Liver T2* Measurement of Iron Overload: an Investigation of Optimal Methods of Quantification

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INTRODUCTION

Iron overload is common in thalassaemia major and sickle cell disease (due to frequent blood transfusions) and in hereditary hemochromatosis. The traditional method to determine total body iron is liver biopsy, as this is the site where iron is first stored. In recent years, non-invasive iron quantification based on MRI [1,2] has been developed, and a FDA-approved T2-based technique (FerriScan™) is currently available as a surrogate to liver biopsy. Potentially more attractive, however, are very rapid T2*-based acquisitions adopted in cardiac overload studies, but these techniques are not approved for the liver, and the reliability associated with different analysis models in the presence of noise is not well understood. In this study, we investigate the accuracy of three common analysis models for T2* quantification of iron levels typically encountered in this patient group.

METHODS

T2* signal decay with echo time (TE) is most simply modeled as a mono-exponential function ($S=S_o e^{-TE \bullet R2^*}$, $R2^*=1/T2^*$). To correct for noisy signal at late echoes, both a constant offset ($S=S_o e^{-TE \bullet R2^*}+C$) and a truncated model (fitting data with $S>2\sigma_{noise}$ to a mono-exponential) have been used. Simulated data were generated to mimic decay in liver on a multi-echo gradient sequence used clinically (TR=500 ms, FA=60°, T1=586 ms). Eleven equally spaced echoes up to 30 ms were sampled, and two different starting echo times, 1.0 ms or 2.39 ms, were compared. Four noise levels ($SNR=M_o/\sigma_{noise}$) were assessed, where M_o is the fully relaxed magnetization. For each SNR and R2* level, 10,000 curves were generated, each fit to all three models, and the median R2* computed. Data fitting was performed using non-linear least-squares fit based on Levenberg-Marquardt (Matlab v.7.0).

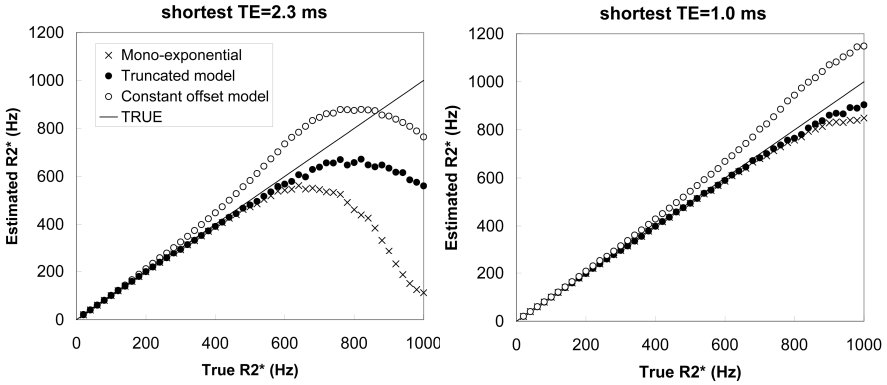

Fig. 1. Accuracy of R2* measurement using three different analysis models for two different starting echo times. The R2* range corresponds to iron levels up to 26 mg/g. SNR=100.

RESULTS

Fig.1 compares the performance of all three analysis models using two different starting TEs. A short starting TE is required to measure high iron concentrations, and 1.0 ms is shown to reliably measure iron levels up to 26 mg/g (corresponding to R2*=1000 Hz [2]). Of the three models, the monoexponential model is the most sensitive to noise and is limited to measurement of low iron levels. Better performance is achieved with the other two models: 1) the constant offset model is robust to noise over a greater range of R2* but generally overestimates the true iron content, 2) the truncated model is more sensitive to noise at high iron levels but generally provides the most accurate quantification.

Fig.2 shows the influence of SNR on accuracy, using TE_{min}=1.0 ms and three representative R2* values for low, moderate, and high iron content. The truncated model provides the most accurate measurement for low to moderate R2* species, even at the lowest SNR. The constant offset model offers an advantage only for high R2* species at low SNR, where larger errors are seen with other models.

Table 1 compares in three pediatric patients T2* measurements of iron content versus a reference value obtained using Ferriscan. As predicted from simulations, the constant offset model tends to overestimate. The truncated model, even with a modest TE_{min}=2.3 ms, provides the best accuracy for moderate iron levels and can be expected to cover a higher range of iron levels with optimal echo time selection.

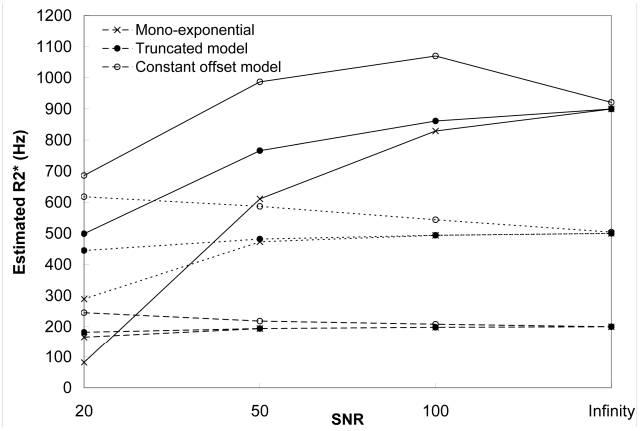

Fig. 2. The influence of SNR on the quantification of low (R2*= 200 Hz), moderate (500 Hz), and high (900 Hz) iron levels.

Table 1. Iron concentrations [Fe] by T2* MRI (SNR>100)

Patient	Reference [Fe] *	T2* [Fe] Measurement	
		Truncated model	Constant offset model
1	2.5	2.6	2.8
2	11.4	11.3	13.0
3	21.4	14.4	25.9

* Reference [Fe] values (mg/g) obtained from Ferriscan™.

CONCLUSIONS

This study addresses our limited knowledge on the accuracy of T2* estimation of liver iron obtained from different analysis models under varying levels of noise. Our results confirm other reports that the widely used constant offset model generally overestimates iron content [3,4], but we also show that it is the most robust to noise over a greater dynamic range. An important finding is that the most accurate quantification is achieved with the truncated model, which has been limited to cardiac iron assessment [4] but is herein shown to be suited for liver iron measurements when high SNRs and short TEs are achieved. These results demonstrate that rapid T2*-based liver iron quantification is possible, and they provide guidelines on minimum SNR requirements and the expected reliability from various models over different ranges of iron concentrations.

REFERENCES: [1] St. Pierre et al. Blood 2005; 105:855. [2] Wood JC et al. Blood 2005; 106:1460. [3] Positano V et al. Conf Proc IEEE Eng Med Biol Soc 2007; 2007:2895. [4] He T et al. MRM 2008; 60:350.