

ORIGINAL ARTICLE | Abdominal Imaging

MRI calculated liver fat mass as a new biomarker for steatosis grade evaluation in middle age population

Panagiotis Koussis¹, George Thiveos⁵, Angeliki Meritsi²,
Anastasia Thanopoulou², Eleni Lamprou³, Emanuel Manesis⁴

¹ Medical Physics Department, BIOIATRIKI SA, Athens, Greece

² Diabetic Center, 2nd Department of Internal Medicine, Medical School,
National and Kapodistrian University of Athens, Athens, Greece

³ 1st Senior High School of Kifissia, Athens, Greece

⁴ Liver Unit, Euroclinic, Athens, Greece

⁵ Diagnostic & Therapeutic Nuclear Medicine Department, Henry Dunant Hospital Center, Athens, Greece

SUBMISSION: 18/04/2026 | ACCEPTANCE: 11/05/2026

ABSTRACT

Purpose: Steatosis, the condition where intracellular excess fat accumulates in the liver, is a growing health concern worldwide.

This is a meta-analysis from MRI data, that was initially produced to investigate the relation of Hepatic Steatosis with abdominal obesity and PNPLA3 molecu-

lar variability in Metabolic dysfunction-associated steatotic liver disease patients. It aims to investigate and statistically confirm any correlation of fat mass in liver with steatosis grade by using MRI-PDFF as a diagnostic tool and introduce liver fat mass as a new biomarker for steatosis grade assessment.



KEY WORDS

Fat Mass, Liver Volume, Steatosis, Fat Fraction



CORRESPONDING AUTHOR, GUARANTOR

George Thiveos, Medical Physicist MSc, Davaki 39 Str, Chaidari, Athens, Greece
Tel: 00306972083811, E-mail: geothiv@yahoo.com

Panagiotis Koussis, BSc, MEd, MSc, PhD (candidate), Irodou Attikou 30
15233 Athens, Greece
Tel: ++30 6974008372, E-mail: p_koussis@yahoo.gr, pkousis@bioiatriki.gr

Material and Methods: A sample of 162 Metabolic dysfunction-associated steatotic liver disease patients and healthy volunteers (average age 60.3y) participated and had abdomen MRI scan with a 3D-GE IQ-IDEAL and a 3D-LAVA sequences. Fat fraction, liver fat mass and liver volume were calculated. Statistical analysis was performed to evaluate data, including Shapiro-Wilk test, Kruskal-Wallis test, Dunn's post-hoc test with Bonferroni correction and Ordinal Logistic Regression.

Results: Statistical analysis proves that there is a strong positive correlation between liver fat mass and steatosis grade; higher fat mass is associated with higher grades of steatosis. From the Predicted Probabilities diagram, we calculated, as a sum of probabilities, the steatosis grade from a given liver fat mass, in a non-discrete steatosis scale.

Conclusions: MRI fat mass estimation could serve as a reliable and clinically meaningful biomarker for Metabolic dysfunction-associated steatotic liver disease (MASLD). The ability to calculate steatosis grade in a more precise non-discrete form may help to better evaluate and monitor a patient's condition through time.

Introduction

Steatosis, the fatty liver disease, is the condition where intracellular excess fat accumulates in the liver. Though it is related to conditions like alcoholism, viral hepatitis, HIV etc., it is a growing health concern in non-alcoholic population worldwide, mostly in developed countries. According to the World Health Organization, 25%-30% of the adult population are affected by the condition. The broader term Metabolic dysfunction-associated steatotic liver disease (MASLD) includes simple Fatty Liver (mild steatosis condition) and Metabolic dysfunction-associated Steatohepatitis (MASH, severe condition). While mild steatosis may not affect liver function, potential progression to MASH may result in hepatic fibrosis, cirrhosis or carcinoma. Risk factors for steatosis include obesity, insulin resistance, high cholesterol, BMI and triglyceride levels.

