Myocardial T2* Relaxometry in Secondary Haemochromatosis: Impact of Technical Variations

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AIM

This study aimed to provide independent replication of the experiments suggesting T2* relaxometry as a method of assessing myocardial iron loading [1,2]. In addition, we wished to explore the impact of additional samples at shorter TE, and the noise level readings in the later echoes of tissue with very short T2*, as these could conceivably contribute to variability in measured T2*.

METHOD

30 independent measurements have been made on 25 adults aged 26 to 43 years (Mean 32.6 years, standard deviation 6.14 years). Their primary conditions were ß-thalassaemia major (20), ß-thalassaemia intermedia (3), HbE/ ß-thalassaemia (1), one case of Diamond Blackfan anaemia. All are managed with regular transfusions of packed red cells and conventional iron chelation. All subjects gave written informed consent, and the investigation was conducted with the approval of the Royal Adelaide Hospital ethics review committee.

MRI studies: Subjects were examined on a 1.5Tesla cardiac MR scanner Siemens Sonata with advanced IPA and CP body array coil. T2* relaxometry acquisition were based on a published scanner specific method[3] with the following variations. Two earlier TE samples were acquired (TE 3.6, 4.6 ms), and the inter-line TR of the ECG triggered segmented GRE sequences was fixed across all TE values. Eleven single breath-hold scans were obtained:. Interline TR 20.66 TE 3.6 – 9.6 in 1 ms steps, & 12 – 18 in 2 ms steps. Flip 35^o FOV 350 x 350 mm, Matrix 256 x 144, slice thickness 10mm slice.

Relaxometry analysis: Myocardial T2* estimates (apparent T2*) were obtained using a method described by the original paper [1]. Where details were not clear, we explored personal communication and commonly available tools. Using Image-J, an ROI was defined in the intraventricular septum.. The mean and standard deviation of pixels values was recorded. The location of the ROI was adjusted manually as needed to accommodate relative motion between the images. The same measurements were collected with the ROI outside the body in the phase encoding line to establish noise and phase ghost values for each echo. ROI values of noise were subtracted from the myocardial values and the resultant "signal minus noise" values were plotted against the echo time using Excel ™. A regression curve was obtained with the general formula $Y= a.e^{-bX}$ so that b=1/T2*. The regression coefficient (R^2) was recorded to assess the relative accuracy of the process. ROI data from each echo was tested to decide if it could be confidently distinguished from noise. We considered data to represent a "true" septal signal where (Septal Mean - Septal SD) – (Noise Mean + Noise SD) >0. Four methods of T2* analysis were used on each data set. Method 1 is the best approximation of the method used by the reference authors. Exponential curves were fitted to ROIs from nine TE values from 5.6 – 18 ms. (Reference Method). Method 2 fitted curves to the ROI values from all eleven measurements. Method 3 fitted curves to the subset of data from method 1 where the echoes tested as True. Method 4 fitted curves to the subset of data from method 2 where the echoes tested as True

Data analysis: Descriptive statistics were obtained for all methods. Methods 2 - 4 were compared to method 1 using the Bland – Altman limits of agreement approach[4]. The results where later echoes were affected by noise were examined separately.

RESULTS

T2* values for this population using reference method ranged between 4 and 34 ms, in a broad negatively skewed distribution. 12 readings were below 10mS, 20 were below the normal boundary suggested by Anderson et al, and 5 more below the 25 mS normal limit suggested by Wood et al, roughly approximating the results of the subjects reported by Westwood et al. Each of the 3 alternate methods showed minimal bias and acceptable limits of agreement in the context of the previously published 5 msec discrepancies in the setting of a threshold normal value. Only 8 cases recorded noise affected ROI, so the strongest agreement is seen between methods 1 and 3. The limits of agreement are largest with methods 2 and 4 suggesting that the extra earlier TE samples have an effect on the T2* reading. Mean R^2 of the exponential curve fitting remained similar for all methods but the minimum R^2 improved with the addition of earlier echoes (Method 2,4) from a reference level of 0.58 to 0.72 & 0.78 respectively, suggesting a slight advantage in Method 4. The worst curve fits were not associated with noise affected echoes, but appear to be due to non-specific signal fluctuations, possibly patient motion or artefacts from irregular heart rates.

msec	M2	M3	M4
Mean Diff	0.02	0.13	0.10
SD diff	1.75	1.01	2.09
95% LOA	-3.40	-1.84	-3.99
95% LOA	3.45	2.11	4.20

CONCLUSION

We have provided independent replication of the myocardial T2* estimation method and explored options in acquisition and curve fitting method. Refinements that were thought to deliver more robust results have not demonstrated a clear advantage, but don't display a resultsbias. The addition of earlier echoes has a greater effect on the limits of agreement than the application of a noise test, and while both modifications deliver limits of agreement acceptable in the context of the weak associations with cardiac dysfunction, the methods would not be interchangeable if testing for small effects such as monitoring therapy change or seeking a correlation with experimental myocardial iron loads.

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