Liver DTI of Obese Insulin Resistant Subjects with Fatty Liver Disease

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is a major world-wide health problem affecting approximately one third of all adults. NAFLD can progress to Nonalcoholic Steato-Hepatitis (NASH), and further to Hepatocellular Carcinoma (HCC) [1-2]. One key limitation in understanding NAFLD is the lack of a non-invasive means to detect and assess disease progression to fibrosis. Recent studies suggest diffusion-weighted (DWI) and diffusion tensor MRI (DTI) as a promising tool in studying hepatic diseases including fibrosis [3-4]. However, these studies were conducted to study hepatitis / cirrhosis. Few, if any, DTI studies have been conducted with patients with NAFLD. In this study, we used DTI to investigate the diffusion parameters in obese, insulin resistant adults with hepatic steatosis in comparison with healthy volunteers. Our results show that Fractional Anisotropy was significantly increased while diffusivity was significantly decreased for obese subjects in comparison to healthy controls. These results suggest diffusional changes are indicative of hepatic adipocyte accumulation and not fibrosis. Therefore, hepatic lipids can complicate the utility of DWI/DTI in the study hepatic fibrosis associated with NAFLD/NASH.

Methods

Eleven obese (BMI≥30), insulin resistant subjects with early-stage NAFLD were recruited from the liver clinic for MRI. Seven lean, healthy subjects were also scanned for comparison. Fatty Liver Disease was confirmed by MRS (data not shown). Ten transverse images were acquired with a respiratory-triggered single-shot DTI-EPI sequence (TR/TE=2000/81ms, 6 directions, NA=6, TH=5mm, FOV=384x280mm, Fat suppression) on a 1.5T Siemens Espree MRI scanner. A b-value of 400 sec/mm^2 was chosen to provide reasonable SNR and limit capillary perfusion effects [5]. The images were processed offline with Matlab and diffusion parameters including fractional anisotropy (FA), apparent diffusion coefficient (ADC), and diffusion eigenvalues (λ_1, λ_2 and λ_3) were computed. For each slice, T_2-weighted images were used to select liver regions of interest (ROIs, Fig. 1). Overall, ten ROIs from different layer of liver for each subject were examined to ensure a robust assessment.

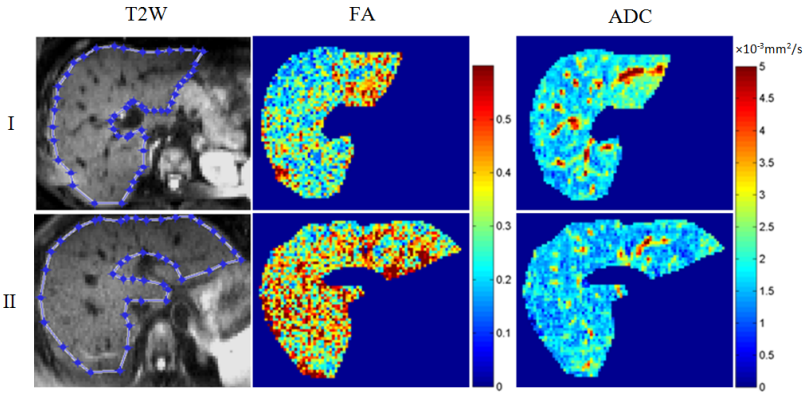

Fig. 1: Representative T_2-weighted images as well as FA and ADC maps for a healthy volunteer (I) and a subject with fatty liver disease (II). Representative ROIs of liver are shown in T2W images.

Results

Representative images of a healthy subject (I) and a subject with fatty liver (II, 19% liver fat by MRS) are shown in Fig. 1. The FA maps demonstrate that the increased FA in the obese subjects are homogeneous throughout the liver. As a group, the mean FA was increased by ~33% in obese subjects (Fig. 2a, $p<0.01$) while the diffusivity was decreased by ~10% (Fig. 2b, $p<0.01$). Evaluation of the diffusion eigenvalues showed a decrease in all diffusion eigenvalues accounting for the decreased diffusivity. However, a disproportionately larger change was observed for λ_2 and λ_3 (Fig. 2c) in obese subjects resulting in the large increase in FA for the obese subjects.

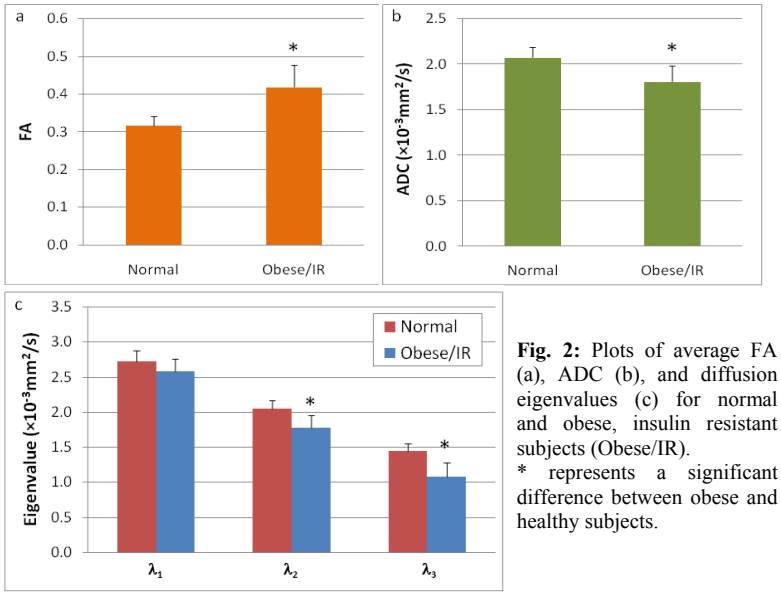

Fig. 2: Plots of average FA (a), ADC (b), and diffusion eigenvalues (c) for normal and obese, insulin resistant subjects (Obese/IR). * represents a significant difference between obese and healthy subjects.

Discussion

Our liver DTI results show ~33% increase in FA and ~10% decrease in ADC for subjects with obese, insulin resistant subjects with hepatic steatosis. Previous hepatitis and cirrhosis studies have demonstrated diffusion changes associated with hepatic fibrosis and not hepatic steatosis (liver fat). Here, the dramatic diffusion changes are most likely due to adipocyte accumulation and not fibrosis as all subjects had normal liver enzymes (ALT/AST). In addition, the FA appears to decrease in response to short-term exercise intervention (data not shown). We hypothesize that the increase in adipocytes is physically impinging hepatocytes resulting in the decrease in (λ_2 and λ_3). Overall, these results suggest that the use of DWI/DTI techniques to detect fibrosis may be greatly complicated by the presence of excessive lipid accumulation. However, DTI may be a useful alternative to MRS in the study liver steatosis.

References

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