Protein density fat fraction is a highly accurate biomarker of hepatic steatosis in adolescent girls and young women

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Target audience: Clinical radiologists and physicians who provide care to children, including specialists in pediatric endocrinology, gastroenterology and hepatology, and primary care providers in pediatrics and family medicine.

Purpose: 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. Traditional methods of detecting fatty liver, such as ultrasound or serum aminotransferases, miss early changes. A rapid, clinically relevant, non-invasive method for early detection and staging of NAFLD is urgently needed.3 The purpose of this work was to evaluate the accuracy of a novel quantitative MRI technique to quantify hepatic steatosis in adolescents.

Methods: Subjects: This is a cross-sectional study involving 132 females with BMI Z-scores ranging from -2.20 to 2.71 (mean 1.07 ± 1.12), aged 11 to 21 years (mean 13.30 ± 2.01), 27% Hispanic, 73% Non-Hispanic; 64% Caucasian, 31% African American and 5% Asian. Fifty-five percent of subjects were overweight or obese (BMI > 85%). Subjects were recruited through a local middle school and pediatric clinics.

 Anthropometric and Laboratory Measures: Blood samples were collected within 1 month of imaging for assays including insulin, glucose, total and HDL cholesterol, and ALT after an overnight fast. All labs were performed in the same laboratory. Anthropometric measurements included height, weight, and waist circumference (WC). Homeostasis model of assessment - insulin resistance (HOMA-IR) was calculated as [fasting glucose (mg/dL) x fasting insulin (U/ml)]/405.

 Imaging: Imaging was performed on a clinical 3T scanner (MR750, GE Healthcare, Waukesha, WI) using an investigational version of a chemical shift encoded water-fat separation method (IDEAL IQ) and a 32-channel phased array body coil. Single voxel STEAM spectroscopy and fat-water separation over the liver were acquired4. 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.

 Table 1: All Study Subjects (n=132)

<table>
<thead>
<tr>
<th>MRI-PDFF (%)</th>
<th>MRS-PDFF (%)</th>
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<tr>
<td>r = 0.97, p &lt;0.001</td>
<td>Slope Estimate = 0.983</td>
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<tr>
<td>Intercept Estimate = 0.795</td>
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Discussion: Quantitative MRI is a feasible and accurate measure of hepatic triglyceride content in a diverse group of adolescents and young women. It is highly reliable for identifying early hepatic steatosis and correlates with metabolic risk factors (insulin resistance, low HDL). In contrast, BMI was not predictive of HS in the overweight and obese girls. The strong correlation of ALT with PDFF in HS subjects is evidence of hepatocellular injury; however 18 of these subjects had an ALT within the normal range and would be missed by current pediatric HS screening guidelines. Thus, ALT is not a sensitive screening tool for early HS. The ability to use PDFF as an accurate biomarker for hepatic steatosis 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 MR elastography to measure liver stiffness and identify progression of fatty liver disease in children and adolescents.

Conclusion: Liver PDFF measured with quantitative MRI is a rapid, clinically relevant, non-invasive method for early detection and quantitative staging of hepatic steatosis in adolescent girls and young women. This novel quantitative MRI technique holds promise as a method for early identification of NAFLD, thus allowing intervention prior to development of irreversible hepatic injury and progression of metabolic disease.

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