QIBA and Imaging Biomarkers for Fat Quantification

Liver Forum, April 2022

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Outline

3 main biomarkers will be discussed

- **Attenuation**
- **Speed of sound**
- **Backscatter coefficient**

- Physics
- Availability
- Clinical results

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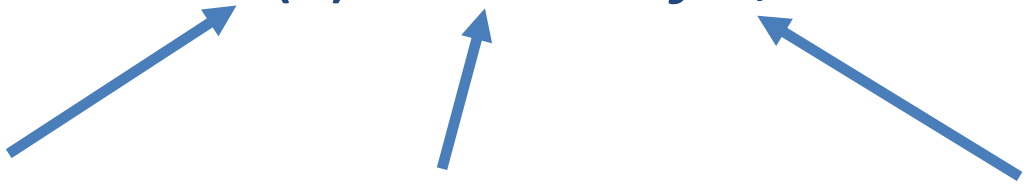
Physics

Attenuation coefficient = Loss of wave amplitude due to acoustic phenomena, esp. absorption and scattering

The magnitude of the loss = $A(z) = A0 - \alpha f z,$



Amplitude (in dB) after the wave propagates a distance z (in cm)

Initial ultrasonic wave amplitude in decibel (dB)

Total loss of wave amplitude

A(z) is the f is the ultrasonic frequency in MHz, and α is the attenuation coefficient (AC; in dB/cm-MHz).

Han A, Andre MP, Deiranieh L, Housman E, Erdman JW Jr, Loomba R, Sirlin CB, O'Brien WD Jr. Repeatability and Reproducibility of the Ultrasonic Attenuation Coefficient and Backscatter Coefficient Measured in the Right Lobe of the Liver in Adults With Known or Suspected Nonalcoholic Fatty Liver Disease. J Ultrasound Med. 2018 Aug;37(8):1913-1927. doi: 10.1002/jum.14537. Epub 2018 Jan 23. PMID: 29359454; PMCID: PMC6056350.

Availability

- Most vendors have attenuation measurement technology
- Methods may differ
- Ongoing clinical trials (NCT04440540, NCT04012242)

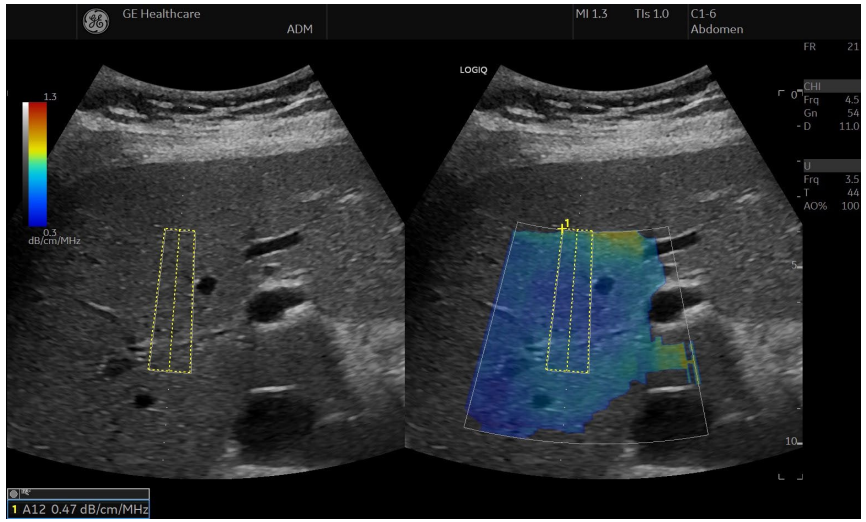


Image from, https://www.gehealthcare.com.au/-/jssmedia/global/products/files/ultrasound/logiq-e10/logiq-e10-guided-attenuation-parameter-anz-jb76082xx-2.pdf?rev=-1

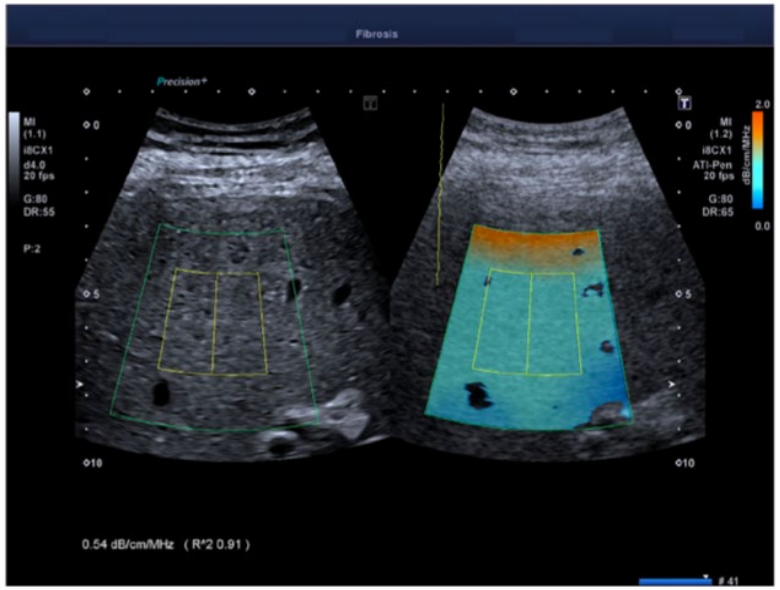
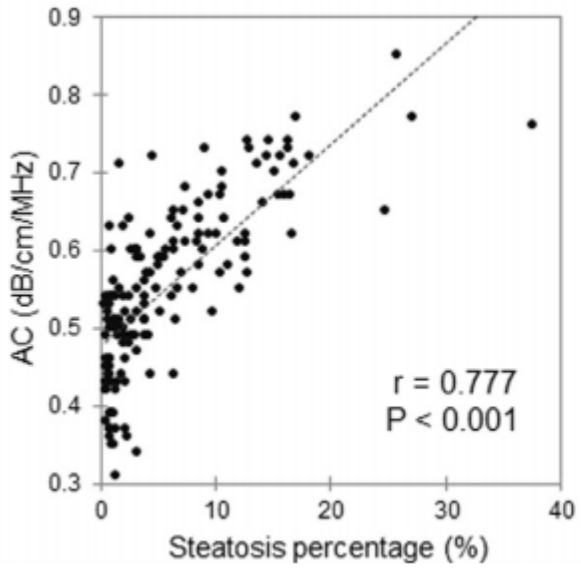


