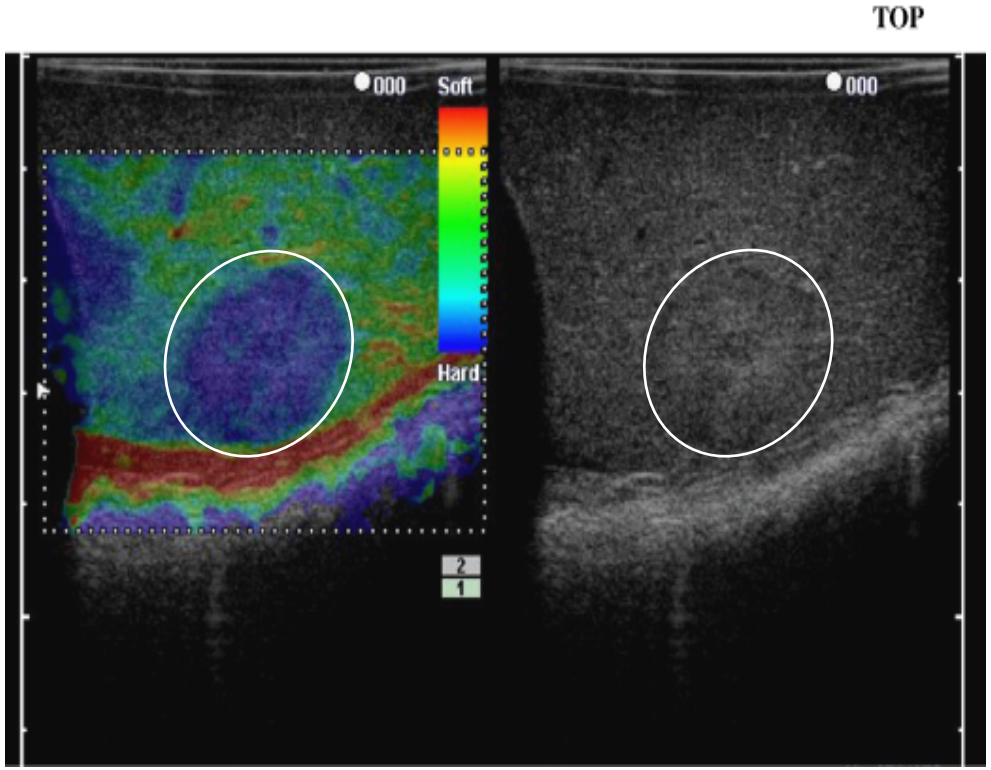
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Colon adenocarcinoma; type D

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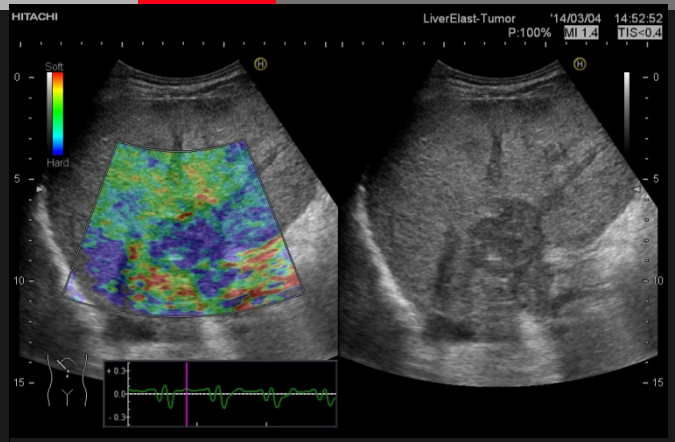


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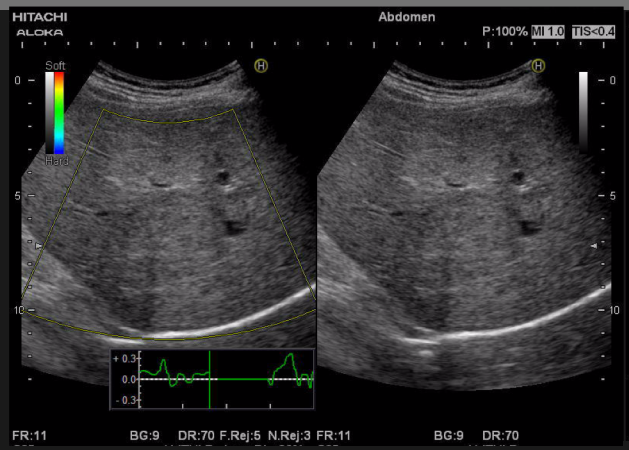
HI-RTE: C715 probe (focal lesions)

Kinki University Hospital, Faculty of Medicine, Yada MD.

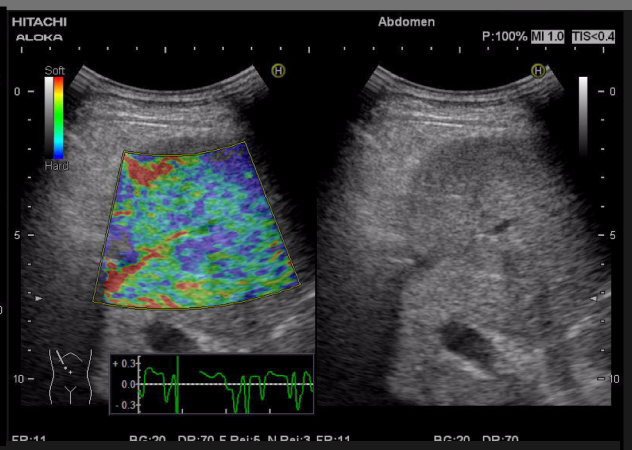
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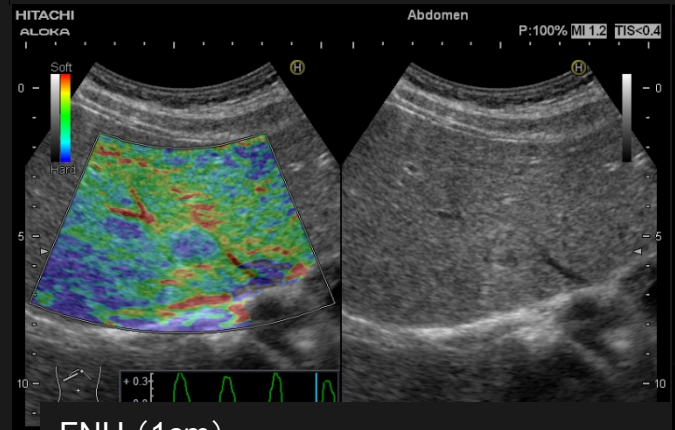
Hepatocellular carcinoma



