

## Performance and limitations of R2\* relaxometry liver iron measurements

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### Introduction

Accurate measurement of liver iron concentration (LIC) is critical in the management of iron overload states, in the evaluation of iron reduction therapies, and in the understanding of iron loading physiology. R2 and R2\* relaxometry are currently the predominant methods used. R2 relaxometry at 1.5Tesla is the basis of a commercial method (FerriScan<sup>1</sup>) recognized as equivalent to liver biopsy. R2\* relaxometry can be implemented on most scanners with multi-echo GRE and T2\* mapping options. Two groups have published R2\* or T2\* to LIC calibration equations but there has been little independent investigation of their performance against gold standards. In a group of clinical patients, we compared the commercial liver T2\* mapping tool and the published calibration curves using LIC results from FerriScan as the reference method.

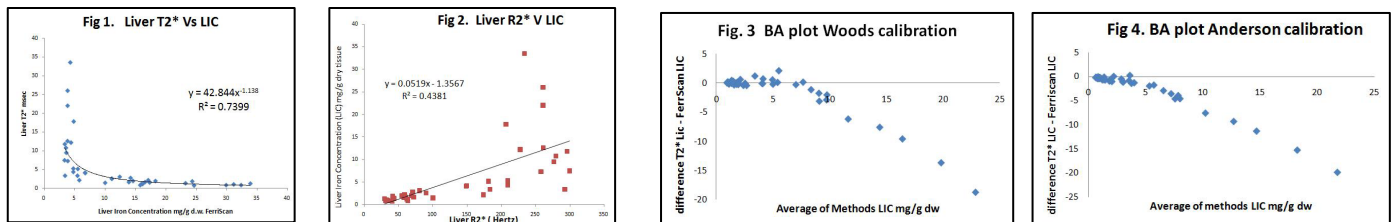
### Method

43 patients aged 7 – 70 years (mean 41.5), 19 males were included. Presenting for MR liver iron assessment with thalassaemia (23), genetic haemochromatosis(13), or other haemoglobinopathies (7). T2\* relaxometry was performed in addition to the clinical protocol (FerriScan). Scans were performed on a Siemens AVANTO SQ 1.5T (VB15). FerriScan examinations followed the dictated protocol (TR 2500 ms; TE 6,9, 2, 15,18 ms) with analysis and calibration by Resonance Health Analysis Services. R2\* relaxometry used a single breath-hold GRE (TR200ms, TE 0.99 to 16.5 ms, echo-spacing 1.41 ms, voxel size 3.1 x 3.1 x 10 mm) and MAPIT in-line T2\* maps. Five GRE scans were performed sequentially on each subject. To obtain T2\* only for the liver parenchyma, mean T2\* was calculated from non-zero value pixels within a ROI outlining the liver, excluding the hepatic vessels. The five mean T2\* values were averaged to give the Liver T2\* value and R2\* value (1/T2\*). The estimated LIC was derived using two calibration equations; the Anderson equation<sup>2</sup> ( $\log_e \text{LIC} = 2.65 - 1.07 \log_e T2^*$ ) and the Wood equation<sup>3</sup> ( $\text{LIC} = .0254R2^* + 0.202$ ). We analysed linear correlation between R2\* and LIC, and for the limits of agreement<sup>4</sup> (LOA) of LIC values of each equation and the reference method.

### Results

Two patients were excluded because respiratory artefacts rendered the T2\* maps unreadable. (LIC=1.4 & 4.6) LIC values ranged from 0.8 to 43 mg/g (mean 6.8 sd 9.2), in a skewed distribution (23/41 under 2 mg/g). R2\* values were 30 – 299 Hertz (mean 141 Hz., sd 94Hz.). Plotting T2\* against LIC appeared to show the theoretical inverse relationship (fig1) however the linear relationship between R2\* and LIC is poor ( $R^2=0.28$ ) and breaks down above a threshold LIC. (Fig 2). Iterative analysis suggest a threshold of approximately 7 mg/g d.w..

The LOA plots (fig 3,4) show small differences for low LIC, increasingly linearly after a threshold, suggesting a breakdown of the calibration above an LIC threshold. The threshold is estimated as 7.5 mg/g d.w. (Woods equation), and 3.5 mg/g (Anderson equation).



### Discussion

The R2\* relaxometry sequence and published calibrations have limited value in estimating clinical LIC. The linear Woods equation gives better estimates than the logarithmic Anderson equation, but both display substantial and increasing underestimation above a threshold LIC value. This reflects the observed breakdown in the linear relationship between R2\* and LIC above a similar threshold, demonstrating a specific sensitivity threshold for the R2\* relaxometry sequence used. The “saturation threshold” has been described previously<sup>5</sup> using gradient echo sequences with intensity ratio analysis, but has not been previously described in T2\* relaxometry. The level of the saturation limit indicates that present methods are too sensitive to T2\* across the range of LIC encountered in clinical practice. Further work is required to establish more appropriate parameters for liver R2\* relaxometry through decreasing sensitivity to T2\*.

<sup>1</sup> FerriScan (R) Resonance Health Analysis Services [www.ferriscan.com](http://www.ferriscan.com)

<sup>2</sup> Anderson LJ et al EIJ 2001 22;2171-79

<sup>3</sup> Wood JC et al BLOOD 2005 106;1460-65

<sup>4</sup> Bland JM, Altman DG Lancet 1986 i:307-310

<sup>5</sup> Gandon Y et al 2004 357-61