Detection of Iron in an Animal Model of Hepatic Iron Overload using T2*-IDEAL

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Introduction: Hepatic iron overload is an important component in chronic liver disease, including in non-alcoholic steatohepatitis, where hepatic steatosis and iron overload can occur simultaneously[1]. Consequently, the presence of iron can corrupt fat measurements due to rapid T_2* decay. Here, we applied a T_2*-IDEAL method* to a rat model of iron overload in order to correlate imaging findings with chemical extraction of iron.

Methods: Three 10-week old male Sprague-Dawley rats with a body weight of 275-300 g were fed a ferrocene-supplemented diet[2] (Harlan Teklad, Madison, WI) containing 833mg Fe/kg diet to create a 5mg daily iron intake, and one identical rat was fed standard rodent chow (Harlan Teklad, Madison, WI) for control. Rats were housed individually with controlled humidity, temperature, lighting and ventilation and remained on the ferrocene diet for nine weeks in accordance with a university-approved animal protocol.

The IDEAL water-fat decomposition method provides robust separation of fat and water[3], and has been modified to measure T_2*, in addition to water and fat[4]. Using an online reconstruction program, fat, water, field map, in-phase and out-of-phase images are constructed. In T_2*-IDEAL, based on the above multi-echo IDEAL, decomposed water and fat images are corrected from the T_2* decay and an additional R_2* map is generated from the online reconstruction[4].

Prior to imaging, rats were sacrificed and perfused with phosphate buffered saline to eliminate motion and susceptibility artifacts from deoxygenated blood. All imaging was performed on a 3.0T Signa GE clinical scanner (V12.0, Waukesha, WI) with a home-built quadrature bird cage coil using a multi-echo sequence with a flip angle of 5° to minimize the effects of T_1 bias. Imaging parameters included: TE = 2.3 ms, echo train length = 12, echo spacing = 1.9 ms, TR = 30 ms, BW = ± 100 kHz, FOV =12 cm, slice = 1.5 cm, and 256 x 256 matrix.

After imaging, the rat livers were excised and sections were stained with Prussian Blue to visualize iron deposits. Additionally, iron content was quantified in samples of homogenized liver using an iron assay kit (BioAssay Systems, Hayward, CA); half-lobe pieces were analyzed and the concentration of iron per sample was obtained. Samples submitted for Histology were taken from the lobe subjected to iron quantification.

Results: Figures 1A and 1B display water images for an experimental and control rat, respectively, whereas figures 1C and 1D show corresponding R_2* maps. The histology slides from these livers are shown in Figures 2A and 2B, where blue, or positive Prussian Blue staining, indicates the presence of iron. For the three ferrocene-fed rats, iron concentrations were found to be 4.76 ± 0.13, 4.96 ± 0.07 and 4.50 ± 0.12 µg Fe/g liver, whereas the control rat had 1.81± 0.09 µg Fe/g liver. Figure 3 shows the relationship between iron concentration in the liver and measured T_2* values for the corresponding regions.

Discussion: For rats on ferrocene-supplemented diets, increased R_2* values and iron concentrations agree with histology findings and signify hepatic iron overload as compared to control rats. T_2*-IDEAL provides water, fat, and R_2* images, which are an indirect measure of iron concentration. Our preliminary results in a rat model of iron overload indicate that T_2*-IDEAL has excellent potential to measure iron overload in patients with chronic liver disease.

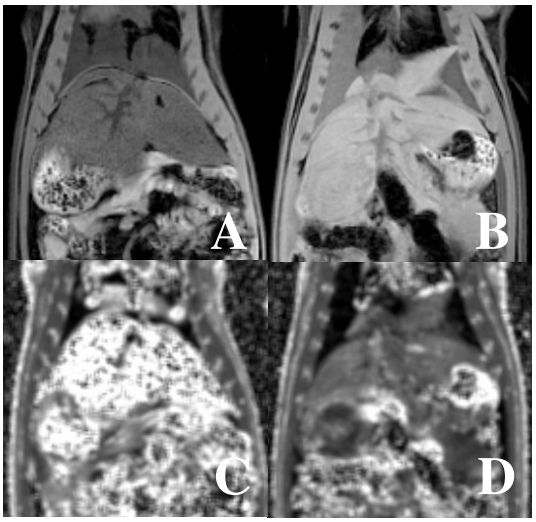

Figure 1: Water images of ferrocene-supplemented (A) and control (B) rats and R_2* maps of ferrocene-supplemented (C) and control (D) rats. T_2* (=1/R_2*)values for the sections analyzed for iron content were 14.5ms and 29.4ms for the experimental and control rats, respectively.

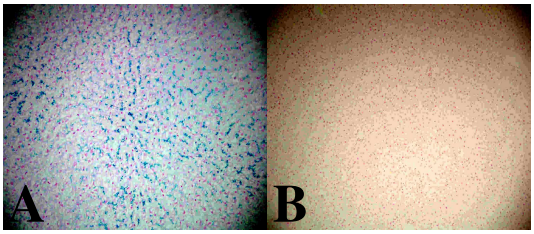

Figure 2: Prussian Blue stain of iron overloaded (x100) (A) and control rat (x100) (B), where blue indicates the presence of iron.

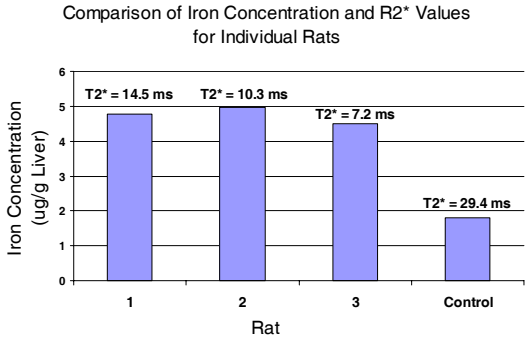

Figure 3: Comparison of iron concentration (µg Fe/g liver) and R_2* values for the ferrocene-supplemented and control rats.

References:

[1] George, et al. Gastroenterology 1998; 114(2):311-318.
[2] Longueville, et al. Biochemical Pharmacology 1986; 35(21):3669-3678.
[3] Reeder, et al. Magn Reson Med 2001; 51(1):35-45.
[4] Huanzhou Yu, et al. ISMRM 2006.