

Transverse Relaxation Rates (R_2^* , R_2 , and R_2') of Iron-Overloaded Livers of Thalassemic Mice at 1.5T and 3T

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Introduction

Liver biopsy for the determination of iron concentration is typically required in the clinical management of patients with iron-overloading diseases such as thalassemia. In recent years, MRI has been explored as an alternative tool to non-invasively estimate iron concentration. Although relaxation rates R_2 (1-3) and R_2^* (4) of iron-overloaded liver both have separately been shown to increase with higher iron levels, these parameters, as well as the reversible relaxation component R_2' , and their dependence on the field strength, have not been thoroughly investigated. In this work, the relaxation parameters R_2^* , R_2 , and R_2' are analyzed using the GESFIDE (gradient-echo sampling of free induction decay and echo) technique (5) in a mouse model of thalassemia at 1.5 and 3T field strengths.

Methods

Mouse Model: Heterozygous β -thalassemic mice were created by mating transgenic sickle mice with wild type (WT) mice (homozygotes die in utero). In addition to WT and thalassemic (TH) mice, a sub-group of TH mice were periodically transfused with blood from other mice (approx. 0.5 cc, twice a week) for durations ranging from 8 to 16 weeks to achieve varying degrees of iron overload. A total of 16 mice were used in this study (5 WT, 5 TH, 6 TH with transfusion).

Scan Protocol: Liver samples were harvested and individually inserted into saline-filled plastic vials. The vials were mounted in a larger Plexiglas tube, in which heated water was circulated and maintained at 37°C. The setup was oriented parallel to the magnetic field to minimize field perturbations. A single axial slice was imaged with GESFIDE (5 echoes per echo train, 6.6 ms inter-echo spacing, TR = 500 ms, 3 mm slice thickness, 10 cm FOV, matrix size = 256x256, receiver bandwidth = ± 60 kHz). Up to 4 averages were used to ensure adequate SNR. R_2^* ($= R_2 + R_2'$) and R_2' ($= R_2 - R_2^*$) maps were first obtained on a pixel-by-pixel basis by fitting the exponential decays of the trains of gradient echoes pre- and post-180° refocusing pulse, respectively. R_2 and R_2' were then computed by subsequent linear combination. The measurements were performed on Siemens 1.5T Sonata and 3T Trio MR scanners.

Results and Discussion

Figure 1 shows that R_2^* , R_2 and R_2' are all well-correlated with iron concentration at both field strengths ($r = 0.72-0.79$). The slopes (or relaxivities) of these parameters are 16.7, 9.7, and 7.0 Hz/(mg/g), respectively, at 1.5T, while they approximately double at 3T (33.6, 17.5, 16.1). Such dependence on field is in agreement with previous observations in the liver (6). The doubling of the relaxivities indicates that the potential gains in SNR at 3T may be negated by the higher rate of signal decay, particularly in highly iron-overloaded subjects, in whom R_2^* could exceed 1000 s⁻¹ at 1.5T.

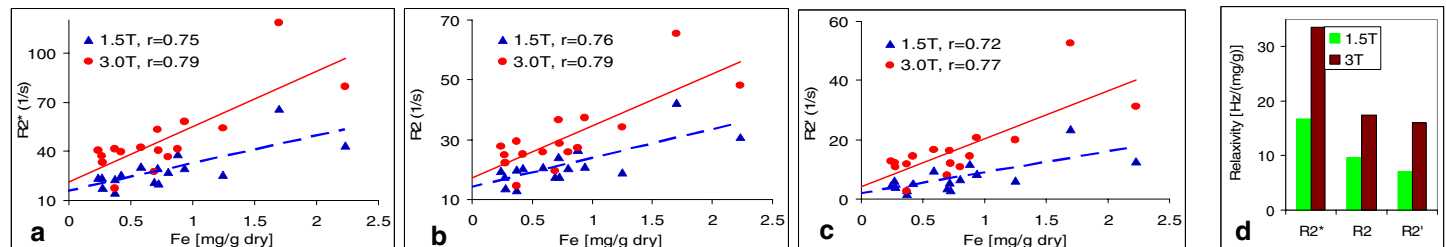


Fig. 1 (a-c) Relaxation rates (R_2^* , R_2 , R_2') vs. iron concentration at 1.5 and 3T. (d) Relaxivities at 1.5 and 3T.

Fig. 2 shows the correlations among relaxation parameter pairs. A nearly perfect correlation between R_2^* and R_2 along with results from Fig. 1 indicates that parameters obtained using either spin echo (R_2) or gradient echo (R_2^*) sequences would have yielded similar relationships with iron concentration. In addition, the high degree of correlation between R_2 and R_2' , as well as the linear increase in the relaxivities with field, indicates that while exchange of spins between the ferritin surface and free water protons occurs (affecting R_2) (6), spin refocusing under the static dephasing regime also takes place (affecting R_2'). Moreover, since R_2 and R_2^* may be preferentially sensitive to different forms of iron storage compounds (ferritin vs. hemosiderin) (7), the linearity of the fits may indicate that the relative fraction of these two compounds remains constant within the range of iron levels that were studied. Finally, results of Figs. 1 and 2 indicate that the acquisition of all three rates may not improve the ability to estimate iron levels compared to just a single parameter, and that a gradient echo sequence alone (presumably the simplest) is sufficient for the purpose.

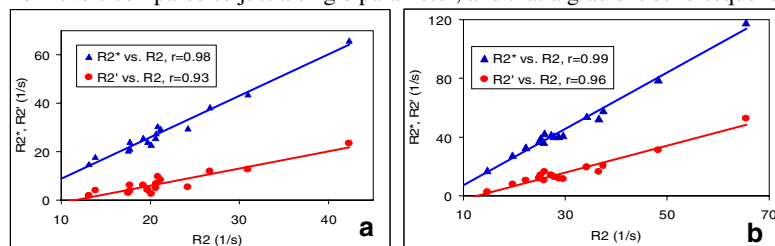


Fig. 2 R_2^* and R_2' vs. R_2 at 1.5T (a) and 3T (b).

References: (1) Brasch, RC, et al, Radiology 150:767-771 (1984). (2) Stark, DD, et al, Radiology 154:137-142 (1985). (3) Thomsen, C, Acta Radiol Suppl 401:1-34 (1996). (4) Gandon, V, Radiology 193:533-538 (1994). (5) Ma, J, et al, J Magn Reson B111:61-69 (1996). (6) Gossuin Y, et al, NMR Biomed, 17:427-432 (2004). (7) Haque, TL, et al, Eur. J. Radiol 48:230-236 (2003).

Conclusion

The relaxation parameters R_2^* , R_2 and R_2' were all well correlated with murine liver iron content at both 1.5 and 3T. The relaxivities for all three rates are approximately doubled at the higher field strength. Within the range of iron concentrations investigated, there is a high degree of linear correlation among the three parameters. The GESFIDE sequence was capable of measuring these parameters efficiently in a single scan.

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