Affecting a quarter of the world's population [1], MASLD is increasing in parallel with Type 2 Diabetes and metabolic syndrome. It is currently estimated that 70% of subjects with Type 2 Diabetes have MASLD [2, 3] and 20-30% Non-Alcoholic Steatohepatitis (NASH). This specific population is at high risk of progressing

to advanced fibrosis and cirrhosis [4], or even worse to hepatocellular carcinoma (HCC). Thus, it is important to recognize high-risk people with MASLD in order to provide them with optimal management.

Liver biopsy remains the golden standard for high-risk NASH and advanced fibrosis population. Nevertheless, its invasive nature, high cost and potential inter and intra-observer heterogeneity, make it less attractive as a diagnostic, monitoring and screening population tool [5].

MRI data used in this study were initially produced to investigate the relation of Hepatic Steatosis with abdominal obesity and PNPLA3 molecular variability in Non-Alcoholic Fatty Liver Disease (MASLD) patients [6, 7].

The aim of this study post-processed analysis, is to investigate and statistically confirm any correlation of fat mass in liver with steatosis grade by using MRI-PDFF as a diagnostic tool. Proven correlation could introduce liver fat mass as a new biomarker for assessment of steatosis grade.

Material and Method

a. Sample

A sample of 162 Non-Alcoholic Fatty Liver Disease patients (91 male / 71 female) with average age 60.3y, had liver MRI in our lab. The initial population of 120 patients included in references 6 & 7 was increased by 42 patients who also met the criteria and participated in the study. All participants were fully informed about the study and provided written consent to participate in it. Their privacy and data protection were ensured in accordance with the applicable General Data Protection Regulation protocols. In general population males have larger liver volumes than females. Male liver volumes decline faster than those of females with age, so that at the age of 60y (55-65y) liver volumes are effectively about the same size [13, 14]. As the average age of the participants was 60.3y, we did not separate males from females.

b. Specifications and parameters

The scans were performed using GE MR 750 Discovery 3.0T scanner. The protocol included the sequences: GE IQ IDEAL with 6 echo time (from 1.0 to 4.8 ms) field-of-view 46cm, slice thickness 8mm, TR = 6.2 ms,

frequency/phase 192/160, bandwidth 125Hz, and GE 3D LAVA echo time 1.1 ms, field-of-view 44cm, slice thickness 4mm, TR = 3.8 ms, frequency/phase 320/224, bandwidth 166.7Hz.

c. Fat fraction calculation

IQ IDEAL, is a multi-echo MR sequence using Dixon's technique for fat and water separation. It automatically produces 4 sets of images: (a) WATER only signal (b) FAT only signal (c) T2 star and (d) Fat Fraction as seen on Image 1. The last set of images gives the ability to easily perform fat fraction measurements of the appearing tissues [8].

On this set of images, fat fraction was measured in each liver segment, and the total liver fat fraction was considered as the average from all segments.

d. Liver volume calculation

Images from GE 3D LAVA sequence were reformatted in axial and coronal planes in slices of 10mm with no gap, then measurements of liver volumes were taken manually from each plane, excluding big vessels and any other non-liver structure. The total liver volume,

expressed in cubic cm, was estimated to be the average volume measurement from the two planes, to eliminate any systemic errors in the mandatory measurement procedure. This task was performed using General Electric Company ReportCARD 4.0 (2008-9) software which was initially designed for Cardiac MRI calculation but is also able to perform volumetric measurements.

e. Fat mass calculation

Fat mass in the liver (FML), measured in grams, was calculated considering fat fraction, liver volume, and triglycerides density (FD) in body temperature, which is 0.9gr/cm³ [9]. Knowing the liver volume (LV) and fat fraction (FF), the volume of fat in the liver (FLV) is calculated by the formula: $(FLV) = (FF)(LV)$. Fat mass in the liver was then calculated from the density equation as: $(FML) = (FLV)(FD)$.