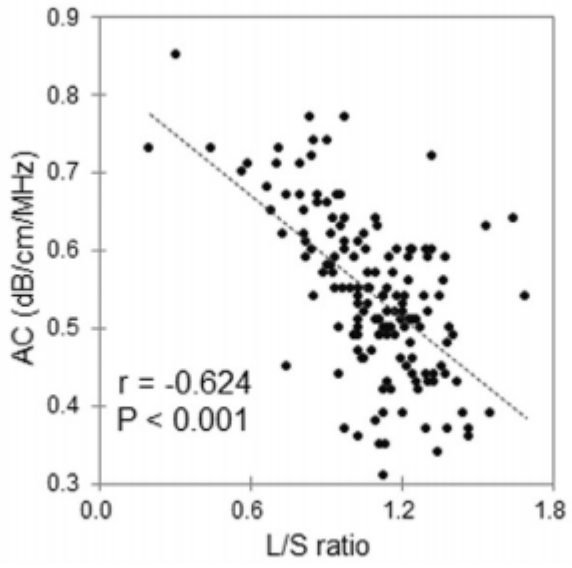
Image from Ferraioli et al. 2021

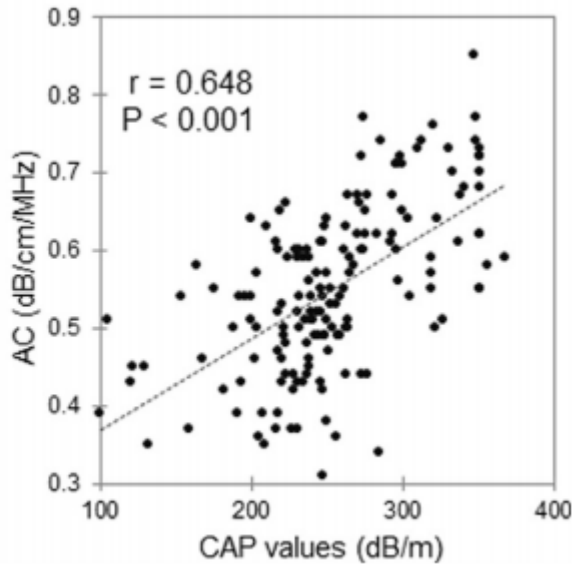
Ferraioli G, Maiocchi L, Savietto G, Tinelli C, Nichetti M, Rondanelli M, Calliada F, Preda L, Filice C. Performance of the Attenuation Imaging Technology in the Detection of Liver Steatosis. J Ultrasound Med. 2021 Jul;40(7):1325-1332. doi: 10.1002/jum.15512. Epub 2020 Sep 22. PMID: 32960457; PMCID: PMC8246860.

Clinical results

Increased attenuation values at higher steatosis percentages and CAP values. Negative correlation with CT defined Liver-to-spleen ratio (L/S).

