Aixplorer MACH® Protocols

Multiparametric Assessment of the Liver: Visco-elasticity, Attenuation and Sound Speed quantification.

Introduction

Chronic liver disease is a major cause of morbidity and mortality worldwide [...] The progression of disease is characterised by ongoing inflammation and consequent fibrosis, although hepatic steatosis [...] However, the current gold standard method of quantifying and staging liver disease, histological analysis by liver biopsy, has several limitations and can have associated morbidity and even mortality. Therefore, there is a clear need for safe and non-invasive assessment modalities to determine hepatic steatosis, inflammation and fibrosis. [...] non-invasive imaging and blood biomarker assessments that can be used as an alternative to information gained on liver biopsy.[1]

The stage of the fibrosis has been proven to be correlated 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 be correlated 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 be correlated to the attenuation and to the sound speed of the liver. It seems that the combination of both of them allows to improve the diagnosis performance for staging steatosis.[7,8]

ShearWave™ Elastography (SWE) performed with Aixplorer® MACH platform 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) imaging performed with Aixplorer® MACH platform 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)** measurements performed with Aixplorer® MACH platform are quantitative measurements through a region of interest.

From a clinical standpoint, staging liver fibrosis, liver steatosis, and liver inflammation is of major importance [1, 9]:

- to assess a prognosis,
- to follow up the evolution of chronic liver diseases,
- to monitor antifibrotic, antiviral, and NASH treatments.

Noteworthy: the presence of ascites is not a limitation for the evaluation of liver fibrosis and viscosity with SWE nor Vi PLUS.

References

1. Hepatic steatosis and fibrosis: Non-invasive assessment. Rustam N Karanjia et al. World J Gastroenterol. 2016 Dec 7; 22(45): 9880–9897.

2. Quantitative viscoelasticity mapping of human liver using supersonic shear imaging: preliminary in vivo feasibility study. Muller M, Gennisson JL, Deffieux T, Tanter M, Fink M. Ultrasound Med Biol. 2009 Feb;35(2):219-29.

3. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: A pilot study. Ferraioli G, Tinelli C, Dal Bello B, Zicchetti M, Filice G, Filice C; on behalf of the Liver Fibrosis Study Group. Hepatology. 2012 Dec;56(6):2125-2133.

4. Supersonic shear imaging: A new technique for soft tissues elasticity mapping. Bercoff J, Tanter M, Fink M. IEEE Trans Ultrason Ferroelectr Freq Control 2004c;51(4):396–409.

5. Viscoelasticity measurement in rat livers using shear-wave uselastography, Katsutoshi Sugimoto et al., Ultrasound in Med. & Biol., 2018

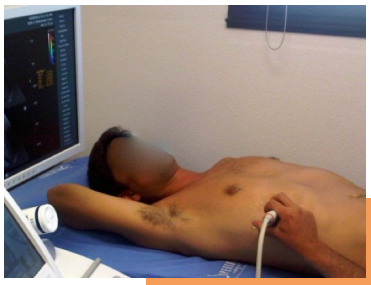
6. Deffieux T et al, Shear Wave Spectroscopy for In Vivo Quantification of Human Soft Tissues Visco-Elasticity, IEEE Transactions on Medical Imaging, 2009

7. The B-mode image-guided ultrasound attenuation parameter accurately detects hepatic steatosis in chronic liver disease, Fujiwara et al., Ultrasound in Med. & Biol., 2018

8. Ultrasonic Adaptive Sound Speed Estimation for the Diagnosis and Quantification of Hepatic Steatosis: A Pilot Study, Dioguardi Burgio et al., Ultraschall Med. 2018 Nov 5.