f. Fat mass and steatosis grade

Fat mass data were grouped according to the steatosis grade, which typically is based on the number of cells with intracellular vacuoles of fat. According to this scale: grade 0 (normal) equals to less than 5% affected cells, grade 1 (mild) equals from 5% to 33% of cells, grade 2 (moderate) equals from 34% to 66% cells and grade 3 (severe) equals to more than 67% affected cells. But the percentage of the affected cells does not correspond directly to the fat-fraction percentage as calculated with MRI PDFF [12]. So, we used reliable bibliography [10], where histological results considered, to relate PDFF fat fraction with steatosis grade.

g. Statistical analysis

We performed Shapiro-Wilk test ($\alpha=0.05$) to investigate if data is normally distributed. Because non-parametric statistical methods were employed, Kruskal-Wallis test was used to compare the steatosis grade with calculated fat mass in liver (expressed in gr). To further assess pairwise differences for Type I error due to multiple comparisons, Dunn's post-hoc test with Bonferroni correction was performed. This allowed adjusted p-values and robust interpretation of group-wise differences. Analysis was performed using the online platform Statistics Kingdom (2017): Shapiro Wilk Test, Kruskal-Wallis test, Dunn's post-hoc test, Ordinal Logistic Regression.

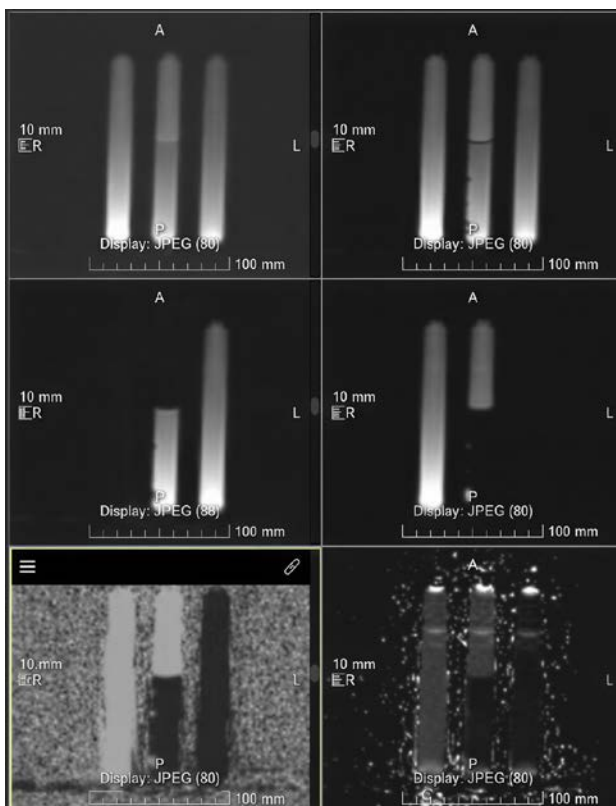


Image 1: MR IQ Ideal sequence

Results

In the total population, with steatosis grade 0 average liver mass was found to be 58.69 gr, with steatosis grade 1 average liver mass was found to be 182.11 gr, with steatosis grade 2 average liver mass was found to be 374.01 gr, with steatosis grade 3 average liver mass was found to be 672.15 gr (Table 1).

Table 1: Steatosis Grade and average liver fat mass

STEATOSIS GRADE	FF (%)	Avg FAT MASS (gr)
0 (normal)	0 - 6,4	58,69
1 (mild)	6,5 - 17,4	182,11
2 (moderate)	17,5 - 22,1	374,01
3 (severe)	> 22,2	672,15

Based on the Shapiro-Wilk test ($\alpha = 0.05$), the p-value was < 0.001 . Since p-value $< \alpha$, we reject the null hypothesis (H_0) and conclude that the data are not normally distributed. In other words, the difference between the data sample and the normal distribution is big enough to be statistically significant. The test statistic W equals 0.6972, which is not in the 95% region of acceptance: (0.9901, 1). The observed effect size KS - D is large, 0.2957. This indicates that the magnitude of the differ-

ence between the sample distribution and the normal distributions is large.