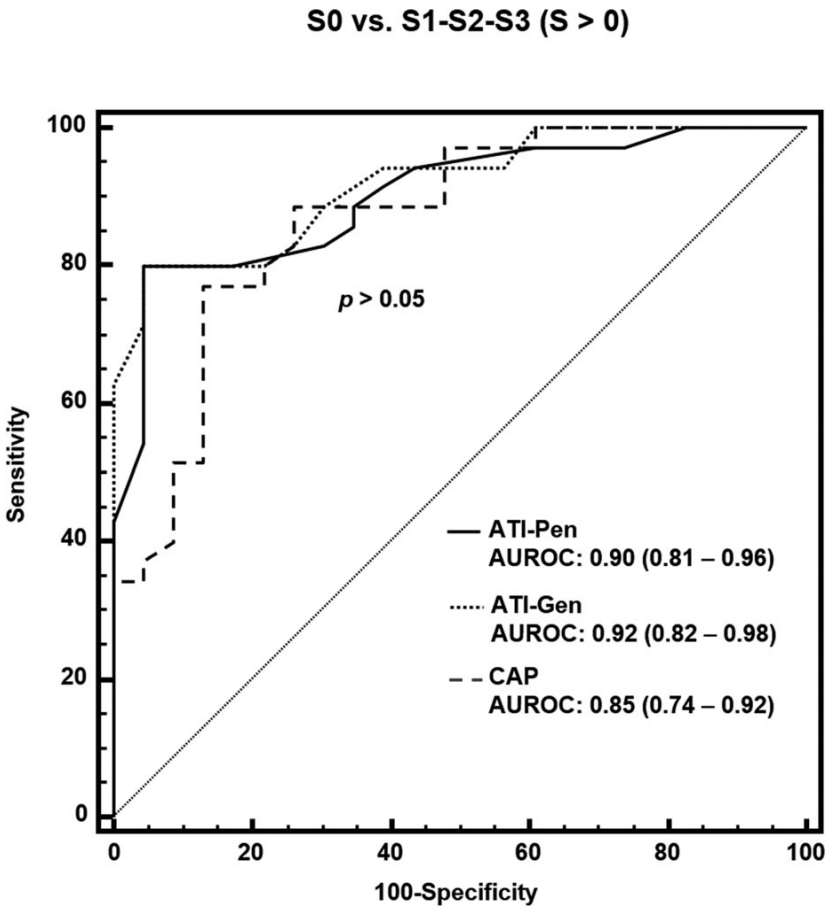






Fujiwara Y, Kuroda H, Abe T, Ishida K, Oguri T, Noguchi S, Sugai T, Kamiyama N, Takikawa Y. The B-Mode Image-Guided Ultrasound Attenuation Parameter Accurately Detects Hepatic Steatosis in Chronic Liver Disease. Ultrasound Med Biol. 2018 Nov;44(11):2223-2232. doi: 10.1016/j.ultrasmedbio.2018.06.017. Epub 2018 Aug 2. PMID: 30077415.

Clinical results



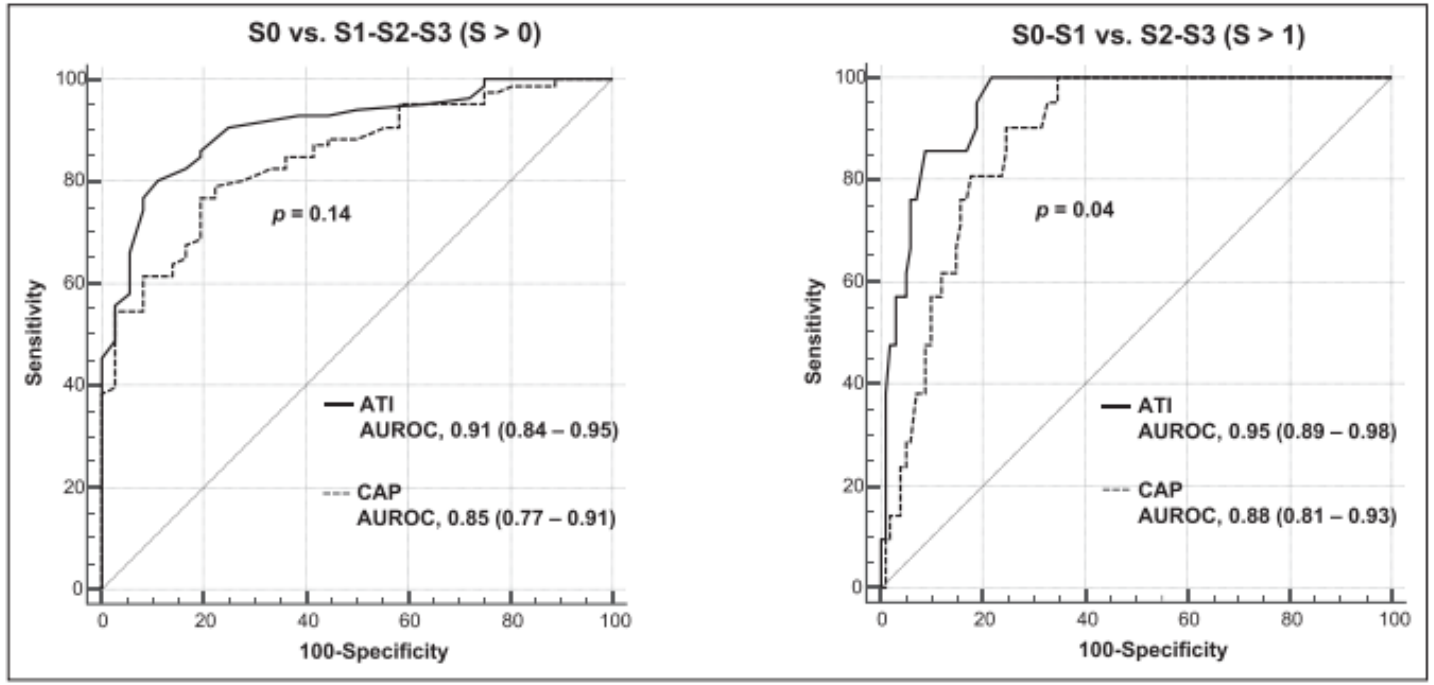
Comparison of receiver operating characteristic curves for 2 attenuation commercial implementations for S0 versus S1 to S3 (S > 0), as defined by MRI-PDFF of greater than 5%.

ATI-Pen (3.0 MHz), ATI-Gen (4 MHz)

Ferraioli G, Maiocchi L, Savietto G, Tinelli C, Nichetti M, Rondanelli M, Calliada F, Preda L, Filice C. Performance of the Attenuation Imaging Technology in the Detection of Liver Steatosis. J Ultrasound Med. 2021 Jul;40(7):1325-1332. doi: 10.1002/jum.15512. Epub 2020 Sep 22. PMID: 32960457; PMCID: PMC8246860.

