GE HealthCare

Ultrasound-Guided Fat Fraction (UGFF)

A noninvasive, accurate, and accessible approach for hepatic steatosis assessment

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Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as NAFLD, represents a growing global health burden. Driven by the increasing prevalence of obesity and metabolic syndrome, MASLD is projected to become the leading cause of hepatocellular carcinoma (HCC) and liver transplantation (LT) worldwide. Annual HCC cases related to MASLD in the US are expected to nearly double by 2046-2050 (from 11,483 to 22,440), with liver transplantation needs increasing fourfold (from 1,717 to 6,720), as compared to the time period from 2020-2025.[1,2]

To combat this trend, major liver-focused societies (e.g., AASLD, AACE, EASL, APASL, AGA) have recommended stepwise diagnostic pathways incorporating blood biomarkers, followed by imaging for hepatic fat quantification and elastography.[3-6] Accessible, accurate, and reproducible tools for liver fat evaluation are thus urgently needed to support this growing demand.

Diagnostic landscape of MASLD and MASH

Test	Strength	Limitation
Liver biopsy	The current gold standard for steatosis evaluation offers direct histological insight into hepatocyte lipid content.	It is invasive, carries procedural risks, and is prone to sampling errors and interobserver variability.[6]
MRI-PDFF	Proton Density Fat Fraction (PDFF) via MRI provides whole-liver assessment with excellent reproducibility.	Its accuracy may be confounded by hepatic fibrosis, and its high cost and limited availability restrict broad adoption.[7]
FibroScan® CAP	Controlled Attenuation Parameter (CAP) via the FibroScan device is widely available at the point of care and has strong supporting literature.	As a non-imaging A-mode technique, CAP lacks precise anatomical localization and may yield variable results between operators.[8]
Conventional ultrasound	B-Mode ultrasound (US) is often the first-line modality post-elevated liver enzyme detection.	Tools like hepatic-renal index (HRI) or shear wave elastography (SWE) provide some quantitative insight, but are limited by operator dependency, depth constraints (in obesity), and inter-vendor variability.[9]

These limitations in today's diagnostic landscape highlight the need for innovative approaches that can provide comprehensive tissue characterization through multiparametric analysis.[10]

Innovation in ultrasound: From UGAP to UGFF

UGAP (Ultrasound-Guided Attenuation Parameter) is a clinical application tool that measures the ultrasound attenuation coefficient to estimate the grade of hepatic steatosis. Available since 2020, the UGAP software incorporates several auto-tuning algorithms designed to minimize errors caused by noise, artifacts, and anatomical obstacles, thereby providing a reliable, reproducible, and noninvasive method for fat quantification. GE HealthCare conducted a multicenter cohort study involving more than 1,000 patients across six hospitals and identified clinically useful cutoff values for each steatosis grade.[11]

While UGAP has been clinically valuable, its single-parameter approach limits the ability to fully characterize tissue properties. Recent advances in ultrasound platforms have enabled sophisticated tissue characterization using both physical and statistical modeling. Quantitative ultrasound (QUS) parameters such as the **Attenuation Coefficient (AC)**, **Integrated Backscatter Coefficient (IBSC)**, and **Signal-to-Noise Ratio (SNR)** have emerged as quantifiable imaging biomarkers for hepatic steatosis. This evolution addresses the need for greater diagnostic accuracy and reproducibility in liver fat quantification.

The **Ultrasound-Guided Fat Fraction (UGFF)** algorithm integrates these multivariable acoustic features to enhance the accuracy and reproducibility of liver fat quantification. By combining physical and statistical tissue characterization, UGFF represents a significant advancement beyond UGAP, delivering a more comprehensive and precise estimation of liver fat fraction to support improved diagnostic confidence and clinical decision-making.

The following text offers a brief explanation of each parameter and its measurement methodology.

Attenuation Coefficient (AC)

AC is measured using the current UGAP plus UGFF. It quantifies the ultrasound deep attenuation. As the amount of fat droplets in the liver increases, the backscatter and absorption of the ultrasound propagation also increases, resulting in deep attenuation.

AC is measured using reference phantom method (RPM),[12] which compensates for ultrasound system-dependent characteristics (such as the non-linear depth gain profile and focusing conditions during image reconstruction, etc.) *(Figure 1)*. The slope of the amplitude profile in the depth direction presents ultrasound deep attenuation; however, the actual amplitude profile of echo signal is complicated by system-dependent factors such as settings and transducers.

The RPM compensates for these characteristics by using reference signals from an industry-standard tissue-mimicking phantom with known acoustic properties. The echo signals for AC measurement are always acquired under fixed transmission and reception conditions, and the slope (AC) is calculated from signals in which the system-dependent characteristics are calibrated using the reference signals. This calibration process is performed in advance within the UGAP/UGFF mode to promote measurement consistency.