Therefore, the Kruskal-Wallis test was used to compare the steatosis grade with calculated fat mass in liver expressed in grams. The result ($H=137.9728$, p-value: 1.03×10^{-29}) indicates a highly significant difference in fat mass across steatosis grades. Results are graphically presented in figure 1 (Fig. 1).

To further assess pairwise differences for Type I error due to multiple comparisons, Dunn's post-hoc test with Bonferroni correction was performed. This allowed adjusted p-values and robust interpretation of group-wise differences. Dunn's Post-hoc Test (Bonferroni-adjusted p-values) proves that Grades 0 vs 1, 0 vs 2, 0 vs 3, and 1 vs 3 show strong significant differences while 1 vs 2 is borderline significant ($p \approx 0.0485$) and 2 vs 3 is not significant after Bonferroni correction. Results are shown in Table 2 (Table 2).

The Ordinal Logistic Regression analysis on the dataset of liver fat mass and steatosis grade yielded statistically significant results: Fat Mass Coefficient: Estimate 0.0415 with p-value: < 0.001 . This means that as liver fat mass increases, the odds of being in a higher steatosis grade also increase. This relationship is statistically significant. The Thresholds Between Grades (cut-points for transitions between ordinal categories): Grade 0/1: 4.40, Grade 1/2: 2.15, Grade 2/3: 1.51. These values help define the boundaries between steatosis grades in the

Figure 1. Bar plot with results and p-values that present statistical significance of liver fat mass between steatosis grades

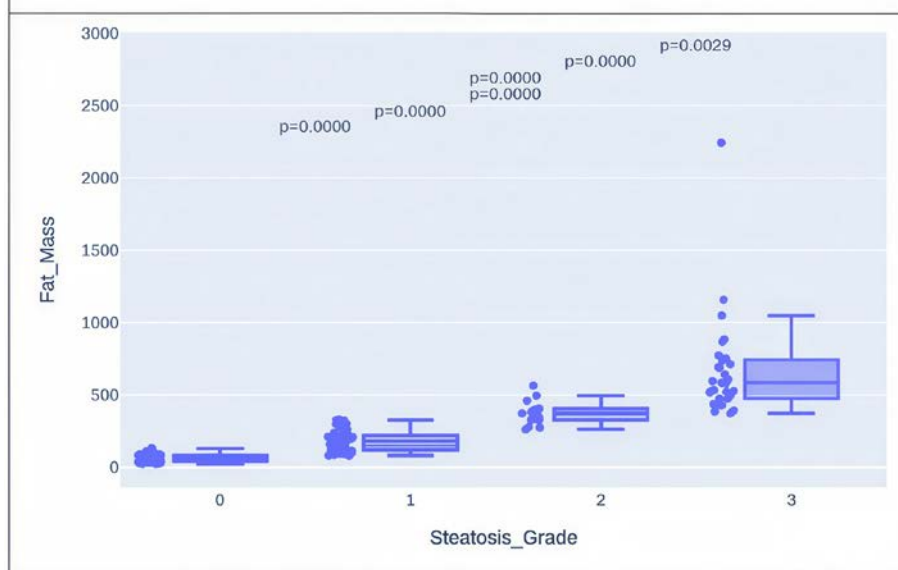


Table 2: Dunn's Post-hoc Test results

Comparison between Grades	z-score	p-value
0 vs 1	6.5256	4.06×10^{-10}
0 vs 2	6.8979	3.17×10^{-11}
0 vs 3	10.7499	$< 1 \times 10^{-12}$
1 vs 2	2.6484	4.85×10^{-2}
1 vs 3	5.2148	1.10×10^{-6}
2 vs 3	1.3444	1.00 (not significant)

logistic model. There is a strong positive correlation between liver fat mass and steatosis grade. The model confirms that higher fat mass is associated with higher grades of steatosis. The visualization of predicted probabilities is presented in figure 2 (Fig. 2).

