MR Diffusion and ^{1}H MR Spectroscopy in Non-alcoholic Fatty Liver Disease

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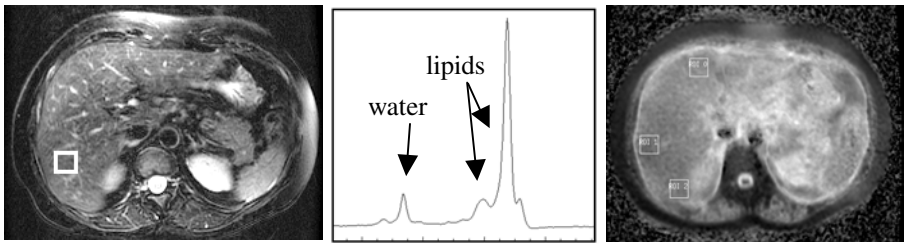
Introduction Nonalcoholic fatty liver disease (NAFLD) is a disorder of increasing prevalence with a propensity to progress to serious liver disease. Currently, a liver biopsy is required to determine the severity of fatty liver infiltration (steatosis) and to identify and characterize inflammation and fibrosis. MR imaging, including diffusion and spectroscopy, has the potential to noninvasively diagnose, grade and follow this disease, providing significant practical and clinical impact. Both MR diffusion and proton MRS show changes with steatosis (1-5). The combination of MR diffusion and MR spectroscopy, and its comparison to pathological biopsy results, have not been evaluated in NAFLD patients.

Methods MR anatomic imaging, diffusion imaging and spectroscopy were performed in 10 healthy volunteers and 12 patients undergoing assessment for NAFLD. Steatosis and inflammation grades and fibrosis stage were determined by liver biopsy. MR diffusion imaging utilized a single-shot fast spin-echo (SSFSE) diffusion tensor imaging sequence (5,6). Directionally-averaged apparent diffusion coefficient (Dav) values were calculated and averaged from three locations in the liver. Liver MRS was obtained from an 8cc voxel placed in the liver to avoid vessels and the edges of the liver in all dimensions. Data was acquired using a 128 acquisition time series of PRESS single voxels with a TR/TE= 2500/30ms. 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. The total area of peaks attributed to CH_2 and CH_3 lipids were summed and a ratio of total lipids: water was calculated for each subject.

Results

Figure 1 – MRI (left), showing MRS voxel placement, MR spectrum (middle) and Dav (right) for a subject with grade 2 steatosis, grade 0 inflammation and stage 0 fibrosis.



In general, Dav results decreased whereas total lipids: water increased with increasing steatosis grade, inflammation grade and fibrosis stage. To separate grades of steatosis with Dav, a Tukey-Karmer test showed significant differences between healthy and the other steatosis grades. Also, grade 1 was significantly different from grade 2 steatosis ($p<0.05$). A logistic regression model using Dav yielded an $R^2=0.38$. MRS lipids:water better separated the steatosis grades. Healthy was not significantly different from grade 1, but grades 2 and 3 were significantly different from each other and the other groups ($p<0.05$, Tukey-Kramer). With logistic regression, a model based on lipids:water yielded $R^2=0.82$. However, when Dav and MRS were combined, the logistic regression model completely separated steatosis grades, $R^2=1$. When investigating fibrosis, a stepwise logistic regression model only showed significance for Dav (not lipids: water). However, with the few cases of high fibrosis in this study, the R^2 was only 0.24. When separated by grade of steatosis, the subjects with stage 2 or 3 fibrosis and those with grade 2 inflammation had the lowest Dav and the highest lipids: water of the subjects with the same steatosis grade as shown in Figure2.

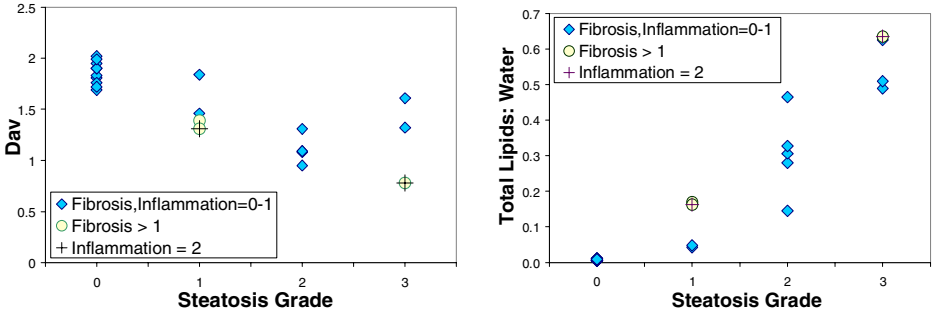


Figure 2 – Dav (left) and total lipids : water (right) versus steatosis grade. Note that the subjects with fibrosis stage = 2-3 have the lowest Dav and highest lipids:water of their respective steatosis grade groups.

Discussion This study demonstrated that liver diffusion and liver proton spectroscopy show changes with steatosis and seem to show differences with fibrosis and inflammation. Spectroscopy more clearly separated subjects based on steatosis grade and Dav more clearly separated subjects based on fibrosis stage than the other MR measure. When combined, a model based on Dav and lipids:water completely separated subjects by steatosis grade. Of note, the very clinically relevant presence of inflammation and/or fibrosis produced the most extreme results within a steatosis grade category. This study showed that the combination of MR diffusion and MR spectroscopy of the liver holds great promise for the noninvasive evaluation of nonalcoholic fatty liver disease.

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. 4. Noworolski S, et al. ISMRM 2005:479. 5. Vigneron D, et al. ISMRM 2005:1888. 6. 1. Xu D, et al.. Magn. Reson. Imaging 2004; 22:751-759.