

Field Strength Reproducibility of Hepatic Proton Density Fat Fraction Estimation by a Complex-data, T1-independent, T2*-corrected, Spectrum-Modeled MRI Technique

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the United States. It affects tens of millions of adults and children, contributes to the development of cardiovascular disease and type II diabetes, and may progress to cirrhosis and hepatocellular carcinoma. Currently, the clinical gold standard for diagnosing NAFLD is histological analysis of a liver biopsy. Unfortunately, biopsy is invasive, and thus not suitable for screening, or for the repeated measurements that would be necessary to examine a response to potential treatment. Conventional MRI is regularly used to assess liver fat, but confounders such as relaxation and multi-peak spectral interference effects often lead to inaccurate estimates of liver fat content. Advanced MRI techniques have recently been developed that address the confounders and permit estimation of Proton Density Fat Fraction (PDFF), the fraction of the protons in the liver attributable to liver fat. To validate PDFF as a biomarker of liver fat content, it must demonstrate not only accuracy against an independent reference standard, but also repeatability and reproducibility. While recent work^{1,2,3} has demonstrated high accuracy of PDFF measured by both magnitude and complex based MRI techniques, reproducibility across field strength has not yet been verified. The purpose of this study was to assess the reproducibility of MRI-derived PDFF across field strength using a complex based MRI technique.

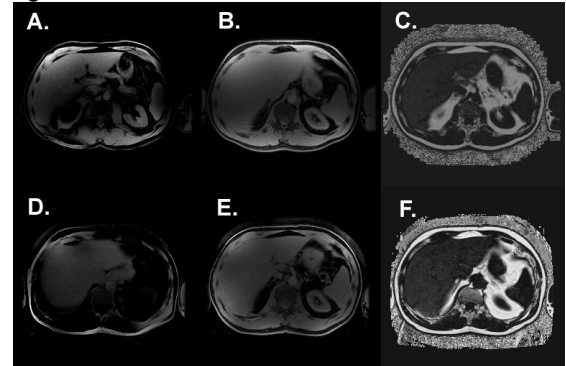
Methods: We enrolled 15 subjects (10 males, 5 females, mean age 44.5 yrs, age range 16-80 yrs), four normal controls and 11 subjects with known fatty liver disease. Imaging was performed at both 1.5T (Discovery MR450, GE Healthcare, Milwaukee, WI) and 3.0T (GE Signa EXCITE HD; GE Healthcare, Milwaukee, MI) using an investigative variant of the quantitative IDEAL (Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation)^{4,5,6} MRI technique to calculate PDFF, allowing for the correction of multiple confounding factors including T₁ bias, T₂^{*}, spectral complexity of fat, eddy currents, and noise bias. Imaging parameters for these scans are listed in **Table 1**. The technique generates source images from which field maps, water-based anatomic maps, and fat-fraction maps are generated⁷. Subjects first had an exam at either 1.5T or 3.0T. Within 15 minutes of completion of the first exam, subjects underwent an exam at the other field strength. A trained technologist reviewed images on a Picture Archiving and Communication System (PACS) workstation and manually placed a region of interest (ROI) on a water map image using anatomic landmarks to ensure similar placement in both 1.5T and 3.0T studies. PACS software then automatically propagated ROIs to the fat-fraction maps for liver fat estimation. The average PDFF values for the given ROIs were recorded. Following data collection, PDFF values collected from 1.5T scans were compared by linear regression analysis to those from 3.0T scans using the R software package.

Results: PDFF in the 15 subjects ranged from 0-2% to 22-24%. Representative images generated by the MRI technique are illustrated in **Figure 1**. Linear regression analysis comparing average PDFF values measured at 1.5T to those measured at 3.0T is demonstrated in **Figure 2**. The regression analysis resulted in a slope of 0.98 +/- 0.5, and an intercept of 0.1% +/- 0.6%.

Discussion: This study demonstrates high reproducibility of PDFF across field strength in subjects spanning a clinically relevant range of liver fat. The high reproducibility across field strength provides further evidence that MRI-derived PDFF measurements are invariant to confounding factors (T₁, T₂^{*}, spectral complexity of fat, etc), particularly those that vary with field strength (T₁ and T₂^{*}).

References: [1] Hines, *et al* JMRI 2009 [2] Meisamy ISMRM 2009 [3] Yokoo T *et al.* Radiology 2009 [4] Yu *et al.* JMRI 2007 [5] Yu *et al.* MRM 2008 [6] Bydder, *et al* MRM 2008 [7] Reeder *et al.* JMRI 2007

Figure 1.



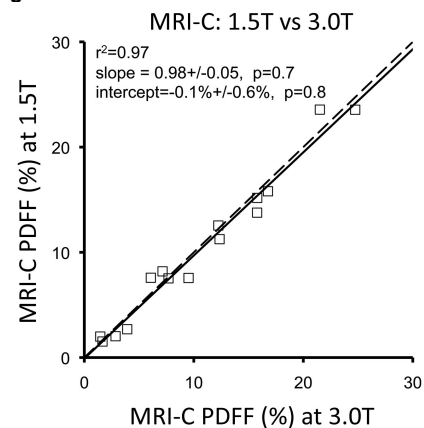
Note. Representative MR images from one patient at both 1.5T (above) and 3.0T (below). From left to right the images illustrate: the IDEAL source images (A,D), the anatomic water maps (B,E), and the fat-fraction maps (C,F)

Table 1.

Seq.	PSD	B ₀	TE (ms)	BW	TR (ms)	FA	ST	Matrix	
								Nx	Ny
MRI-C	3D IDEAL	3.0T	1.0, 1.8, 2.6, 3.4, 4.2, 5.0 3 echoes/TR, 2 interleaves	200	7	6°	8	192	192
		1.5T	1.0, 2.8, 4.6, 5.4, 6.2, 8.0 6 echoes/TR, 1 interleave	200	14	6°	8	192	192

Note. MRI-C=Complex PSD = pulse sequence design IDEAL = Iterative Decomposition of water and fat with Echo Asymmetry and Least squares estimation. B₀ = field strength (3.0T or 1.5T), TR = repetition time (msec), FA = flip angle (degrees), TE = echo time (msec), ST = slice thickness (mm), Nx = readout matrix, Ny = phase encode matrix, BW = receive bandwidth (kHz).

Figure 2.



Note. Linear Regression of PDFF values measured by advanced MRI techniques at 1.5T vs. 3.0T is displayed. The linear regression, represented by the dashed line, is very close to the line X=Y (solid line) indicating high reproducibility across field strength.