

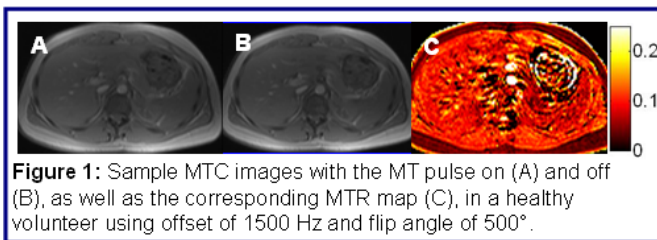
DIAGNOSIS OF CIRRHOSIS WITH MRI: IS MAGNETIZATION TRANSFER CONTRAST WORTH PURSUING?

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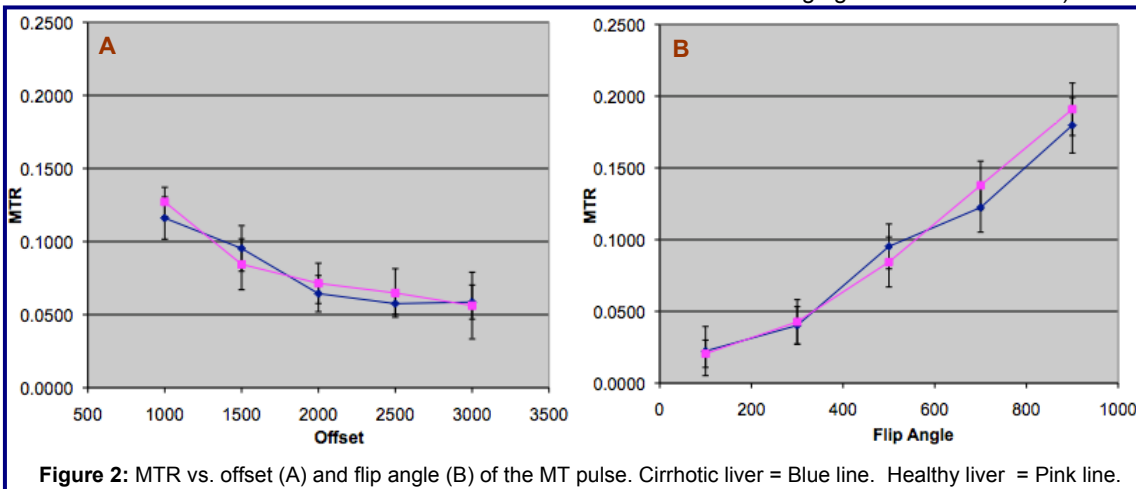
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Introduction: Liver biopsy, which serves as the clinical standard for the detection and surveillance of liver fibrosis and cirrhosis, is an invasive procedure that is prone to sampling error and interobserver variability. Magnetization-transfer contrast (MTC) imaging employs off-resonance radio-frequency pulses to selectively pre-saturate signal from macromolecule-bound protons via chemical exchange with free water and may offer a non-invasive means of detecting the collagen and other macromolecules deposited in the extracellular matrix of the liver in the setting of fibrosis and cirrhosis. While several studies have previously examined the utility of MTC imaging in this setting, these studies used differing imaging parameters for the magnetization transfer (MT) pre-pulse and have achieved variable and inconclusive results [1-5]. In this study, we attempt to optimize the ability of MTC imaging to separate healthy and cirrhotic livers via the use of an MTC sequence with adjustable MT pulse parameters.

Methods: 8 patients (6 male, 2 female; mean age 61±5 yrs) with a diagnosis of liver cirrhosis and 8 healthy volunteers (8 male, 0 female; mean age 29±7 yrs) with no history of liver disease were included in this ongoing prospective IRB-approved study. All individuals were imaged on a 1.5T Siemens Avanto scanner using multiple applications of an adjustable MTC sequence, obtained as a single axial 2D slice using a spoiled gradient-echo acquisition with the following parameters: 70/4.76/28°, 1 average, no parallel imaging, FOV 350 x 262 mm, matrix 128 x 80, slice thickness 8.0 mm, receiver bandwidth 200 Hz/pixel. Over the course of a single 13s breath-hold acquisition, the same slice was imaged with and without a 20,000 microsecond Gaussian-shaped MT pre-pulse. This MTC sequence was performed repeatedly in each subject with the frequency offset of the MT pulse varying from 1000 Hz to 3000 Hz in increments of 500 Hz while the flip angle of the MT pulse was held fixed at 500°, and with the flip angle of the MT pulse varying from 100° to 900° in increments of 200° while the frequency offset was held fixed at 1500 Hz. A single radiologist placed a 0.75 cm² region of interest (ROI) on all images over the right lobe of the liver in an area free of lesions, vessels, and artifacts. The magnetization transfer ratio (MTR) was calculated for each MTC sequence in each patient as $MTR = (S_0 - S) / S_0$, where S_0 and S represent the mean signal intensity of the ROI obtained with the MT pulse off and on, respectively. MTR was compared between healthy and cirrhotic livers for each of the assessed MTC sequences using an unpaired Student's t-test.



Results: Figure 1 shows a representative pair of images with the MT pulse off and on, as well as the corresponding MTR map. MTR increased as frequency offset decreased and as flip angle of the MT pre-pulse increased for both cirrhotic and healthy liver (Figure 2), with values ranging from 0.007 to 0.215 across all subjects. There was substantial overlap in the measured MTR between cirrhotic and healthy livers for all of the assessed MTC sequences, with none of the differences between these two groups being statistically significant (p-values ranging from 0.092 to 0.819).



Conclusions: The observed trends in MTR as a function of frequency offset and flip angle are consistent with previous simulations of the behavior of MTC contrast in phantoms and in vivo [6,7]. However, unlike some previous studies, we observed no difference in MTR between healthy and cirrhotic liver across a wide range of frequency offsets and flip angles. Possible explanations include the confounding effect of edema and

inflammation in the setting of cirrhosis, the contribution of direct water saturation to the measured MTR, and volume averaging of fibrotic bands with adjacent regenerative nodules in cirrhotic patients. It is also possible that the MT pre-pulse in the MTC sequence we used lacks specificity for the particular macromolecules deposited in the extracellular matrix in the setting of liver fibrosis. Data from additional subjects may further support our preliminary results that, contrary to the claims of previous authors, MTC imaging is unable to differentiate healthy and cirrhotic liver.

References: [1] Guo K, et al. JMRI 2003;18:321-7. [2] Chen JH, et al. Hepatogastroenterology 1999;46:2872-7. [3] Chen JH, et al. JMRI 1999;9:257-65. [4] Aisen AM, et al. JMRI 2000;14:79-87. [5] Kim H, Radiology 2008;247:696-705. [6] Martirosian P, et al. Invest Radiol 2008;43:16-26. [7] Morrison C, et al. MRM 1995;33:475-482.