Quantification of Hepatic Steatosis with MRI: The Effects of Accurate Fat Spectral Modeling

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is increasingly prevalent, affecting up to 30% of the US population [1], and 10% of all children [2]. The clinical utility of biopsy, the current gold standard for diagnosis of NAFLD, is limited by its high cost, morbidity and high sampling variability. Non-invasive quantitative biomarkers using MRI have the potential to provide quantitative assessment of hepatic steatosis over the entire liver in a single breath-hold and could allow earlier detection and treatment of disease. The purpose of this work is to investigate the use of IDEAL (Iterative Decomposition of water and fat with Echo Asymmetry and Least squares estimation) water-fat separation for quantitative estimation of hepatic fat content. In this work, we compare a new multi-peak IDEAL reconstruction, which accounts for signal from all spectral peaks of fat, to conventional IDEAL and spectroscopy in 31 patients.

Methods: All imaging was performed on a 1.5T Signa HDx scanner (GEHC, Waukesha, WI) using an 8-channel phased array cardiac coil. IDEAL imaging was performed using a 3D multi-echo spoiled gradient echo (SPGR) pulse sequence with echo times selected to optimize the SNR of the water-fat decomposition [3,4,5].

The signal model for IDEAL was expanded to include the multiple spectral peaks of fat. This modification, which will be described in detail in a separate submission, assumes that the relative frequencies of the various fat peaks are known *a priori*. In this work, the relative frequencies of the fat peaks were measured with a point resolved spectroscopic (PRESS) acquisition [6] without water suppression, in the subcutaneous fat of several volunteers, and the relative amplitudes measured using a 16 point IDEAL acquisition to be described elsewhere.

After obtaining IRB approval and informed consent, a total of 33 patients (11 with suspected steatosis, and 22 patients referred for MRI of the liver for unrelated reasons) were imaged. One patient was excluded due to large body habitus and the inability to use the phased array coil and a second patient due to motion between the IDEAL and PRESS acquisitions. Of the remaining 31 patients there were 15 men (age=23-68yrs) and 16 women (age=21-71).

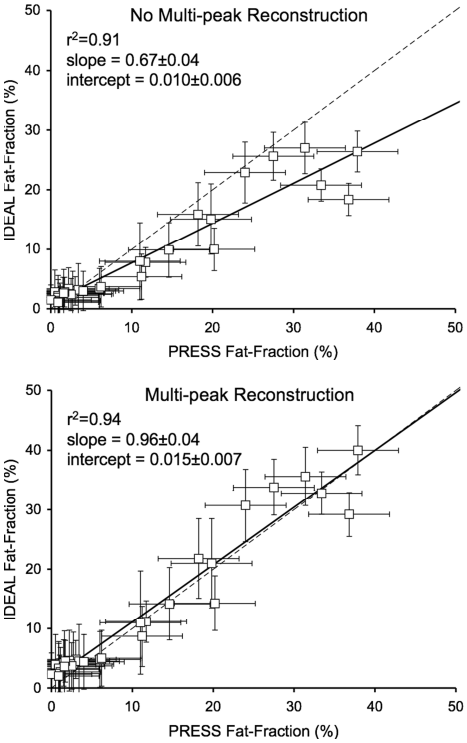

Figure 2: *IDEAL vs PRESS fat-fraction in 31 patients, using A) conventional IDEAL and B) multipeak IDEAL. Although excellent correlation is seen with both IDEAL reconstruction methods, close agreement with a slope near one is only achieved with multipeak reconstruction, demonstrating the importance of including all spectral peaks of fat. Dashed line is the line of unity.*

