

# Complex and Magnitude MRI for Quantification of Hepatic Steatosis – Correlation with MR Spectroscopy and Biopsy

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) is an emerging condition increasingly recognized as the most common type of chronic liver disease and affects up to 30% of the US population and 75% of obese individuals [1]. Currently it is diagnosed based on a combination of clinical history such as risk factors for metabolic syndrome, elevated serum aminotransferases, and lack of alcohol consumption. Definitive diagnosis, however, requires liver biopsy. Liver biopsy is limited to assess NAFLD not only because it is invasive and expensive, but also because NAFLD is an inherently heterogeneous disease that leads to tremendous sampling variability in biopsy results. In recent years, quantitative MR methods developed for accurate measurement of hepatic steatosis have been developed. Validation of these methods has been typically performed through comparison with single voxel MRS as the reference standard. These methods have demonstrated excellent correlation and agreement between proton density fat-fraction ("fat-fraction" for brevity) and MRS so long as all confounding factors are addressed [2-4]. Confounders include: T1 related bias, T2\* correction, spectral complexity of fat, noise related bias, and eddy currents. The purpose of this study was to compare two quantitative MRI methods for fat quantification, using MR spectroscopy and liver biopsy as the reference standard.

**Methods:** In this on-going IRB-approved and HIPAA-compliant study, 12 patients referred for liver biopsy (47.1±12.3years, 81.7±18.1kg) were recruited and studied after written informed consent was obtained.

**MR-Imaging.** Studies were conducted within one month after non-targeted liver biopsy was performed to evaluate for diffuse liver disease. Imaging was performed on a clinical 3T scanner (GE Discovery MR 750, Waukesha, WI) using a 32-channel body coil (NeoCoil, Pewaukee, WI). MR fat-fraction was quantified using three (3) different methods. First, a previously described 3D complex-based (MRI-C) gradient echo method [4] with acquisition parameters including: 6 echoes/TR, TR=8.6 ms, TE<sub>min</sub>=1.2ms, ΔTE=1.0ms, full readout, BW=±125kHz, FOV=40x36cm, slice=8mm, 256x160 matrix, 32 slices, and a total scan time of 23sec. The second MRI method is a previously described 2D magnitude-based (MRI-M) gradient echo method [3] with the following imaging parameters: 6 echoes/TR, TR=130 ms, TE<sub>min</sub>=1.1ms, ΔTE=1.1ms, full readout, BW=±125kHz, FOV=44x40cm, slice=8mm, 224x144 matrix, 28 slices, ASSET factor=2, for a total scan time of 19sec. Fat-fraction images for both MRI-C and MRI-M were reconstructed using two separate on-line reconstruction algorithms. Both algorithms use spectral modeling of fat [5,6] and T2\* correction [7], while MRI-C also corrects for eddy currents and noise-related bias [8,9]. Flip angles of 3° and 10° were used to minimize T1 related bias for MRI-C and MRI-M data respectively [9]. Correction for residual T1 bias was performed for both methods using the method of Hines et al [10].

For comparison, single breath-hold MRS was performed by using single voxel STEAM (Stimulated Echo Acquisition Mode) without water suppression. A 2x2x2cm<sup>3</sup> voxel was placed in the posterior segment of the right hepatic lobe free from large vessels. Acquisition parameters included: 2048 readout points, 1 signal average, TR=3500, and at 5TEs, all acquired in the same 21s breath-hold. MRS data were postprocessed by an MR physicist who was blinded to the MR imaging results as previously described [4]. For both MRI-M and MRI-C fat-fraction was measured from ROI's co-registered with the MRS voxel.

**Liver Biopsy.** All histological slides were stained with H&E and/or Masson's tri-chrome stain, and were re-evaluated for this study. Histology was graded using the Brunt classification that assesses the number of cells affected with macrosteatosis (grade 0-3): 0 is < 5%, 1 is 5-32%, 2 is 33-66%, 3 is >66%.

