Quantitative MRI/MRS of Nonalcoholic Fatty Liver Disease (NAFLD)

W. H. Perman[1], B. Neuschwander-Tetri[2], E. Brunt[3], E. Bialecki[4], D. Palmer[4], I. Akduman[5], J. Olynyk[6], G. Balci[5]

[1]Department of Radiology, Saint Louis Univeristy School of Medicine, St. Louis, MO, United States, [2]Department of Internal Medicine, Saint Louis University, St. Louis, MO, United States, [3]Department of Pathology, Saint Louis University School of Medicine, St. Louis, MO, United States, [4]Department of Internal Medicine, Saint Louis University School of Medicine, St. Louis, MO, United States, [5]Department of Radiology, Saint Louis University School of Medicine, St. Louis, MO, United States, [6]School of Medicine and Pharmacology, University of Western Austrailia, Fremantle, Australia

BACKGROUND: Nonalcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease in many countries. NAFLD encompasses a spectrum of liver disease. In some cases, there is only fat accumulation in the liver (simple steatosis) which may be associated with liver enzyme abnormalities. When there are associated significant necroinflammatory changes in the liver, this is termed steatohepatitis. Similar changes may be seen with the consumption of alcohol, and therefore the term nonalcoholic steatohepatitis (NASH) is used. NASH is a subtype of NAFLD also accompanied by hepatocyte ballooning with or without Mallory's hyaline and fibrosis. The significance of the presence of NASH is that it may induce liver fibrosis and progressive liver disease leading to cirrhosis (2,3). Currently the only method of detecting NASH is by liver biopsy. CT scan and ultrasound can reliably detect significant fat (>33%) in the liver with a sensitivity of 93% and 100% (PPV of 76% and 62%), however they are unable to detect steatohepatitis.(4) Ultrasound used to diagnose a fatty liver gives an incorrect diagnosis in 25-33% of cases(5). Proton Magnetic Resonance Spectroscopy (MRS) has recently been found reliable in quantitating hepatic fat(6), however its utility in detecting NASH and liver fibrosis has yet to be determined.

OBJECTIVE: The purpose of this work was to perform quantitative MRI and MRS on patients diagnosed with NAFLD and to correlate the histologic measures of the disease (steatosis, inflammation, and fibrosis) with the MR parameters of calculated T1 and T2, percent fat, percent magnetization transfer, and diffusion coefficient.

MATERIALS and METHODS: The MRI/MRS protocol was approved by the Institutional Human Subjects Committee and informed consent was obtained from each subject prior to the MRI/MRS examination. Patients scheduled for liver biopsy to confirm the working diagnosis of NAFLD were recruited into this study undergoing proton MRI/MRS within one week of their liver biopsy. Liver biopsies were evaluated by one pathologist (EMB) in the context of routine patient care according to a previously described scoring system (ref). The proton MRI/MRS was performed on a 1.5 T General Electric Signa MR unit running version 9.1 software using the body coil for homogeneous excitation and reception of the MRI/MRS signal. All proton MR imaging was performed with breath-holding. Percent fat content was determined using in-phase and out-of-phase short-echo gradient echo multiple-slice imaging with TR-125 ms, Te = 2.2 and 6.6 ms, and single voxel PRESS proton spectroscopy with and without water suppression TR=1.5s, TE=57 ms, 2x2x2 cm^3 voxel. T1 was calculated from multiple breath hold gradient echo acquisitions with TE=2.2 ms (in-phase), and TR=1800, 1200, 800, 600, 450, 225, 150 and 75 ms. T2 was calculated from multiple 4-shot breath hold EPI image acquisitions with constant TR and TE values of 18.8,28.4, 38.0, 47.6, and 57.2 ms. Percent magnetization transfer (MT) was determined by acquiring two breath hold acquisitions one without and one with two MR rf pulses 1200 Hz off resonance. The diffusion coefficient was determined from a single slice single-breath hold 2D spin echo EPI acquisition with b-value encodings of 0, 100, 200, 300 and 400.

RESULTS: A total of 25 NAFLD subjects completed the MRI/MRS examination. The results are summarized in Table 1. Inflammation alone significantly elevated T1 but did not have a significant effect on T2. Fibrosis with inflammation elevated T1 and decreased T2 at the higher fibrosis levels. Increased percent fat decreased T1 to levels at or below normal and decreased T2 at higher (40-70 %) fat levels. While large changes in MT and D were observed, these changes did not appear to correlate with a histologic parameter. Significantly increased T2 values of 50 ms were observed in two patients but the increased T2 did not appear to correlate with a given histologic change. T1 relaxation increases with inflammation, is relatively insensitive to fibrosis, and decreases with increases in percent fat. T2 relaxation is relatively insensitive to inflammation, decreases with significantly increased percent fat (40-60 %), and is significantly increased due to a process that does not correlate with a histologic change.

CONCLUSION: Quantitative MR imaging is sensitive to changes in liver due to NAFLD, but the changes can be confounding (e.g. increased percent fat and inflammation have offsetting effects on T1) and do not always correlate with histologic parameters.

T1 and T2 Changes with Inflammation, Fibrosis and Steatosis

	T1		T2	
Inflammation Grade (number of subjects)	mean	stdev	mean	stdev
0 (4)	401.8	20.7	43.1	3.3
1 (3)	465.6	28.4	42.8	2.1
3 (2)	496.7	12.6	41.4	3.4
Fibrosis/Inflammation (number of subjects)				
2/3 (3)	456.0	67.2	45.4	2.6
3/3 (2)	467.6	64.0	38.0	3.8
Steatosis/Fibrosis/Inflammation (number of subjects)				
10-15%/0-2/1-2 (2)	465.3	44.0	51.2	0.5
25-35%/3/1-3 (4)	394.8	18.4	40.3	4.4
49-66%/0/1-3 (2)	309.3	42.2	34.0	0.9
Normal Liver				
10 subjects	329.9	24.3	42.3	4.3