# Accuracy and reproducibility of T2* measurement of liver iron overload in pediatric patients

Hai-Ling Margaret Cheng[1,2], Stephanie Holowka[3], Rahim Moineddin[4], and Isaac Odame[5]

[1]*Medical Biophysics, University of Toronto, Toronto, ON, Canada,* [2]*Physiology & Experimental Medicine, The Hospital for Sick Children, Toronto, ON, Canada,* [3]*Diagnostic Imaging, The Hospital for Sick Children,* [4]*Family and Community Medicine, University of Toronto,* [5]*Haematology/Oncology, The Hospital for Sick Children*

## INTRODUCTION

Iron overload is a common occurrence in children who require frequent blood transfusions to treat anemia (e.g. thalassemia, sickle cell disease) or as a result of excess iron absorption (e.g. hereditary hemochromatosis). Assessment of iron levels is conventionally performed with biopsy of the liver. The liver provides a good indication of total body iron stores, and the assessment is done to determine risks for liver damage and cardiac failure. Non-invasive measurement of absolute liver iron content (LIC) can be made with T2 [1] and T2* [2] relaxation times, as these have been calibrated against LIC. In fact, FerriScan®, a T2-based commercially available regulatory approved service, has replaced biopsy procedures in many centres. Unlike T2-based measurements, validation of the T2* technique in a clinical setting has been scarce. In this study, we evaluate the accuracy and reproducibility of T2*-based LIC measurements against reference measurements (i.e. FerriScan) in children with iron overload. Our goal is to offer a better imaging platform to children, one that requires significantly less acquisition time without sacrificing accuracy.

## METHODS

Ninety-nine ($N = 99$) pediatric patients with iron overload were enrolled in this IRB-approved prospective study. Axial T2 and T2* data were acquired on a 1.5T Siemens (Avanto). The T2 protocol used a multi-slice spin-echo sequence (TR=2500 ms, TE=6,9,12,15,18 ms); liver iron concentrations calculated from the T2 data by FerriScan were used as a reference standard. The T2* protocol employed a multi-echo gradient echo sequence (TR=500 ms, FA=60°, eleven echoes starting at TE=2.39 ms up to 30 ms). The T2* data were then analyzed on a pixel-wise basis using in-house software developed in Matlab (v.7.0). Data were fitted to a constant offset model ($S=S_0e^{-TE\bullet R2^*}+C$, $R2^*=1/T2^*$). All fitting employed Levenberg-Marquardt non-linear least-squares. ROIs were drawn on R2* maps to encompass the entire liver and excluding blood vessels and ducts. The iron concentration for each patient was determined from the median R2* through the liver calibration curve given in Ref [2]. Two independent observers performed the analysis and prescribed ROIs with no prior knowledge of FerriScan's results. Their results were compared to determine inter-observer reproducibility. Analysis was also repeated in each patient on a different imaging slice to determine intra-observer reproducibility.

## RESULTS

Fig.1 illustrates a R2* map in the liver of a Thalassemic pediatric patient and a manually determined ROI of the liver. Fig.2 compares in all patients the LIC measured using the T2* method versus standard measurements obtained on FerriScan. Excellent agreement was achieved, with a Pearson correlation of $r$=0.94 ($P$<0.0001) and an intra-class correlation of ICC=0.92. The inter- and intra-observer agreement was also very high (Table 1).

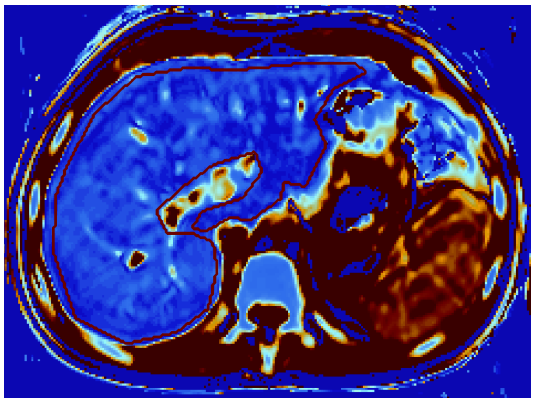

**Fig. 1** R2* map in a Thalassemic pediatric patient. Red outline is the manually determined liver ROI.

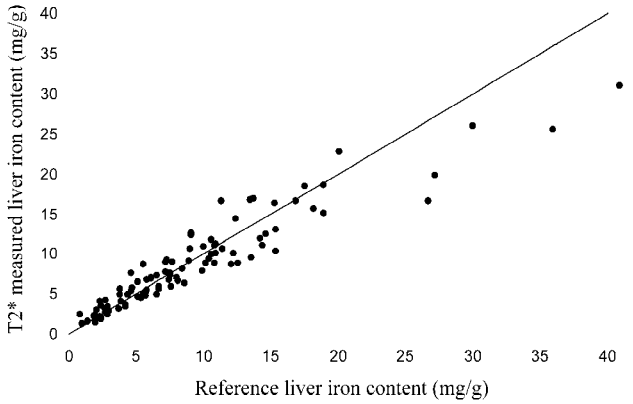


**Fig. 2** Comparison of T2* measured absolute liver iron content versus reference standard (FerriScan) in 99 patients. Line of identity is shown.

**Table 1** Statistical analysis on T2* measured absolute liver iron content

| | T2* versus reference comparison | Inter-observer comparison | Intra-observer comparison |
|---|---|---|---|
| $r$ ($P$-value) | 0.94 ($P$ <0.0001) | 0.99 ($P$ <0.0001) | 1.0 ($P$ <0.0001) |
| ICC | 0.92 | 0.99 | 1.0 |

## CONCLUSIONS

Our ongoing pediatric study supports the use of T2*-based quantification of liver iron content, which offers distinct advantages to young children because of a rapid acquisition protocol and is shown to be as reliable as FerriScan, the current non-invasive standard for liver iron measurement. Our results demonstrate that excellent agreement is achieved, particularly in the lower to mid-range where accuracy is extremely important in determining whether or not a child has abnormal liver iron content and in guiding decision-making on intensity of iron-chelator therapy. Future work will assess the value of the T2* approach for monitoring chelation therapy.

**REFERENCES:** [1] St. Pierre TG et al. Blood 2005; 105:855. [2] Wood JC et al. Blood 2005; 106:1460.