Clinical results

ROC analysis- Diagnosing PDFF proven steatosis %



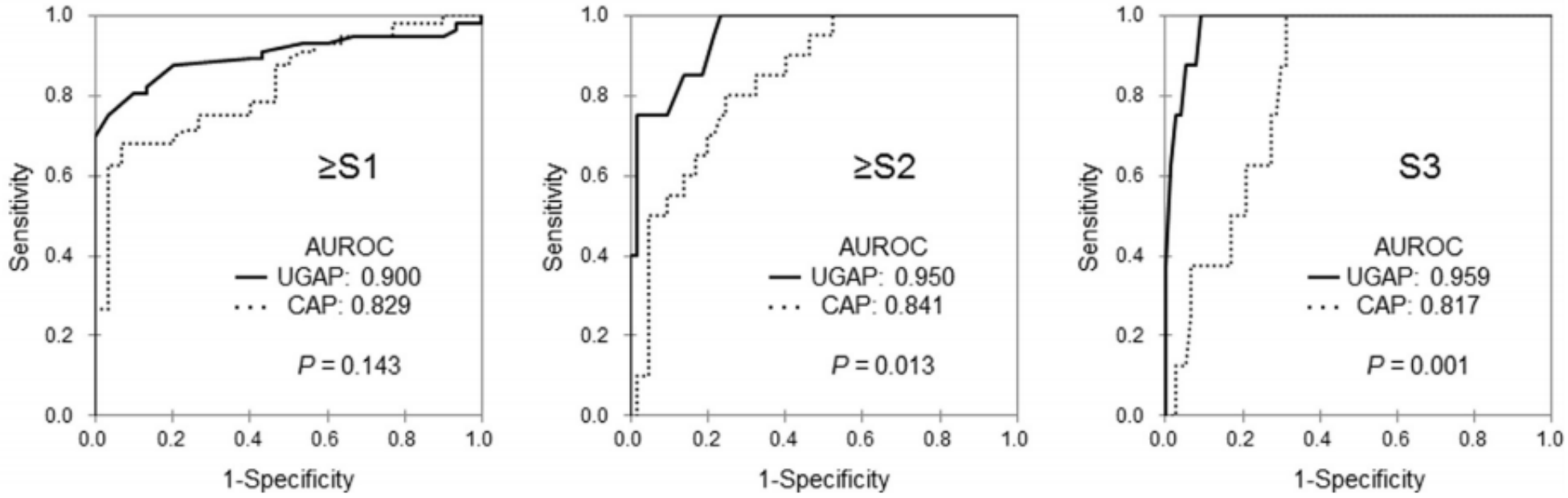
Reference standard: MRI-PDFF ≥ 5%

MRI-PDFF ≥ 16.3%

Ferraioli G, Maiocchi L, Raciti MV, Tinelli C, De Silvestri A, Nichetti M, De Cata P, Rondanelli M, Chiovato L, Calliada F, Filice C. Detection of Liver Steatosis With a Novel Ultrasound-Based Technique: A Pilot Study Using MRI-Derived Proton Density Fat Fraction as the Gold Standard. Clin Transl Gastroenterol. 2019 Oct;10(10):e00081. doi: 10.14309/ctg.0000000000000081. PMID: 31609745; PMCID: PMC6884349.

Clinical results

ROC analysis- by steatosis stage



Fujiwara Y, Kuroda H, Abe T, Ishida K, Oguri T, Noguchi S, Sugai T, Kamiyama N, Takikawa Y. 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. doi: 10.1016/j.ultrasmedbio.2018.06.017. Epub 2018 Aug 2. PMID: 30077415.

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Physics

Focusing methods

- SoS assumed to be 1540 m/s.
- Deviation of true tissue SoS leads to image degradation.

