Multislice multiecho T2* cardiovascular magnetic resonance can detect heterogeneous myocardial iron distribution in thalassemia patients

V. Positano[1], A. Pepe[1], A. Ramazzotti[1], D. De Marchi[1], B. Favilli[1], E. Cracolici[2], M. G. Brizi[3], M. F. Santarelli[1], M. Lombardi[1], and L. Landini[4]

[1]MRI Lab, Institute of Clinical Physiology, Pisa, Italy, [2]Department of Radiology, University of Palermo, Palermo, Italy, [3]Department of Radiology, A. Gemelli University Hospital, Roma, Italy, [4]University of Pisa, Pisa, Italy

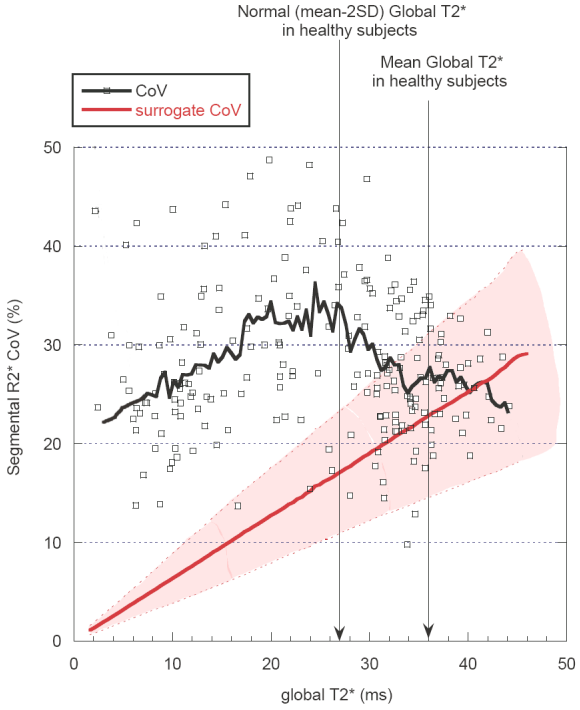
Introduction: Segmental distribution of T2* values can be assessed in heart iron overloaded patients by multislice, multiecho T2* cardiovascular MRI [1]. A significant heterogeneity in T2* segmental distribution was demonstrated in previous studies in thalassemia major (TM) patients [2,3]; however it is not clear yet if that may represent true heterogeneous iron density or it could be generated by geometric and susceptibility artefacts. In this study we investigate the relationship between T2* heterogeneity and iron overload progression in a large patient population in order to understand if susceptibility artefact may account for inhomogeneous T2* values segmental distribution.

Materials and methods: 230 TM patients consecutively affered to our laboratory were studied. Informed consent was obtained for all of them. MRI was performed using a 1.5 T MR scanner (GE Signa, CV/i). For the measurements of myocardial T2*, a fast gradient echo-multiecho sequence (FA=25°, matrix=256x192, FOV=35x35 cm, thickness=8.0 mm, NEX=0.75) was used with ECG triggering. Each slice was acquired at nine echo times (2.2-20.3 ms, with echo spacing of 2.26 ms) in a single end-expiratory breath-hold. Three short axis views (basal, medium, and apical) of the left ventricle were obtained and analyzed using a custom-written, previous validated software (HIPPO MIOT®) [1,2]. The myocardium was automatically segmented into a 16-segments standardized LV model and the T2* value on each segment was calculated as well as the global T2* value. The level of heterogeneity of the T2* segmental distribution on each patient was evaluated by computing the coefficient of variation (CoV) as the standard deviation of the absolute value of differences between the segmental T2* values and the global T2* value divided by their means, and expressed as the percentage.

A surrogate data set was obtained stating that the inhomogeneous segmental distribution of R2* would be generated only by susceptibility artefacts that are additive in the R2* domain. These artefacts were characterized by the analysis of the segmental R2* distribution in normal subjects in a previous study [2]. Under this hypothesis, the surrogate segmental R2* distribution for the patient *p* was modelled adding the artefacts effect to the global R2* value $R2_G^*(p)$:

$$R2^*(p,s) = R2^*_G(p) + \Delta_{R2^*}(s) + \sigma_{R2^*}(s)\, N_{0,1}(s),$$

where *s* was the segment location, $\Delta_{R2*}(s)$ and $\sigma_{R2*}(s)$ were the mean difference and the standard deviation of the difference between $R2^*$ values in the segment *s* and the global value measured on normal subjects, and $N_{0,1}(s)$ represented the Normal distribution. CoV of surrogate data was of course inversely proportional to $1/R2_G^*$ and directly proportional to $T2_G^*$.



Results: Results of the Montecarlo simulation performed on 10,000 surrogate data sets are shown in figure. Patients were sorted using the global T2* value. The CoV of all patients (square markers) and the mean CoV value averaged on a 20 patient window (black line) are plotted vs. the global T2*. For surrogate data, the mean CoV value (red line) is shown together with the region inside the mean±2SD limits. Mean and normal global T2* value assessed in a previous study [2] for healthy subjects was shown as well.

Discussion and Conclusions: T2* heterogeneity for patients without iron overload was compatible with the hypothesis that the heterogeneity was generated only by additive susceptibility artefacts. Below the normal limit of global T2* the heterogeneity abruptly increased of about 10%. Starting from this level, the heterogeneity decreased linearly returning to 25% in patients with high iron overload levels.

In conclusion, T2* segmental heterogeneity in TM patients cannot be explained by the effect of susceptibility artefacts, that are additive in the R2* domain and should vanish at high iron overload levels. A possible interpretation is that a true heterogeneity in iron overload distribution is present in TM patients. This heterogeneity seems more important in the early development of iron overload and reduces when the iron overload level increases.

References: [1] Pepe A et al. JMRI 2006;23(5):662-668. [2] Positano V et al. NMR Biomed 2007;20:578-590. [3] Ghugre NR et al. JMRI 2006;23(1):9-16.