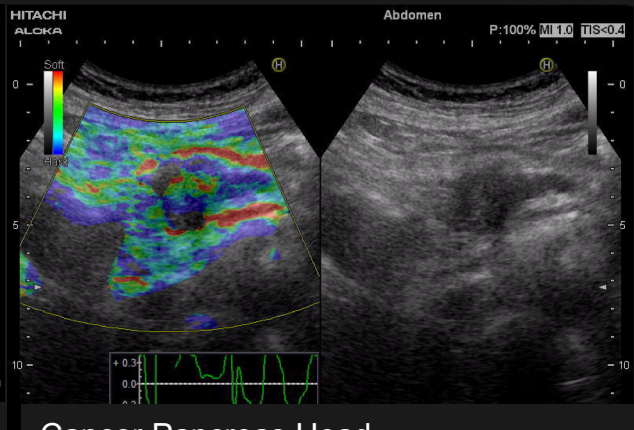
FNH（5cm）



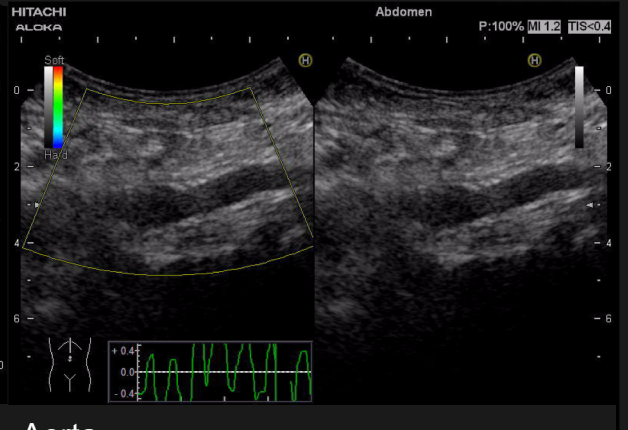
Recurrent HCC after RFA - TAE



FNH（1cm）



Cancer Pancreas Head



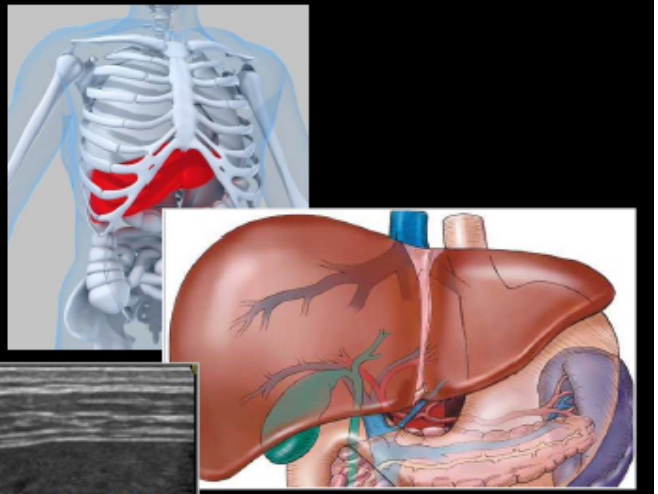
Aorta

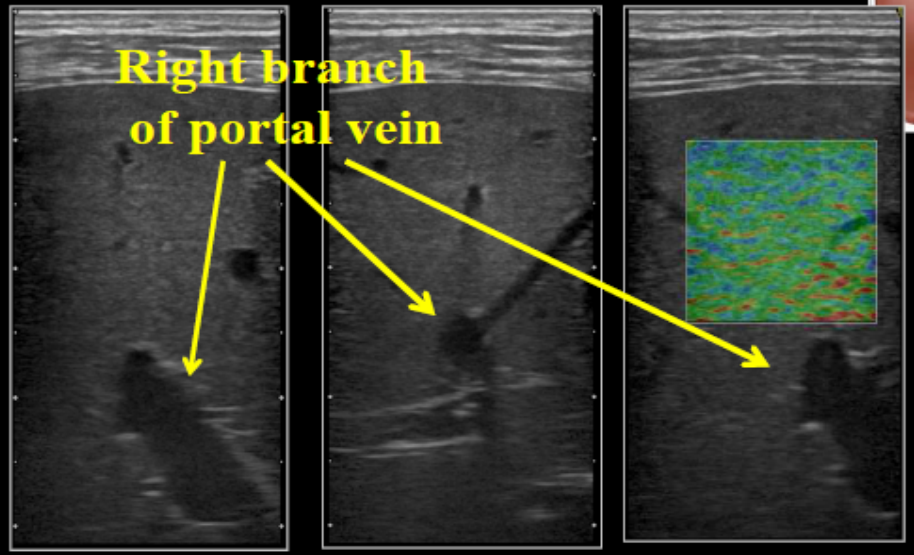
Methodology of RTE in LF evaluation

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SCAN TECHNIQUE

Observe right branch of portal vein in US image

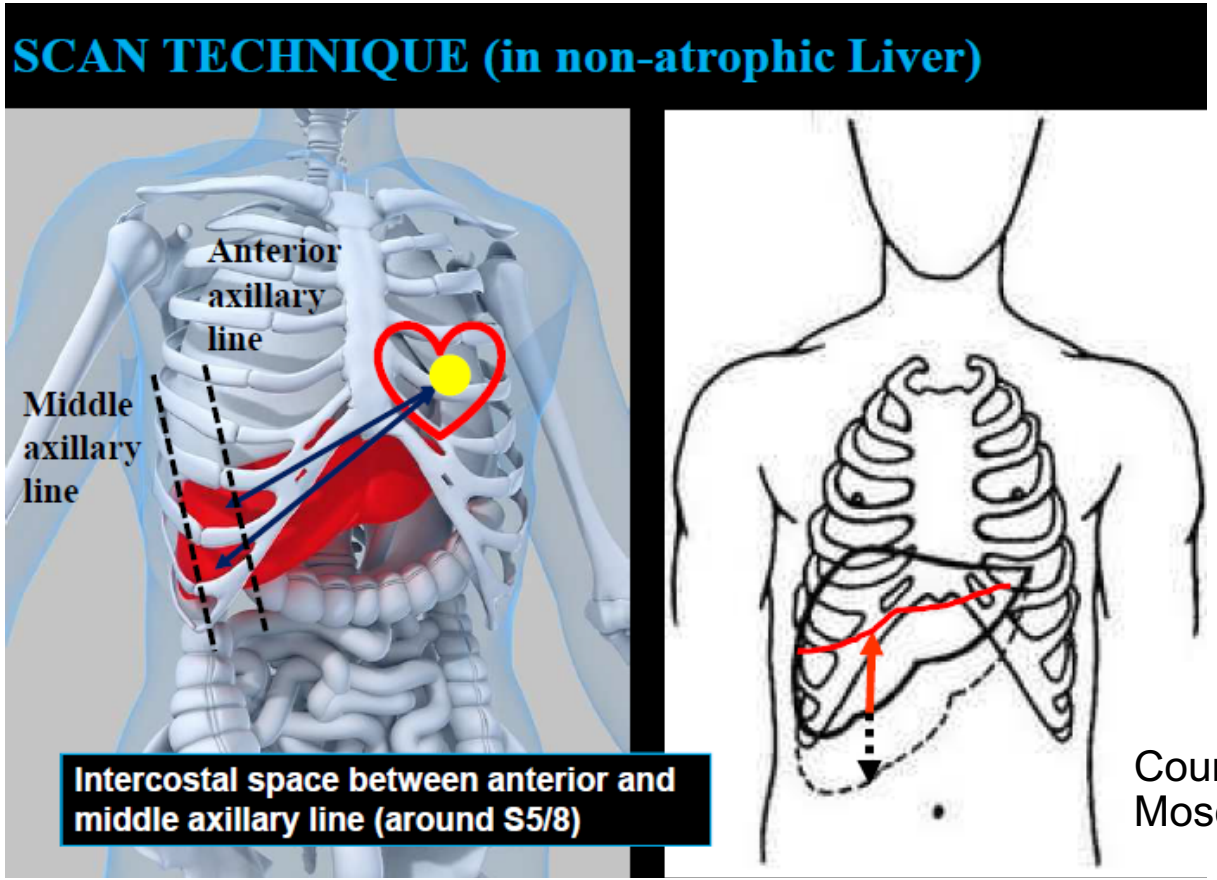


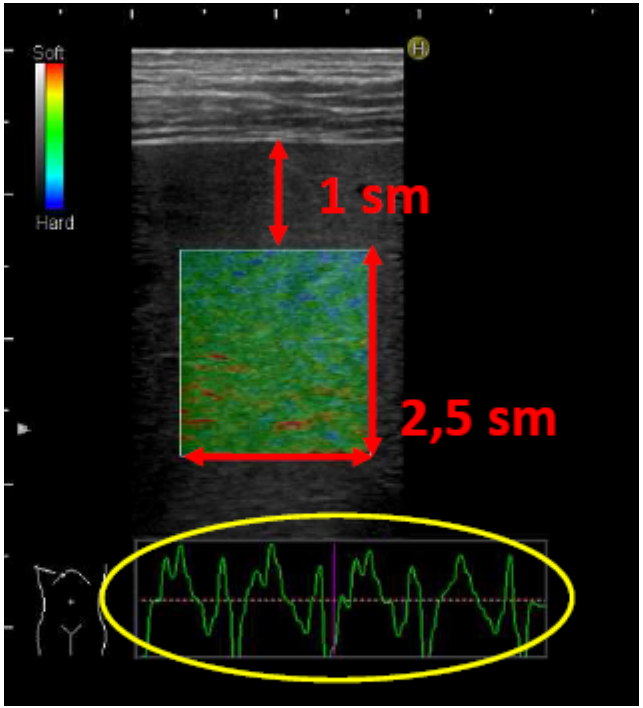


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Methodology of RTE in LF evaluation

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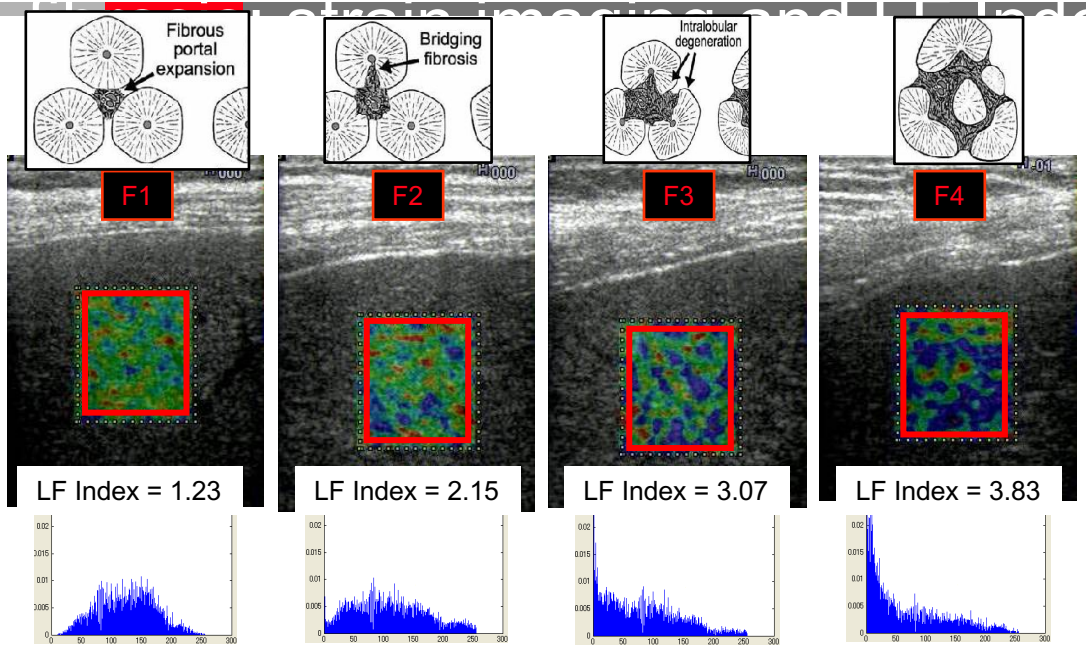