Coherence methods

- Specialized signal processing
- Channel-data
- Depth specific SoS

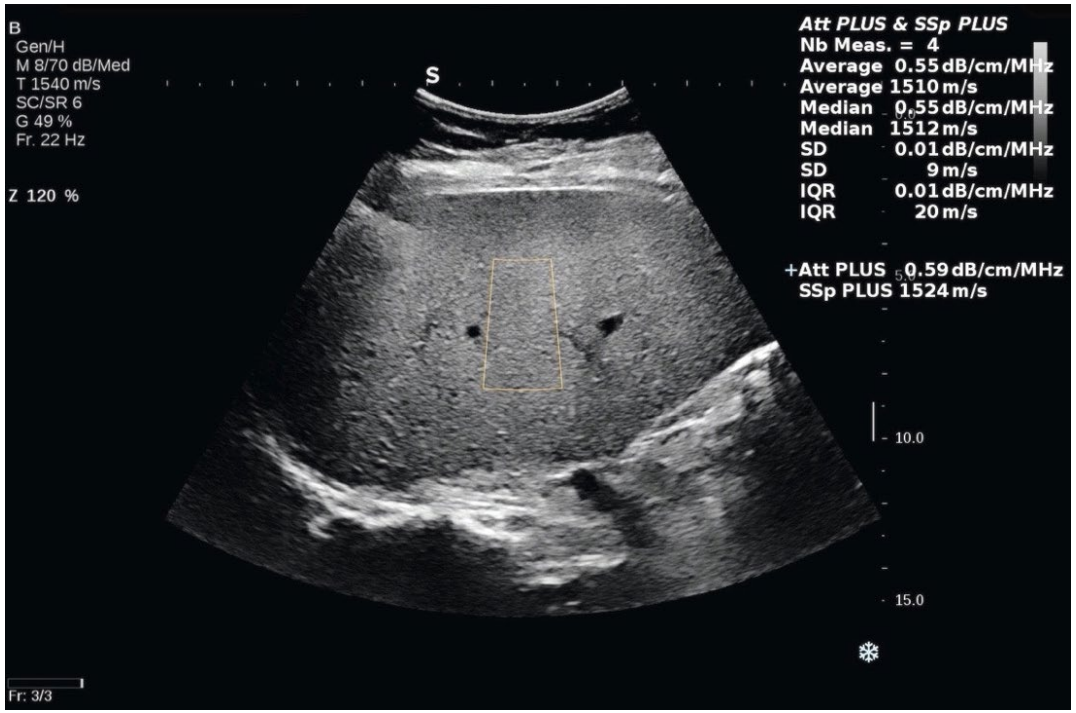
Compounding methods

- Uses different transmit steering angles to cause spatial shift misregistration
- Real-time SoS maps

Imbault M, Faccinetto A, Osmanski BF, Tissier A, Deffieux T, Gennisson JL, Vilgrain V, Tanter M. Robust sound speed estimation for ultrasound-based hepatic steatosis assessment. Phys Med Biol. 2017 May 7;62(9):3582-3598. doi: 10.1088/1361-6560/aa6226. Epub 2017 Feb 22. PMID: 28225357..
Sanabria SJ, Ozkan E, Rominger M, Goksel O. Spatial domain reconstruction for imaging speed-of-sound with pulse-echo ultrasound: simulation and in vivo study. Phys Med Biol. 2018 Oct 26;63(21):215015. doi: 10.1088/1361-6560/aae2fb. PMID: 30365398.

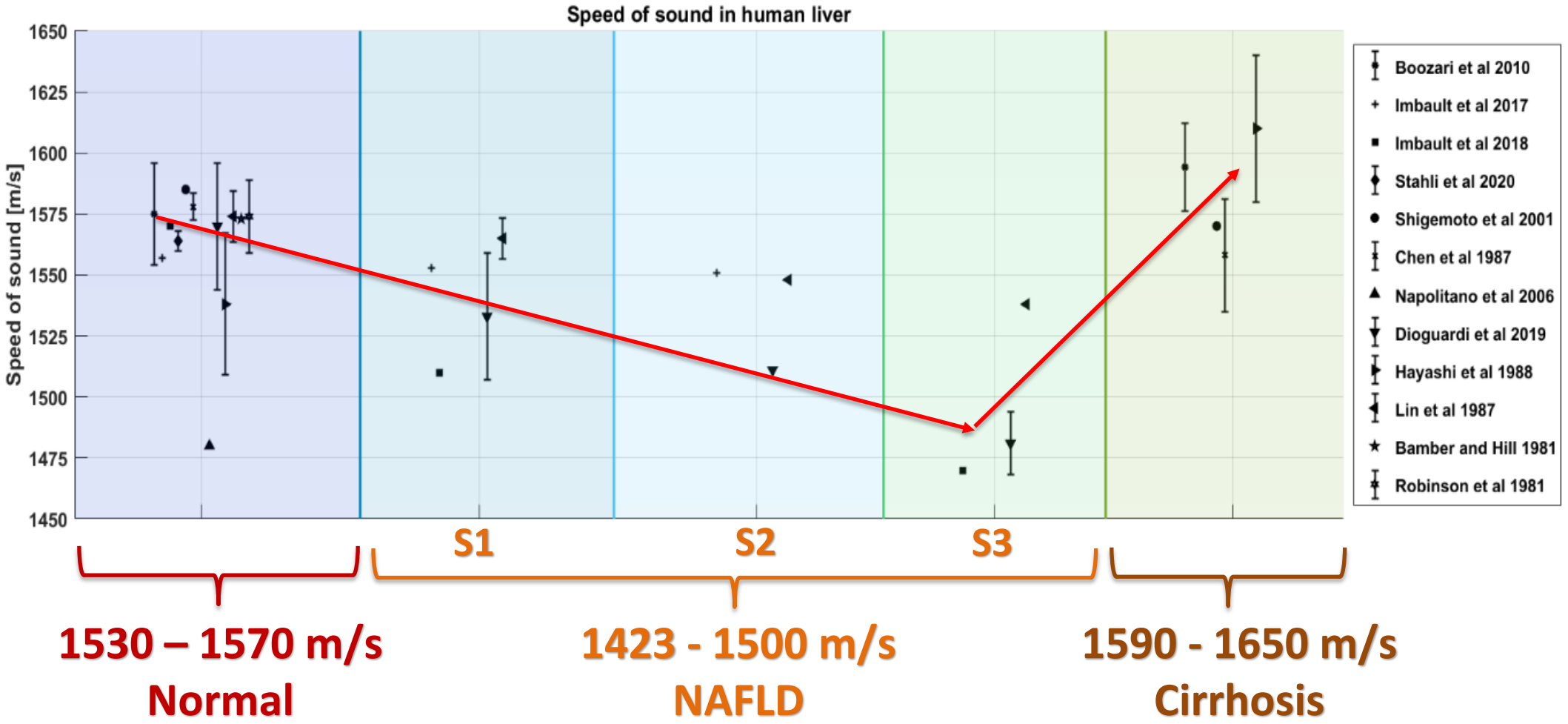
Availability

- Limited availability
- Ongoing clinical trials to assess variability and diagnostic performance are needed. Active trials (NCT04782050)