For each additional gram of liver fat, the odds of being in a higher steatosis grade increase by ~4.2%. This increase is consistent and statistically significant, meaning it's unlikely to be due to chance. The confidence interval confirms that the true effect is likely between 3.0% and 5.3% increase per gram. An Example: If a patient's liver fat increases from 100g to 110g, the odds of being in a higher steatosis grade increase by approximately: $1.04210 \approx 1.52$.

That's a 52% increase in odds, a clinically meaningful change.

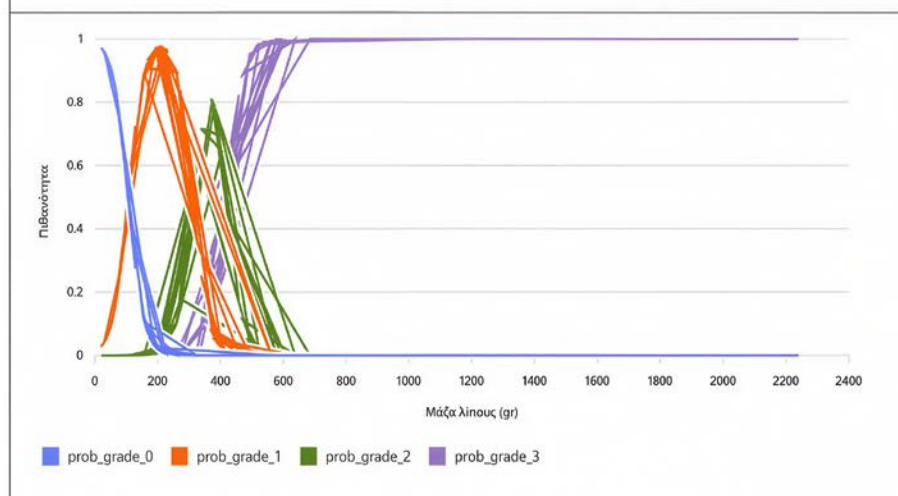
From figure 2 it is easy to calculate (as a sum of probabilities) the steatosis grade from a given (calculated) liver fat mass, in a more precise non-discrete scale. An example is given in figure 3 (Fig. 3).

