Advances in Quantitative Imaging Assessment of Hepatic Steatosis

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Abstract: The liver serves as a critical site for lipid metabolism. Under pathological conditions such as obesity and metabolic disorders, disrupted lipid metabolism leads to abnormal accumulation of triglycerides within hepatocytes. Persistent and excessive fat accumulation may exacerbate hepatocyte injury, progressively evolving into steatohepatitis, liver fibrosis, and even hepatocellular carcinoma. Therefore, quantifying hepatic fat content is crucial for early diagnosis and disease management. This article summarizes advances in imaging techniques for assessing hepatic steatosis, with a focus on the clinical application and progress of magnetic resonance imaging proton density fat fraction in quantitative hepatic fat measurement.
***Keywords*:** hepatic steatosis, MRI-PDFF, MASLD

1. Introduction

Hepatic steatosis, with lipid accumulation exceeding 5% of hepatocytes, is the pathological basis of metabolic dysfunction-associated steatotic liver disease (MASLD). This condition can progress to metabolic dysfunction-associated steatohepatitis (MASH), cirrhosis, and hepatocellular carcinoma, affecting approximately 30% of the global population[1]. Therefore, early detection and quantification of hepatic steatosis are critically important. This paper recapitulates the latest progress in quantitative imaging studies related to hepatic fat content.

2. Imaging Methods for Assessing Liver Fat Content

2.1 Ultrasound

Conventional ultrasound serves as the first-choice approach for detecting hepatic steatosis, though its sensitivity and specificity are lower for mild fatty liver disease. Quantitative ultrasound techniques based on radiofrequency signals enable more objective quantification of liver fat. Quantitative ultrasound techniques primarily include attenuation coefficient(AC), backscatter coefficient(BSC), and sound velocity measurement. Ultrasound propagation through the liver is influenced by fat content. Lipid deposition can lead to increased sound energy attenuation and enhanced acoustic scattering, manifesting as elevated attenuation coefficients and backscatter coefficients, along with reduced sound velocity.

Ultrasound-Guided Attenuation Parameter Imaging (UGAP) is an emerging ultrasound technique for quantitative analysis of hepatic steatosis by measuring the liver attenuation coefficient (AC).Huang[2] reported that UGAP demonstrated high diagnostic accuracy for grading hepatic steatosis (S1-S3) with an AUC ranging from 0.88 to 0.91. The cutoff values for diagnosing ≥S1, ≥S2, and S3 steatosis using UGAP were 0.62 dB/cm/MHz, 0.76 dB/cm/MHz, and 0.82 dB/cm/MHz, respectively. In a study [3]of 1,010 chronic liver disease patients and another of 100 confirmed MASLD patients [4], UGAP exhibited excellent diagnostic efficacy for the grading of steatosis, with AUC values spanning 0.89-0.91 and 0.78-0.82 correspondingly. Additionally, UGAP measurements demonstrated high interoperator and intraoperator consistency, where the intraclass correlation coefficients (ICC) were 0.92 and 0.95, respectively.

Combining AC and BSC, the composite ultrasound technique referred to as ultrasound-determined fat fraction (UDFF) demonstrates high diagnostic performance. Nakamuraet al.[5] demonstrated a strong association between UDFF and histopathological fat assessment, and its sensitivity for mild steatosis surpassed 90%. In a multicenter study of 790 MASLD patients[6], using reference standards including histopathological diagnosis (n=342), MRI-PDFF (n=396), and 1H-MRS (n=52), UDFF demonstrated diagnostic cutoff values of approximately 8%, 14%, and 20% for ≥S1, ≥S2, and S3, respectively. In a 300-patient study with MRI-PDFF as the reference standard, the diagnostic threshold values of UDFF for ≥S1, ≥S2, and S3 were 7.6%, 15.9%, and 22.3%, respectively [7]. In Cao Xinge's study[8],identified the optimal UDFF cutoff values as 6.02%, 15.12%, and 22.98% for these respective grades. Even when using the same reference standard, cutoff values varied across studies. Wang [9]found that UDFF measurements significantly correlated with the presence of hepatic steatosis in chronic liver disease. The UDFF threshold for diagnosing liver steatosis in patients with chronic liver disease was 5.8%, with an AUC of 0.861, sensitivity of 76.7%, and specificity of 82.0%. As a highly precise and reproducible detection technique,UDFF is suitable for large-scale population screening and follow-up monitoring.

