The use of appropriate calibration curves can correct the systematic differences between softwares in hepatic R2* estimation

Antonella Meloni[1], Hugh Young Rienhoff[2], Amber Jones[2], Aessia Pepe[1], Massimo Lombardi[1], and John C Wood[3]

[1]*CMR Unit, Fondazione G. Monasterio CNR-Regione Toscana and Institute of Clinical Physiology, Pisa, Italy,* [2]*FerroKin BioSciences, Inc, San Carlo, California, United States,* [3]*Division of Cardiology, Children's Hospital Los Angeles, Los Angeles, California, United States*

Introduction. Liver R2* can be used as a surrogate for liver iron concentration (LIC) in iron overloaded subjects [1]. Two different signal decay models, truncated exponential [2,3] and exponential plus constant [1,4], have been validated for R2* estimation and calibrated to liver biopsy [5]. However, reported calibration curves for these two analysis methods differ by 15%. Our aim was to evaluate if the different fitting models yielded significantly different R2* estimates and if these differences disappeared once R2* estimates were converted to LIC units using method-appropriate calibration curves.

Materials and methods. A single-center (N=45) and a multi-center cohort (N=47) of patients were used. Gradient echo images optimized for R2* estimation were collected at each site according to local clinical practice. R2* values were generated using the CMRTools introduced by the Pennel's group (truncated exponential model; $R2^*_{Pennell}$) and custom Matlab code (exponential plus constant model; $R2^*_{Wood}$). R2* values were converted to dry weight liver iron concentration using calibrations published by Garbowski (equation 1) [5] and Wood (equation 2) [1], respectively:

$$LIC_{Pennel} = 0.03 * R2^*_{Pennell} + 0.7 \quad \textit{(equation 1)} \qquad LIC_{Wood} = 0.0254 * R2^*_{Wood} + 0.2 \quad \textit{(equation 2)}$$

Bland Altman analysis was performed with respect to both R2* and LIC estimates.

Results. For the single-center cohort the $R2^*_{Pennell}$ values ranged from 28.1 to 1219.5 s^{-1}, with a mean value of 367.5 ± 380.6 s^{-1}. The $R2^*_{Wood}$ values ranged from 29.7 to 1344.9 s^{-1}, with a mean value of 422.3 ± 445.6 s^{-1}. Figure 1a shows $R2^*_{Wood}$ values as a function of $R2^*_{Pennell}$ values. The line of best fit had a slope of 1.160 ± 0.024, significantly different from 1 (P<0.0001), an intercept of -3.992 ± 12.723 s_{-1}, and an R-squared value of 0.982. Figure 1b is the Bland-Altman plot. Results were unbiased for R2* < 300 s^{-1}, but R2* values obtained using exponential plus constant were systematically larger at higher R2* and the difference increased with increasing values. The mean difference was 54.7 ± 85.7 s-1 (95% confidence intervals of the difference: lower 28.9 and upper: 80.5 s-1), corresponding to a percentage difference in R2* values of 9.1 ± 11.8%. The bias was eliminated following conversion to LIC units. The $LIC_{Pennell}$ values ranged from 1.5 to 37.3 mg/g dry, with a mean value of 11.7 ± 11.4 mg/g dry. The LIC_{Wood} values ranged from 0.95 to 34.4 mg/g dry, with a mean value of 10.9 ± 11.3 mg/g dry. The line of best fit had a slope of 0.982 ± 0.020, not significant different from the unity (P=0.382), an intercept of -0.589 ± 0.334 mg/g dry (Figure 2a). Figure 4b is the Bland-Altman plot. LICPennell values were systematically higher for LIC's up to 10 mg/g and the two estimates were unbiased thereafter. The mean difference was -0.8 ± 1.5 mg/g dry (95% confidence intervals of the mean difference: lower -1.3 and upper: -0.3 mg/g dry). 95% confidence intervals of the individual LIC estimates were -3.8 – 2.2 mg/g dry weight

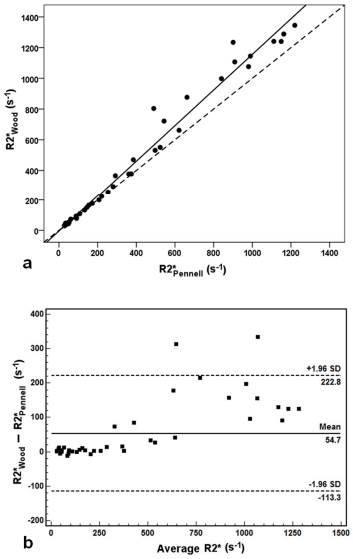

Figure 1.

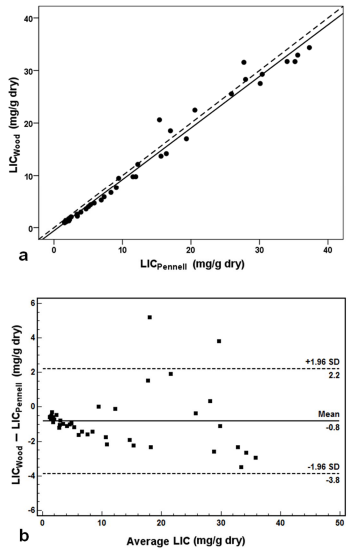

Figure 2

Similar differences in R2* estimation were found in the multi-center cohort and the conversion of R2* values to LIC units again removed the disparity.

Conclusion. R2* values vary with post-processing method but yield statistically identical LIC values when technique-appropriate calibration curves are used. LIC, rather than R2* values, should be reported and compared across studies.

References.

[1] Wood JC et al. Blood 2005;106(4):1460-1465. [2] Tanner MA et al. Haematologica 2006;91(10):1388-1391. [3] Kirk P et al. Circulation 2009;120(20):1961-1968. [4] Meloni A et al. J Magn Reson Imaging 2011;33(2):348-355. [5] Garbowski MJ et al. Blood 2009.