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GUIDE
Multiparametric Assessment of the Liver

Viscoelasticity, Attenuation and Sound Speed Quantification

There is a clear need for new modalities to safely and noninvasively assess hepatic steatosis, inflammation and fibrosis. These noninvasive imaging and blood biomarker assessments can be used as an alternative to information gained on liver biopsy:[1]

• The stage of the fibrosis has been proven to correlate to the stiffness of the liver, which is also correlated to the velocity of the shear wave.[2,3,4]

• The level of the inflammation is being proved to correlate to the viscosity of the liver, which is also correlated to the shear wave dispersion.[5,6]

• The stage of the steatosis has been proven to correlate to the attenuation and to the sound speed of the liver. It seems that the combination of both improves diagnostic performance for staging steatosis.[6,7]

ShearWave™ PLUS Elastography (SWE) is a 2D imaging mode[2,3,4] that provides a view of the organ and a quantitative map of stiffness over a region of interest.

Viscosity PLUS (Vi PLUS) is a 2D imaging mode that provides a view of the organ and a quantitative map of viscosity over a region of interest.

Attenuation PLUS (Att PLUS) and Sound Speed PLUS (SSp PLUS) are quantitative measurements through a region of interest.

Att PLUS & SSp PLUS

① The patient lies supine with the right arm in maximal abduction.

② Choose C6-1X probe/Abdominal/Liver or Abdomen preset.

③ Apply a generous layer of gel on the patient.

④ Locate the 7th to 9th right intercostal space, and place the probe in between the ribs, parallel to the intercostal space.

⑤ Find the optimal acoustic window:

   a. Ensure the probe length is parallel to the ribs, and its axis is orthogonal to the liver capsule.

   b. Apply strong pressure on the probe to eliminate acoustic shadowing from the loss of contact on the edges of the probe.

⑥ Press « Att PLUS & SSp PLUS ROI » available on the touchscreen.

⑦ Ensure the Region of Interest is totally free of vessels, nodules or structures other than liver parenchyma.

⑧ Ask the patient to hold his or her breath so you can stabilize the image.

⑨ Press « Att PLUS & SSp PLUS Acquisition », available on the touchscreen.
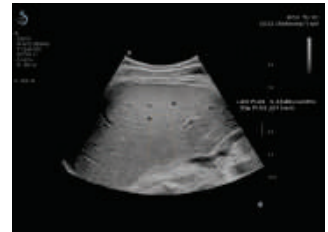
Repeat acquisitions 3 times to collect 3 valid measurements of liver attenuation and speed of sound.

The accepted mean value of liver attenuation and liver sound speed is the average value of the 3 independent values.

The sound speed in the liver is 1385 m/s - 1705 m/s.

The attenuation coefficient in the liver is 0,20 dB/cm/MHz - 2,0 dB/cm/MHz.

ShearWave™ PLUS and Vi PLUS

(1)(2)(3)(4)   Repeat steps 1 to 4.

(5)   Find the optimal acoustic window before engaging
the SWE & Vi PLUS modes.
   a. Press "AutoTGC".
   b. Ensure the liver area is free of major vessels.
   c. Ensure the probe length is parallel to the ribs, and its axis
      orthogonal to the liver surface.

(6)   Apply strong pressure on the probe to eliminate acoustic
shadowing from the loss of contact at the probe edges.

(7)   Ask the patient to hold his or her breath.

(8)   Activate "SWE" mode.

(9)   Stabilize your hand, the probe and the image. (Complete stillness is required.)

(10)   Position the SWE and Vi PLUS boxes. (Vi PLUS box is a duplicate of SWE box.)

   a. Over an area of uniform parenchyma.

   b. Avoid vessels in the middle of the box.

   c. Avoid visible nodules, gallbladder or any other structures.

   d. At least 2 cm below the liver capsule, and ideally centered
      at around 5 cm in depth.

(11)   When the image has stabilized for 3 seconds, press "Measure".

(12)   Adjust the Q-Box diameter to 15-20 mm.