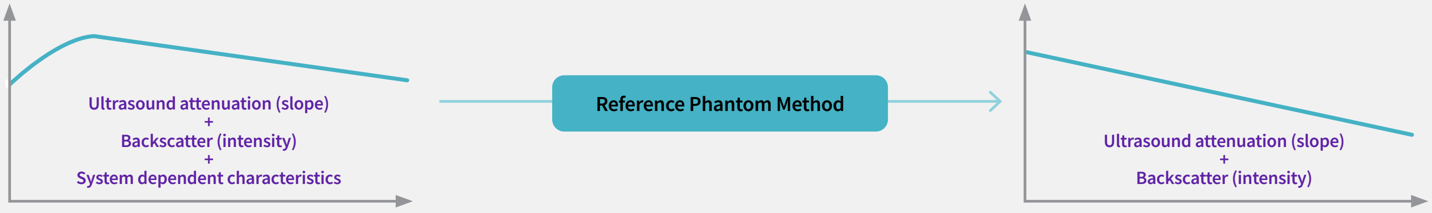


Figure 1: Reference Phantom Method for Attenuation Coefficient Measurement.

Integrated Backscatter Coefficient (IBSC)

IBSC is a new quantitative ultrasound parameter measured by UGFF. It quantifies the intensity of echo signals (brightness of B-Mode images). As the amount of fat droplets in the liver increases, the backscatter also increases, resulting in higher echo signal intensity.

IBSC is also measured using RPM, the intensity is measured from echo signals which the system-dependent characteristics and effect of ultrasound attenuation (slope) are compensated for during the measurement *(Figure 2)*.

Figure 2: Integrated Backscatter Coefficient Measurement.

Signal-to-Noise Ratio (SNR)

SNR is another novel quantitative ultrasound parameter measured by UGFF. It quantifies the homogeneity of B-Mode image texture. SNR is known as a parameter of Rayleigh distribution and is defined as the reciprocal of Rayleigh parameter.

In a normal healthy liver, the texture of B-Mode images is not homogeneous due to the presence of structures such as blood vessels. Conversely, in severe fatty liver, fat droplets become the dominant scatterers and mask these structures, resulting in a more homogenous texture. Consequently, SNR increases with the amount of fat droplets and the homogeneity of B-Mode image texture.

SNR is the ratio of average and standard deviation of the linear amplitude. The linear amplitude is calculated using tissue harmonic B-Mode data acquired under fixed transmission and reception conditions. UGFF has the scan sequence to acquire fundamental B-Mode base data for AC/IBSC measurement and tissue harmonic B-Mode base data for SNR measurement continuously *(Figure 3)*.