9. The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases. Naga Chalasani et al., HEPATOLOGY, VOL. 67, NO. 1, 2018

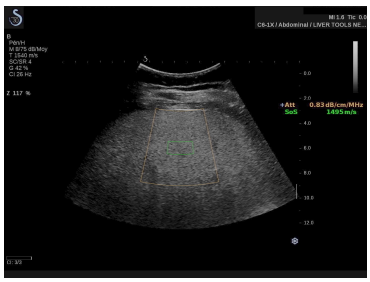
Attenuation PLUS & Sound Speed PLUS



1. The patient lies supine with the right arm in maximal abduction.
2. Choose C6-1X probe/ Abdominal / Liver or Abdomen.
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 sufficient pressure on the probe to get rid of acoustic shadowing from the loss of contact on the edges of the probe.

6. Press « Att PLUS & SSp PLUS ROI » available on the touch screen.
7. Position the upper part of the largest box (Attenuation) **ON** the liver capsule, ensuring the area in this box is free of major vessels or nodules as much as possible.
8. Ensure the smallest box (Sound Speed) is **TOTALLY** free of vessels or other structure than liver parenchyma.
9. Ask the patient to stop breathing in order to stabilize the image.
10. Press " Att PLUS & SSp PLUS Acquisition ", available on the touch screen.



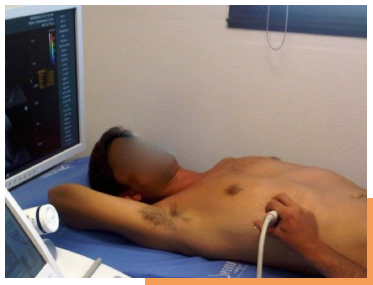
Repeat acquisitions 3 times to collect 3 valid measurements of liver attenuation and speed of sound.

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 from 1450 m/s to 1600 m/s.

The attenuation coefficient in the liver is from 0,20 dB/cm/MHz to 1,60 dB/cm/MHz.

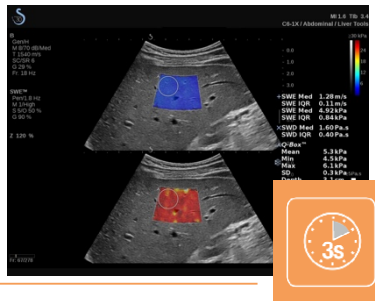
SWE & Vi PLUS



1. The patient lies supine with the right arm in maximal abduction.
2. Choose C6-1X probe/ Abdominal / Liver or Abdomen.
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 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 is orthogonal to the liver surface.

6. Apply sufficient pressure on the probe to get rid of acoustic shadowing from the loss of contact on the edges of the probe.
7. Ask the patient to stop breathing.
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.

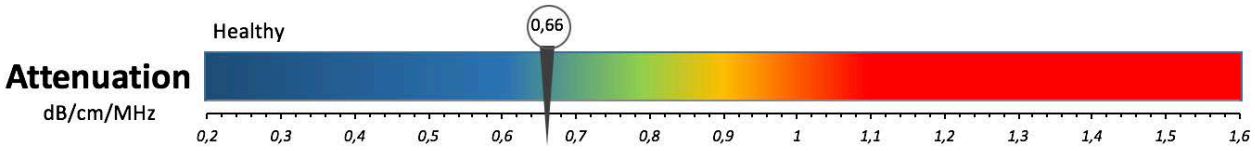
The accepted Mean Value of liver stiffness and liver viscosity is the average value of the 3 independent values.

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.

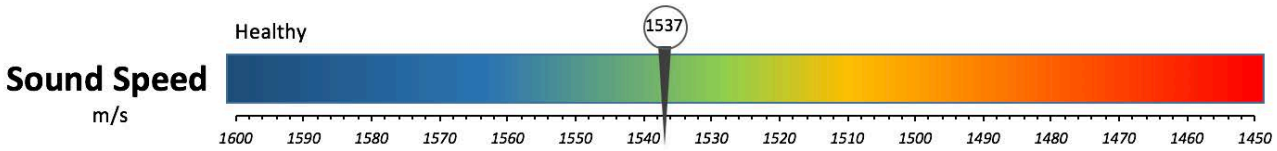
If signal is lacking and all conditions above are satisfied, switch "Optimization” setting to “Penetration”.