Popa A, Bende F, Șirli R, et al. Quantification of Liver Fibrosis, Steatosis, and Viscosity Using Multiparametric Ultrasound in Patients with Non-Alcoholic Liver Disease: A "Real-Life" Cohort Study. *Diagnostics (Basel)*. 2021;11(5):783. Published 2021 Apr 26. doi:10.3390/diagnostics11050783

Clinical results

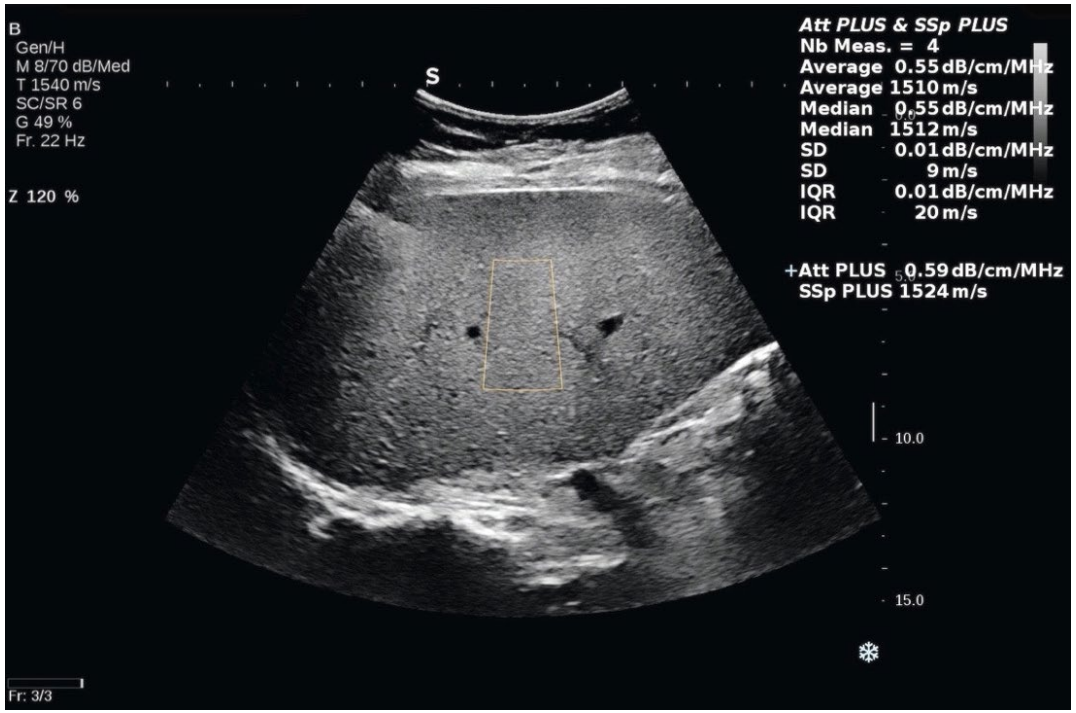


Courtesy of Xiaohong Wang, UITC 2021

Clinical results

- Majority of studies are animal and ex-vivo studies.
- Limited clinical studies
- Popa et al. 2021, AUC to detect S2,S3 steatosis

Cut-off	<1524 m/s
AUC(95%CI)	0.88 (0.82-0.92)
Sens	75.5 %
Spec	93.4 %



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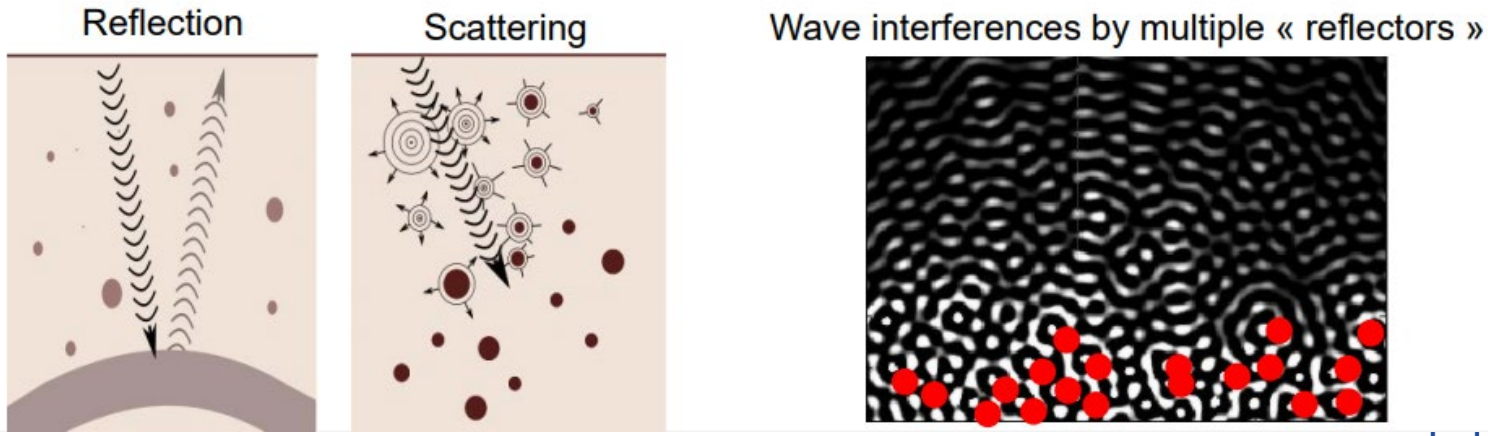
Physics