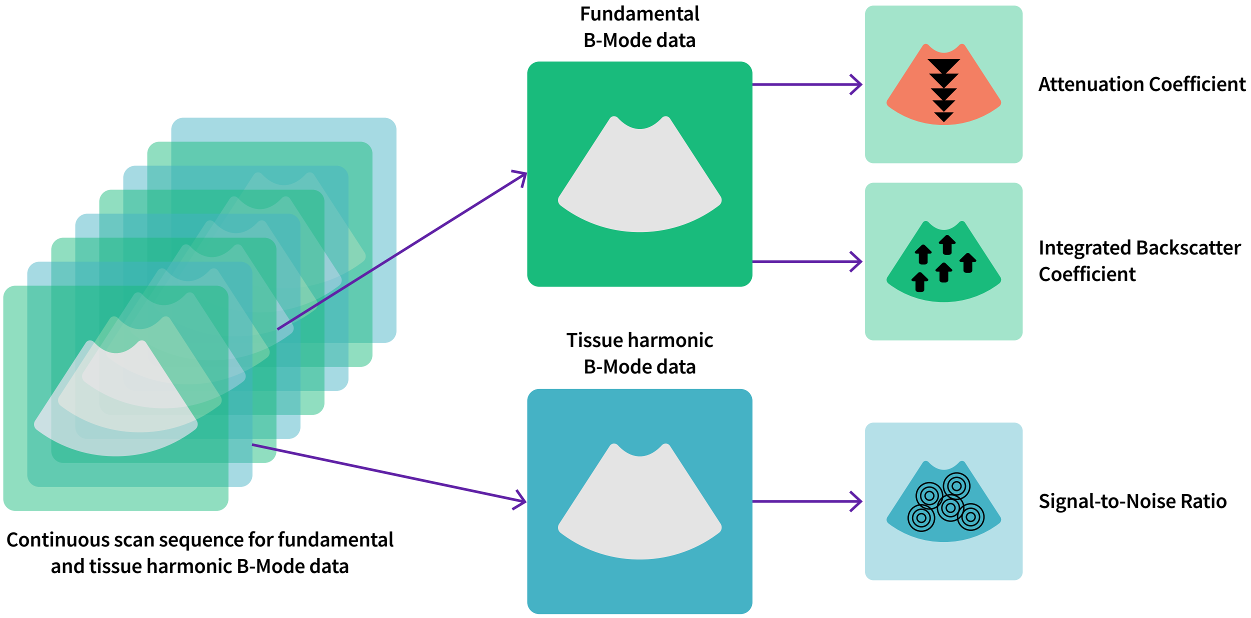


Figure 3: Continuous scan sequence for fundamental and tissue harmonic B-Mode data.

Study review[13]

Study design and methods

This prospective multicenter study enrolled a total of 582 patients with chronic liver disease (CLD) between 2020 and 2021 across six liver centers in Japan. The objective was to evaluate the diagnostic performance of ultrasound-derived parameters for the noninvasive assessment of hepatic steatosis, using MRI-PDFF as the reference standard. Each participant underwent ultrasound examinations to measure three QUS parameters: UGAP, IBSC, SNR. These measurements were performed five times per patient to evaluate interobserver repeatability and ensure data robustness.

Based on these parameters, the authors constructed four logistic regression models to predict the presence of ≥ 5% liver fat content:

- **Model 1 (UGAP) included AC alone**
- **Model 2 combined AC and IBSC**
- **Model 3 combined AC and SNR**
- **Model 4 (log UGFF) integrated all three parameters — AC, IBSC, and SNR**

This structured approach allowed the authors to directly compare the additive diagnostic value of each parameter and to determine the most accurate model for clinical application.

Results

The area under the curve (AUC) values for Models 1, 2, 3, and 4 (log UGFF) were 0.92 (0.90-0.94), 0.93 (0.91-0.95), 0.95 (0.94-0.97), and 0.96 (0.94-0.97), respectively. Among these, Models 3 and 4 showed significantly better discriminative performance than Models 1 and 2 (p<.01). Notably, log UGFF demonstrated the highest AUC, achieving 89.1% sensitivity and 90.2% specificity at a cutoff value of 0.74 *(Table 1, Figure 4A)*. Furthermore, log UGFF showed statistically significant positive correlations with the log MRI-PDFF (p<.01) *(Figure 4B)*.

	Model 1 (UGAP) (AC)	Model 2 (AC + IBSC)	Model 3 (AC + SNR)	Model 4 (log UGFF) (AC + IBSC + SNR)
AUC (95% CI)	0.92 (0.90-0.94)	0.93 (0.91-0.95)	0.95 (0.94-0.97)	0.96 (0.94-0.97)
Cutoff value	0.65	0.55	0.69	0.74
Sensitivity	0.92 (0.89-0.95)	0.89 (0.85-0.92)	0.87 (0.83-0.90)	0.89 (0.86-0.92)
Specificity	0.75 (0.69-0.80)	0.84 (0.79-0.89)	0.93 (0.89-0.96)	0.90 (0.85-0.93)
PPV	0.86 (0.83-0.89)	0.90 (0.87-0.93)	0.95 (0.93-0.98)	0.94 (0.91-0.96)
NPV	0.85 (0.81-0.91)	0.81 (0.76-0.86)	0.81 (0.76-0.86)	0.83 (0.79-0.88)

Table 1: Performance of various parameters for discrimination of ≥5% steatosis.

