

Agreement of 2-, 3-, 4-, 5- and 6-echo MRI-PDFP with MRS-PDFP in 580 adults with known or suspected non-alcoholic fatty liver disease (NAFLD)

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Target Audience: Researchers and clinicians with interest in liver fat quantification using MRI proton density fat fraction (PDFP)

Purpose: To compare agreement of 2-, 3-, 4-, 5- and 6-echo MRI-PDFP with MRS-PDFP in 580 adults with known or suspected non-alcoholic fatty liver disease (NAFLD)

Methods: This retrospective, cross-sectional, IRB-approved, HIPAA-compliant study was conducted from 2009 to 2013. Adult subjects with known or suspected NAFLD who underwent previous prospective research MR examinations as part of other studies were consecutively enrolled. Those studies included MRI of the whole liver to measure PDFP, with MRS at a single location in the right lobe of the liver as reference standard. Unenhanced axial spoiled gradient-recalled-echo images were obtained with low flip angle (10°) and repetition time ≥ 100 ms to minimize T1 dependence. Magnitude images were acquired alternately in- and out-of-phase to correct for T2* decay. MRS spectra were acquired using a STimulated Echo Acquisition Mode (STEAM) sequence to minimize j-coupling effects. Other parameters used were a TR of 3500 ms, a TM of 5 ms, a single voxel (20 x 20 x 20 mm³) placed in the right lobe of the liver, and five spectra obtained in a single breath-hold to correct for T2 effects. Regions of interest (ROIs) were manually placed at three consecutive MRI slices, the 1st ROI was co-localized to the MRS voxel location, and the 2nd and 3rd ROIs were placed above and below the 1st one to ensure coverage of the entire MRS voxel. The three ROIs were propagated to the original six TE images and a custom Matlab algorithm was used to calculate PDFP from the first 2, 3, 4, 5 echoes and all 6 echoes. MR spectra were analyzed using Advanced Method for Accurate, Robust, and Efficient Spectral fitting (AMARES) in the jMRUI software package^{1,2}, with MRS-PDFP calculated as integrated sum of fat peaks at 2.7, 2.2, 1.3, and 0.9 ppm (corrected for 5.3 and 4.2 ppm peaks) divided by sum of fat and water peaks (4.7 ppm)^{3,4}.

Results: Regression analysis results are shown in **Table 1**. 3-echo MRI-PDFP informally shows the closest agreement with MRS-PDFP (regression intercept=0.102%, slope=1.013, R²=0.981); 2-echo MRI PDFP showed the worst agreement (regression intercept=3.167%, slope=0.960, R²=0.963). Correlation of MRI- with MRS-PDFP was not significantly different using 3, 4, 5 or all 6 echoes (all have r=0.990), but was different (worse) using 2 echos (r=0.981). **Figures 1 and 2** show regression results for 2-echo and 3-echo MRI methods, compared to MRS.

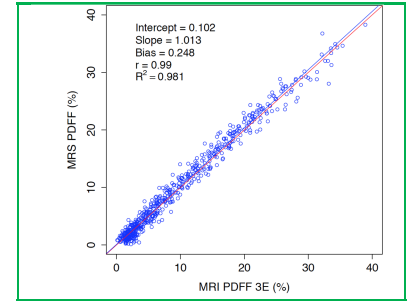


Figure 1: 3-echo MRI- vs. MRS-PDFP

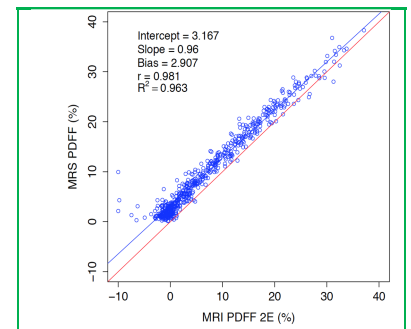


Figure 2: 2-echo MRI- vs. MRS-PDFP

Table 1. Regression analysis for 2-, 3-, 4-, 5- and all 6-echo MRI-PDFP vs. MRS-PDFP

	6-echo vs. MRS	5-echo vs. MRS	4-echo vs. MRS	3-echo vs. MRS	2-echo vs. MRS
Intercept	0.609	0.415	0.306	0.102	3.167
95% CI	0.472-0.745	0.273-0.554	0.173-0.450	-0.041-0.238	2.972-3.451
Slope	0.994	0.999	1.005	1.013	0.960
95% CI	0.978-1.008	0.984-1.014	0.991-1.020	0.997-1.027	0.934-0.979
Bias	0.555	0.407	0.361	0.248	2.907
95% CI	0.465-0.651	0.306-0.508	0.254-0.460	0.133-0.362	2.779-3.071
r	0.990	0.990	0.990	0.990	0.981
95% CI	0.988-0.991	0.988-0.991	0.988-0.992	0.988-0.992	0.968-0.986
R ²	0.980	0.980	0.981	0.981	0.963
95% CI	0.976-0.983	0.976-0.983	0.977-0.984	0.977-0.984	0.936-0.972

Discussion: Five MRI analysis methods to estimate hepatic PDFP were compared to MRS. 2-echo MRI-PDFP showed a closer agreement with MRS compared to the other methods, mainly because 2-echo calculations neglect T2* decay, and instead assume that the difference between in- and out-of-phase echoes is due only to fat-water interference. A limitation of this study is that co-localization of MRI with MRS is not exact since each is acquired in a separate breath-hold. Further work is needed to determine diagnostic accuracy of each method using MRS as reference standard.

Conclusion: MRI accurately quantifies hepatic PDFP in adults, with the 3-echo MRI-PDFP method informally showing the closest agreement with MRS, and the 2-echo MRI-PDFP method showing the worst agreement.

1. Naressi A et al, *MAGMA* **2001**; 12:141-152.
2. Vanhamme et al, *J Magn Reson* **1997**; 129:35-43.
3. Johnson et al, *JMRI* **2013** [Apr 17; Epub ahead of print].
4. Hamilton et al, *NMR in Biomedicine* **2011**; 24:784-790.