If desired, the system is able to provide the stiffness and viscosity quantification in real time in the entire boxes. To activate this feature, go to Syst. Config./ System Display/ Scanning Preferences and check "Auto Display of Real Time Median". In this case, please follow the same guidelines provided above from step #1 to step #11 (but press Freeze instead of Measure in this case). Be careful that no structures other than liver parenchyma is in the box, otherwise stiffness values can be oversestimated.

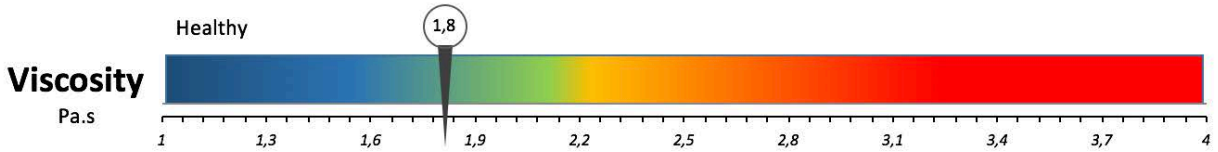
Suggested thresholds



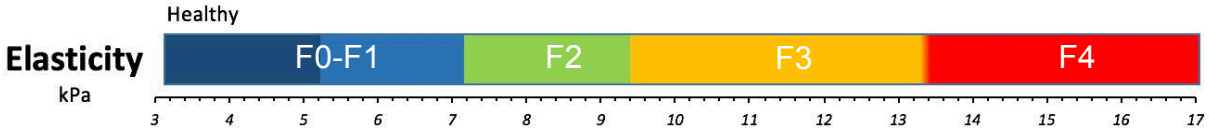
The higher the Attenuation value, the higher the liver fat content.



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



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



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

References

Ronot M et al. EASL LiverTree™. Apr 22, 2017 - Dioguardi Burgio M et al. Ultraschall Med. 2018 Nov 5
Imbault et al. Phys Med Biol. 2017 May 7 - Internal R&D Data. 2016 June 14

*Further on-going studies are warranted to confirm this finding.
**NASH Context

Example of Liver Report

AIXPLORER mach30 | Anonymous Anonymous 20/06/2019

Exam Report

Patient: Anonymous Anonymous
Patient ID: Aixplorer_298721652
DoB:
Gender:
Height:
Study description:

Accession #:
Sonographer:
Ref MD:
Exam start date: 20/06/2019
Weight: BMI:

Liver

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%

Cassinotto C, Boursier J, De Ledinghen V, Lebigot J, Lapuyade B, Cales P, Hiriart JB, Michalak S, Le Bail B, Cartier V, Mouries A, Oberti F, Fouchard-Hubert I, Vergniol J, Aube C. Liver stiffness in nonalcoholic fatty liver disease: A comparison of Supersonic Shear Imaging, FibroScan and ARFI with liver biopsy. Hepatology. 2015 Dec 13. doi: 10.1002/hep.28394.

The above measurements are not from the exam. They are extracted from the selected publication and are shown for reference only. Liver stiffness measurements have been proposed as a non-invasive indirect marker of liver fibrosis severity in patients presenting with chronic hepatopathies. Liver stiffness values have to be interpreted by a clinician who specializes in hepatology and especially in chronic liver diseases, while taking into account the level of reliability of stiffness measurements, and any other clinical and diagnostic information for a given patient, and especially liver stiffness confounding factors. The determination of these diagnostic cut-off values depends on the diagnostic goal, the type of population studied (disease etiology, global severity of disease, confounding factors…). Readers should be aware of these limitations before generalizing clinical results.