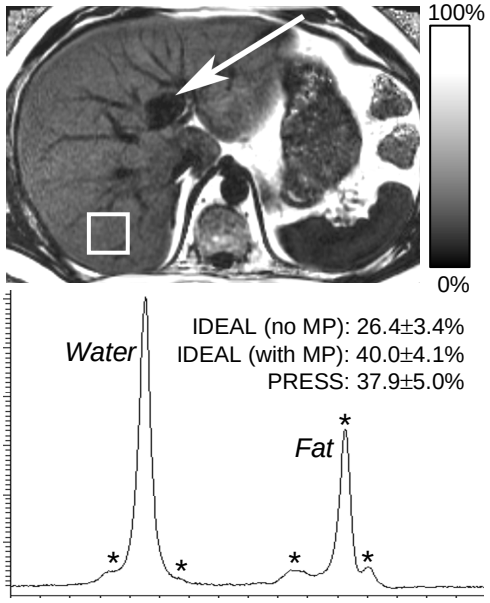

Figure 1: *Fat-fraction measured in a patient with steatosis demonstrates good agreement between PRESS and IDEAL when multipeak (MP) reconstruction is used. The PRESS voxel (square) was acquired from posterior segment of the liver. Note the multiple spectral peaks of fat (*), and the fatty sparing near the gall bladder fossa (arrow).*

Acquisition parameters included: 3 echoes/TR, TR=7.4ms, TE=2.0/3.6/5.2ms, BW=±143kHz, FOV=35cm, slice=8-10mm, 224-256x160-192 matrix, 18-22 slices, total scan time = 18-22s. A 5° flip angle was used to minimize bias from T_1 differences between water and fat [7]. Water-fat separation was performed with an on-line reconstruction using a region-growing algorithm [8], providing separate water and fat images, as well as fat-fraction images: $\eta = W/(W+F)$. A magnitude discrimination algorithm was used to prevent bias that occurs at low fat-fractions when magnitude images are used to calculate fat-fraction [7]. Fat-fraction measurements were made from ROIs that attempted to match the location of the PRESS voxel (below).

For comparison, breath-held spectroscopic acquisitions were performed in one or more locations using PRESS, without water suppression. A 2.0-2.5cm cubic volume (8.0-15.6cc) was selected in a region of the liver free from large vessels, usually in the posterior segment of the right lobe of the liver. Acquisition parameters included: TR/TE=2500/25ms, BW=±2500Hz, 4 averages, readout points=2048, total scan time=20s. Raw spectroscopy data were post-processed (blinded to IDEAL results) using in-house analysis software (Mathworks, Natick, MA) to estimate area under the water peak and total area under the fat peaks, in order to estimate fat-fraction.

Results: Fig. 1 shows an IDEAL fat-fraction image and corresponding PRESS spectrum in a patient with steatosis. Excellent agreement between IDEAL (40.0±4.1%) and PRESS (37.9±5.0%) was observed when multipeak reconstruction was used. Fig. 2 plots fat-fraction for PRESS and IDEAL, without (fig. 2a) and with (fig. 2b) multipeak reconstruction. Direct agreement between PRESS and IDEAL is achieved with a slope close to 1.0 (slope=0.96±0.04, intercept=1.5%±0.7%) when the multipeak method is used.

Discussion: This clinical study demonstrates excellent correlation between IDEAL and MR spectroscopy for the measurement of fat-fraction *in vivo*. Accounting for the multiple spectral peaks of fat improves the agreement between the two methods, particularly at higher fat-fractions. IDEAL is a promising non-invasive method for quantification of hepatic steatosis, offering potentially improved accuracy and safety compared to biopsy. Future work will investigate correlation of IDEAL with steatosis grading from biopsy.

References: **1.** Harrison, *et al.* Clin Liver Dis 2004; 8:861-879. **2.** Papandreou et al Semin Liver Dis 2007 26:409-415, **3.** Reeder et al, MRM 2005 54:636-44, **4.** Reeder et al, ISMRM 2006, pg 2444, **5.** Pineda et al, MRM, 2005 54:625-35, **6.** Bottomley et al Ann NY Acad Sci, 1987 508: 333-48, **7.** Liu et al MRM 2007 58:354-364, **8.** Yu et al, MRM, 2005 54:1032-9 8.