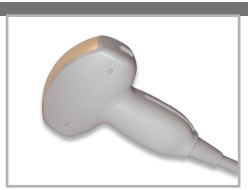
Courtesy: Dr.N.Postnova NVD Hospital Moscow

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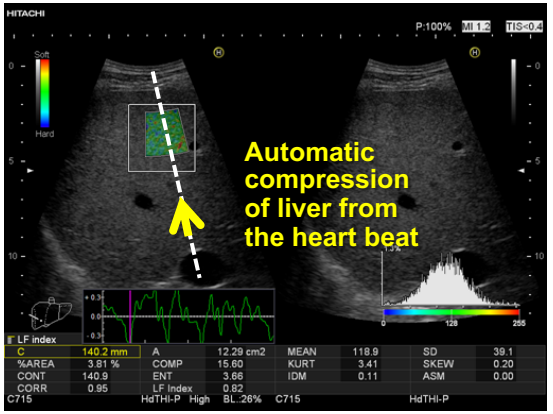
RTE (Real-time Tissue Elastography)

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convex transducer



- Use the same transducer as for B-mode imaging
- Wide FOV enables easy ROI position free from vessel artifacts and rib shadowing
- Good reproducibility
- Very good penetration for difficult-to-image patients

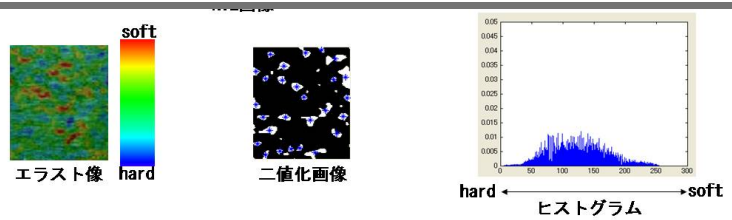
Fujimoto K. et al ; Kanzo 51(9) ; 539-541 (2010)

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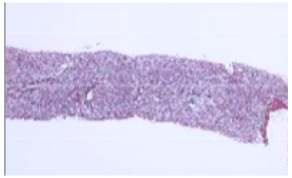
Strain histogram - background

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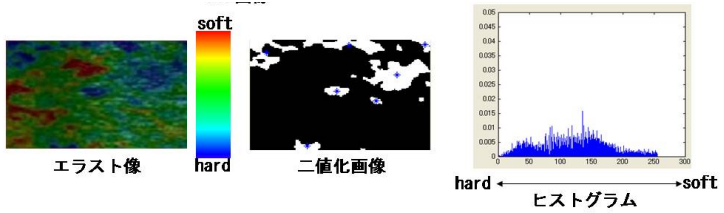
Colored area is comparatively uniformly in green



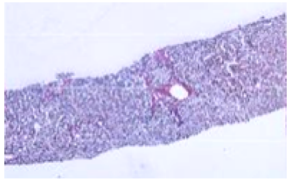
F1



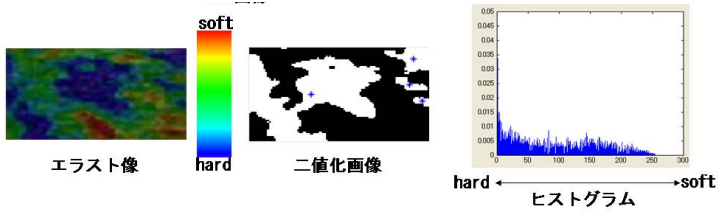
Blue color is mixed in a part of green area like worm holes.



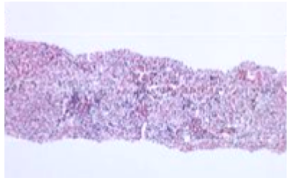
F2



Green and blue colors are mixed in the colored area.



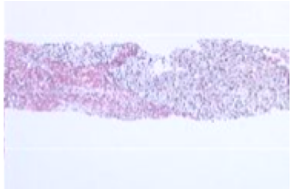
F3



Most colored area is displayed in blue.



F4



Presented in JDDW 2008
Courtesy: Dr. Kenji Fujimoto, National Hospital Organization, Minamiwakayama Medical Center

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Paramiters used to calculate LF index

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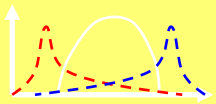
1. MEAN
(Average of relative strain)
Contents: Average value of strain in the ROI classified in 256 scales from the average of strain

2. SD
(Standard deviation)
Contents: standard deviation of relative strain in the ROI

3. %AREA
(Area of blue parts)
Contents: Ratio of pixels of relative strain in the ROI which is lower than threshold = Pixels lower than threshold/Pixels in the ROI

4. COMP
(Complexity)
Contents: Divide relative strain in the ROI in 2 types to detect the blue parts. Calculate the complexity from the boundary length and area of blue parts. Complexity = boundary length^2/Area

5.SKEW
(Skewness)
Contents: Tertiary center moment.
Used as a scale of asymmetry



6. KURT
(kurtosis)
Contents: Quartic center moment. This value gets bigger when a part of value is far from others.
If all valuesare near the average, this value gets smaller.



7. CONT
(Contrast)
Contents: This value gets bigger when matrix value is distributed far from main diagonal. In other words, it means big concentration difference.

8. ENT
(Equality)
Contents: This value gets bigger when values are allotted equally.

9. IDM
(Complication)
Contents: Measure Complication

10. ASM
(uniformity)
Contents: This value gets bigger when specific pairs of pixels exist a lot.

11. CORR
(correlation)
Contents: This value gets the biggest when the value of matrix actor is distributed on main diagonal. Equality in σ direction.
Access the texture's direction.

Item correlated to staging by itself

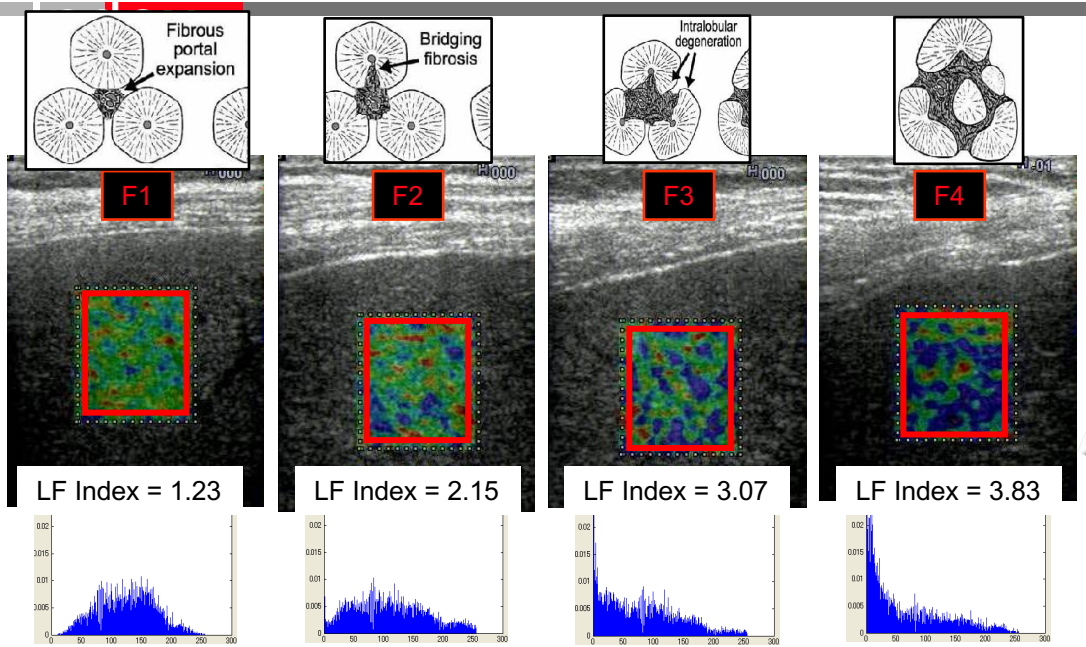
Item to evaluate the shape of Histgram graph

