QUANTIFICATION OF THE HEPATIC FATTY INFILTRATION AND THE METABOLITE CONCENTRATIONS USING MAGNETIC RESONANCE SPECTROSCOPY AND IN AND OUT OF PHASE IMAGING

S. CAVASSILA[1], A. BUCUR[1], H. RATINEY[1], C. CUDALBU[1], O. BEUF[1], and F. PILLEUL[1,2]

[1]CREATIS-LRMN, CNRS UMR 5220, Inserm U630, INSA-Lyon, Université de Lyon, Université Lyon 1, Villeurbanne, France, [2]Imagerie digestive - CHU Herriot, Hospices Civils de Lyon, Lyon, France

Introduction

Despite the increasing prevalence of non-alcoholic fatty liver disease, the criteria used to diagnose the disorder remain poorly defined. Non invasive methods have been developed in order to substitute liver biopsy which is the gold standard. Indeed, proton magnetic resonance spectroscopy (MRS) [1], diffusion-weighted imaging, double-echo imaging (DEI) [2] provide alternative procedures to quantify triglycerides in the liver. The aim of this paper was to quantify the *in vivo* hepatic metabolite and lipid contents from MRS measurements, to determine if the hepatic metabolite and lipid concentrations evaluated from MRS were correlated with the fat fraction determined from DEI.

Method

Twelve patients with suspected liver diseases underwent MR imaging and spectroscopy of the liver (4 women, 8 men; average age: 44 +/- 21 years).

MR Imaging and Spectroscopy acquisitions: All MR studies were performed on a clinical 1.5 T Symphony system (Siemens Medical Solutions, Erlangen, Germany) using phased-array body coils. MR examinations were performed with the following protocol: transverse dual echo in and out of phase T1-weighted FLASH sequences of the upper abdomen (TR/TE 202/2.3–4.6 ms; 70°flip angle, 22 slices acquired in a 23-second breath hold). Slice thickness was 8 mm and matrix size was 256 x 112 (frequency x phase encoding). Localized MRS acquisitions were performed using a short–echo time respiration trigged PRESS sequence (TR/TE 1500/30 ms, 1024 data-points, 128 accumulations, about 6 minutes acquisition time, depending on the patient's respiratory cycle). Based on 3D magnetic fields maps, first- and second- order shims were adjusted for each volume of interest centered in a vessel free zone of the right hepatic lobe (2x2x2 cm^3). The water suppression was achieved with CHESS. The corresponding unsuppressed water signal was acquired for each patient (TR/TE 1500/30 ms, 1024 data-points, 4 accumulations).

MR Imaging interpretation: Fat/water ratios on in- and opposed-phase images of the liver were calculated by dividing the signal intensity measured on out of phase images with the signal intensity measured on in-phase images. Quantification of liver steatosis was performed using the following formula: %Steatosis = [(-79.8)(Fat/Water ratio)] + 91.5 [5].

Quantifications of MRS signals: *In vivo* MRS signals were post-processed in the time-domain. The signals were fitted using a nonlinear least-square method that adjusts the parameters of a Voigt lineshape model function to the measured signals. For each spectrum, ten components were selected to fit the saturated lipids (0.9ppm, 1.3ppm, 1.8ppm), the unsaturated lipids (2.1ppm, 5.2ppm), the water residue (2 components around 4.7ppm) and the metabolite contributions (Choline + Phosphocholine + Glycerolphophocholine + TMAO (3.2ppm), Choline + Phosphorilcholine + Glycerol + Glucose + Glycine (3.5ppm), Choline + Glycogen +Lactate +Glucose (4ppm)). The assignations of the resonances referred to the published values in the references [3, 4]. The water contribution was quantified from the unsuppressed water acquisitions by invoking two components for the model function. The intensities of the metabolite and lipid contributions were normalized to the corresponding estimated water content.

Statistical analysis: The non-parametric Kendall's rank correlations (τ) were computed to determine whether the metabolite and lipid concentration estimates were correlated with the fat/water ratios determined on the in and out-of phase images.

Results

For each *in vivo* liver spectrum, eight main groups of resonances originating from different types of lipids, compounds of Choline, TMAO, Glucose and Glycogen were successfully quantified (Figure 1). The saturated and unsaturated lipid/water ratios and the metabolite/water ratios were then calculated. The saturated and unsaturated lipid/water ratios were in the range of 0.74-54.2% and 0.46-12.1% respectively. Percentages of liver steatosis estimated from in- and out-of phase imaging were in the range 6.6-74.7%. Both saturated and unsaturated lipids/water ratios showed positive and strong correlations (τ=0.727, n=12, p<0.001) with the percentage of liver steatosis estimated from DEI. The metabolite resonances at 3.2ppm (τ=0.576, n=12, p<0.01), 3.5ppm (τ=0.667, n=12, p<0.01) showed also correlations with the % of liver steatosis estimated from DEI (Fig 2).

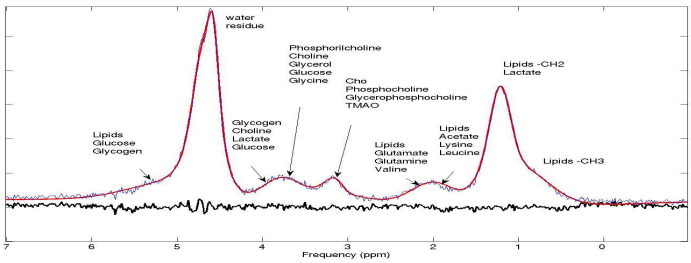

Figure 1: ^{1}H water-suppressed spectrum acquired at 1.5T from the right hepatic lobe of a patient (blue line), estimated spectrum as a sum of Voigt lineshape resonances (red line) and the residue (black line). For this patient, the fat/water ratio estimated from DEI was 14.8%; and the levels (relative to water) of saturated lipids, the unsaturated lipids and compounds of Cho estimated from MRS data were 2.9%, 1.8% and 0.2% respectively.

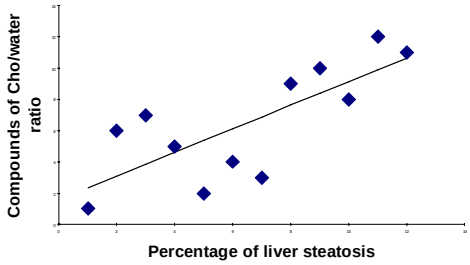

Figure 2: Correlation between the level (relative to water) of the group of metabolites at 3.2 ppm determined by MRS and the percentage of liver steatosis determined by DEI.

Conclusion

Both saturated lipids/water and unsaturated lipids/water ratios showed strong correlations with the percentage of liver steatosis estimated from DEI. Moreover, the levels (relative to water) of the groups of metabolites at 3.2 ppm and 3.5ppm determined by MRS showed also correlations with the % of liver steatosis determined by DEI. A larger number of patients will be investigated in order to confirm these results.

Acknowledgments: Authors thank Dr Berthold Kiefer from Siemens Medical Solutions for support with WIP spectroscopy sequence.

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