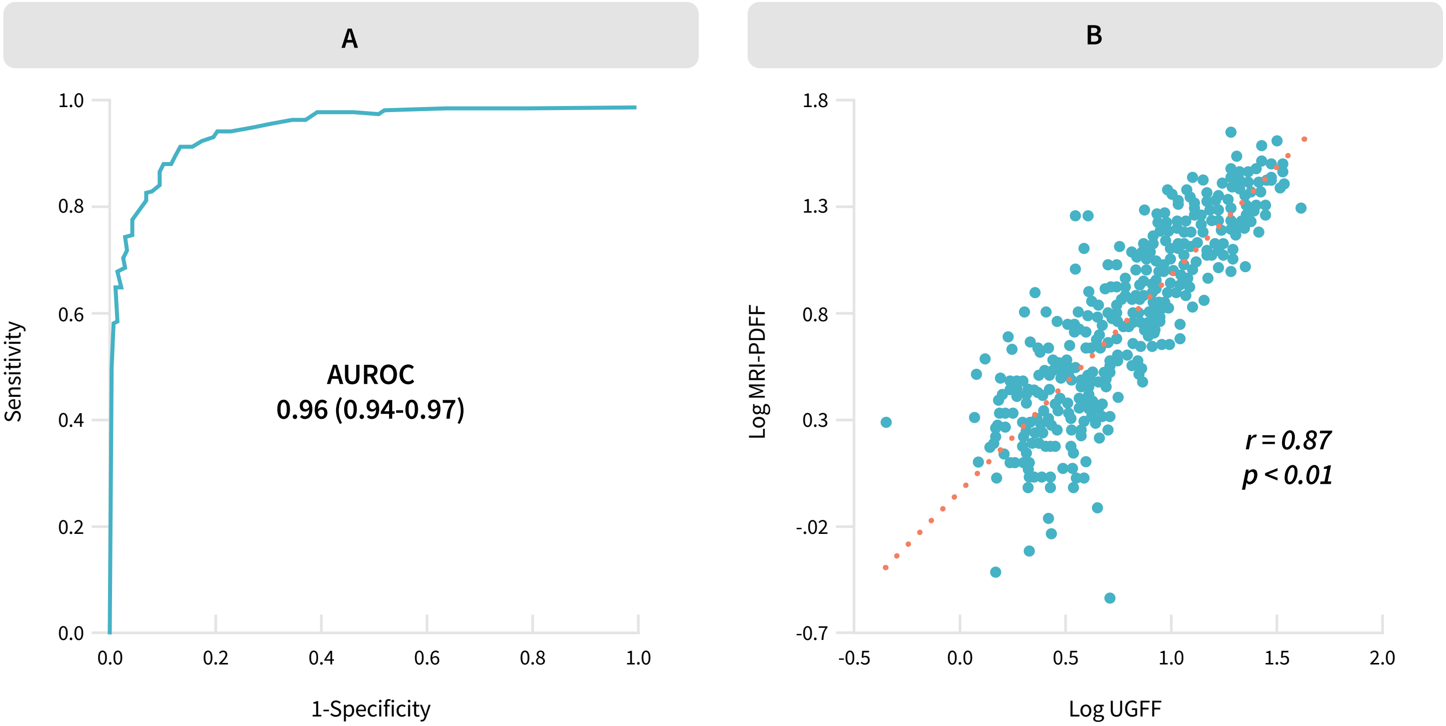


Figure 4: Receiver operating characteristic (ROC) curve for discrimination of ≥5% steatosis by UGFF **(A)** and its relationship with log MRI-PDFF **(B)**.

Sub-analysis

Model 4 (log UGFF) showed excellent diagnostic performance with all subgroups having AUC values ≥0.91, including participants aged ≥64 years, no NAFLD, BMI >25, and advanced fibrosis stages. By etiology, AUC values for discriminating Hepatitis B virus, Hepatitis C virus, non-alcoholic fatty liver disease and alcoholic liver disease were 0.96 (0.93-0.99), 0.95 (0.88-1.00), 0.94 (0.91-0.98), and 0.94 (0.87-1.00), respectively *(Figure 5)*.