(13)   Place the Q-Box preferably at the center of the SWE and Vi PLUS boxes
(Vi PLUS Q-box is a duplicate of SWE Q-Box), avoiding large vessels
if any, and the edges of the boxes.

(14)   Reject any Q-Box location that achieves less than 90% stability index SI.
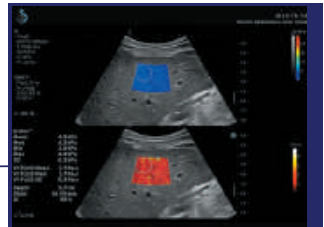
Repeat acquisitions 3 times to collect 3 valid measurements of liver stiffness and liver viscosity.

The accepted mean value of liver stiffness and liver viscosity is the average value of the 3 independent values.

Do not continue scanning in SWE and Vi PLUS modes while the patient is breathing. Complete stillness should be achieved before entering the combined modes.
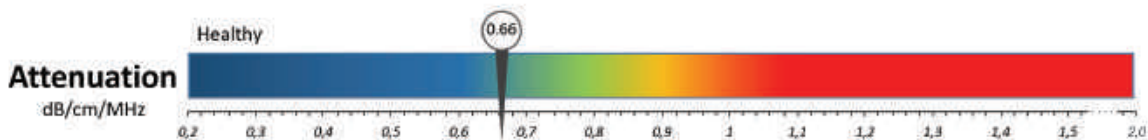
If a signal is lacking and all conditions above are satisfied, switch "Optimization" setting to "Penetration".

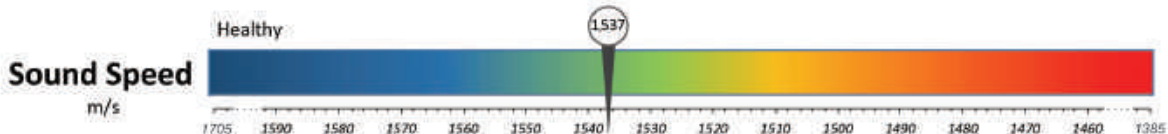The system is able to provide the stiffness and viscosity quantification in real time in the entire box. To activate this feature, go to Syst. Config./System Display/Exam/Scanning Preferences and check "Auto Display of Real Time Median". Please follow the same guidelines provided above from step #1 to step #11, but press "Freeze" instead of "Measure". Be careful that no structures other than liver parenchyma are in the box; otherwise stiffness or viscosity values can be overestimated.
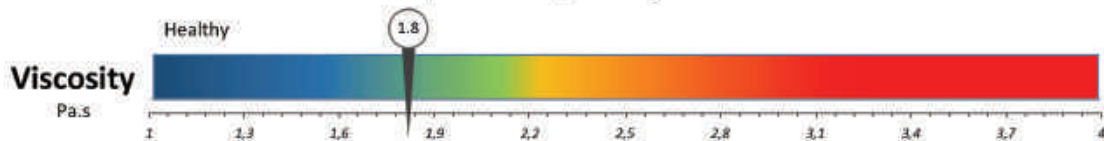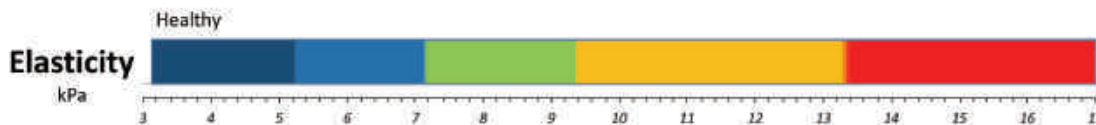
Suggested thresholds

Attenuation
dB/cm/MHz

Healthy ··· 0.66

| 0,2 | 0,3 | 0,4 | 0,5 | 0,6 | 0,7 | 0,8 | 0,9 | 1 | 1,1 | 1,2 | 1,3 | 1,4 | 1,5 | 2,0 |

The higher the Attenuation value, the higher the liver fat content.

Sound Speed
m/s

Healthy ··· 1,537

| 1705 | 1590 | 1580 | 1570 | 1560 | 1550 | 1540 | 1530 | 1520 | 1510 | 1500 | 1490 | 1480 | 1470 | 1460 | 1385 |

The lower the Sound Speed value, the higher the liver fat content.

