R2* as a Surrogate Measure of Ferriscan® Iron Quantification in Thalassemia

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Background:
Accurate monitoring of liver iron concentration is an important clinical concern in patients with thalassemia [1]. Ferriscan® is an FDA approved, commercially available service for the non-invasive measurement of liver iron ([Fe]) using MRI [2]. R2* measurement sequences are readily available on most commercial scanners, and prior studies have demonstrated a correlation between R2* and liver biopsy based iron measurements [3, 4]. However, it is not easy to translate this result to different vendor platforms; this is part of the value of the Ferriscan® service. If R2* measurements were highly correlated with Ferriscan® iron measurements, it would be possible to reduce costs by developing a calibration curve between R2* measurements from a given scanner and Ferriscan® results. Once this is done, assuming FDA approval is not required for the given application, iron measurements can be derived without the need to send all cases for Ferriscan® analysis, thus reducing costs. The aim of this study is to determine the accuracy of using R2* values in measuring liver iron concentration by demonstrating a correlation between R2* relaxation rates and Ferriscan® determined liver iron concentration.

Materials and Methods:
Eighty-eight patients with thalassemia major were retrospectively evaluated in the study. Imaging was performed using a 1.5 Tesla system (Siemens Avanto, Erlangen, Germany) using the Body Coil. R2* data maps were generated from a multiecho gradient echo sequence (Figure 1) using a monoexponential decay model (TR=2500 ms and TE echo times of 6, 9, 12, 15, and 18 ms). A noise floor was determined by measuring the mean signal in air. Three elliptical regions of interest (2 in the right lobe and 1 in the left) were selected in each patient, encompassing as much liver parenchyma as possible while excluding vessels and biliary tree. The results were then averaged to obtain R2* data. R2 data was obtained as previously described according to the Ferriscan® protocol [2]. These results were analyzed by Ferriscan® and the resultant liver iron concentrations were correlated with the R2* data, with the assumption of a linear relationship between R2* and liver iron concentration. R2* values of paraspinal muscles were also determined for each patient to serve as internal controls.

Results:
The mean age was 35.7 ± 2.1 yrs and gender distribution was equal with 44 males and 44 females. Hepatic R2* values ranged from 57.5 to 1032.5 1/s with a mean of 334.7 ± 249.6 1/s. Ferriscan® determined liver iron concentrations ranged from 17 to 769 mmol/kg with a mean of 224.9 ± 207.3 mmol/kg. Mean R2* value for paraspinal muscle was 55.2 ± 12.9 1/s. There was a very strong linear correlation between our R2* values and Ferriscan® determined liver iron concentration with the estimated Spearman correlation being 0.976 (95% CI: 0.963, 0.984). The prediction equation from regression analysis was (liver iron concentration) = 0.80(R2*) – 44.1 (r=0.968, r^2=0.937, 95% CI: 0.911, 0.951, $p<0.0001$) (Figure 2). Simulated models based on our data predicted that a minimum of 21 measurements would be needed on other MRI scanners in order to calibrate R2* values with Ferriscan® results (r^2 confidence interval width=0.15, probability > 0.80).

Conclusion:
Determination of liver iron concentration by R2* methods may be helpful as a diagnostic surrogate for Ferriscan® iron measurements and could help save costs. In addition, Ferriscan® may be a valuable tool for interscanner and intervendor calibration of R2* measurement. Further prospective validating studies using our model are needed.

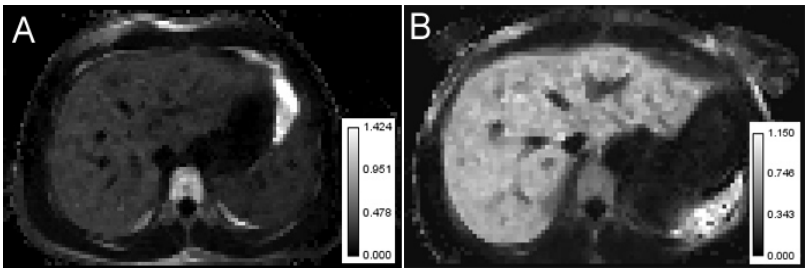

Fig 1. Representative R2* maps with mean R2* values of (a) 195.5 ± 8.1 1/s for a liver [Fe] of 94 mmol/kg (as determined by Ferriscan®) and (b) 780.5 ± 20.6 1/s for a liver [Fe] of 700 mmol/kg. R2* value scales are provided (units=1/s).

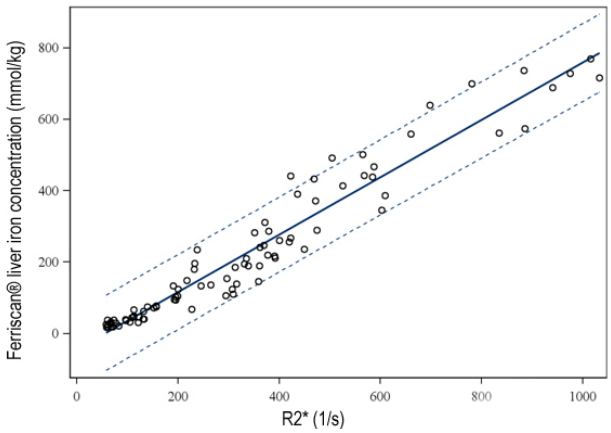

Fig 2. Scattergram showing linear correlation between liver R2* values and Ferriscan ® liver [Fe] (r=0.97, r^2 = 0.94, $p<0.0001$, n=88). Dashed lines represent 95% prediction limits.

References:
1) Angelucci, E., et al. N Engl J Med, 2000. 343(5): p. 327-31.
2) St Pierre, T.G., et al. Blood, 2005. 105(2): p. 855-61.
3) Christoforidis, A., et al. Eur J Haematol, 2009. 82(5): p. 388-92.
4) Wood, J.C., et al. Blood, 2005. 106(4): p. 1460-5.