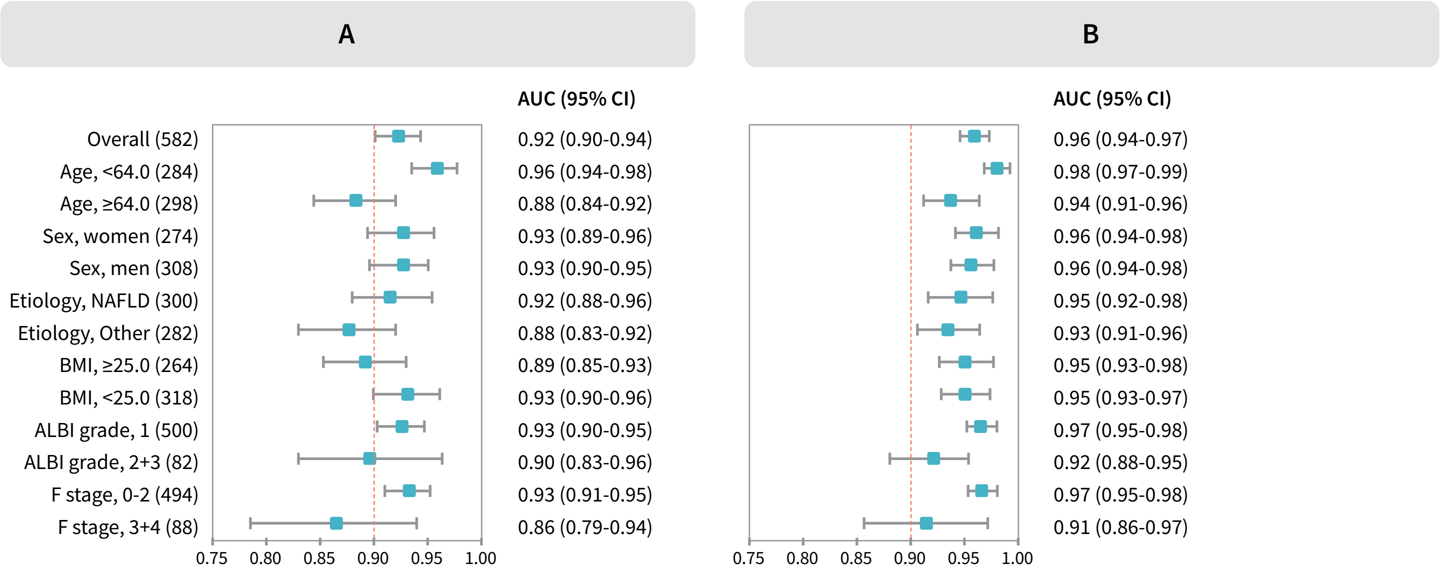


Figure 5: ROC subgroup analysis. Model 1 (UGAP). **(A):** suboptimal AUC in high-risk subgroups. Model 4 (log UGFF) **(B):** AUC ≥0.9 in all subgroups.
Abbreviations: NAFLD, nonalcoholic fatty liver disease; BMI, body mass index; ALBI, albumin-bilirubin index; F stage, fibrosis stage.

UGFF: Clinical workflow and practical implementation

Recommended workflow

As described above, the UGFF algorithm offers a clinically practical and noninvasive method for quantifying hepatic steatosis. The following steps outline the process for completing a UGFF measurement evaluation.

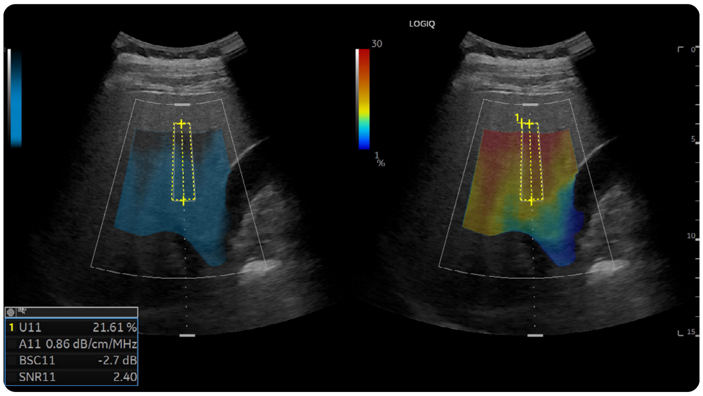
i. The examination begins with a **standard B-Mode ultrasound scan**. The probe should be positioned in an **intercostal approach**, and the operator should confirm that the liver **parenchyma is clearly visualized** with minimal interference from large vessels, ribs, or other anatomical structures.

ii. Once a relatively homogeneous liver section is identified, the operator activates **UGFF mode**. When an appropriate B-Mode image of the liver parenchyma is obtained, the operator starts UGFF data acquisition. As the UGFF algorithm uses B-Mode signals for its calculation, a few seconds of scanning is typically sufficient to acquire the necessary data frames.

iii. The operator presses the **Freeze** button to measure UGFF from the cine loop images. The **region-of-interest (ROI)** is initially placed at the center of the image. If large vessels or artifacts are included within the ROI, the position should be adjusted using the trackball. (Notably, the UGAP software includes an automatic ROI adjustment algorithm — minor obstructions or artifacts are either excluded in the background calculation, or prompt the operator to repeat the measurement.)

iv. Once the ROI is optimized, pressing the **Set** button will immediately display the calculated **UGFF value (% ultrasound fat fraction)**. The next cine frame is automatically selected, and the same procedure is repeated. In total, **five measurements** are performed or recommended per examination.

In addition to the UGFF value, an optional display of component parameters — **AC (UGAP), IBSC and SNR** — can be enabled. While these parameters are not required for the UGFF examination, it is recommended to display all of them as supplementary reference values.



1 U11 21.61 %
A11 0.86 dB/cm/MHz
BSC11 -2.7 dB
SNR11 2.40

Liver UGFF in Dual View, C1-6-D

Validation of the auto measurement algorithm

According to the WFUMB guidances for ultrasound-based attenuation measurement, the recommended ROI (3 cm in axial direction) should be positioned **2 cm below the liver capsule**. This recommendation is based on the need to avoid signal interference from superficial tissues such as the abdominal muscles and subcutaneous fat, which may cause multiple reflections that affect liver parenchymal signals. While this fixed-depth guideline is reasonable in many cases, the degree of such influence can vary depending on individual patient anatomy and scanning conditions. The study evaluated whether the automatic measurement adjustment algorithm implemented in UGFF provides results that are consistent with the WFUMB guidance recommendation.