The sound velocity in liver tissue is measured using plane wave ultrasound. Current research has paid relatively little

attention to sound velocity. Halima Gottfriedova[10]evaluated 56 patients with liver biopsies confirming fatty degeneration. The results showed that the AUC values for sound velocity in distinguishing the presence or absence of fatty degeneration and moderate-to-severe fatty degeneration were 0.78 and 0.89, respectively, indicating a high diagnostic capability for moderate-to-severe fatty degeneration.

2.2 Computed Tomography

CT measures liver fat through variations in X-ray attenuation, with units in Hounsfield units (HU). Liver fat content can be reflected by the level of CT values, but these results are susceptible to interference from iron deposition and other pathologies. Plain CT scans are generally preferred over contrast-enhanced CT, as iodine contrast agents increase liver attenuation values, thereby affecting comparisons of hepatic fat content. Enhanced CT has also made significant advances in assessing hepatic steatosis. Research using a 3D U-Net deep learning model[11] demonstrated that inputting enhanced liver CT images can generate predicted MRI-PDFF images and fat fractions. Although numerical discrepancies exist between the two methods, they exhibit high consistency in low-fat classifications (<15%), achieving 86.4% classification accuracy and a kappa coefficient of 0.75. This approach eliminates reliance on organs like the spleen. Leveraging TotalSegmentator automated segmentation and a three-phase attenuation equation enables screening for severe steatosis. Kappa coefficient of 0.75), with a predicted root mean square error of 4.27%, eliminating reliance on organs like the spleen. Utilizing TotalSegmentator automated segmentation and the three-phase attenuation equation enables screening for severe fatty liver disease (three-phase AUROC of 0.92–0.97)[12]. Additionally, China's United Imaging has developed the 3D Fatty Analysis and Computation Technology (FACT) sequence. The FACT sequence achieved AUC values of 0.99, 0.963, and 0.963 for assessing mild, moderate, and severe fatty liver disease, respectively. The optimal cutoff values for diagnosing different degrees of fatty liver were 4.9%, 12.17%, and 23.19%[13]. These studies demonstrate that clinically widely available CT can be utilized for liver fat screening and quantitative assessment.

Quantitative CT (QCT) is a non-invasive method for measuring bone density and fat content based on existing CT images. Studies have confirmed that liver fat content measured by QCT shows high consistency with MRI and biochemical results, as validated by goose liver samples [14]. AI models based on abdominal plain CT demonstrate good performance in diagnosing steatosis and exhibit high consistency with QCT measurements[15]. In clinical practice, QCT can also assess risks in cirrhotic patients. For instance, elevated hepatic fat content combined with decreased hemoglobin may increase the probability of esophageal and gastric variceal bleeding[16]. Furthermore, multiple studies[17, 18] indicate that multi-energy photon-counting CT (PCCT) can accurately quantify hepatic fat in material images. A recent computer simulation imaging study[19]employed in vivo phantoms and human liver models with material decomposition techniques. It demonstrated that deep silicon detector photon-counting CT (dSi-PCCT) exhibits high accuracy across a 1%-50% fat fraction range, and the correlation between estimated and actual values is exceptionally strong (R^2=0.98), indicating its capacity for liver fat quantification.

2.3 Magnet Resonance Imaging

Clinically, the primary methods for qualitative assessment of fatty degeneration via MRI include chemical shift imaging (Dixon technique) and fat suppression techniques. MRI evaluation of hepatic steatosis has evolved from qualitative to quantitative assessment. Currently, widely applied MR quantitative techniques for measuring liver fat content include magnetic resonance spectroscopy and multi-echo chemical shift encoding MRI.

The primary peaks in liver MRS originate from hydrogen protons in fat and water molecules. Direct comparison of fat and water peak areas enables quantitative fat analysis. This technique is extensively used for metabolite assessment in liver diseases. The breath-hold single-unit high-speed T2-corrected multi-echo 1H magnetic resonance spectroscopy (MRS) sequence enables quantitative liver fat analysis via compensation for R2 relaxation effects in water and fat.. Studies indicate high consistency between MRS and MRI-PDFF in quantifying hepatic fat content, with MRS being less susceptible to interference from iron deposition, liver fibrosis, and other hepatic lesions. However, MRS also has limitations. 1H MRS imaging acquisition includes both mono- and multi-voxel scans. Mono-voxel scans measure only the liver region, potentially introducing errors due to localized fat deposition and exhibiting lower repeatability. While multi-voxel scans cover a larger liver area, they increase patient scan time. Furthermore, some MRI machines lack MRS software configuration, limiting MRS application.