Viscosity
Pa.s

Healthy ··· 1.8

| 1 | 1,3 | 1,6 | 1,9 | 2,2 | 2,5 | 2,8 | 3,1 | 3,4 | 3,7 | 4 |

The higher the viscosity value, the higher the liver inflammation level.[*]

Elasticity
kPa

Healthy

| 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |

The higher the stiffness value, the higher the liver fibrosis stage.[**]

*Further on-going studies are warranted to confirm this finding.
**NASH Contact – For more details, please refer to the Guide for assessing liver fibrosis and steatosis.

References

Ronot M, Rautou P-E, Dioguardi Burgio M et al. Prospective comparison of shear-wave elastography, CAP and conventional ultrasound for non-invasive detection and grading of steatosis. EASL LiverTree™, 2017 Apr; 168432

Dioguardi Burgio M, Imbault M, Ronot M, et al. Ultrasonic Adaptive Sound Speed Estimation for the Diagnosis and Quantification of Hepatic Steatosis: A Pilot Study. Ultraschall Med. 2019;40(6):722-733.

Imbault M, Faccinetto A, Osmanski BF, et al. Robust sound speed estimation for ultrasound-based hepatic steatosis assessment. Phys Med Biol. 2017;62(9):3582-3598.

Internal R&D Data; 2016 June 14

Example of Liver Report

ShearWave™ Elastography

	Depth	Diam	SI	Elasticity					Velocity				
				Min	Max	Mean	Med	SD	Min	Max	Mean	Med	SD
Q-Box 1	4.2 cm	16.00 mm	98 %	3.8 kPa	5.2 kPa	4.4 kPa	4.4 kPa	0.3 kPa	1.1 m/s	1.3 m/s	1.2 m/s	1.2 m/s	0.0 m/s
Q-Box 2	3.8 cm	16.00 mm	92 %	3.9 kPa	4.9 kPa	4.3 kPa	4.3 kPa	0.2 kPa	1.1 m/s	1.3 m/s	1.2 m/s	1.2 m/s	0.0 m/s
Q-Box 3	4.2 cm	16.00 mm	92 %	4.0 kPa	6.0 kPa	4.7 kPa	4.6 kPa	0.4 kPa	1.2 m/s	1.4 m/s	1.3 m/s	1.2 m/s	0.1 m/s
Mean	4.1 cm	16.0 mm		3.9 kPa	5.4 kPa	4.5 kPa	4.4 kPa	0.3 kPa	1.1 m/s	1.3 m/s	1.2 m/s	1.2 m/s	0.0 m/s

Mean	4.5 kPa	1.2 m/s
Median	4.4 kPa	1.2 m/s
IQR	0.4 kPa	0.1 m/s
SD	0.2 kPa	0.0 m/s

Reference

Cassinotto C, Hepatology 2016, NAFLD/NASH patients

Fibrosis NASH CRN stage	Median (IQR)	AUROC (95%CI)	Youden Cut-off value (kPa)	Rule-out cut-off value (kPa)	Rule-in cut-off
F0-F1	6.0 (2.7)				
F2	8.0 (3.4)	0.86 (0.79-0.90)	8.9 (Sens: 68% | Spec: 94%)	6.3 (Sens: 90% | Spec: 50%)	8.7 (Sens: 71%
F3	12.0 (5.0)	0.89 (0.83-0.92)	9.3 (Sens: 84% | Spec: 83%)	8.3 (Sens: 91% | Spec: 71%)	10.7 (Sens: 71%
F4	17.0 (13.6)	0.88 (0.82-0.92)	10.0 (Sens: 95% | Spec: 69%)	10.5 (Sens: 90% | Spec: 72%)	14.4 (Sens: 58%