To assess this, the raw data from 568 patients with chronic liver disease included in the previously published multicenter UGAP study was reanalyzed.[11] After skilled hepatologists or experienced sonographers manually adjusted the lateral position of the ROI, UGFF values were calculated in two conditions: (a) using the auto measurement algorithm, and (b) using a manually placed ROI at exactly 2 cm below the liver capsule, in accordance with WFUMB guidances.

The comparison results are shown in *Figure 6*. A strong and statistically significant correlation was observed between the two measurements (correlation coefficient = 0.972). In 96.3% of patients, the absolute difference between the two methods was within the limits of agreement (LOA), and the outliers were the same cases previously noted in the UGFF validation study.

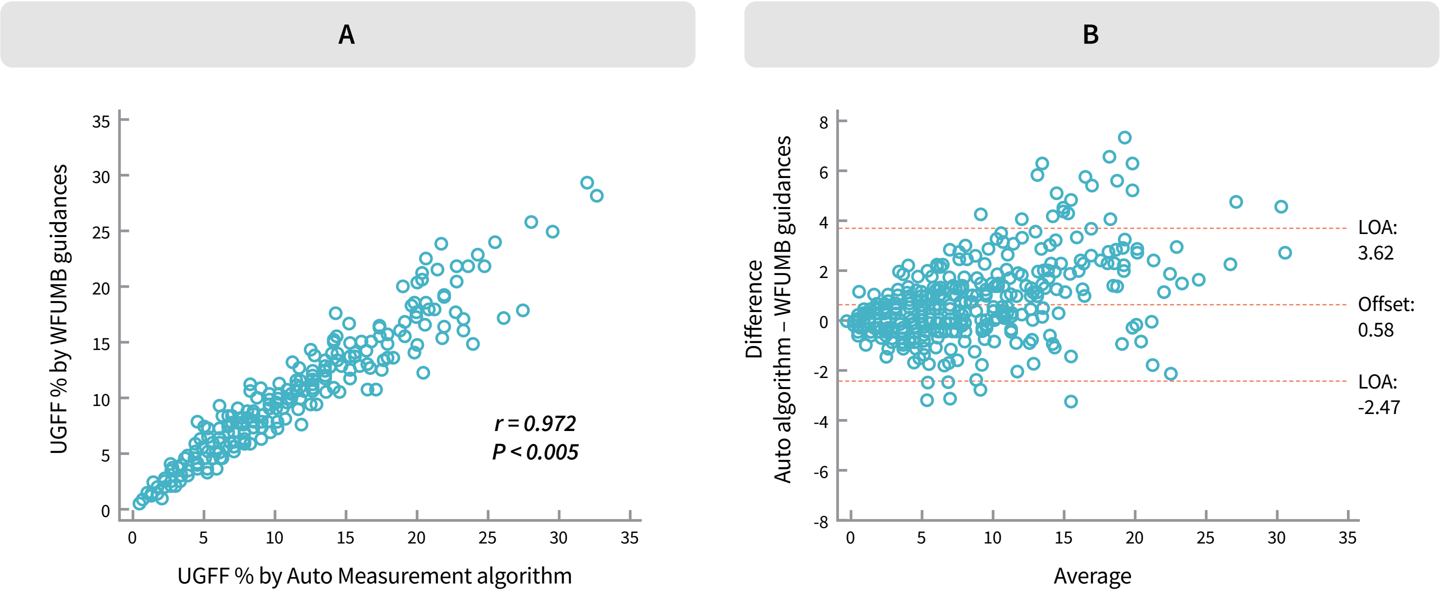


Figure 6: (A) Correlation between UGFF measurements obtained using the automatic measurement algorithm and those obtained with manual ROI placement at 2 cm below the liver capsule, as recommended by the WFUMB guidances. **(B)** Bland-Altman plot comparing the two methods.

Validation of the auto measurement algorithm *(continued)*

Furthermore, *Figure 7* presents the AUROC results for steatosis grading, based on MRI-PDFF as the reference standard. No significant differences were found in diagnostic performance between the UGFF values obtained by auto adjustment and those obtained with manual ROI placement at 2 cm below the liver capsule.

