Non-invasive quantification of hepatic steatosis with 3.0 Tesla MR Spectroscopy in an experimental rat model

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Introduction:

Hepatic steatosis is characterized by fat accumulation in the liver and is associated with features of the metabolic syndrome, e.g. obesity, insulin resistance and dyslipidaemia; conditions that are increasing in prevalence the Western population. Hepatic steatosis has been identified as a risk factor in liver surgery or in living donor liver transplantation. Invasive needle biopsy of the liver remains the gold standard for histopathological assessment of hepatic steatosis, but is subject to underscoring and associated with an increased risk of complications. Magnetic Resonance proton Spectroscopy (^{1}H-MRS) could be a non-invasive alternative to needle biopsy, but is not yet validated. Therefore the purpose of this study was to quantify hepatic steatosis with 3.0 T ^{1}H-MRS in an experimental rat model and correlate these ^{1}H-MRS measurements with both histopathological and biochemical analysis of hepatic fat.

Materials and Methods:

Hepatic steatosis was induced by feeding rats a methionine choline deficient (MCD) diet for 0, 1, 3 or 5 weeks (n=5 per group). ^{1}H-MRS was performed using a 3.0 Tesla Philips Intera scanner using an experimental micro-coil. A voxel of 8 x 10 x 15 mm was positioned in the rat liver (see fig. 1). Spectra were acquired using a PRESS sequence with TE/TR=36/2000 ms and 64 signal acquisitions. Two ratios from the ^{1}H-MR spectra were calculated: ratio 1 defined as the total fat peak versus the reference H_2O peak and ratio 2 defined as the unsaturated fat peak versus the H_2O peak. A hepatopathologist blinded for ^{1}H-MRS results quantified macrovesicular hepatic steatosis percentage. Correlations (Spearman correlation coefficient) were studied between both ^{1}H-MRS ratios, histopathology and total fatty acid concentration (gas chromatography).

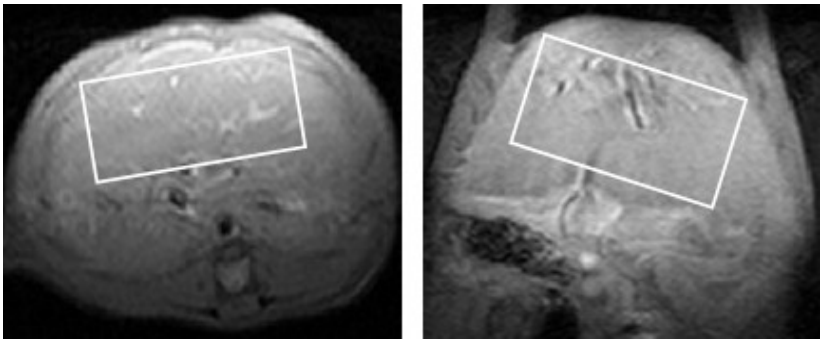


Figure 1: voxel position in the rat liver at an axial (left) and coronal (right) slice

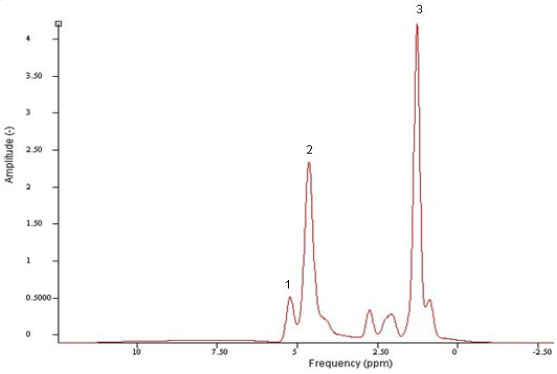


Figure 2: 1= unsaturated fatty acids at 5.4 ppm, 2= H_2O at 4.65 ppm, 3= total fatty acids at 1.2 ppm

Results:

The median hepatic fat ratio measured by ^{1}H-MRS increased from 0.003 at baseline to 0.460 after 5 weeks of MCD diet (see fig. 3). This increasing ratio significantly differed per MCD diet group (p<0.001, Kruskal-Wallis analysis). Fig. 2 provides an example of a water suppressed spectrum of a steatotic rat liver after 5 weeks of diet. A large fat peak is visible at 1.2 ppm arising from both unsaturated and saturated lipid methylene protons. Next to the suppressed water peak at 4.65 ppm, the spectrum contains a peak at 5.4 ppm from the unsaturated lipid protons. Furthermore we found significant correlations between the total fat/water (1) and unsaturated fat/water (2) ratios and histopathological macrovesicular steatosis (ratio 1: r= 0.92, p<0.001 and ratio 2: r= 0.84, p<0,001) and biochemical assessed total and unsaturated fatty acids in the rat liver (ratio 1: r=0.92, p<0.001 and ratio 2: r= 0.88, p<0.001), see table 1 and fig. 4.

Table 1: ^{1}H-MRS ratio 1 and 2 correlation coefficients
Figure 3: boxplot representing increasing hepatic fat during diet
Figure 4: correlation between ^{1}H-MRS and total fatty acids

Table 1

	Histopathological liver fat content	Biochemical fatty acids
Ratio 1 Total fat/ water	r= 0.92 p< 0.001	r= 0.92 p< 0.001
Ratio 2 Unsaturated fat/ water	r= 0.84 p< 0.001	r= 0.88 p< 0.001

Figure 3:

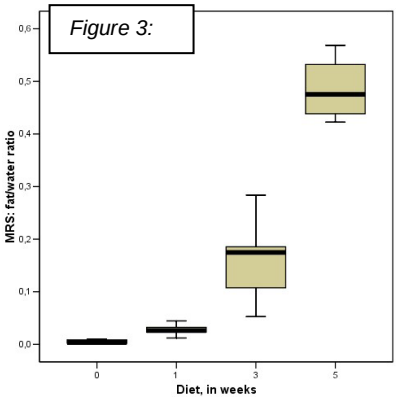
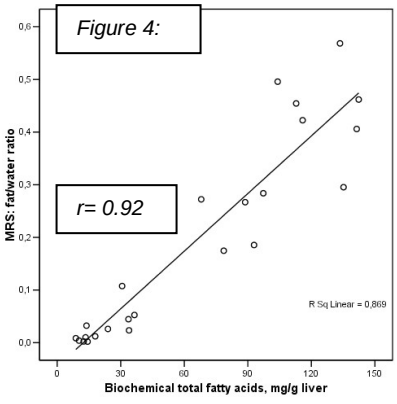


Figure 4:



Conclusion:

3.0 Tesla ^{1}H-MRS is able to accurately measure hepatic fat content in this rat model and strongly correlates with histopathological and biochemical analysis of hepatic fat. When applied in a human model the assessment of hepatic steatosis with ^{1}H-MRS may replace invasive liver biopsy in clinical practice. To our knowledge this is the first time the unsaturated ^{1}H-MRS fat/water ratio was correlated with both histopathological and biochemical parameters. Further research must be implemented to investigate the additional value of the unsaturated H-MRS fat/water ratio in hepatic steatosis.