MR Spectroscopy of Non-alcoholic Fatty Liver Disease

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is a disorder of increasing prevalence with a propensity to progress to serious liver disease. Currently, a liver biopsy is required to determine the severity of fatty liver infiltration (steatosis) and to distinguish it from nonalcoholic steatohepatitis. MR spectroscopy has the potential to noninvasively diagnose, grade and follow this disease, providing significant practical and clinical impact. The noninvasive assessment of fatty liver disease is particularly important in HIV and hepatitis C co-infected (HIV/HCV) patients who are at increased risk for steatosis and accelerated liver disease progression. Proton MRS has been used to study fatty liver disease (1-3), but has not been evaluated in HIV/HCV patients.

Methods

MR imaging and spectroscopy were performed in 8 healthy volunteers, 9 patients undergoing assessment for NAFLD, and 14 patients co-infected with both HIV and hepatitis C. Steatosis grade was determined by liver biopsy. An 8cc voxel was placed in the liver, avoiding vessels and away from the edges of the liver in all dimensions. The proton MR spectroscopy was acquired using a 128 acquisition time series of PRESS single voxels (8cc, TR/TE= 2500/30. Unsuppressed water spectra with 8 acquisitions also were acquired at each location. Each spectrum was Fourier transformed, baseline subtracted, and phase and frequency corrected. Any data with artifacts were removed and the remaining spectra were averaged for each location.

Results

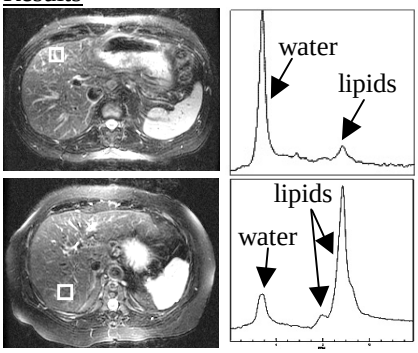

Fig 1: MRI & MRS from a normal (top) and Grade 1 steatosis subject (bottom).

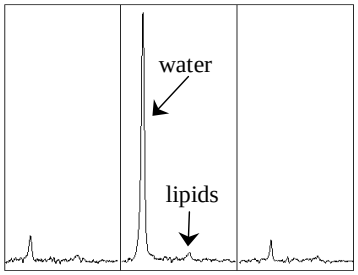

Fig 2: 3 consecutive spectra from a patient showing large respiration or other artifact.

The MRS lipid:water ratios among NAFLD patients with grades 1, 2, and 3 steatosis were statistically different from each other and from healthy subjects ($p< 0.008$). MRS lipid:water were higher in the NAFLD patients than the healthy subjects (17 ± 14 vs. 0.1 ± 0.06, $p<0.0001$) and increased dramatically with grade ($p<0.008$). See Table 1. A peak at 2.1ppm attributed to free fatty acids was also higher (vs. water) in the patients (3:1 vs. 1:80, $p<0.02$). A peak at 3.2ppm (choline, phosphocholine, and trimethylamine oxide) was observed in the healthy controls and not measurable in all but one NAFLD patient (grade 1). Example spectra from a healthy individual and a subject with grade 1 steatosis are shown in Fig 1. When all patients were combined, the 19 subjects without steatosis had lipid:water less than the 6 subjects with grade 1 steatosis (0.26 ± 0.3 vs, 3.2 ± 2.2, $p<0.00001$).

Table 1: Lipid:Water (mean ± sd) by population and steatosis grade. Numbers are in ()'s.

	Healthy(8)	**NAFLD (9)**			**HIV/HCV (14)**	
		Grade 1 (3)	Grade 2 (3)	Grade 3 (3)	Grade 0 (11)	Grade 1 (3)
Lipid:water	0.11±0.06	4.3±2.9	13±1.7	35±5	0.36±0.31	2±0

In the HIV/HCV patients, 3/14 had histopathological evidence of steatosis (grade 1) with a mean lipid:water of 2, within the range of the NAFLD grade 1 steatosis patients. Of the remaining patients, who did not have steatosis on biopsy, 4/11 had lipid:water <0.17, in the range of the healthy subjects, and 7/11 had intermediate levels of lipid:water (0.2– 1).

Acquiring a time series of spectra allowed the evaluation of respiratory or other temporal variations. Most subjects had some phase variations and small lipid:water amplitude variations during the exam, however 6 had lipid:water vary 1.5-fold - 10-fold (Fig 2). Averaging the signal without the artifact spectra yielded lipid:water ratios up to 2-fold larger.

Discussion

This study demonstrated that liver MRS shows very significant differences among healthy volunteers and patients with different grades of steatosis. MRS showed a range of lipid:water ratios in the HIV/HCV patients. The 3 patients with steatosis had lipid:water ratios within the range found in the NAFLD patients with comparable steatosis. Four patients had values in the normal range. The remaining 7 had values between the values found in the healthy population and the values found in grade 1 steatosis. This may represent a broader range of normal lipid:water ratios than demonstrated by our healthy population or may represent a progression towards steatosis. Several subjects had large variations in their lipid:water during the spectral acquisition, likely due to tissues shifting from motion, a large concern for MR spectroscopy of the body. Such artifacts need to be evaluated and compensated before interpreting spectra in these patients. Regardless, this study shows that liver MRS holds great promise for the noninvasive evaluation of steatosis in nonalcoholic fatty liver disease, including evaluation of HIV/HCV patients.

References: 1. Longo R, et al. J Magn Reson Im 1995; 281-285. 2. Szczepaniak LS, et al. Am J Physiol 1999; 276:E977-89. 3. Heiken JP et al. Radiology 1985; 157:707-10.