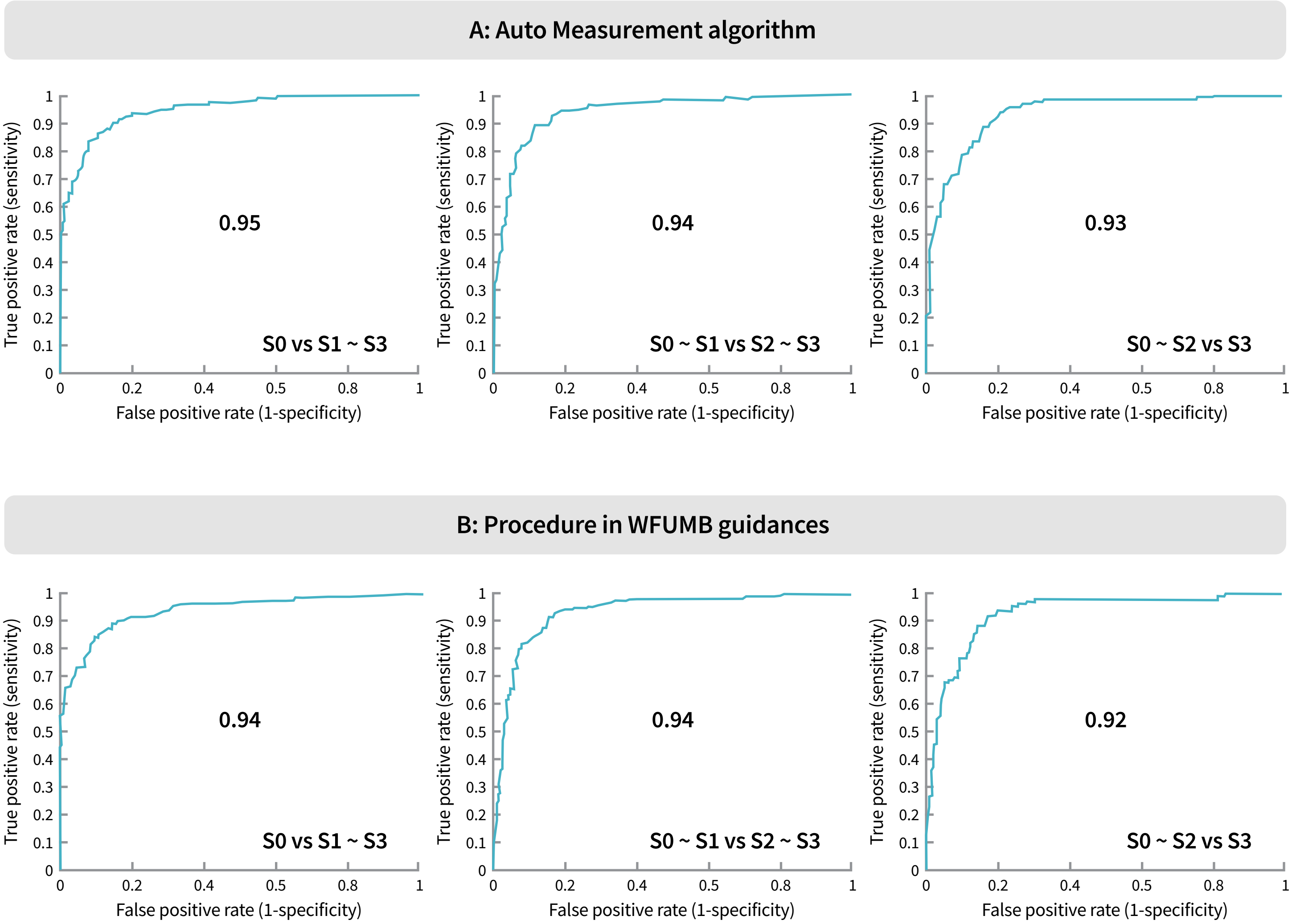


Figure 7: Comparison of diagnostic performance (AUROC) for each steatosis grade using **(A)** UGFF values derived from the automatic measurement algorithm and **(B)** manual ROI placement at 2 cm below the liver capsule.

Results

These findings indicate that the UGFF auto measurement algorithm can reliably produce results consistent with those recommended by the WFUMB guidances — without the need to manually measure the distance from the liver surface. This allows for improved workflow efficiency and reduced operator burden during clinical examinations.

UGFF: Cutoff values

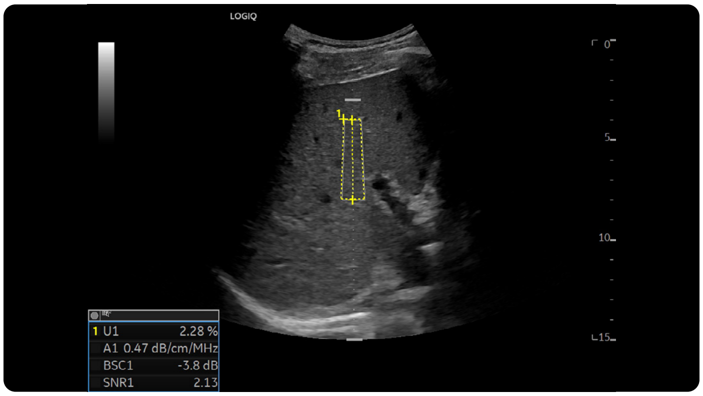
UGFF enables clinicians to accurately determine whether the liver contains more than 5% fat content, a critical threshold for the diagnosis of early-stage MASLD and MASH. AUROC and cutoff values for UGFF, AC, IBSC and SNR to diagnose each steatosis grade are shown in *Table 2*.

