Noninvasive quantitation of liver triglycerides in steatosis patients using MR methods

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Introduction

Hepatic steatosis is characterized by an excess of triglycerides following a prolonged inflammation of the hepatocytes. Asymptomatic, it can often precede more severe diseases like diabetes or cancer (1,2). Histopathologic analysis remains the standard method to diagnose steatosis but the associated biopsy procedure is invasive and potentially dangerous for the patient. Moreover, the tissue sample withdrawn may not be representative of the whole liver. Noninvasive techniques such as proton MRS (3), diffusion-weighted imaging (DWI), double echo imaging (DEI) and bioassays provide alternative procedures to quantity triglycerides in the liver without the need for biopsy. The goal of this project is to be able to determine which methods and which parameters are best suited to measure the triglyceride content in the liver of steatosis patients.

Methods

Patients and control subjects: Seven patients (6 men, 1 woman; 60 ± 10 years) diagnosed with steatosis by histopathologic analysis and 13 control subjects (5 men, 8 women; 41 ± 17 years) were recruited. Blood and urine samples were collected before MR examination. All MR experiments were performed during breath holding on a GE Signa 1.5 T instrument using a surface coil.

MRS: Single-voxel proton MRS data were acquired in three different areas of the liver (lower, central and upper locations) using the PROBE protocol with the PRESS sequence. Acquisition parameters were: voxel size = 2 x 2 x 2 cm^3, TE = 30 ms, TR = 1200 ms, spectral width = 2500 Hz, number of scans = 16, water suppression = off, total acquisition time = 22 s. MR spectra were processed and quantified using *LCModel*.

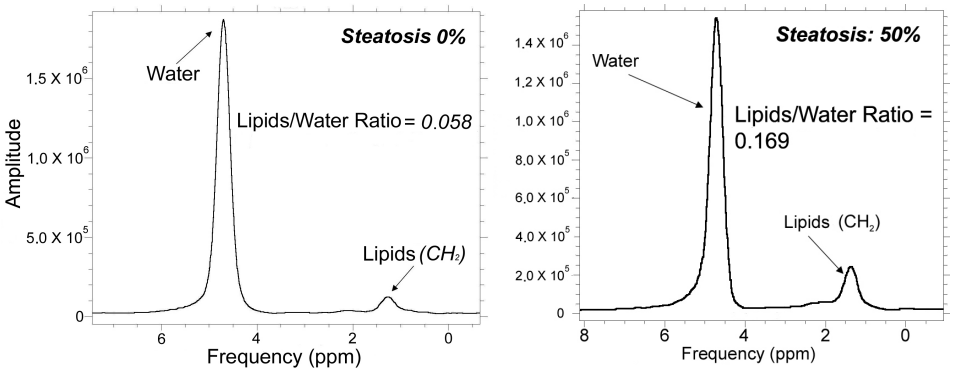

Figure 1 : MR spectra from the liver of (left) a control subject and (right) a patient with a percentage of steatosis of 50% determined by histopathology.

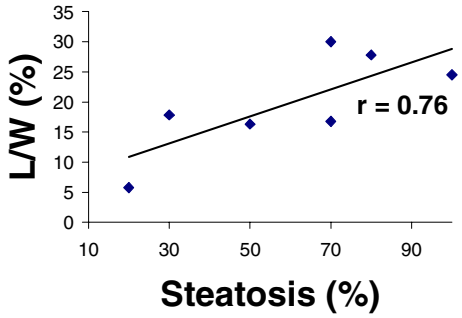

Figure 2 : Correlation between the lipids/water ratio determined by MRS and the percentage of steatosis determined by histopathology.

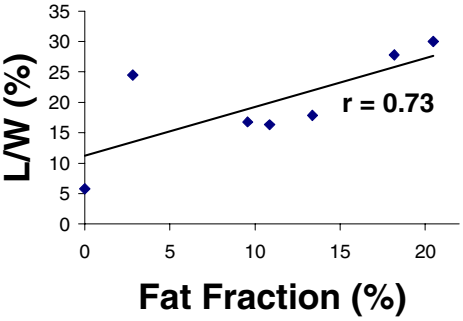

Figure 3 : Correlation between the lipids/water ratio determined by MRS and the fat fraction determined by DEI.

DEI: The fast spoiled gradient-recalled (SPGR) dual-echo sequence was used for in phase/out of phase MRI acquisition. Data were obtained using the following parameters: TR = 140 ms, TE = 2.2 and 4.4 ms, FOV = 36 x 36 cm^2, matrix = 256 x 160, flip angle = 90°, bandwidth = 62.5 kHz, total acquisition time = 17 s. Axial slices (13) covering most of the liver were used with a thickness of 7 mm and a gap of 3 mm. Data were analyzed with the GE *FUNCTOOL* software.

DWI: DWI data were acquired using the EPI sequence with TR = 3500 ms, TE = 85 ms, FOV = 38 x 38 cm^2, matrix = 96 x 128, bandwidth = 62.5 kHz, gradient factors b = 50, 100, 200, 300, 400 s/mm^2, total acquisition time = 16 s. Axial slices (16) covering most of the liver were used with a thickness of 7 mm and a gap of 3 mm. Analysis of DWI data was performed with the GE *FUNCTOOL* software.

Bioassays: Blood enzyme activities were determined for alanine aminotransferase (ALT), alkaline phosphatase (AP) and γ-glutamyltransferase (γ-GT). Triglycerides and total lipid content were also assayed.

Results

Fig. 1 presents spectra from the liver of a control subject and a steatosis patient showing a much higher lipids/water ratio (L/W). Fig. 2 presents the most significant correlation between the L/W determined by MRS and the percentage of steatosis measured by histopathology (r = 0.76). A good correlation (r = 0.74) was also found between L/W and the fat fraction calculated from DEI data (Fig. 3). Correlations between blood enzyme activities and MR parameters were weaker. The analysis of DWI data is complicated by the presence of iron in some cases.

Discussion

The MR results obtained so far suggest that MRS is the most accurate method to quantify liver steatosis noninvasively. However, DEI data also show a good potential and the combination with other noninvasive measurements such as bioassays and metabonomics data should lead us to an accurate method to quantitate liver steatosis without using biopsy.

References

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