Derived by multi-echo chemical shift encoded MRI (CSE-MRI) water-fat separation technology, the MRI-PDFF value stems from the ratio of fat signal intensity to the combined total signal intensity of water and fat. This sequence employs small flip angles and multi-echo acquisition to minimize interference from T1 effects and iron deposition. Manual ROI delineation enables precise measurement of MRI-PDFF and R2* values. MRI-PDFF enables whole-liver fat content assessment, effectively avoiding the trauma and sampling errors associated with needle biopsy.

MRI-PDFF demonstrates high concordance with liver histopathology findings,and outperforms other imaging

techniques in quantitative liver fat analysis, establishing it as a clinical trial endpoint for evaluating drug efficacy. Hepatic steatosis serves as the histopathological cornerstone of MASLD and is closely associated with disease progression. Numerous studies have employed MRI-PDFF to analyze steatosis in MASLD. In the Loomba trial[20], a ≥30% decline in MRI-PDFF correlated strongly with meaningful histological response. This response translates to a reduction of at least 2 points in the MASLD Activity Score, encompassing improvements in steatosis, inflammation, and ballooning, with no progression in fibrosis stage.The probability of achieving an histologic response was 19% in patients with an MRI-PDFF decrease <30% and 50% in those with a decrease ≥30%. Comparing responders and non-responders based on MRI-PDFF, significant improvements in histological features were observed, with 85% versus 25% of patients achieving ≥1-grade reduction in steatosis, and 50% versus 26% in ballooning. This improvement was further quantified in a meta-analysis of 346 subjects, which showed that over half (51%) of patients with a >30% MRI-PDFF reduction achieved the primary histological endpoint, corresponding to a robust odds ratio of 6.98 [21]. Similarly, achieving this MRI-PDFF threshold was associated with a six-fold greater likelihood of fibrosis improvement (≥1-stage) in a later prospective study[22]. MRI-PDFF response was significantly correlated with NAS improvement and fibrosis regression. These findings collectively suggest that histological response correlates with PDFF, and a relative decrease in MRI-PDFF of ≥30% may serve as an imaging endpoint for evaluating treatment efficacy in the MASH trial.

2.4 Radiomics

Radiomics and artificial intelligence offer new perspectives for precise assessment and risk prediction of hepatic steatosis. Studies by Nasir and Derstine[11, 12] enabled in-depth investigation of fat content within conventional CT imaging techniques. Chen's team[23]employed MRI-PDFF combined with deep learning models to identify PNPLA3 carriers, revealing characteristic hepatic fat distribution in homozygous patients—particularly pronounced perivascularly in the hepatic hilum—enabling early intervention and targeted therapy opportunities. Multiple machine learning models integrating demographic and clinical features now exist for screening MASLD occurrence in populations. A machine learning model incorporating eight baseline variables (e.g., age, education level) from 10,007 outpatient cases achieved an internal ROC curve of 0.798–0.806 for predicting MASLD occurrence via logistic regression, with external validation yielding 0.831[24]. Another European study[25] demonstrated that 19 conventional clinical indicators obtained through blood tests and outpatient examinations could predict advanced MASLD outcomes (MASH and fibrosis), with ROC curves ranging from approximately 0.719 to 0.994. Artificial intelligence demonstrates high diagnostic performance and clinical applicability in assessing hepatic steatosis imaging, enabling not only quantitative assessment of fat content but also identification of early-stage liver fibrosis. Machine learning models utilizing routine clinical data demonstrate significantly superior performance in detecting advanced fibrosis among MASLD patients compared to conventional scoring systems like FIB-4 and the NAFLD fibrosis score, attaining an area under the curve of 0.91. A pooled analysis[26] incorporating 15 studies confirmed that AI models based on abdominal imaging demonstrate high diagnostic performance for detecting liver fibrosis and MASLD, with sensitivities, specificities, and AUC values of 0.85, 0.81, and 0.92, and 0.86, 0.95, and 0.99, respectively. This demonstrates the diagnostic advantages of multimodal imaging approaches, enabling early identification and management of high-risk populations for MASLD.

3. Conclusion

In summary, the aforementioned quantitative imaging techniques all hold value for quantifying hepatic fat content. Offering non-invasiveness, whole-liver assessment, and robust reproducibility, MRI-PDFF has become the imaging standard for analyzing hepatic fat content and an indicator for evaluating drug efficacy. A relative decline of 30% or more in MRI-PDFF correlates with histological improvement and is also linked to the amelioration of liver fibrosis.However, the direct relationship between this metric and cirrhosis or adverse hepatic events remains unclear. Furthermore, current studies are predominantly small-sample, single-center clinical investigations, with limited data in populations such as children and diabetic patients. Therefore, large-scale, multicenter clinical studies across diverse populations are needed, combined with radiomics approaches to achieve more intelligent diagnosis and assessment.

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