Characterizing MRI Parameters of Iron Loaded Rat Liver

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Introduction

Iron is a physiologically vital substance, but it also can be toxic and has been associated with numerous pathological states in various tissues. The excess iron may be deposited in liver, heart, and brain. The liver iron concentration is an important index of total body iron load. Accurate non-invasive assessment of the body iron is essential for iron-removal treatment. The established, clinical used device for non-invasive measurement of liver iron stores is currently biomagnetic susceptometry using Superconducting Quantum Interference Device (SQUID) magnetometers. The cost, complexity, and technical demands limit access to this technique [1]. Many previous studies have indicated that NMR parameters (T2, T2*) change with iron concentration in liver tissue, but no clear protocol has been established to measure iron content in tissue accurately [2]. The exact dependence of NMR parameters on iron concentration and the forms of the stored iron is unclear. This problem can be addressed only by combining studies of iron metabolism with studies of fundamental nuclear relaxation mechanisms and the development of advanced MRI measurement protocols. We combine the study of an animal model of iron overload, NMR techniques, and SQUID susceptibility imaging.

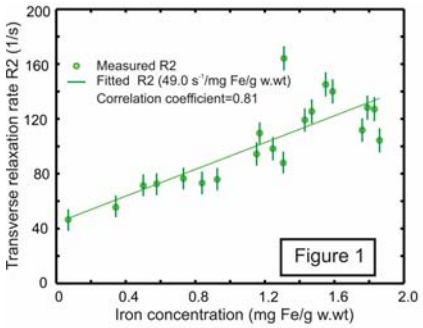
Methods

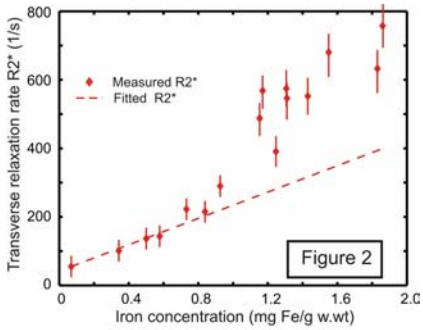
Iron overload was induced in rats by high iron-content diet (0.1% TMH- Ferrocene). Total 44 adult male rats were used: 36 rats with iron diet, and 8 rats with normal diet. The rats were scanned in vivo, started from one week after the iron feeding, then every week for 26 weeks. After MRI scan, the rat was sacrificed and perfused and fixed with 10% formalin. The lager lobe was scanned by SQUID magnetometer, and other two lobes were sent for iron content analysis and histological analysis.

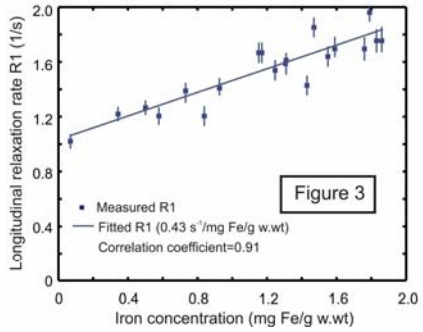
The Varian 4.7 T magnet, with a quadrature coil, was used for MRI scan. With respiratory gating, a single slice, multi-spin -echo sequence (TR=1200ms, TE=6.5ms, 16 echoes) was used for T2 weighted images, and a single slice, multi-echo gradient echo sequence (TR=1000ms, TE = 1.5ms, 16 echoes) was used for T2* weighted images. Seven T1 weighted images were obtained using an inversion-recovery prepared snapshot sequence (TR = 5s, TI = 0.025 - 4s, TE=0.9ms). Three areas, corresponding to three lobes and excluding vascular structures, were selected. The intensity of each area was the average value over the pixels within the area which includes at least 9 pixels. T1, T2 and T2* were fitted by mono-exponential decay for each area. There is slightly variation of 1-5% between the three areas for T1 and T2, however, the larger variations of 10% - 15% for T2*. Then the averaged value over the three areas was used for the correlation of the iron content.

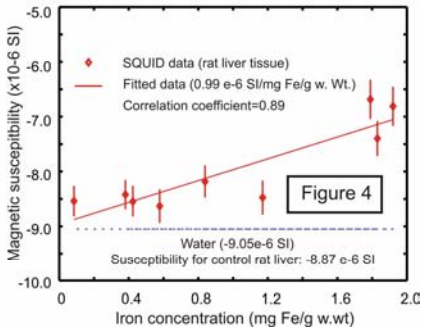
The magnetic susceptibility of liver was measured using a SQUID susceptometry, including a gradiometer with 3 mm pick-up coil and a 0.5 gauss room temperature magnet. The susceptibility was calibrated by water.

Results and Discussion









The liver iron concentration was from 0.077(control) to 1.8 mg Fe/ g wet weight. The relaxation time T1, T2 and T2* were obtained by fitting the intensity using mono-exponential function (Matlab LSQCURVEFIT). Figure 1 and 2 show the transverse relaxation rates R2 and R2*. Figure 1 shows R2 increases linearly with iron concentration. The R2 values are comparable with the results published by A. Fenzi et al. [3]. The slope of the relaxation rate is 49.0 s^{-1}/mg Fe/g wet weight, and the correlation coefficient is 0.81. Figure 2 shows that R2* is more sensitive to the iron content than R2, however, it increase linearly with iron concentration only if the iron concentration is below 0.8 mg Fe/g wet weight. J.C. Wood et al have reported that the correlation between R2 and R2* for human liver, using 1.5T scanner, is good only when R2* is less than 1000s^{-1} [4]. Figure 3 is the longitudinal relaxation rate R1, which is also linear with the iron concentration. Though R1 is less sensitive to iron concentration than R2, the correlation coefficient of 0.91 is higher than R2 (0.81). Figure 4 shows the magnetic susceptibility measured by SQUID for the liver tissue in vitro. The susceptibility of a control rat liver is -8.87e-6 (SI), which is very close to the susceptibility of water -9.05e-6 (SI). The susceptibility of the rat liver with 2mg Fe/g w.wt. is about -7.0 e-6 (SI), which is still highly diamagnetic. The difference between the liver and water is due to the iron content in the liver. It is about 0.99 e-6 (SI) for 1mg Fe/g liver, which is lower than the published value of human liver, 1.6e-6 (SI) [5]. The susceptibility is linear with the iron content. The correlation coefficient is 0.89. It should be noticed that the susceptibility was measured at B=0.5 gauss, which is weak compare to 4.7T. Further investigation for the magnetic susceptibility at higher magnetic fields is suggested.

Acknowledgement

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