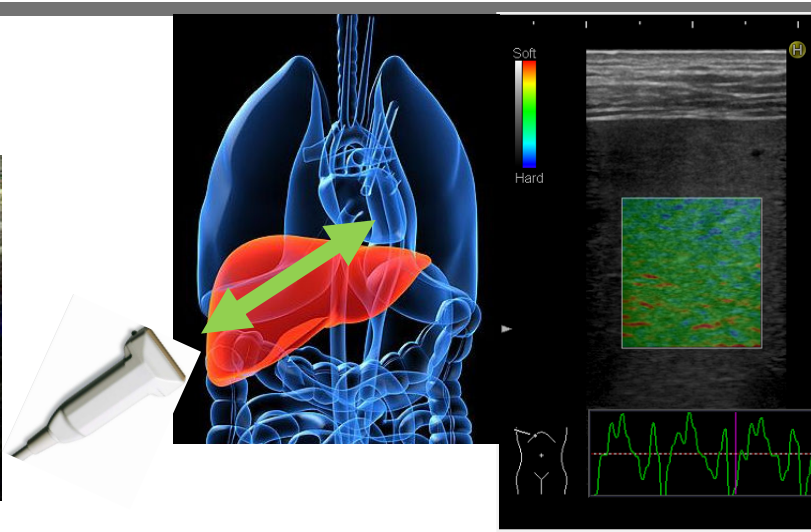
Item used for Texture analysis

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Strain Elastography

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

Fujimoto K. et al ; Kanzo 51(9) ; 539-541 (2010)

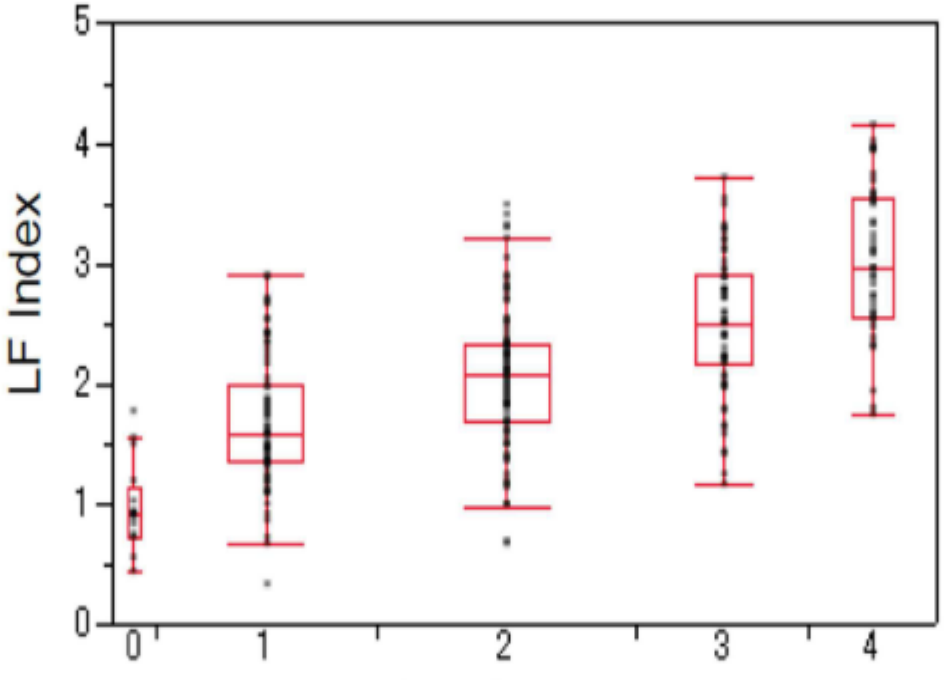
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Russian Liver Fibrosis study

Quantitative values of LFI according to the average values

	Average values
F0 - F1	2.29 (2.00 – 2.76)
F2	2.72 (2.30 – 3.22)
F3	3.21 (2.8 – 3.4)
F4	4.38 (3.56 – 5.09)

Japonese Liver Fibrosis study

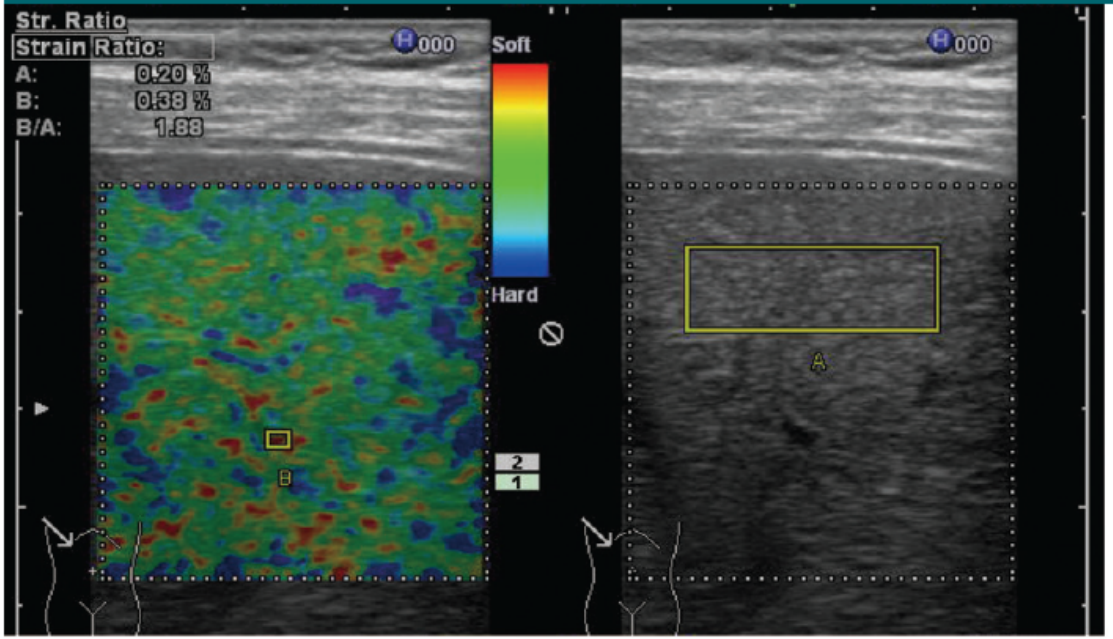


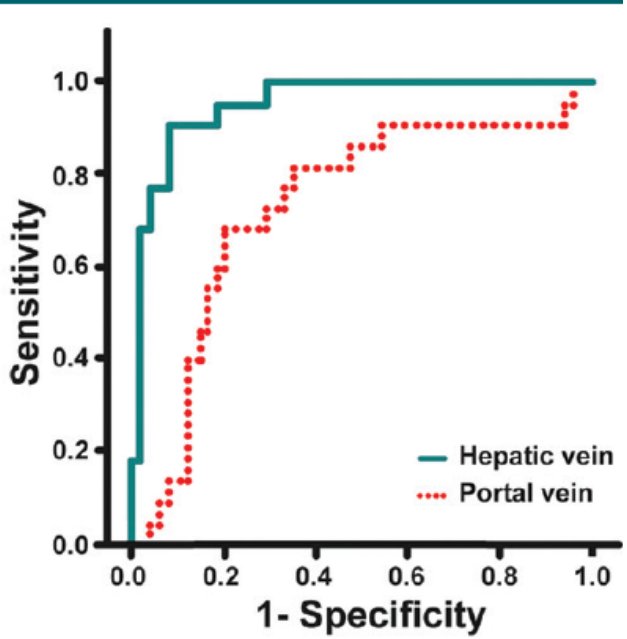
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Strain ration in LF evaluation

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Figure 2





a. b.

Figure 2: **(a)** The elastic ratio is measured between the tissue compressibility of the liver (right) and that of the intrahepatic small vessel (left). Red indicates that tissue is soft, and blue indicates that it is hard. Information about displacement becomes the basis of the elastic information and is obtained by using a supersonic wave signal. **(b)** Receiver operating characteristic (ROC) curves of the elastic ratio obtained by using the hepatic vein or portal vein as an internal control.

