Fatty Liver Disease in Overweight Adolescent Girls Measured with Quantitative MRI and MR Spectroscopy

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Introduction: The prevalence of non-alcoholic fatty liver disease (NAFLD) in children ranges from 1-10% worldwide and 28% to 38% in overweight children[1]. In fact, NAFLD is anticipated to be the leading cause of liver cirrhosis, failure, and transplant in the future - surpassing alcoholic liver disease, viral hepatitis and liver cancer.[2] Therefore, early identification of NAFLD is important for intervention and prevention of progression. Unfortunately, traditional methods of detecting fatty liver, such as ultrasound or liver enzyme blood screening, miss early changes. A rapid, clinically relevant, non-invasive method for early detection and staging of NAFLD is urgently needed[3,4]. In this work, we conducted a feasibility study in overweight, ethnically diverse adolescent girls comparing traditional serum and anthropometric biomarkers of metabolic risk to a non-invasive quantitative method for early diagnosis and quantitative grading of fatty liver disease, using magnetic resonance imaging (MRI).

Methods:

Subjects: This is a cross-sectional study involving 24 overweight/obese, pubertal girls with a mean age of 13.5 years ± 1.956, 75% non-Caucasian. Subjects were recruited through a local middle-school and pediatric endocrinology clinics.

Anthropometric and Laboratory Measures: Blood was collected on the same day as imaging, for assays of glucose, insulin, lipids (total cholesterol, HDL, LDL, and triglycerides), ALT and AST after an overnight fast. All labs were performed in the same laboratory. Anthropometric measurements included height, weight, hip and waist circumference and blood pressure.

Imaging: Imaging was performed on a clinical 3T scanner (MR750, GE Healthcare, Waukesha, WI) using an investigational version of a chemical shift based water-fat separation method (3D-IDEAL-SPGR) and a 32-channel phased array body coil. Single voxel STEAM spectroscopy and fat-water separation over the liver were acquired. First, single voxel STEAM without water suppression was acquired in the posterior right lobe using the following parameters: TE = 10, 15, 20, 25, 30 ms acquired in a single TR of 3800ms, 2x2x2cm voxel, 1 signal average, 2048 points, and a spectral width of 5000, all acquired in a breath-hold of 23 seconds. Next, an investigational version of a quantitative chemical shift based MRI method (IDEAL) was acquired over the liver using the following parameters: FOV = 44x40cm, first TE/TR = 1.2/8.6ms, echo spacing = 2.0ms, echo train length = 6 (2 shots of 3 echoes), BW = ±111kHz, flip = 3° to minimize T1 bias, 8mm slices, 28 slices, and 256x160 matrix. 2D parallel imaging (ARC) with R=2.86 was used to reduce total imaging time to a 23 second breath-hold. An on-line reconstruction algorithm was used to perform T2* correction, spectral modeling and eddy current correction to create quantitative proton density fat-fraction maps over the entire liver. Fat-fraction measurements were made from PDFF maps using a 2x2cm^2 voxel co-localized to the MRS voxel.

Statistics: Associations between fat fraction and other outcomes was examined using Spearman's correlation analysis and linear regression analysis. A two-sided p-value of <0.05 was regarded as significant.

Results: Figure 1 demonstrates excellent agreement between hepatic MR spectroscopy and quantitative MRI hepatic fat concentration. Liver fat fraction correlated strongly with ALT (r=0.84, p=<0.0001), and moderately with fasting insulin (r=0.69, p=0.0003), triglycerides (r=0.58, p= 0.0036), and waist-hip ratio (r=0.50, p=0.0175). Mean BMI was elevated at 30.9 kg/m^2 ± 4.162. However, BMI did not correlate significantly with liver fat fraction. Figure 2 illustrates these correlations in patients with low, moderate, and high liver fat fractions. Prevalence of hepatic steatosis (defined as fat fraction greater than 5.56%[5]) is 28% (7/24) in the girls studied.

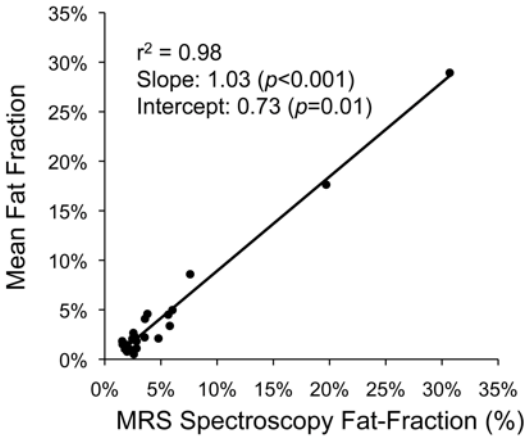

Figure 1: *Quantitative MRI methods are equivalent to MRS for measuring hepatic triglyceride concentration (fat fraction)*

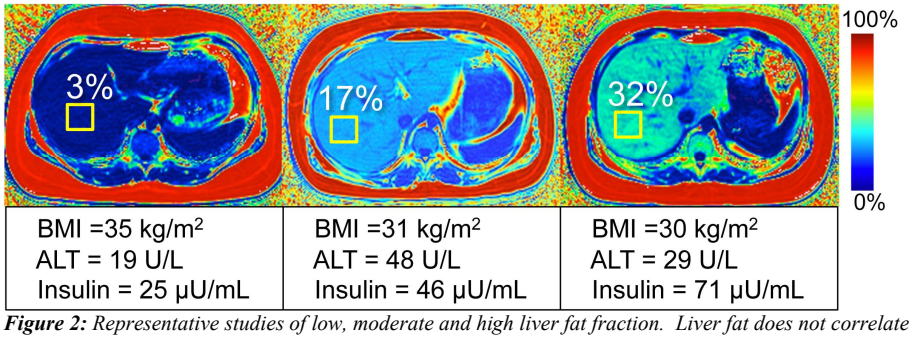

Figure 2: *Representative studies of low, moderate and high liver fat fraction. Liver fat does not correlate with BMI but has moderate correlation with ALT and fasting insulin.*

Discussion: Quantitative MRI is a feasible and accurate measure of NAFLD in overweight adolescents and correlates with metabolic risk factors including insulin resistance, HDL, triglycerides and waist-hip ratio. In contrast, BMI a common pediatric screening tool, does not offer predictive value of NAFLD risk. While ALT correlates strongly with liver fat fraction, only one of the subjects with NALFD had an abnormally high ALT. Thus ALT is not a sensitive screening tool for early NAFLD. This novel MRI fat fraction technique offers a strong advantage over traditional measures in identifying NAFLD risk and following the effectiveness of interventions for NAFLD in obese adolescents. Future work will include the use of quantitative MRI to measure change in liver fat in prospective intervention studies

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