Early Hepatic Lipid Changes in Fatty Liver Rat Model by In Vivo Short-TE 1H-MRS at 3T

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Introduction

Non-alcoholic fatty liver disease is the most common cause of chronic liver diseases [1]. Liver lipid content has been suggested to play an important pathogenic role in the development of liver fibrosis and cirrhosis [2]. In addition, hepatic fat plays a major role in metabolic diseases including obesity, diabetes, and non-alcoholic fatty liver disease [3] Proton magnetic resonance spectroscopy (^{1}H-MRS) allows the study of cellular biochemistry and metabolism, and provides a non-invasive mean to determine disease abnormalities and progression in vivo and longitudinally. ^{1}H-MRS permits longitudinal assessment of fat fraction, saturated and unsaturated [4]. The aim of this study was to characterize early hepatic lipid changes in fatty liver rat model by in vivo short-echo time (TE) ^{1}H-MRS.

Materials and Methods

Twelve male Sprague-Dawley rats with 60% high fat diet were included in this study. MR imaging an single-voxel ^{1}H-MRS was performed using a PRESS sequence at 3T (e.g., Philips Achieva TX System with a 4-channel receive-only array animal coil). The examinations (voxel size, 8×8×8 mm^3) were measured from liver parenchyma in rats at 0 week and 2 weeks followed by high fat diet, respectively. The typical water peak linewidth (FWHM) ranged from 4 to 8 Hz. After shimming procedure water suppression was accomplished with "VAPOR" pulses. The spectral acquisition parameters were TR/TE = 2500/35 ms, and 256 acquisitions for averaging. A fully relaxed, unsuppressed spectrum was also acquired to measure the water peak (16 averages). LCModel fitting was conducted using experimental basis sets (e.g., lipid-8). Lipid signals and choline-containing compounds (Cho) were quantified by dividing peak are of H_2O. In addition, total saturated fatty acid (TSFA), total unsaturated fatty acid (TUFA), total unsaturated bond (TUB), and polyunsaturated bond (PB) were estimated. For multivariate statistical analysis, SIMCA-P 13.0 software (Umetrics Inc.) was used to process the numeric data. Principal component analysis (PCA) and partial least squares regression discriminant analysis (PLS-DA) were performed to distinguish between the two groups. To identify which variables were responsible for the separation, the variable influence on the projection (VIP) parameter was used.

Results

Figure 1 shows the typical liver MR image and ^{1}H-MRS spectra from a rat animal assessed at 0 week and 2 weeks after the start of high fat diet. Significant increase in lipid signals, 0.9, 1.3, 2.1, 2.3, 2.8, and 5.3 ppm was found in animals with 2 weeks ($p < 0.01$). However, no significant differences were observed in Cho, TSFA, TUFA, TUB, PB, and UI between baseline and 2 weeks ($p>0.05$). In a PLS-DA model, the relative discriminatory potential of the ^{1}H-MRS measures in the differentiation of the two groups are shown in Figure 3 (bottom) in terms of VIP. 5 ^{1}H-MRS measures (e.g., Lipids, 0.9, 1.3, 2.1, 2.3, and 5.3 ppm) with VIP>1 are those detectable in ^{1}H-MRS spectra. Using these 5 ^{1}H-MRS measures an optimal model was constructed, and it did allow a significant separation between the two groups (Figure 3(top)).

Discussion

The present study demonstrated that in vivo ^{1}H-MRS can be used to detect the hepatic lipid abnormalities in fatty liver disease [5]. The main observation in this work was the significant increase of lipid signals in the liver parenchyma of fatty liver rats with high fat diet. The optimal PLA-DA model allowed a good separation of the two groups (e.g., at 0 week and 2 weeks). In this study, the total saturated fatty acid was high in the fatty liver rats, but not significant ($p>0.05$). The TSFA increase in liver may reflect the lipid-induced cell toxicity, which has been suggested to be related with activated apoptosis induced by saturated fatty acids. Therefore, ^{1}H-MRS is useful in detecting and characterizing various hepatic lipid alterations as early as 2 weeks for the start high fat diet.

Reference

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Acknowledgement: This work was supported in part by KBSI- #E34600.

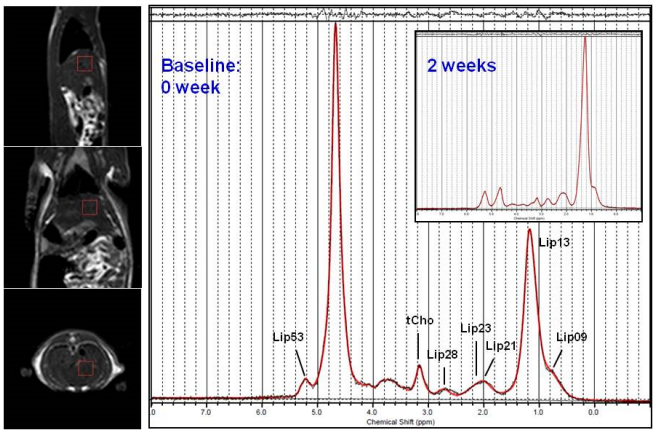

Figure 1. 3T MR imaging showing volume of interest (Left) and in vivo ^{1}H-MRS spectra of the rat liver parenchyma processed using LCModel with basis sets (Right, at week and 2 weeks (insert)).

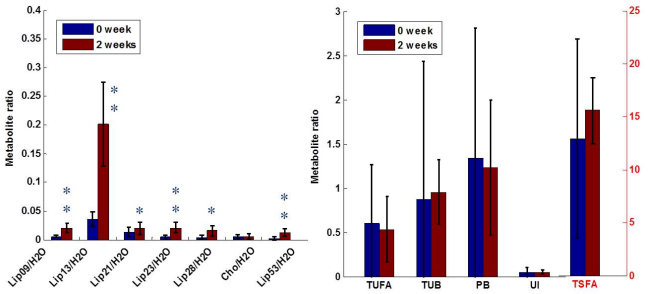

Figure 2. Lipid signals and choline-containing compounds (Left) and fat fraction (Right) quantified in 0 week and 2 weeks after high fat diet. Data shows mean±SD for each group using a two tailed *t*-test with significance threshold of *$p < 0.01$ and **$p < 0.001$.

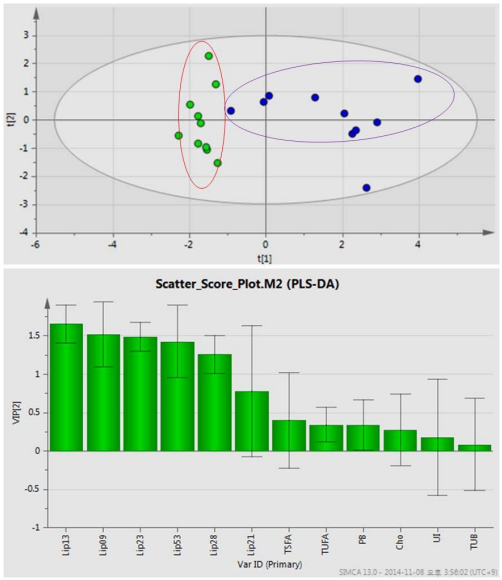

Figure 3. The variables with VIP values in PLS-DA model (bottom) and PLS-DA scores plot (top). The model did allow a good separation of the two groups (e.g., at 0 week and 2 weeks).