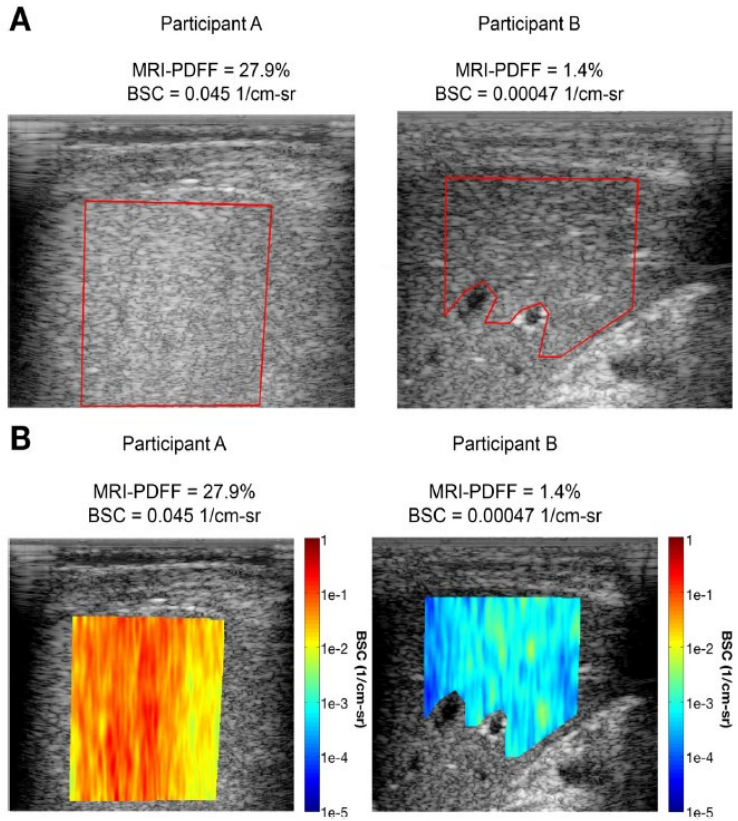
- Backscatter imaging refers to the analysis of echoes received by the ultrasound transducer due to compression wave reflection and scattering
- Quantitatively measure scattering from biological tissue
- Defined as the differential scattering cross-section per unit volume in the 180º direction.



Cloutier G., Destrempes F., Yu F.T.H., Tang A., Quantitative ultrasound imaging of soft biological tissues: A primer for radiologists and medical physicists, Insights into Imaging, in press, 2021.

Availability

- Mostly experimental
- Clinical trials to assess variability and diagnostic performance are needed.



Lin SC, Heba E, Wolfson T, Ang B, Gamst A, Han A, Erdman JW Jr, O'Brien WD Jr, Andre MP, Sirlin CB, Loomba R. Noninvasive Diagnosis of Nonalcoholic Fatty Liver Disease and Quantification of Liver Fat Using a New Quantitative Ultrasound Technique. Clin Gastroenterol Hepatol. 2015 Jul;13(7):1337-1345.e6. doi: 10.1016/j.cgh.2014.11.027. Epub 2014 Dec 3. PMID: 25478922; PMCID: PMC4454635.

Clinical results

		Mean AUC Values	Treshold	Sens%	Spec%
Backscatter Coefficient	Grade 1 vs ≥2	0.854 (0.753-0.966)	0.0112	0.848 (0.681-0.949)	0.815 (0.619-0.937)
	Grade ≤2 vs 3	0.830 (0.719-0.942)	0.0166	0.882 (0.636-0.985)	0.744 (0.588-0.885)
MR-PDFF	Grade 1 vs ≥2	0.962 (0.922-1.000)	13.45	0.848 (0.681-0.949)	0.963 (0.810-0.999)
	Grade ≤2 vs 3	0.929 (0.865-0.933)	16.83	1.000 (0.805-1.000)	0.814 (0.666-0.916)

Paige JS, Bernstein GS, Heba E, Costa EAC, Fereirra M, Wolfson T, Gamst AC, Valasek MA, Lin GY, Han A, Erdman JW Jr, O'Brien WD Jr, Andre MP, Loomba R, Sirlin CB. A Pilot Comparative Study of Quantitative Ultrasound, Conventional Ultrasound, and MRI for Predicting Histology-Determined Steatosis Grade in Adult Nonalcoholic Fatty Liver Disease. AJR Am J Roentgenol. 2017 May;208(5):W168-W177. doi: 10.2214/AJR.16.16726. Epub 2017 Mar 7. PMID: 28267360; PMCID: PMC5512552.