Radiology - February 2011 - Koizumi Hirooke - Liver Fibrosis with Chronic Hepatitis C

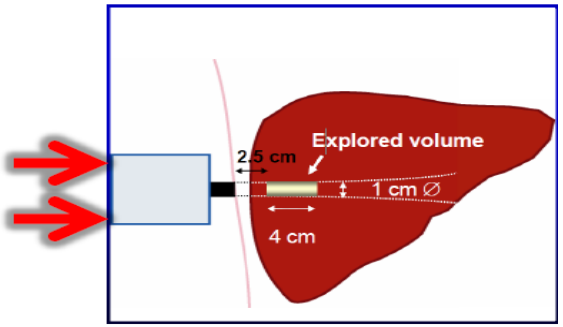
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Transient elastography

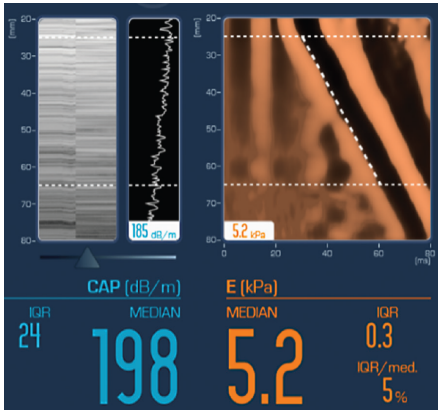
- Low frequency and low amplitude mechanical vibration by probe
- Propagation velocity of pressure wave depends on on tissue stiffness (Young's modulus, $E=3\rho V^{2)}$





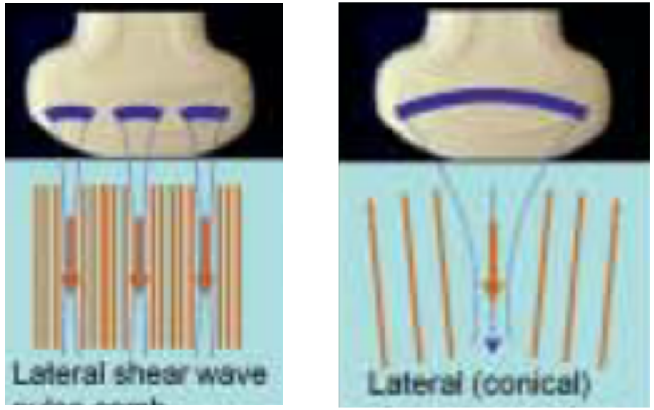


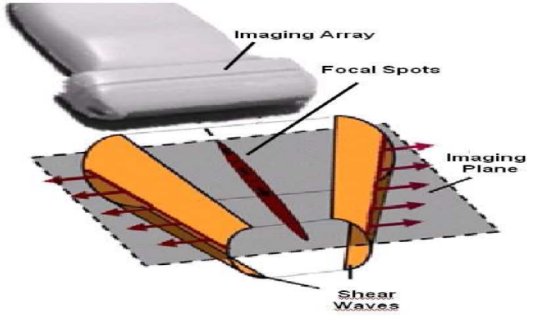


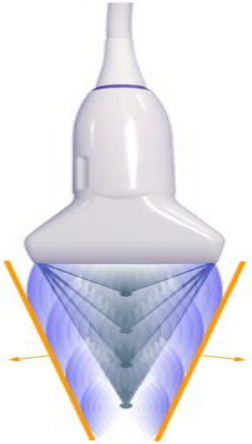


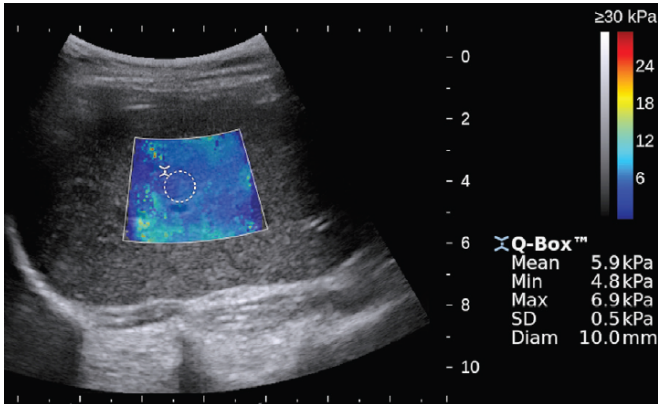
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Shear Wave Elastography (2D SWE)



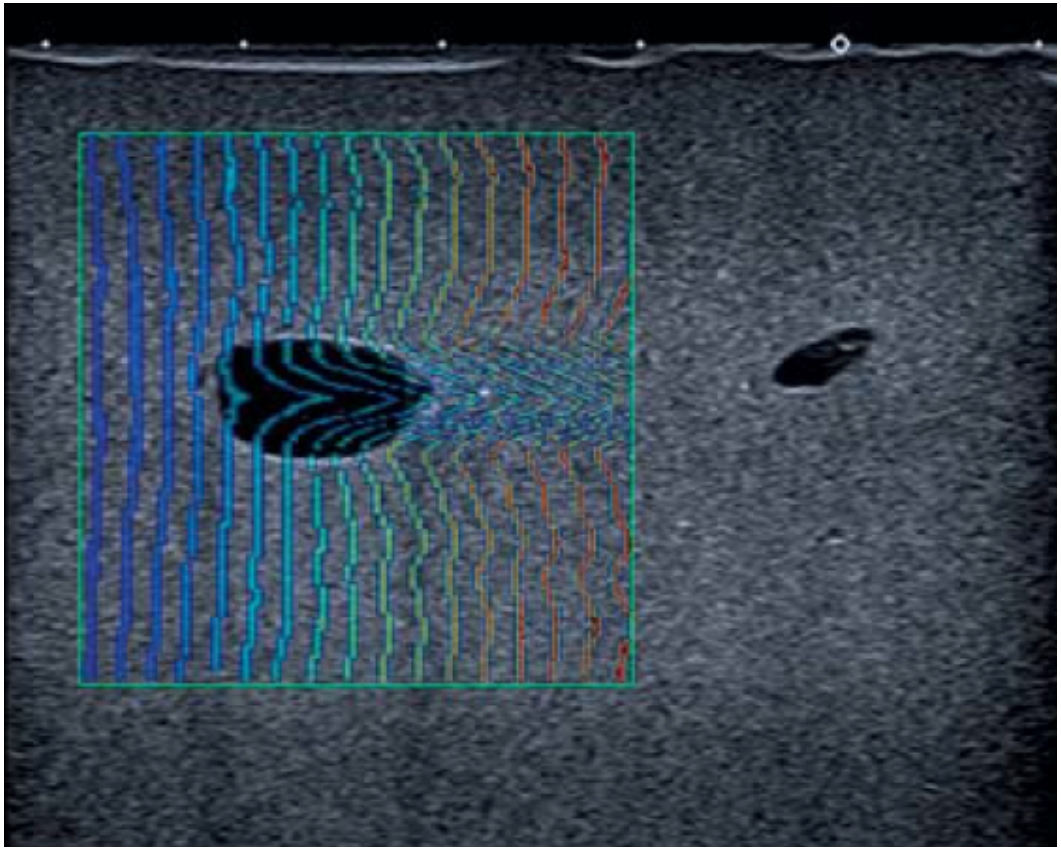






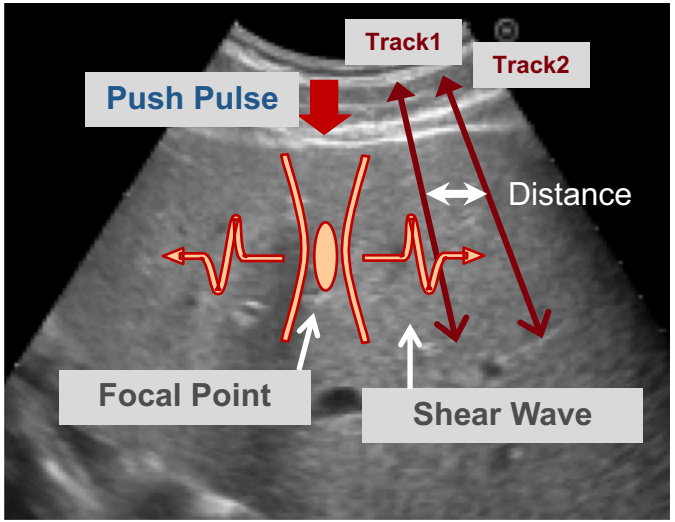
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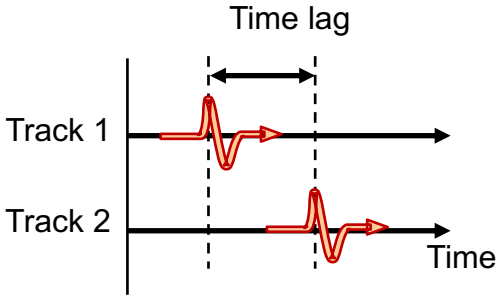
Shear Wave Elastography (2D SWE)



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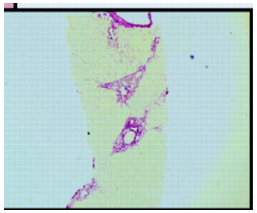
SWM (point sheare wave measurement)



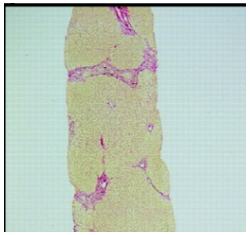


Vs = Distance / Arrival time lag

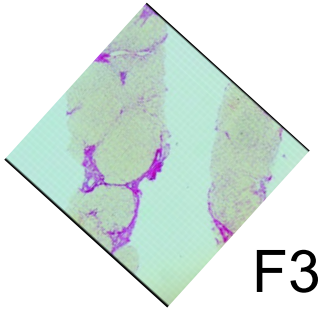
- Calculate Propagation Speed:
  - Tx. Rx. "**Track Pulse (T1,T2)**" continuously
  - Detect arrival time at each position



