Performance and limitations of R2* relaxometry liver iron measurements

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Accurate measurement of liver iron concentration (LIC) is used in the management of iron overload, evaluation of iron reduction therapies, and studying iron loading physiology. MR methods for non invasive assessment of LIC have been explored for several decades with R2 and R2* relaxometry generally used at present. FerriScan[1] is a commercial R2 relaxometry method employing external QA and validation that is equivalent to liver biopsy for LIC measurement. R2* relaxometry has been proposed as a sensitive method to quantify liver iron. Two primary research groups have published LIC calibration equations based on T2* or R2* (1/T2*), but there has been little independent validation of performance in a clinical setting. In this study, we investigated the performance of a commercial liver T2* mapping tool[2] combined with published calibration curves. FerriScan LIC is used as the reference method.

Method

43 patients presenting for MR liver iron assessment were studied. Age 7 – 70 years (mean 41.5), 19 males. Presenting conditions were beta-thalassaemia (23), genetic haemochromatosis(13), other haemoglobinopathies (7). Scans were performed on a Siemens AVANTO SQ 1.5T (VB15). FerriScan examinations followed the dictated protocol with analysis by the reference lab. T2* relaxometry used a single slice, single breath-hold, GRE acquisition with MAPIT in-line T2* mapping. (TR 200ms, Flip 20°, TE 0.99 to 16.5 ms, echo-spacing 1.41 ms, voxel size 3.1 x 3.1 x 10mm)

Five GRE scans were performed sequentially on each subject. A ROI of the liver with numeric exclusion of zero value pixels and excluding hepatic vessels, yielded a mean liver T2* value for each map. The 5 means were averaged to give the analysed Liver T2* and R2* values. An estimated LIC was calculated using two published calibration equations; the Anderson equation[3] (loge LIC = 2.65 – 1.07 loge T2*), and the Wood equation[4] (LIC = 0.0254 x R2*+ 0.202). We analysed correlation between T2* and R2* with LIC, and the Bland-Altman plots between the estimated LIC values and the reference method.

Results

Two patients were excluded as respiratory artefacts made the T2* maps unreadable (LIC=1.4 and 4.6, both GH). Reference LIC values ranged from 0.8 to 41.6mg/g (mean 6.8 SD 9.2), in a negatively skewed distribution (23/41 under 2mg/g). R2* values were 30 – 299Hertz (mean 141Hz., SD 94Hz., bimodal distribution).

T2* values display an inverse relationship with LIC but at higher levels of LIC the T2* plateaus. (Fig 1) The plot of R2* and LIC similarly displays a levelling of R2* values above a threshold (Fig 2). Linear correlation between LIC and R2* across the full range was therefore poor (R2=0.29). Iterative analysis suggested a threshold of correlation at an LIC of approximately 7mg/g d.w.