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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

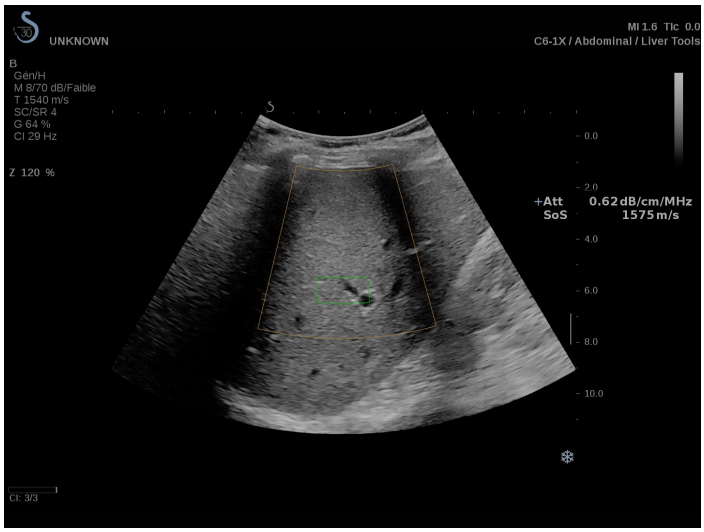
Conclusion

Signature

Signature: ..... Date: .....

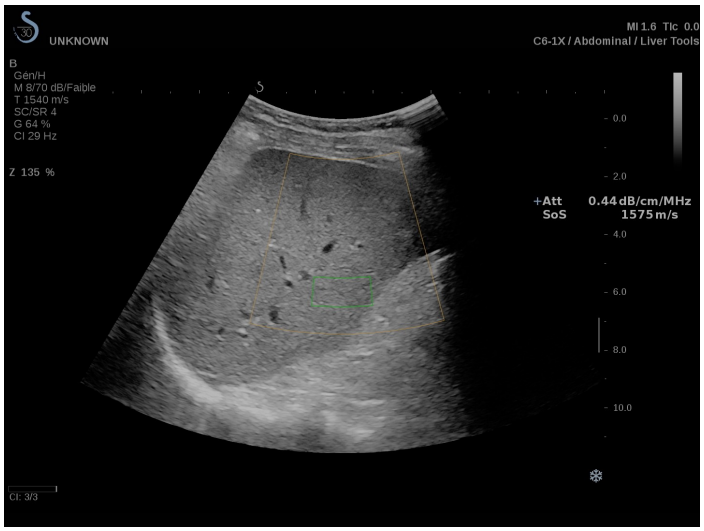
Print Name: .....

Example of acquisitions



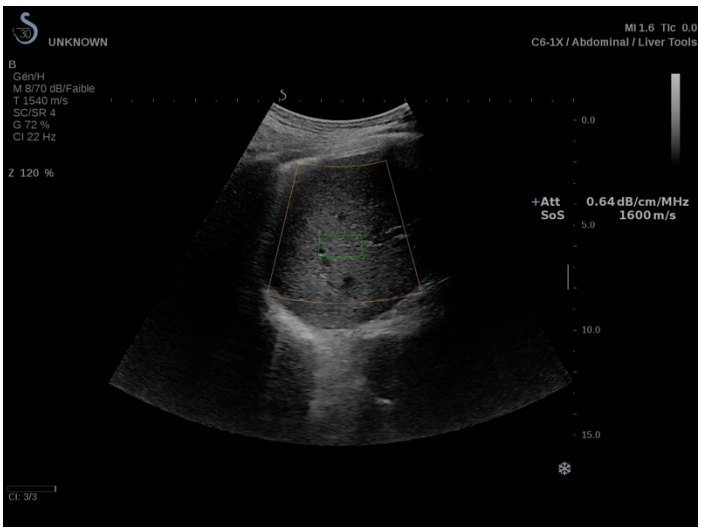
Wrong Attenuation and Sound Speed Acquisition:

- Presence of vessels inside the smallest box (Sound speed meas.)
- Image not optimal due to the presence of acoustic shadowing from ribs.



