Hepatic fat quantification on 3T MRI using a dual-flip multi-echo sequence with MR Spectroscopy and histopathologic correlation

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Introduction: Non alcoholic fatty liver disease (NAFLD) comprises a spectrum of diseases that range from simple steatosis through non alcoholic steatohepatitis (NASH) to cirrhosis. Since fatty liver is the hall mark of NAFLD, it has been used as a surrogate marker to monitor progression of NASH and its response to novel therapies. Our purpose is to utilize a previously developed dual-flip multi-echo gradient-echo (GRE) sequence for hepatic fat quantification at 3T in patients with NASH treated with Leptin, and compare the estimated % hepatic fat with single-voxel MRS estimates and quantitative measurements of hepatic fat on liver biopsy slides as the reference standard in a subset of patients who underwent liver biopsy.

Materials and Methods: Nine patients with known NASH who received Leptin therapy were referred for MRI hepatic fat quantification before and at 6-month intervals after treatment. Patients also underwent liver biopsy before and 1-year after treatment.
Images were acquired on a 3T clinical MR system (Philips Achieva, R2.5) with a 6-channel phased-array coil. The exam consisted of a multi-echo dual flip angle GRE breath hold scan, and a single voxel spectroscopy scan. The sequence parameters for the multi-echo GRE sequence were as follows: multi-slice 2D fast field multi-echo (mFFE), 6 echoes, TR/TE 184/1.15 ms, ΔTE 1.2 ms, dynamic flip angle: 70°/20°, voxel size 2.2x2.47mm, 17 slices at 7 mm thickness and 1 mm gap, FOV 360x280 mm (106x164 matrix), SENSEx1.8, 1135 Hz/pix bandwidth, 24s breath hold duration. Proton MR Spectroscopy was acquired with a single voxel PRESS sequence, TR 4000 ms, TE 45, 65 ms, 2 NSA, 2 phase cycles, 1.95 Hz spectral resolution, 30x30x30 mm3 voxel size placed in a homogenous region of the liver, and 16 sec scan duration.

% hepatic fat was calculated from the m-FFE images using a previously described technique [1]. Integration of water and fat spectral peaks at TE=45 ms and 65 ms allowed for removal of T2 bias in MRS fat estimation [2]. All biopsies were taken from the right lobe of the liver during suspended breathing at end-expiration without imaging guidance. Quantitative histopathology analysis of the H & E slides was performed using the image analysis software (Image J, NIH, USA), which generates a histogram of pixels according to their color intensity. The proportion of bright vs. dark area on histopathology was used as an objective estimate of “true” fat and non-fat content.

Results: In this ongoing study, 33 MRI/MRS studies and 12 biopsies were performed. One MRI study was excluded from the analysis due to extensive motion artifact related to patient claustrophobia. There was a very good correlation between the estimated % hepatic fat using the multi-echo dual flip-angle technique and SV-MRS with T2-correction ($p < 0.001$) (Figure 1), and an excellent correlation with quantitative biopsy analysis ($p< 0.001$) in the 12 patients who underwent liver biopsy (Figure 2).

Conclusions: The dual-flip multi-echo MRI method at 3T is reliable to measure hepatic fat. It correlates well with MRS and quantitative histopathologic measures, though unlike MRS, offers full-liver mapping of fat content and heterogeneity.

References:
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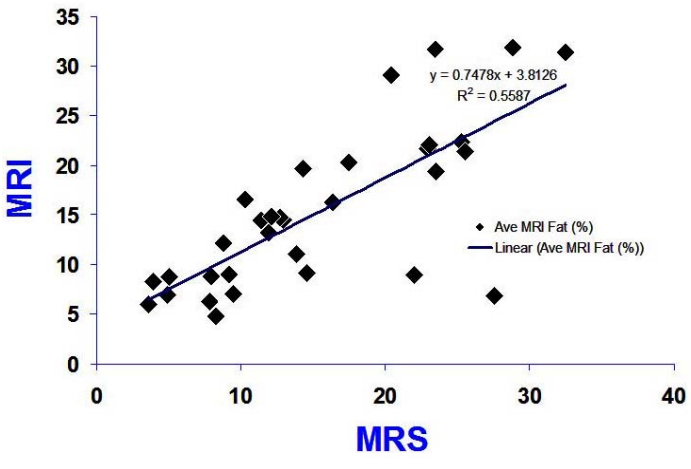

Figure 1

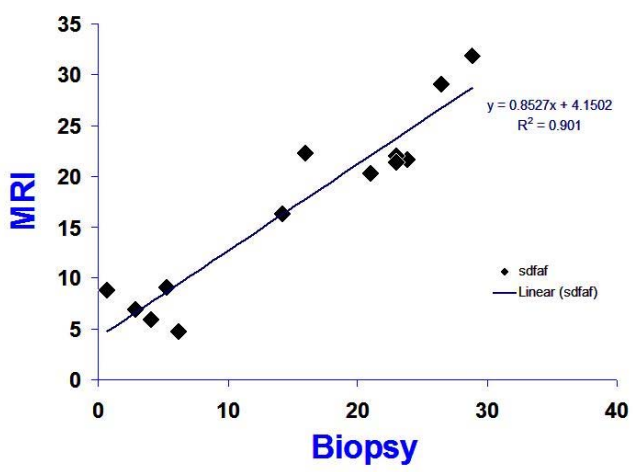

Figure 2