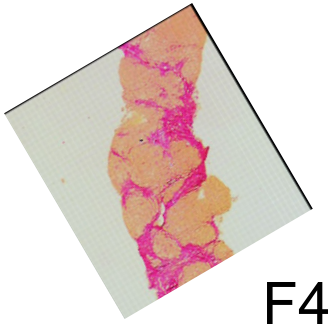
F1



F2



F3

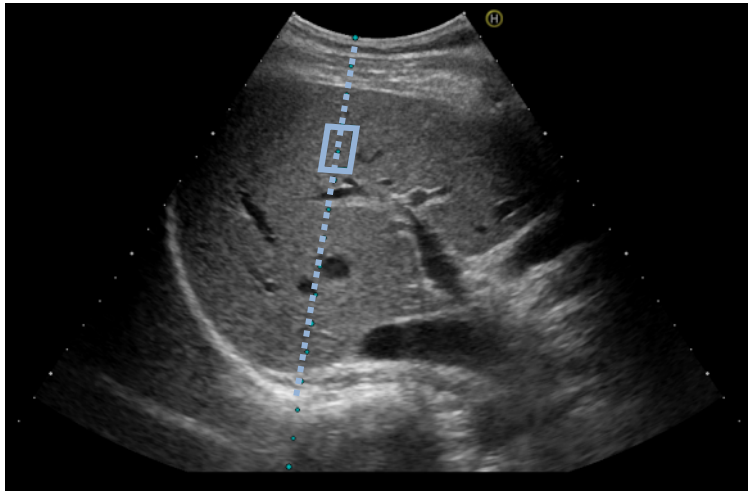


F4

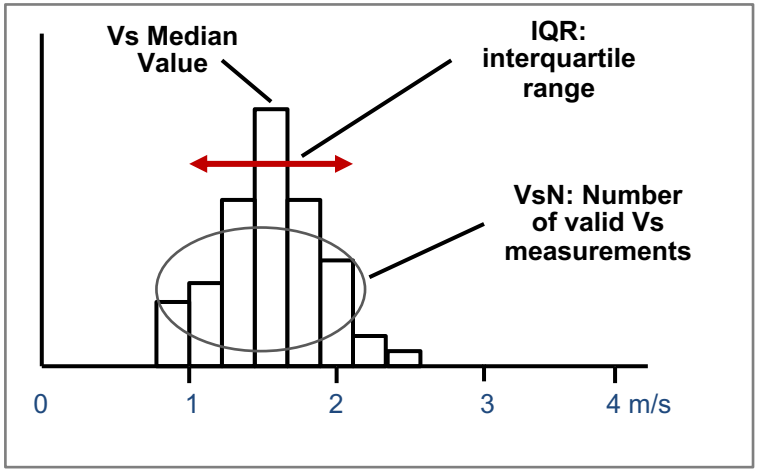
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SWM: Measurement Result (Vs / IQR / VsN)

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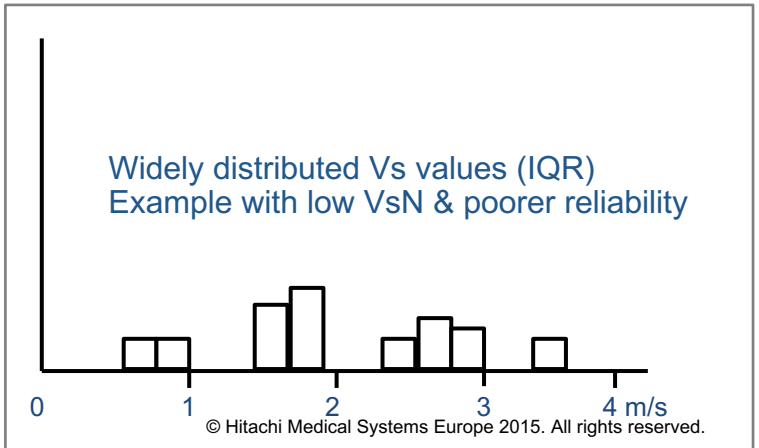


Histogram analysis



Vs : Median Value of the histogram
IQR : Interquartile range of Vs values (±25% of the median)
VsN : Success rate of the Vs (reliability indicator)

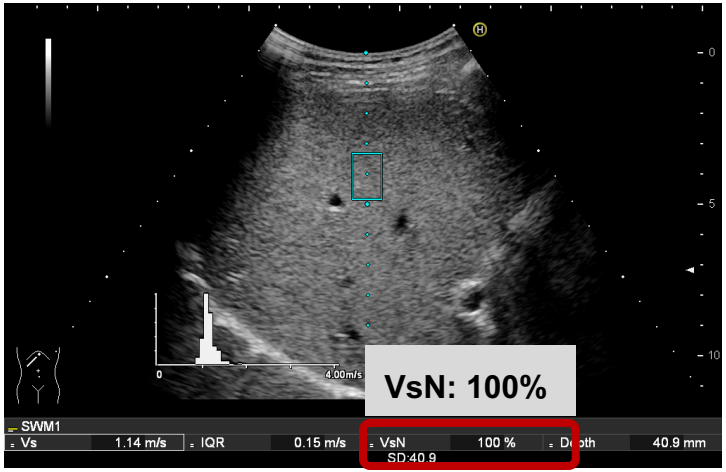
NOTE: If IQR is varied when VsN is high, the variation can be regarded as disease-related.

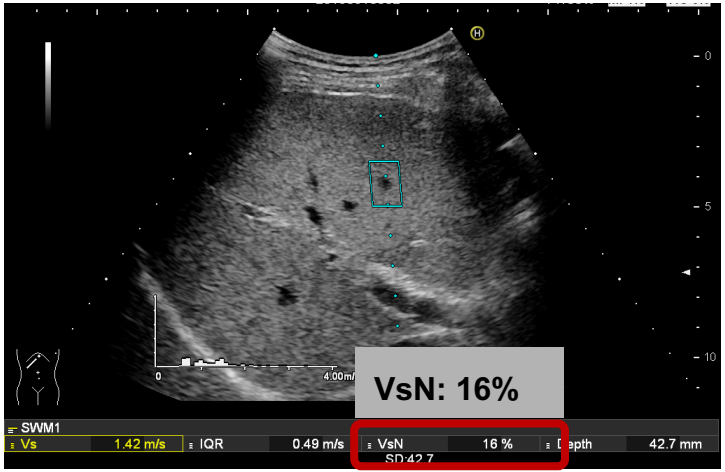


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SWM : Reliability Indicator, VsN (in-vivo examples)

- Higher VsN represents a valid detection of the shear wave propagation velocity.
- Lower VsN represents an inaccurate detection due to the propagation across vessels, hypoechoic regions (shadowing) or body motion.





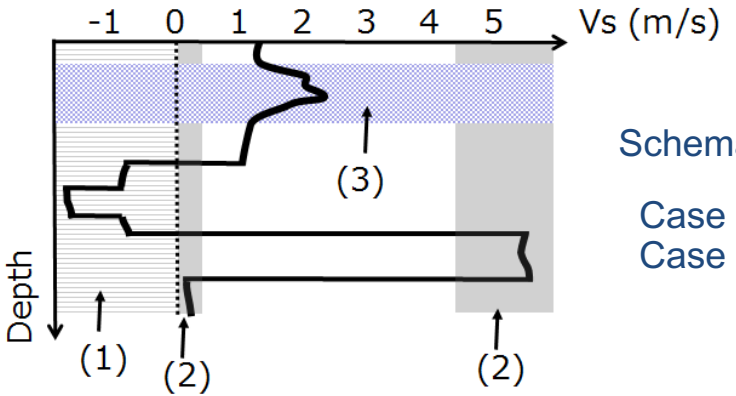
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SWM: Calculation of VsN

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- Rejection conditions:
  - Vs less than or equal to zero (1)
  - Outside a certain defined range of Vs (2): 0.7-4m/s (1.47-48kPa)
  - When phase fluctuations are observed at a particular depth (3) (fluctuations are mainly generated by small blood vessels and/or body motion)

$$\text{VsN (\%)} = \frac{\text{(Total \# Vs pts measured)} - \text{(Rejected \# Vs pts)}}{\text{(Total \# Vs pts measured)}} \text{ X } 100$$



Schematic of 3 rejection conditions:

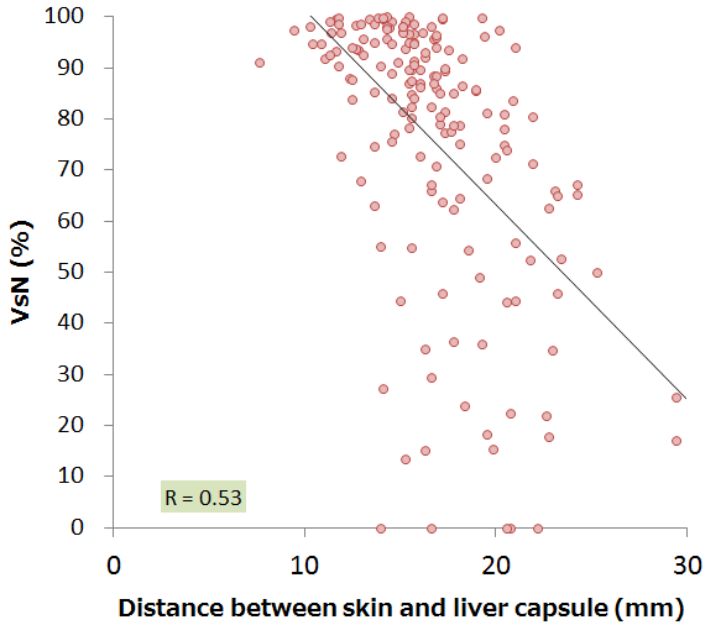
Case (1),(2) : Relative to the Vs axis (horizontal)
Case (3) : Relative to the depth axis (vertical)

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SWM : In-vivo Results / VsN and Skin-Liver capsule depth

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- VsN is related to the skin-to-liver capsule depth
- A skin-to-liver depth > 20 mm, tended to give poor VsN values (< 60%).