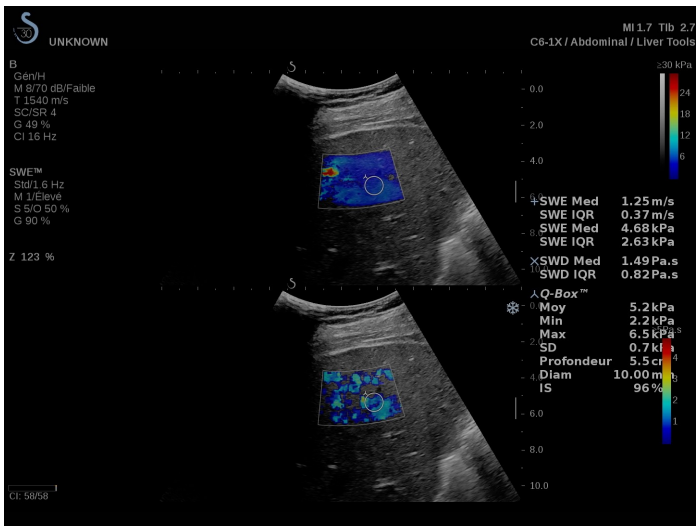
Wrong Attenuation and Sound Speed Acquisition:

- Presence of structures other than liver parenchyma inside the largest box (attenuation meas.)
- Probe orientation not correctly aligned with the liver capsule as upper part of the attenuation meas.box is placed outside liver capsule.



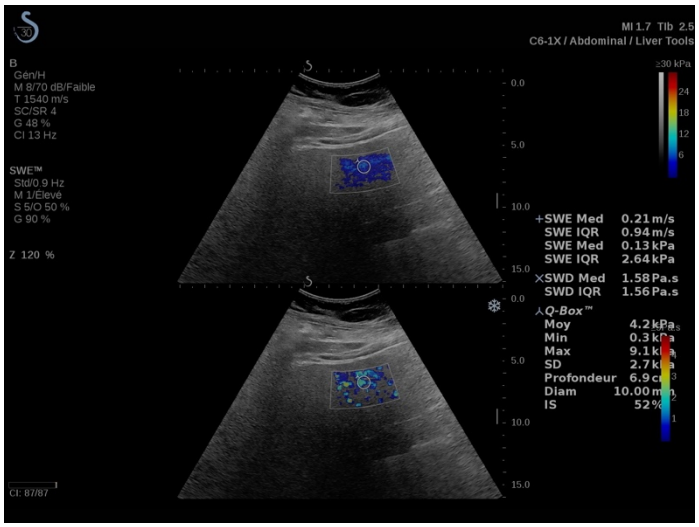
Wrong Attenuation and Sound Speed Acquisition :

- Probe orientation not correctly aligned with the liver capsule as upper part of the attenuation meas. box is placed outside the liver capsule.
- Presence of structures other than liver parenchyma in the biggest box (Attenuation Meas.)
- Presence of vessels in the smallest box (Sound Speed Meas)
- Image not optimal due to presence of acoustic shadowing from the loss of contact on the edges of the probes.



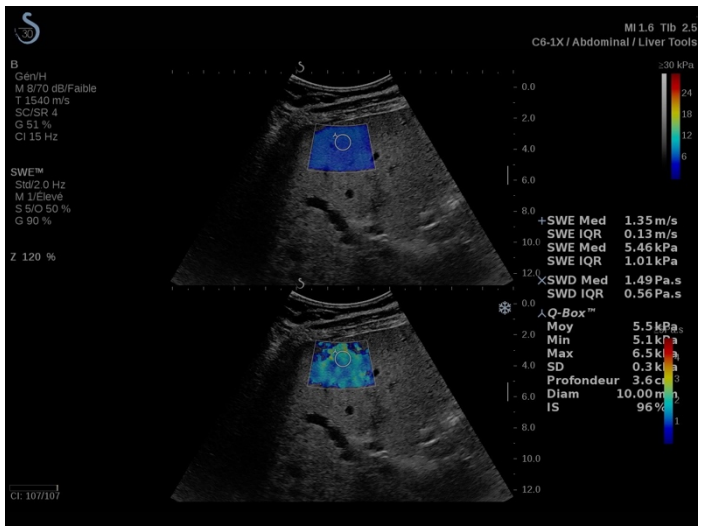
Wrong SWE and Vi PLUS Acquisition:

- Image not optimal due to the presence of 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 meas.