Clinical results

- Biopsy Comparison (Paige, AJR 2017)
  - 61 subjects with biopsy-confirmed NAFLD
  - BSC had a cross-validated grading accuracy of 68%
  - Note that MRI-PDFF had a cross-validated grading accuracy of 71%.
- MRI-PDFF Comparison (Han, Radiology 2020)
  - Study of 102 participants of which 72 had NAFLD
  - BSC had Correlation Coefficient of 0.58 with MRI-PDFF

Han A, Zhang YN, Boehringer AS, Montes V, Andre MP, Erdman JW Jr, Loomba R, Valasek MA, Sirlin CB, O'Brien WD Jr. Assessment of Hepatic Steatosis in Nonalcoholic Fatty Liver Disease by Using Quantitative US. Radiology. 2020 Apr;295(1):106-113. doi: 10.1148/radiol.2020191152. Epub 2020 Feb 4. PMID: 32013792; PMCID: PMC7104700..
Paige JS, Bernstein GS, Heba E, Costa EAC, Fereirra M, Wolfson T, Gamst AC, Valasek MA, Lin GY, Han A, Erdman JW Jr, O'Brien WD Jr, Andre MP, Loomba R, Sirlin CB. A Pilot Comparative Study of Quantitative Ultrasound, Conventional Ultrasound, and MRI for Predicting Histology-Determined Steatosis Grade in Adult Nonalcoholic Fatty Liver Disease. AJR Am J Roentgenol. 2017 May;208(5):W168-W177. doi: 10.2214/AJR.16.16726. Epub 2017 Mar 7. PMID: 28267360; PMCID: PMC5512552.

AIUM/RSNA collaboration

- Radiological Society of North America (RSNA) established QIBA in 2007.
- Mission "to improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, sites, patients and time"

https://www.rsna.org/research/quantitative-imaging-biomarkers-alliance

AIUM/RSNA collaboration

- A new, collaborative effort (PEQUS) to gain knowledge about the;
  - Diagnostic performance of emerging fat quantification techniques
  - Inter and intra-manufacturer variability of these biomarkers

AIUM/RSNA collaboration

- AIUM/RSNA QIBA Pulse Echo Quantitative Ultrasound (PEQUS) Biomarker committee was established in 2020.
- 4 sub-committees were generated.
- Members from different disciplines.

Attenuation working group	Backscatter coefficient working group
Phantom working group	Speed of Sound working group

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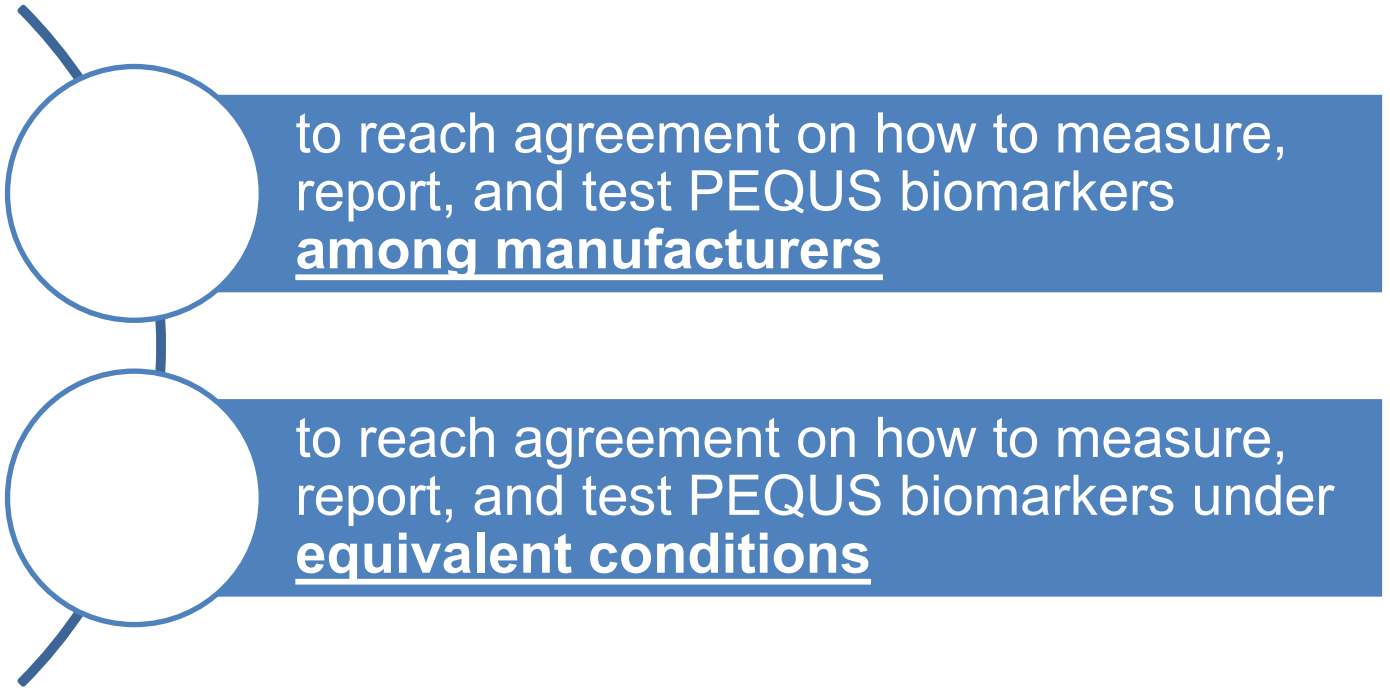
AIUM/RSNA collaboration

- AIUM/RSNA QIBA PEQUS Biomarker committee goals



Thank you for your attention!

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