Validation of Hepatic Fat Quantified on 3T MRI via Histopathologic Correlation in Patients with Non-Alcoholic Steatohepatitis

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Introduction: Non Alcoholic Fatty Liver Disease (NAFLD) represents a wide spectrum of conditions ranging from simple steatosis to Non Alcoholic Steatohepatitis (NASH), cirrhosis and end stage liver disease. While simple steatosis follows a remarkably benign clinical course, NASH is a potentially serious condition associated with a significant increase in overall and liver-related morbidity and mortality. After establishing the initial diagnosis of NASH via liver biopsy, monitoring disease progression and response to therapy requires a reliable and reproducible non invasive method. The % hepatic fat may provide a surrogate biomarker for this purpose. A practical dual-flip angle method for hepatic fat quantification has been developed at 1.5T (1). Our purpose is to utilize the dual-flip angle method for hepatic fat quantification at 3T and to compare the estimated % hepatic fat with single-voxel MRS estimates and quantitative measurements of hepatic fat on liver biopsy slides as the reference standard.

Materials and Methods: Seven patients with suspected or known NASH were referred for MRI to quantify hepatic fat. All patients underwent MR imaging at 3T field strength and liver biopsy within 1 day of the MRI. A previously described (1) dual-echo dual flip-angle (20º and 70º) gradient recalled-echo sequence was acquired through the liver during suspended respiration to resolve the ambiguity of the dominant constituent and eliminate the effect of T1-relaxation. The exam included T2* estimation using a dual IP echo sequence as needed for fat estimation. Single-voxel proton (SV-MRS) was performed in a liver region selected for its relative homogeneity. The PRESS sequence was used to acquire a 3x3x3cm voxel (body-coil transmit/receive; TR=4000msec; TE=36msec and 56msec). Spectra were analyzed offline using in-house software to phase-correct and quantify water and lipid via peak integration and curve fitting. Spectra acquired at TE=36ms and TE=56ms were used to correct for subject-specific T2 and calculate water/fat content at "TE=0ms". All biopsies were taken from the right lobe of the liver during suspended breathing at end-expiration without imaging guidance. Semiquantitative analysis of the hepatic fat content and its severity was estimated visually on H & E liver biopsy slide as the percent hepatocytes involved by macrovesicular steatosis. 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 pixel intensity level at a "notch point" in the histogram was used to segment bright pixels (ie. fat) from dark pixels (ie. non-fat) on the histopathology slide. The proportion of bright vs dark area on histopathology was used as an objective estimate of "true" fat and non-fat content.

Results: The hepatic fat content using the dual flip-angle technique, SV-MRS without T2-correction (i.e. TE 36ms), SV-MRS with T2-correction (TE 0ms), and visual analysis of the histopathology slide as scored by the pathologist are compared with the quantitative histopathology hepatic fat content in all 7 patients as shown in Figure 1. The rms deviations from the line-of-unity were: 3% for dual-flip MRI; 11% MRS at TE36; 5% MRS at TE0; and 36% for subjective pathologist score. An example of these measures in one patient is shown in Figure 2.

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

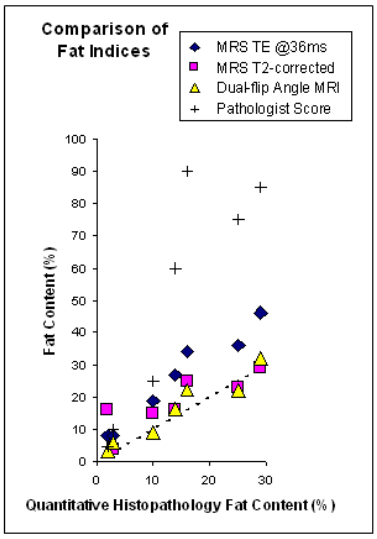

Figure 1

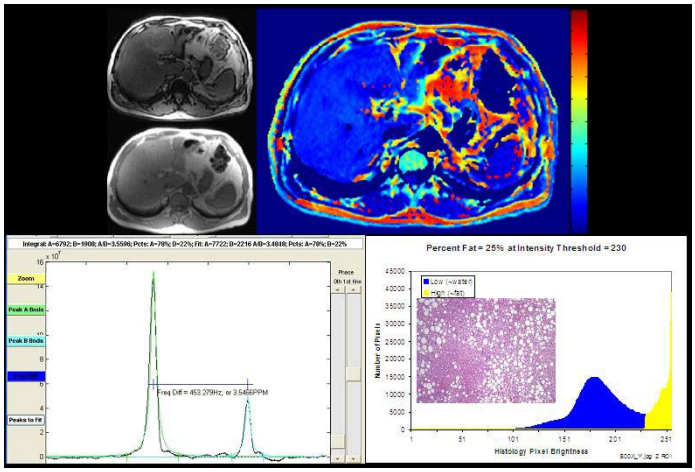

Figure 2

Reference: (1) Hussain HK, Chenevert TL, Londy FJ, et al. Radiology 2005; 237:1048-1055