Comparison Between Digital Biopsy and MRI Quantification of Hepatic Fat in NAFLD

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Target Audience: This study is of interest to researchers and clinicians studying fat quantities in the liver using MRI and or biopsy.

Purpose: Non-Alcoholic Fatty Liver Disease (NAFLD) is the leading form of liver disease worldwide in both adults and children. T1 independent, T2* corrected chemical shift based fat-water separation methods with accurate spectral modelling of fat (quantitative IDEAL) has been demonstrated to give measures of hepatic fat fraction that correlate well with liver triglyceride content measured in animal models of NAFLD and with magnetic resonance spectroscopy (MRS) measurement of fat in humans with NAFLD. (1-4). However, liver steatosis is often diagnosed through biopsy. Here we report on the results of a study comparing hepatic fat measured with MRI to digitally analysed biopsy measurement of hepatic fat in patients with NAFLD.

Methods: After obtaining informed consent, forty-five patients with biopsy confirmed NAFLD were enrolled in a Research Ethics Board approved study where phlebotomy was initiated in each patient to achieve iron depletion (serum ferritin ≤50 or Hgb 100). Data from 20 of these patients is presented here. Patients received two liver biopsies (unguided, taken from the lower right liver lobe), one before phlebotomy commenced and one six months following the cessation of phlebotomy. Biopsy tissues were fixed and stained using haematoxylin and eosin. Images of tissue sections for each biopsy were digitised. The area fat fraction was calculated in regions of interest outlined with confounding structures excluded. The software was calibrated in to gain the best distinction between stained hepatic tissue and non-stained fat vacuoles.

Quantitative IDEAL images (3D IDEAL-SPGR, TR 7.3 ms, TE=1.0,1.8, 2.7, 3.5, 4.3, 5.1 ms, echo train length=3, 5° flip angle, FOV 48cm, 10 mm slices, matrix 24x128x224, BW ±125 kHz, parallel imaging R=1.4) of the entire liver were acquired with an 8 coil torso array on a 3.0 T MRI (Discovery 750, GE Healthcare, Waukesha, WI, USA) just prior to each biopsy. Proton Density Fat fraction maps were reconstructed for each patient and hepatic fat fraction was determined in two regions of interest (ROI) placed in the lower right lobe of the liver. Both ROI's were placed in close proximity to the estimated location of the biopsy. The ROI's were placed in approximately the same location in each patient. Results from two raters were compared to determine reproducibility of the MRI and biopsy derived fat fractions.

Results: Figure 1 shows the correlation between MRI and digital biopsy quantification of fat. The agreement is strong with R^2= 0.66, and a linear fit to the data having a slope of 0.78 and an intercept of 0.09. Figure 2 shows the comparison of digital biopsy between two researchers. The results have a strong correlation with R^2= 0.96, demonstrating excellent inter-rater agreement. Figure 3 shows the comparison of MRI determined fat fraction by two researchers. The correlation here is extremely strong with R^2= 0.92, which is essentially equivalent to the results for digital biopsy analysis.

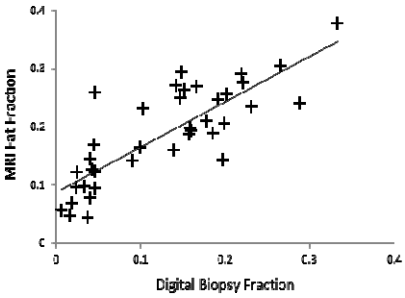

Figure 1: MRI Fat Fraction versus Digital Biopsy Fraction The correlation between fat fractions determined by MRI and digital analysis of unguided biopsy samples is strong, with R^2= 0.66.

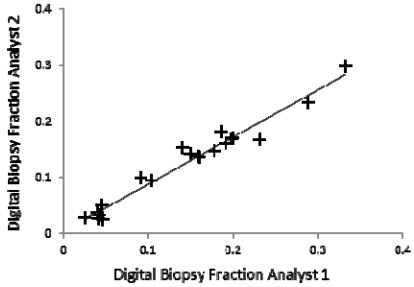

Figure 2: Comparison of biopsy digital analysis results between two analysts. The reproducibility was excellent with R^2=0.96.

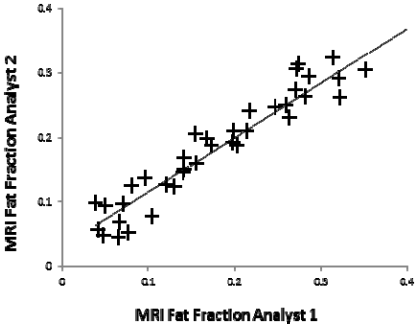

Figure 3: Comparison of MRI results between two analysts. The reproducibility is excellent with R^2 = 0.92

Discussion: Given that the precise location of the biopsies were unknown, the strong correlation of MRI with biopsy is particularly impressive. The intercept was non-zero likely because the biopsy analysis was missing very small vesicles that were only partially sampled in the slices analysed. The inter-rater reproducibility of MRI results is strong and comparable to the biopsy reproducibility, which suggests that MRI is a good non-invasive alternative to quantifying fat globally in the liver. The standardization of MRI fat quantification for use in clinical settings would be of great benefit. MRI should be considered as the standard tool to diagnose, quantify and monitor treatment of hepatic steatosis.

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