Viscosity PLUS

	Depth	Diam	Viscosity			Dispersion		
			Mean	Med	SD	Mean	Med	SD
Q-Box 1	4.2 cm	16.00 mm	1.5 Pa.s	1.5 Pa.s	0.4 Pa.s	4.1 (m/s)/kHz	4.1 (m/s)/kHz	0.8 (m/s)/kHz
Q-Box 2	3.8 cm	16.00 mm	1.5 Pa.s	1.5 Pa.s	0.3 Pa.s	3.9 (m/s)/kHz	4.0 (m/s)/kHz	0.7 (m/s)/kHz
Q-Box 3	4.2 cm	16.00 mm	1.4 Pa.s	1.4 Pa.s	0.2 Pa.s	3.8 (m/s)/kHz	4.0 (m/s)/kHz	0.9 (m/s)/kHz
Mean	4.1 cm	16.0 mm	1.4 Pa.s	1.4 Pa.s	0.3 Pa.s	3.9 (m/s)/kHz	4.0 (m/s)/kHz	0.8 (m/s)/kHz

Mean	1.4 Pa.s	3.9 (m/s)/kHz
Median	1.5 Pa.s	3.9 (m/s)/kHz
IQR	0.1 Pa.s	0.2 (m/s)/kHz
SD	0.0 Pa.s	0.1 (m/s)/kHz

Attenuation and Sound Speed

	Attenuation Coefficient	Sound Speed
1	0.49 dB/cm/MHz	1570 m/s
2	0.40 dB/cm/MHz	1570 m/s
3	0.45 dB/cm/MHz	1575 m/s
Mean	0.45 dB/cm/MHz	1572 m/s

	Attenuation Coefficient	Sound Speed
Mean	0.45 dB/cm/MHz	1572 m/s
Median	0.45 dB/cm/MHz	1570 m/s
IQR	0.10 dB/cm/MHz	5 m/s
SD	0.04 dB/cm/MHz	2 m/s

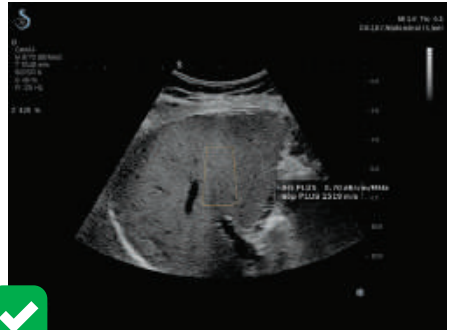# Att PLUS and SSp PLUS
Examples of acquisitions

- Presence of vessels inside the Region of Interest (ROI).
- Image not optimal due to the presence of acoustic shadowing from the ribs or from the loss of contact on the edges of the probe.
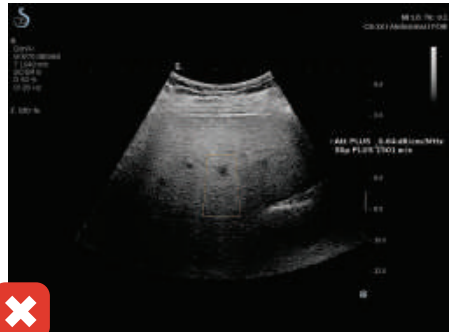
- Presence of structures other than liver parenchyma inside the box.

- Probe surface absolutely not orthogonal to the liver capsule.
- Presence of structures other than liver parenchyma in the box.
- Image not optimal due to the presence of acoustic shadowing from the ribs or from the loss of contact on the edges of the probe.

- Image optimal without any shadowing.
- Sufficient pressure applied on the probe to eliminate acoustic shadowing from the loss of contact on the edges of the probe.
- Probe surface correctly aligned with the liver capsule.
- The area in the ROI is totally void of vessels, nodules or structures other than liver parenchyma.

ShearWave™ PLUS and Vi PLUS
Examples of acquisitions
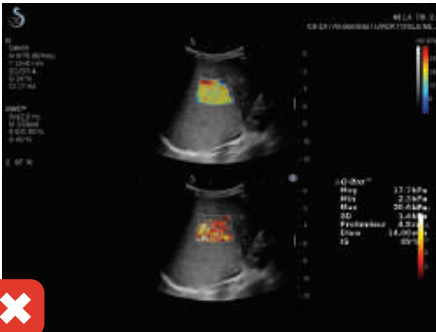
❌

- Image not optimal due to the acoustic shadowing from the loss of contact on the edges of the probe.
- Acquisition not reliable as there is a lack of signal filling for viscosity measurements.