Figure 1

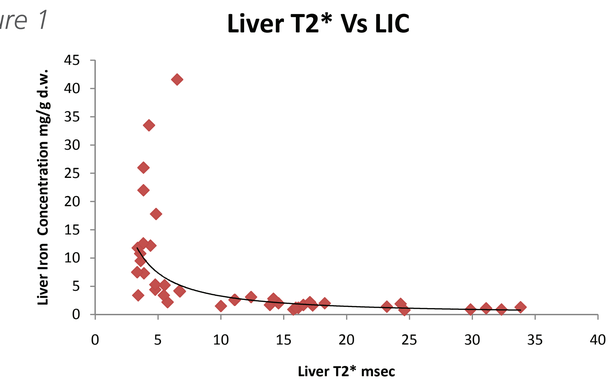


Figure 2

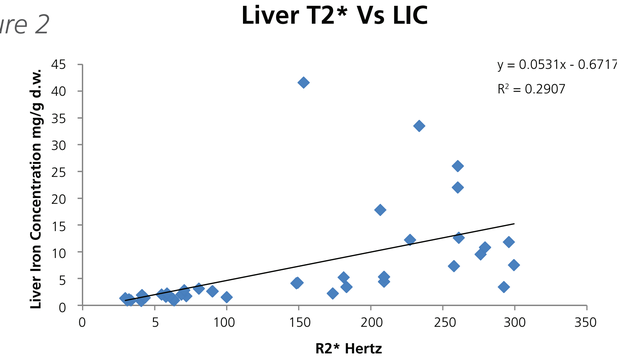


Figure 3

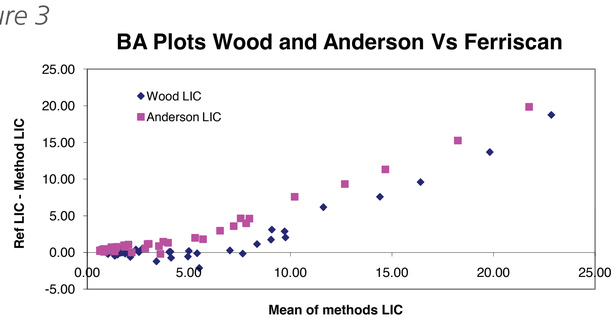


Figure 4

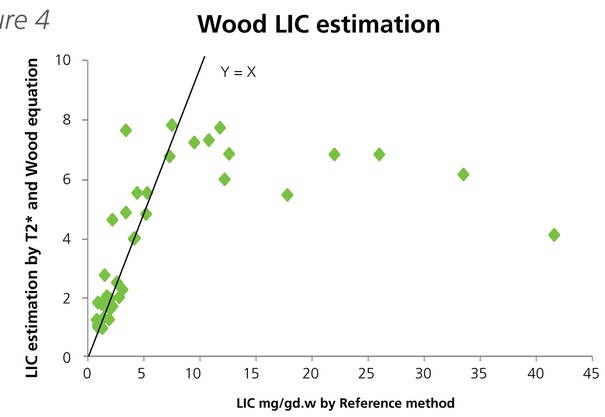
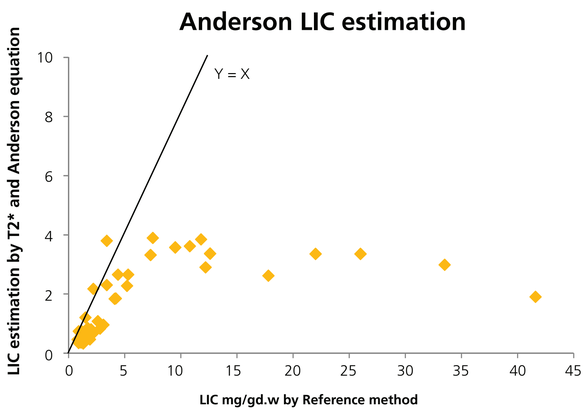


Figure 5



Discussion

The plateau of T2* and R2* values above a specific LIC has been identified in GRE intensity ratio studies[6, 7] and termed the 'saturation threshold'. It has not been observed in GRE relaxometry studies, and points to limitations of the acquisition method, or the regression analysis. The former is common to many published works on liver T2* relaxometry, while the latter is specific to the method described. Calibration equations cannot redress the relaxometry value threshold.

The Bland Altman difference plots for both calibration equations were unhelpful in identifying any limits of agreement (Fig 3). The linear increase in difference values (Y axis) clearly demonstrated the impact of the saturation threshold, but a usable threshold LIC is obscured by the averaging of reference and T2* methods displayed on the X axis.

Calibration performance was better appreciated by plotting the estimated LIC from each equation directly against the reference LIC value.

The Wood equation (Fig 4) gave close estimations of LIC up to 6mg/g d.w., then LIC values displayed a range of four to eight for actual LIC of 7.3-41.6mg/g d.w.. The Anderson equation (Fig 5) substantially underestimated LIC up to 6mg/g d.w., then LIC values displayed a range of 1.9 to 3.9 for actual LIC of 7.3 to 41.6 mg/g d.w..

Analysis of R2* values and reference LIC below 7mg/g d.w. gave a maximum correlation coefficient of 0.75. Application of the local LIC correlation (LIC = 0.0194 x R2* + 0.56) may deliver a useful limited clinical role for the method in detecting LIC below 7mg/g d.w.

Conclusion

Local validation of T2* relaxometry is essential before clinical use. The study method has a limited range of LIC accuracy stemming from an observed 'saturation threshold' in the R2* relaxometry method. A saturation threshold has not been identified in T2* relaxometry previously. The T2* relaxometry method is too sensitive to be useful for the full range of LIC encountered in clinical practice, but could deliver quantification of lower LIC values through local calibration. Further work is required to establish parameters with decreased sensitivity and increased dynamic range, and to examine the basis of the observed limitations.

References

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