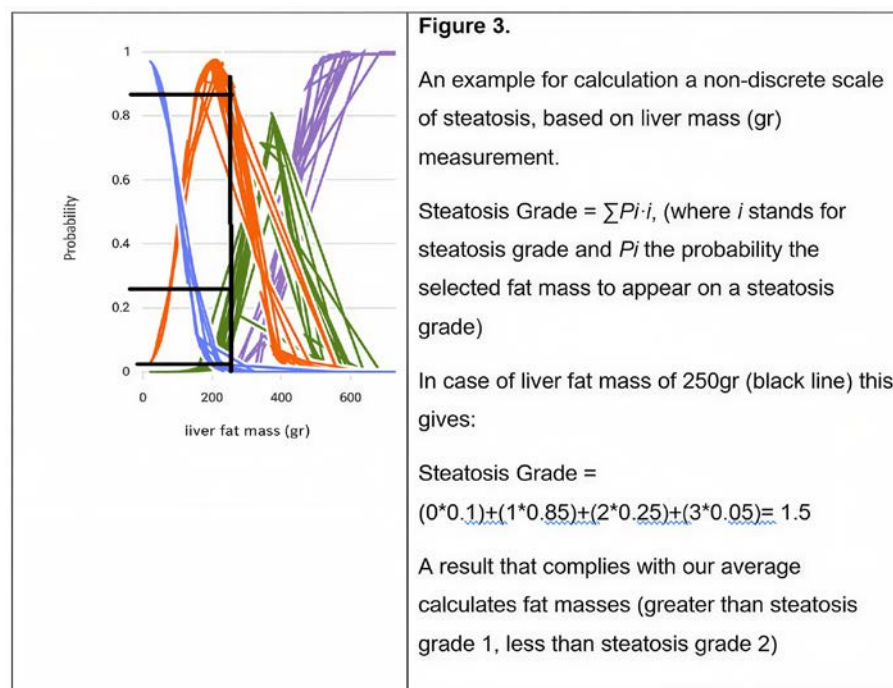
Discussion & Conclusion

Liver biopsy remains the gold standard for assessing steatosis grade; however, it is invasive, costly, and limited by sampling variability, as it evaluates only a small portion of the liver. In contrast, MRI-based proton density fat fraction (PDFF) offers a non-invasive, patient-friendly, and more comprehensive alternative. PDFF enables fat quantification across the entire liver, making it particularly valuable in cases of heterogeneous fat distribution. While other imaging modalities such as ultrasound (US) [11] are more accessible and affordable, they lack the sensitivity and accuracy of MRI-PDFF in detecting and grading hepatic steatosis at least in older US scanners.

Previous studies have shown a strong correlation between hepatic fat fraction and automated liver volume. Notably, we found a strong correlation between liver fat mass and steatosis grade, suggesting that fat mass estimation could serve as a reliable and clinically meaningful biomarker for nonalcoholic fatty liver disease (MASLD). The ability to calculate steatosis grade

Figure 2. Visualization of Predicted Probabilities: The plot shows how the probability of each steatosis grade (0 to 3) changes with increasing liver fat mass. In this context, the odds ratio quantifies how the odds of being in a higher steatosis grade change with each 1 gram increase in liver fat mass. Odds Ratio for fat mass: approximately 1.042, 95% Confidence Interval, p-value: < 0.001 (statistically significant).





in a more precise non-discrete form, may help to better evaluate and monitor a patients' condition through time.

Despite its advantages, PDFF MRI has limitations, including susceptibility to artifacts from metallic implants or air cavities, challenges in patients with claustrophobia or movement disorders, and reduced accuracy in cases of severe iron overload ($T2^* < 2$ ms). Another limitation of this study is that all participants were Greek (white Caucasian race), the measurements for people from other races [13] or geographical places are expected to be different, although this may not affect the main idea of the study: the precise calculation of steatosis grade in a decimal form.

Given the progressive nature of hepatic steatosis and its potential to evolve into nonalcoholic steatohepatitis, fibrosis, or cirrhosis, early and accurate assessment is crucial. Our findings highlight the potential of MRI, particularly fat mass calculation, as a powerful diagnostic and monitoring tool in MASLD management.

In conclusion, MRI-PDFF demonstrates significant promise as a non-invasive, accurate method for assessing hepatic steatosis. Our study adds to the growing evidence supporting its clinical utility and introduces fat mass estimation as a potentially valuable marker. Further large-scale, longitudinal studies are needed to validate these findings and assess their implications in routine clinical practice. **R**

REFERENCES

1. Younossi, Z.M., Koenig, A.B., Abdelatif, D., et al., Global epidemiology of non-alcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016; 64:73-84. doi: 10.1002/hep.28431
2. Bril, F., Cusi, K. Management of Nonalcoholic Fatty Liver Disease in Patients with Type 2 Diabetes: A call to Action. *Diabetes Care*. 2017; 40:419-430. doi: 10.2337/dc16-1787
3. Williamson, R.M., Price, J.F., Glancy, S., et al. Prevalence of and risk factors for hepatic steatosis and non-alcoholic fatty liver disease in people with type 2 diabetes: the Edinburgh Type 2 Diabetes Study. *Diabetes Care*. 2011; 34:1139-1144. doi: 10.2337/dc10-2229. Epub 2011 Apr 8
4. El-Seraq, H.B., Tran, T., Everhart, J.E. Diabetes increases the risk of chronic liver disease and hepatocellular carcinoma. *Gastroenterology*. 2004; 126:460-