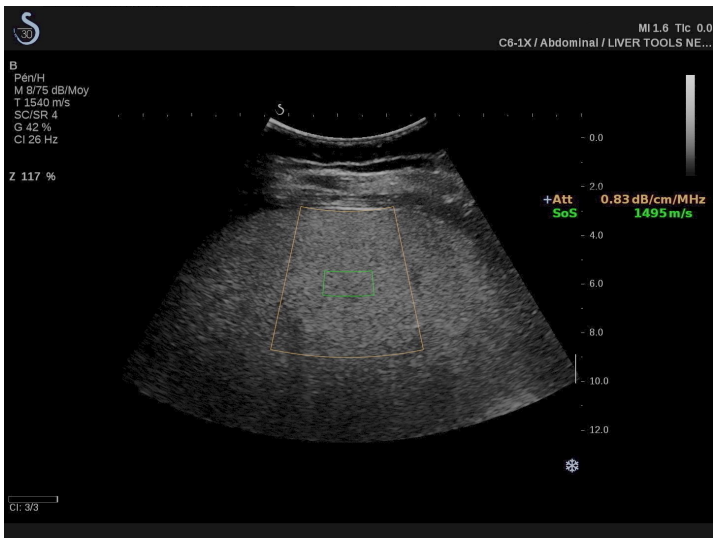
Wrong SWE and Vi PLUS Acquisition:

- Image not optimal due to the presence of acoustic shadowing from the loss of contact on the edges of the probe or from ribs.
- Lack of signal filling, Optimization PEN setting may help.
- Rushed acquisition giving non reliable map and measurements.
- Stability Index: 52% meaning the acquisition must be rejected.



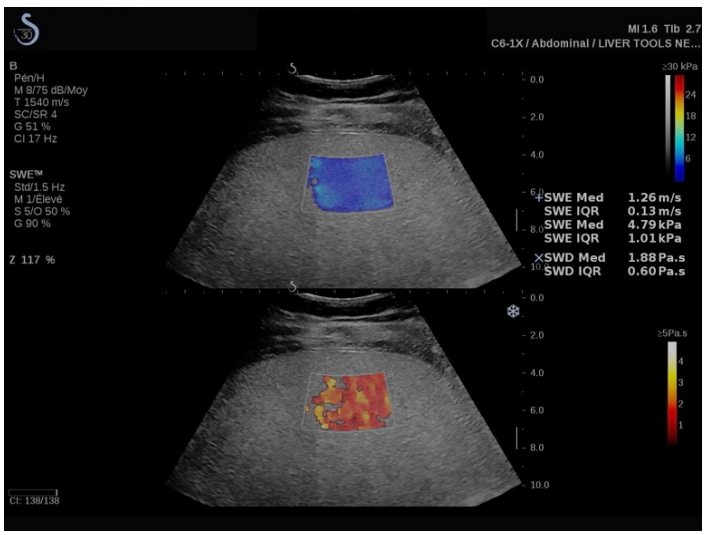
Wrong SWE and Vi PLUS Acquisition:

- 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.



Right Attenuation and Sound Speed Acquisition:

- Image optimal without any shadowing.
- Sufficient pressure applied on the probe to get rid of acoustic shadowing from the loss of contact on the edges of the probe.
- Probe orientation correctly aligned with the liver capsule.
- The upper part of the largest box (Attenuation Meas.) is located correctly on the liver capsule.
- The area in the largest box is void of major vessels or nodules.
- The smallest box (Sound Speed Meas.) is TOTALLY void of vessels or structures other than liver parenchyma.



Right SWE and Vi PLUS Acquisition:

- Image optimal without any shadowing.
- Liver area is void of major vessels.
- Probe orientation correctly aligned with the liver capsule.
- Sufficient pressure applied on the probe to get rid of acoustic shadowing from the loss of contact on the edges of the probe.
- Boxes are located over an area of uniform parenchyma.
- No vessels, nor nodules, gallbladder or any other structures located in the middle of the boxes.
- However, the Optimization Pen. setting could have been used to ensure a better filling.

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