≥ S1	**UGFF**	**AC (UGAP)**	**IBSC**	**SNR**
AUC (95% CI)	0.96 (0.94-0.97)	0.90 (0.89-0.93)	0.86 (0.83-0.89)	0.91 (0.89-0.94)
Cutoff value	5.3%	0.65 dB/cm/MHz	-3.8 dB	2.2
Sensitivity	0.89 (0.85-0.92)	0.79 (0.75-0.83)	0.71 (0.66-0.75)	0.86 (0.82-0.89)
Specificity	0.90 (0.86-0.94)	0.91 (0.87-0.94)	0.86 (0.81-0.90)	0.83 (0.77-0.87)
PPV	0.94 (0.91-0.96)	0.94 (0.91-0.96)	0.90 (0.85-0.93)	0.90 (0.86-0.92)
NPV	0.83 (0.78-0.87)	0.72 (0.67-0.77)	0.64 (0.58-0.69)	0.78 (0.73-0.83)
≥ S2	**UGFF**	**AC (UGAP)**	**IBSC**	**SNR**
AUC (95% CI)	0.95 (0.94-0.97)	0.91 (0.89-0.93)	0.89 (0.87-0.92)	0.90 (0.87-0.92)
Cutoff value	8.8%	0.71 dB/cm/MHz	-3.6 dB	2.3
Sensitivity	0.90 (0.85-0.93)	0.91 (0.87-0.95)	0.87 (0.81-0.91)	0.90 (0.85-0.93)
Specificity	0.89 (0.85-0.92)	0.76 (0.72-0.80)	0.77 (0.72-0.81)	0.75 (0.70-0.79)
PPV	0.82 (0.77-0.87)	0.67 (0.63-0.74)	0.68 (0.62-0.73)	0.67 (0.61-0.72)
NPV	0.94 (0.91-0.96)	0.94 (0.91-0.96)	0.91 (0.87-0.94)	0.93 (0.89-0.95)
S3	**UGFF**	**AC (UGAP)**	**IBSC**	**SNR**
AUC (95% CI)	0.94 (0.91-0.96)	0.89 (0.87-0.92)	0.88 (0.86-0.91)	0.88 (0.85-0.91)
Cutoff value	11.4%	0.77 dB/cm/MHz	-3.5 dB	2.4
Sensitivity	0.87 (0.80-0.92)	0.80 (0.72-0.86)	0.96 (0.9-0.98)	0.81 (0.73-0.87)
Specificity	0.88 (0.84-0.90)	0.84 (0.80-0.87)	0.67 (0.63-0.71)	0.81 (0.77-0.84)
PPV	0.64 (0.57-0.71)	0.56 (0.48-0.63)	0.43 (0.37-0.49)	0.52 (0.45-0.56)
NPV	0.96 (0.94-0.98)	0.78 (0.73-0.83)	0.98 (0.96-0.99)	0.94 (0.91-0.96)

Table 2: AUROC and cutoff values for steatosis grading.

Compared to MRI-PDFF, UGFF offers a **cost-effective, accessible,** and **time-efficient** alternative that can be seamlessly integrated into routine ultrasound examinations. It is particularly suitable for both specialized liver centers and general clinical settings, enabling **timely screening of at-risk patients, stratification, early diagnosis,** and **longitudinal follow-up of fatty liver disease** without requiring additional equipment or advanced imaging modalities.

By combining quantitative accuracy with workflow compatibility, UGFF represents a major step forward in the practical implementation of noninvasive liver fat assessment.



Liver UGFF, C1-6-D

Conclusion

UGFF represents a major advancement in the noninvasive assessment of hepatic steatosis, delivering a unique combination of quantitative precision, clinical accessibility, and workflow integration. By leveraging multiparametric QUS biomarkers, UGFF addresses key limitations of existing modalities and provides clinicians with a scalable solution for accurate liver fat quantification.

With further external validation and integration into clinical guidelines, UGFF has the potential to become a standard component of MASLD diagnostic pathways — particularly in resource-limited or high-throughput environments where efficiency and reproducibility are critical. Beyond diagnosis, this innovation enables improved screening, patient stratification, treatment planning, and disease monitoring — ultimately supporting earlier intervention and better patient outcomes in the face of a growing global liver health crisis.

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