- 468.doi: 10.1053/j.gastro.2003.10.065
5. Rinella, M.E., Sanyal, A.J. Management of NAFLD: a stage-based approach. *Nat Rev Gastro Hepat.* 2016; 13:196-205.doi: 10.1038/nrgastro.2016.3. Epub 2016 Feb 24
 6. Angeliki Meritsi, Emanuel Manesis, Marina Noutsou, Panagiotis Koussis, Stamatia Rapti, Dimitra Latsou, Ioannis Tsorlalis, Eustathios Tsitsopoulos, Hariklia Moshoyianni, Spilios Manolakopoulos, Dimitrios Pektasides, Anastasia Thanopoulou, Factors associated with hepatic steatosis in adult Greek subjects with type 2 diabetes mellitus, *Metabolism*, Volume 128, Supplement, 2022, 154968, ISSN 0026-0495, <https://doi.org/10.1016/j.metabol.2021.154968>.
 7. Meritsi A, Manesis E, Koussis P, Rapti S, Latsou D, Tsitsopoulos E, Moshoyianni H, Manolakopoulos S, Pektasides D, Thanopoulou A. PNPLA3 rs 738409 and Other Nongenetic Factors Associated with Hepatic Steatosis Estimated by Magnetic Resonance Imaging Proton Density Fat Fraction in Adult Greek Subjects with Type 2 Diabetes Mellitus. *Metab Syndr Relat Disord.* 2022 Mar;20(2):124-131. doi: 10.1089/met.2021.0098. Epub 2021 Dec 27. PMID: 34962148.
 8. Eskreis-Winkler S, Corrias G, Monti S, Zheng J, Capanu M, Krebs S, Fung M, Reeder S, Mannelli L. "IDEAL-IQ in an oncologic population: meeting the challenge of concomitant liver fat and liver iron". *Cancer Imaging.* 2018 18:51. doi.org/10.1186/s40644-018-0167-3.
 9. Gouw, T. H., & Vlugter, J. C. (1966). Physical Properties of Triglycerides. I. Density and Refractive Index. *Fette, Seifen, Anstrichmittel*, 68(7), 544-549. doi:10.1002/lipi.19660680705
 10. Tang A, Desai A, Hamilton G, Wolfson T, Gamst A, Lam J et al. "Accuracy of MR imaging-estimated proton density fat fraction for classification of dichotomized histologic steatosis grades in nonalcoholic fatty liver disease". *Radiology.* 2015;274(2):416-425. doi: 10.1148/radiol.14140754.
 11. Beyer C, Hutton C, Andersson A, Imajo K, Nakajima A, et al. (2021) Comparison between magnetic resonance and ultrasound-derived indicators of hepatic steatosis in a pooled NAFLD cohort. *PLOS ONE* 16(4):doi: 10.1371/journal.pone.0249491. eCollection 2021
 12. Reeder SB, Sirlin CB. Quantification of liver fat with magnetic resonance imaging. *Magn Reson Imaging Clin N Am.* 2010 Aug;18(3):337-57, ix. doi: 10.1016/j.mric.2010.08.013. PMID: 21094444; PMCID: PMC3002753.
 13. Harada K, Ishinuki T, Ohashi Y, et al. (2021). Nature of the liver volume depending on the gender and age assessing volumetry from a reconstruction of the computed tomography. *PLoS ONE*, 16(12): e0261094. doi: 10.1371/journal.pone.0261094. [journals.plos.org]
 14. Oliveira, Robson & Dias, Apio & Vieira, Waldônio & Falcão, Aline & Falcão, Luiz & Quaresma, Juarez. (2020). A protocol of hepatic volume measurement using magnetic resonance imaging in individuals from the Eastern Brazilian Amazon population. *PLOS ONE*. 15. e0229525. <https://doi.org/10.1371/journal.pone.0229525>



READY - MADE
CITATION

Panagiotis Koussis, George Thiveos, Angeliki Meritsi, Anastasia Thanopoulou, Eleni Lamprou, Emanuel Manesis. MRI calculated liver fat mass as a new biomarker for steatosis grade evaluation in middle age population, *Hell J Radiol* 2026; 11(3): 40-46.