❌
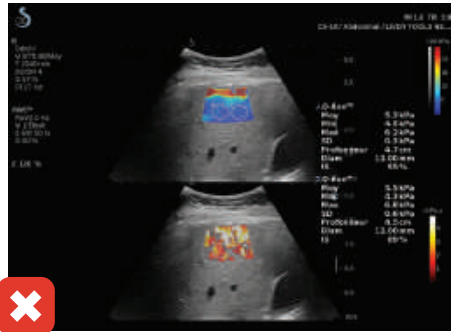
- Image not optimal due to the presence of acoustic shadowing from ribs.
- The boxes are both located on the liver capsule, while they must be located at least 2 cm below the liver capsule, and ideally centered at around 5 cm in depth.

❌
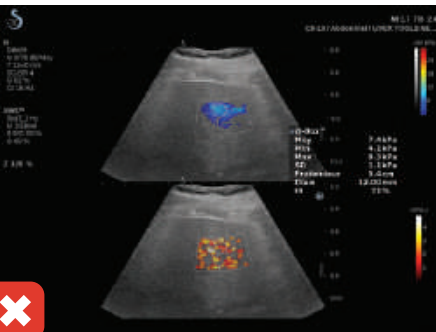
- Image not optimal due to the acoustic shadowing from the loss of probe contact.
- Lack of signal filling; Optimization PEN setting may help.
- Rushed acquisition, delivering non-reliable map and measurements.
- Stability index: 71%, meaning the acquisition must be rejected.

✅
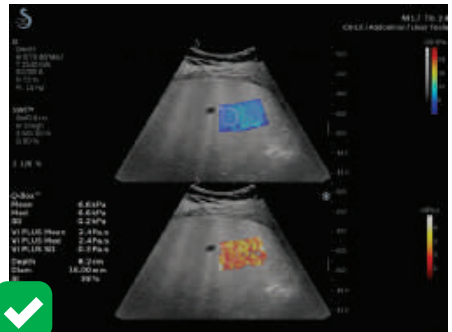
- Image optimal without any shadowing.
- Probe surface correctly aligned with the liver capsule.
- Sufficient pressure applied on the probe to eliminate acoustic shadowing from the loss of probe contact.
- Boxes located at least 2 cm below the liver capsule, centered at around 5 cm in depth and over an area of uniform parenchyma.
- No vessels, nor nodules, gallbladder or any other structures located in the middle of the boxes.
- Q-Box diameter between 15-20 mm and stability index SI>90%.

References

1. Karanjia RN, Crossey MM, Cox IJ, et al. Hepatic steatosis and fibrosis: Non-invasive assessment. *World J Gastroenterol.* 2016 Dec ; 22(45):9880-9897

2. Muller M, Gennisson JL, Deffieux et al. Quantitative viscoelasticity mapping of human liver using supersonic shear imaging: preliminary in vivo feasibility study. *Ultrasound Med Biol.* Feb 2009;35(2):219-229.

3. Ferraioli G, Tinelli C, Dal Bello B, et al. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study. *Hepatology.* 2012 Aug; 56(6):2125-2133.

4. Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. *IEEE Trans Ultrason Ferroelectr Freq Control.* 2004 Apr;51(4):396-409.

5. Internal R&D Data, SuperSonic Imagine. 2018 - Ongoing studies are warranted to confirm this finding.

6. Deffieux T, Montaldo G, Tanter M et al. Shear wave spectroscopy for in vivo quantification of human soft tissues visco-elasticity. *IEEE Trans Med Imaging.* 2009 Mar;28(3):313-322.

7. Fujiwara Y, Kuroda H, Abe T, et al. The B-Mode Image-Guided Ultrasound Attenuation Parameter Accurately Detects Hepatic Steatosis in Chronic Liver Disease. *Ultrasound Med Biol.* 2018 Nov;44(11):2223-2232.

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