MEDIX Vol.63, 2015 (in press) By courtesy of Yada MD, Prof. Kudo, Kinki University, Japan.

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Median values of liver stiffness

Study based on 445 patients

Reliability index VsN > 50% improves diagnostic performance of SWM

Fibrosis Stage	SWM, kPa (interquartile range)
Mild/No fibrosis (F0-F1)	**4.8** (4.0-5.7)
Significant fibrosis (F2)	**7.2** (5.7-9.0)
Advanced fibrosis (F3)	**8.5** (6.7-9.5)
Liver cirrhosis (F4)	**14.0** (11-17)

	Ruling-in F≥2 (95% CI)	Ruling-out F≥2 (95% CI)	Ruling-in F=4 (95% CI)	Ruling-out F=4 (95% CI)
Cutoff, KPa	**6.78**	**5.55**	**9.15**	**8.41**
Sensitivity	76.9	**90.6**	83.3	**90.6**
Specificity	**90.3**	72.2	**90.1**	82.2

Ferraioli et al., J Gastrointestin Liver Dis, 2017

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the shear modulus increases with vascular and interstitial pressure

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- Deep inspiration
- Food
  - Investigation minimum 3 hours after eating
  - Coffee, smoking drinking – stop as above
- Alcoholic hepatitis
  - Stifness decreases after 1-4weeks abstinence
- Exercises
  - Minimum rest 10min
- **Hepatic inflamation**
- **Obstructive cholestasis**
- **Hepatic congestion**
- **Acute toxic hepatitis (drug induced)**
- **Amyloidosis**
- **Lymphomas**
- **Extramedullary hamopoiesis**
- **Steatosis???**

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Other factors influencing SW measurments

- Depth dependance
  - Minimum 1cm below the capsule not deeper than 5cm
- Frequency dependance
  - Higher frequency transducer – higher stifness values
- Region of the liver (left lobe bigger variations)

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Treatment follow up

“Data in patients undergoing IFN-free antiviral therapies suggest that liver stiffness

rapidly declines during treatment, even in patients with advanced fibrosis and cirrhosis.

This decline appears to reflect the reduction

in liver inflammation, restoration of liver function and the

decrease in portal pressure, like an effect of HCV eradication”

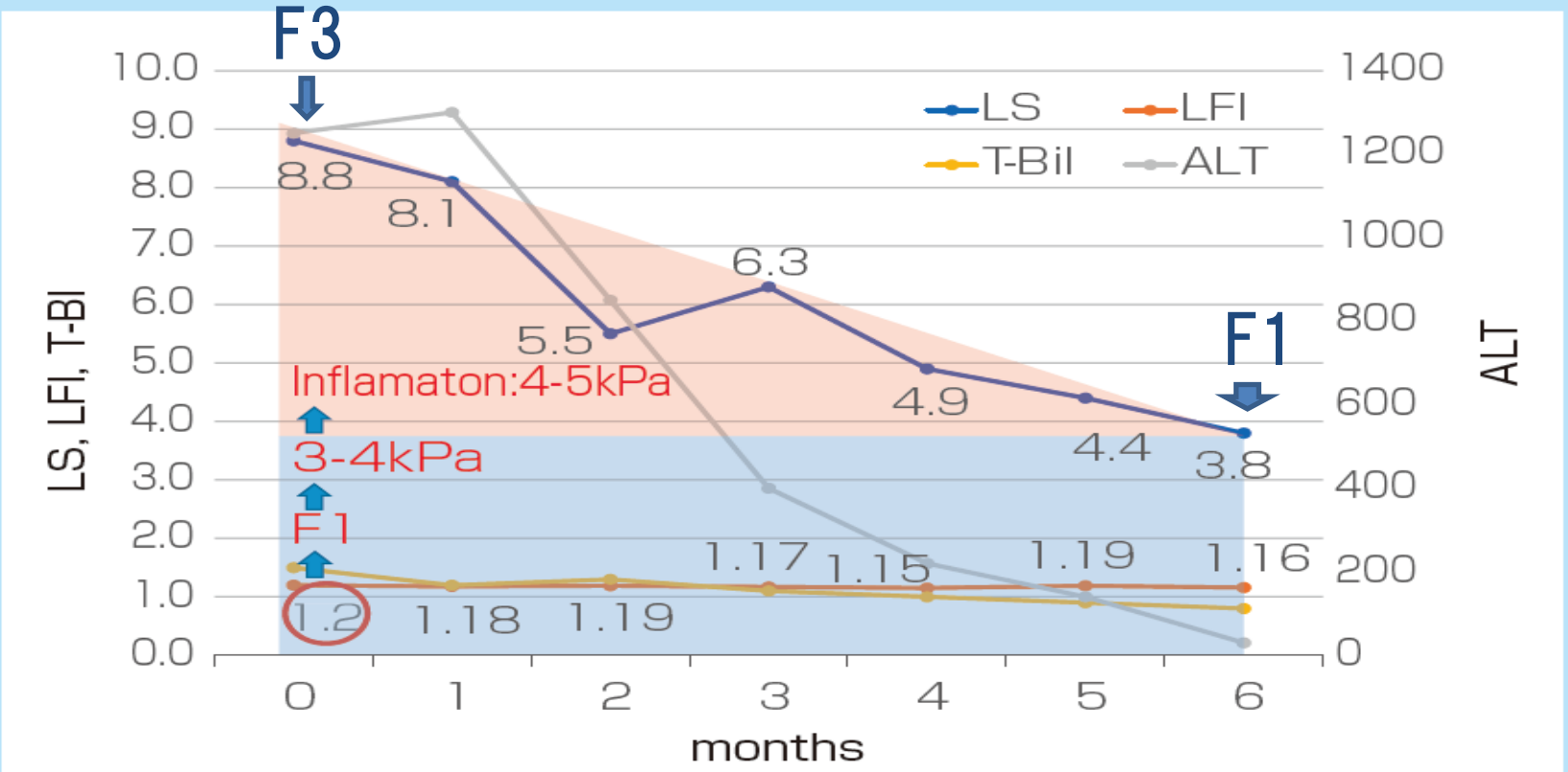
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Complete solution

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- SWM
  - Results in absolute values of spead or elasticity modulus
  - Results not influenced by:
    - steatosis
- RTE
  - Works in ascites
  - Results are not influecnced by:
    - acute inflamation
    - joundice
    - congestion (portal hypertension)

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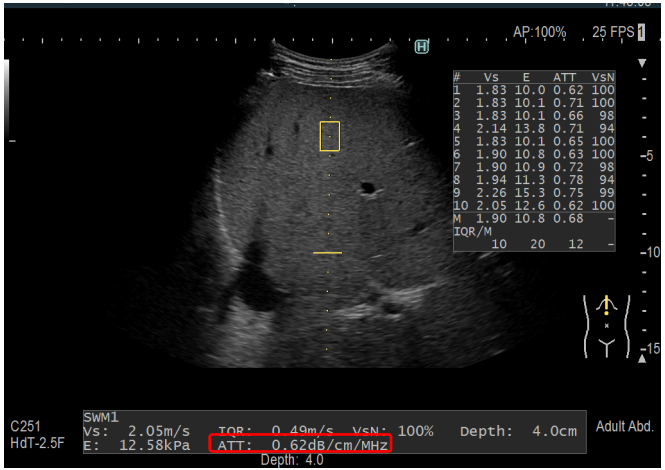

F3
F1
LS
LFI
T-Bil
ALT
LS, LFI, T-Bil
ALT
months
Inflamaton:4-5kPa
3-4kPa
F1
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1400
1200
1000
800
600
400
200
0
0
1
2
3
4
5
6
8.8
8.1
5.5
6.3
4.9
4.4
3.8
1.2
1.18
1.19
1.17
1.15
1.19
1.16

b

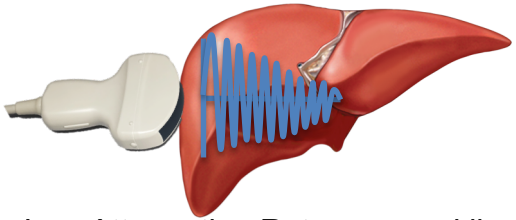
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What Is the Attenuation Measurement Function (ATT)?