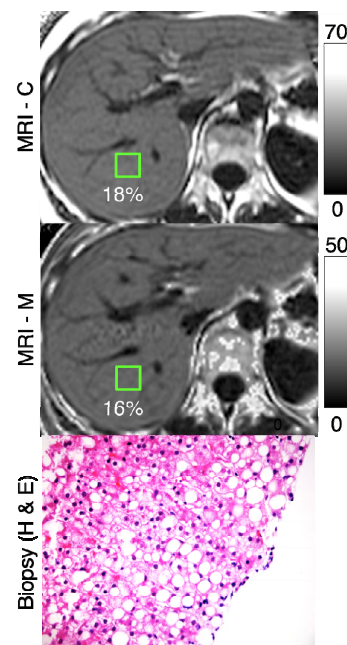
**Results:** Figure 1 shows the calculated fat-fraction image by MRI-C (top) and MRI-M (middle), in a patient with grade 2 (FF>33%) steatosis and a representative histology image from the biopsy specimen (bottom). Figure 2a plots FF from MRI-C and MRI-M vs MRS, and demonstrates excellent correlation ( $r^2=0.99$  and  $r^2=0.96$  for MRI-C and MRI-M respectively). Further, both methods show slope and intercept close to 1.0 and 0.0 ( $m=1.07\pm0.02$ ,  $b=0.04\pm0.15$  and  $m=0.96\pm0.06$ ,  $b=-0.11\pm0.33$ ) for MRI-C and MRI-M respectively) indicating good agreement with MRS. Figure 2b plots FF from MRI-C and MRI-M compared with histological grade. In these preliminary results, both MRI methods had good correlation with liver biopsy based on polynomial fits.

Interestingly, in one subject, the biopsy was reported as normal, but the patient had 7-8% fat-fraction with MRI-C and MRI-M in good agreement with MRS (7.4%). This subject underwent MRI 2 weeks after the biopsy. The discordance between MRI and biopsy is best explained by sampling error or changes in the hepatic steatosis during that interval.

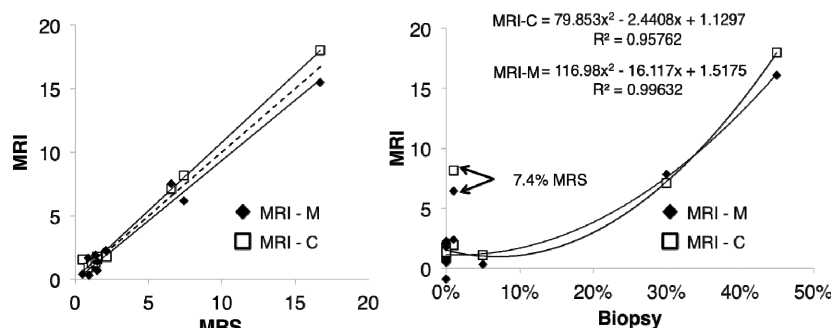
**Discussion:** This preliminary study demonstrates good correlation of fat-fraction measured using MRI-C and MRI-M with both MRS and histological grading of steatosis. Additional studies will be required to determine the sensitivity and specificity of MRI to grade steatosis, and also to determine whether there are differences in the performance between MRI-M and MRI-C.

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**References:** [1] Browning, Hepatology 2007; [2] Yokoo et al Radiology 2009; [3] Yokoo et al Radiology 2011; [4] Meisamy et al Radiology 2011; [5] Bydder et al MRI 2008; [6] Yu et al MRM 2008; [7] Yu et al JMIR 2007; [8] Yu et al MRM 2011; [9] Liu et al MRM 2007; Hines et al ISMRM 2010.



**Figure 1** - Example demonstrating good subjective correlation between MRI-C (top), MRI-M (middle) and histological grading of steatosis (bottom). MRS showed ~17.4% fat-fraction.



**Figure 2** - a. Correlation of MRI-C and MRI-M with MRS (a) and liver biopsy (b).