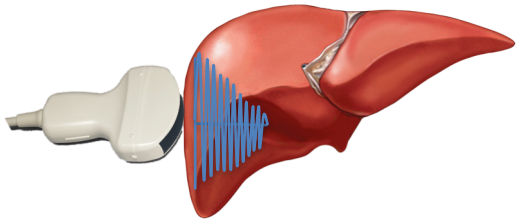
- Fat tissue increases the ultrasonic attenuation.
- ATT is a function to assess the attenuation coefficient generated in the ultrasonic propagation process.
- The extent of fatty liver can be evaluated and estimated by attenuation coefficient value.



Attenuation of normal liver is approx. 0.5〜0.6 (dB/cm/MHz)



Low Attenuation Rate – normal liver



High Attenuation Rate – fatty liver tissue

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ATT concept

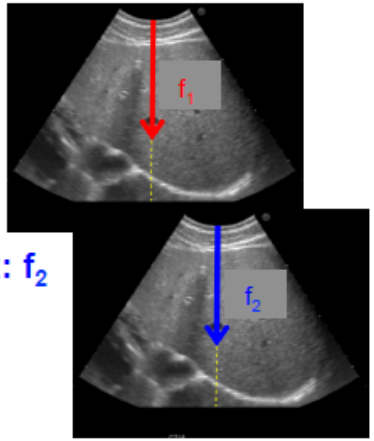
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ATT estimates the attenuation coefficient by calculating the amplitude difference of received signals in two frequencies and determining the slope on its graph (dual frequency method).

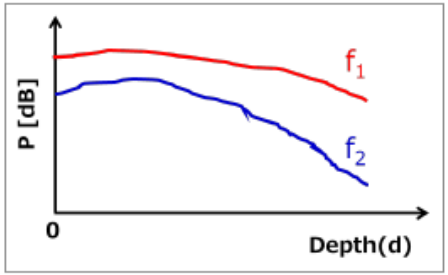
- ATT eliminates the effects of structures along the propagation path such as microvasculature on brightness variation using the Dual Frequency method.

1st Tx: f_1

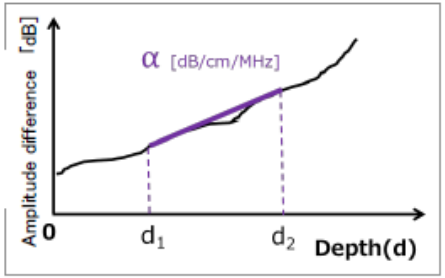
2nd Tx: f_2



Tx and Rx in two different frequencies along the same beamline ($f_1 < f_2$)



Estimates the attenuation coefficient (α) by calculating the amplitude difference of Rx signals and determining the slope



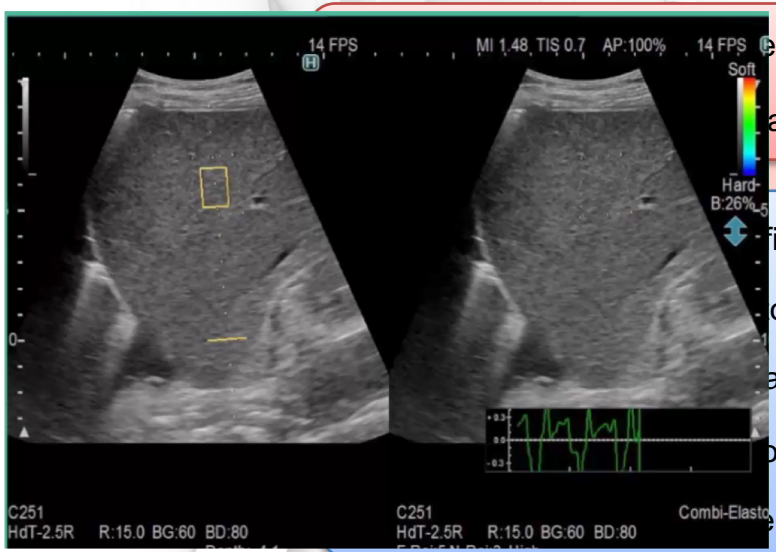
$$\text{ATT [dB/cm/MHz]} = \frac{(P_{f1}(d2) - P_{f2}(d2)) - (P_{f1}(d1) - P_{f2}(d1))\ \text{[dB]}}{2(d_2 - d_1)\ \text{[cm]} \cdot (f_2 - f_1)\ \text{[MHz]}}$$

where, Signal power of Rx at $f_1 = P_{f1}(d)$ and at $f_2 = P_{f2}(d)$
Amplitude difference between $P_{f1}(d)$ and $P_{f2}(d)$ at Depth d_1 =
$= P_{f1}(d_1) - P_{f2}(d_1)$, at Depth $d_2 = P_{f1}(d_2) - P_{f2}(d_2)$
Propagation distance = $2(d_2 - d_1)$ and Frequency difference = $(f_2 - f_1)$

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Combi-Elasto supports the comprehensive evaluation of diffuse liver diseases.



ex calculated from total amount of

agation velocity (median of the Vs)

ibrosis stage calculated from

otal amount of strain histogram and Vs.

activity grade calculated from

otal amount of strain histogram and Vs.

e (degree of attenuation)

Yada N, et al: Diagnosis of Fibrosis and Activity by a Combined Use of Strain and Shear Wave Imaging in Patients with Liver Disease. Digestive Diseases 2017; 35(6): 515-520. doi: 10.1159/000480140.

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Combi Elasto results

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- Fibrosis and inflammation can be evaluated respectively.
- Less dependent on operators' technique, simple operation.



Quantitative index

- Fibrosis F value
- inflammation A value
- Attenuation ATT

Items	Unit	Contents
Vs	m/s	Propagation velocity of shear wave (median of Vs group)
E	kPa	Vs value converted to kPa
ATT	dB/cm/MHz	Attenuation
F		Fibrosis related index
A		Inflammation related index
LFI		LF Index
IQR/M	%	±25% range median/Median

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F index, A index

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- The calculation formulas

➢ F Index = -0.0199×MEAN-0.00685×STD+0.00680×AREA
-0.0214×COM+42.1×ASM+0.00114×CON+8.21×COR+1.67×ENT-1.34xIDM
-0.0772xSKEW+0.0862xKURT+1.39xVs-12.3

➢ A Index = -0.0370×MEAN-0.00189×STD-0.0218×AREA
-0.00590×COM+2.66×ASM+0.000579×CON+15.1×COR-0.360×ENT-5.16xIDM
+0.188xSKEW-0.216xKURT+0.575xVs-7.41

The calculation formulas are based on the results of multicenter study.

Yada N, Tamaki N, Koizumi Y, Hirooka M, Nakashima O, Hiasa Y, Izumi N, Kudo M. Digest Dis, 2017;35(6):515-520. DOI: 10.1159/000480140

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Table 3. Comparison of diagnostic ability of each evaluation value

Diagnosis level	Evaluation value	Cutoff value	Sensitivity	Specificity	Accuracy	AUROC
F≥1	F index	1.162	0.761	0.759	0.760	0.871
	V_s	1.258	0.770	0.778	0.771	0.826
	LF index	1.901	0.746	0.745	0.746	0.809
F≥2	F index	1.524	0.740	0.739	0.740	0.804
	V_s	1.507	0.735	0.735	0.735	0.794
	LF index	2.282	0.587	0.585	0.585	0.621
F≥3	F index	1.748	0.750	0.750	0.750	0.826
	V_s	1.633	0.724	0.725	0.725	0.809
	LF index	2.322	0.553	0.555	0.554	0.594
F=4	F index	1.770	0.690	0.699	0.698	0.799
	V_s	1.617	0.667	0.662	0.662	0.778
	LF index	2.361	0.571	0.573	0.573	0.584
A≥1	A index	0.982	0.868	0.867	0.868	0.936
	V_s	1.220	0.769	0.767	0.769	0.852
A≥2	A index	1.270	0.689	0.690	0.690	0.741
	V_s	1.540	0.702	0.701	0.702	0.750
A=3	A index	1.366	0.667	0.704	0.704	0.763
	V_s	1.643	0.667	0.667	0.667	0.753

The diagnostic ability of F index was the best for each fibrosis stage. In Activity diagnosis, the diagnostic ability of A index is not inferior to V_s.

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EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Long Version)

EFSUMB-Leitlinien und Empfehlungen zur klinischen Anwendung der Leberelastographie, Update 2017 (Langversion)

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