Quantitative MRI in the Detection of Cardiac Iron in Patients with Thalassemia

J. Yamamura[1], R. Grosse[2], R. Engelhardt[2], J. Graessner[3], G. Kurio[4], R. Fischer[4], G. Janka[2], and G. Adam[1]

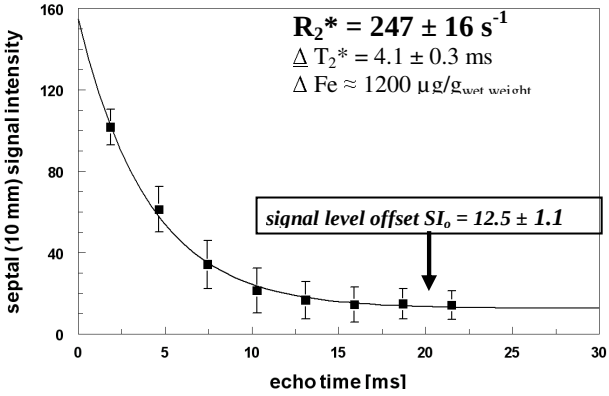
[1]Diagnostic and Interventional Radiology, University Hospital Hamburg-Eppendorf, Hamburg, Hamburg, Germany, [2]University Hospital Hamburg-Eppendorf, [3]Siemens AG, [4]Children's Hospital & Research Center, Oakland, USA

Introduction

Cardiac iron concentration in patients with iron overload can be determined from multiple gradient recalled echo measurements (MRI-R2*) within one breathhold, although there are technical limitations with respect to echo times and analysis methods. These limitations may be less important for diagnosis than for monitoring cardiac iron overload. In a cross-sectional study, in patients coming to our iron metabolism center for routine monitoring of liver iron by biomagnetic liver susceptometry, we also determined R2* in the heart in those being at risk of developing problems from cardiac iron toxicity.

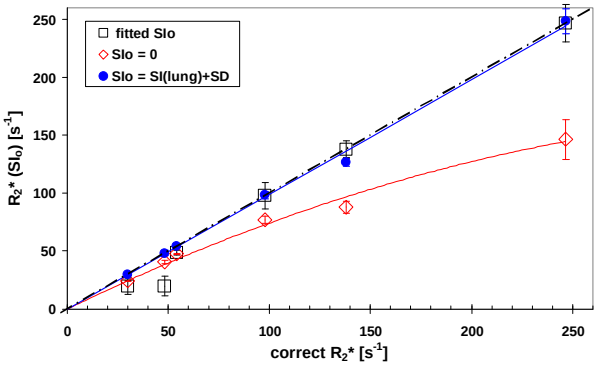
Methods

Breathhold retrospective ECG gating was performed on a 1.5T MRI (Symphony®) on 7 controls and 55 patients with thalassemia major (TM: n=25), thalassemia intermedia without RBC transfusions (5), sickle cell disease (5), Friedreich Ataxia (4), hereditary hemochromatosis (3), and 7 transfused patients after stem cell transplantation (post-SCT) as well as single transfused patients with CDA-II, MDS, Diamond-Blackfan anemia (DBA), and plasmocytoma. Liver and cardiac iron measurements were synchronized within 6 months. A total of 88 MRI-R2* scans were performed, monitoring patients for changes of cardiac iron concentrations within 6 to 12 months under chelation treatment. R2* was analyzed from signal intensities in 10mm mid-papillary short axis slices in the cardiac septum. Data from 9 heartbeats in end-diastole (TE=1.9-21.5ms, TR=223ms, flip angle=20°, TT=400-1000ms) were acquired. Additionally, cardiac functions were assessed from 6mm short and long axis slices of cine series spanning the entire cardiac cycle (25phases). The widely used software (CMRTools®) was applied to assess cardiac function and signal intensities (SI±SD) in delineated septal ROIs. R2* was analyzed by a mono-exponential function with signal level offset (SI_{LO}) based on a weighted Marquardt algorithm (SlideWrite®). For R2*>100s^{-1}, a comparison of a free fit of SI_{LO} and the mean SI+SD of lung tissue within the shim-box could be made with an agreement of ±5% (p<0.001). The deviation between this more precise procedure and an exponential fit without SI_{LO} was found to be 20–40%, especially for R2*>100s^{-1}, even the truncation method still resulted in deviations >20% (He et al, 2006). Cardiac iron concentration (*wet-weight* CIC) was calculated from adjusting the data of Ghugre et al (2006) to the mean R2* of our controls (28.9±4.4s^{-1}) at a mean heart iron concentration from Bush et al (1995). Perfect agreement (>90%) was found with available cardiac biopsy and autopsy data for R2*<200s^{-1} (Westwood et al, 2004; Pennell et al 2005).



Results

In the patients and controls with liver iron concentration (*in vivo/wet-weight* LIC) between 100 and 7680 (converted LIC: 0.6-46.1mg/g-dry wgt, age: 11-67y.o.), we assessed cardiac iron in the septum from 0 to 1777µg/g (R2*: 22–371s^{-1} or T2*: 45.7-2.7ms). Most patients with elevated cardiac iron levels (R2*>50s^{-1}, CIC>143 µg/g) were found in TM (52%). In this group, 81% of patients with LIC>2000µg/g had expected mild to severe cardiac iron overload. Interestingly, one patient (29y.o.) with LIC = 3926µg/g (ferritin: 4787µg/l) did not show elevated CIC (R2*: 35±1s^{-1}) or cardiac function impairment (LVEF=67%). However, at LIC below this recommended threshold, 35% of the patients had unexpected high CIC, some even higher CIC than LIC levels. Nearly all patients (8 TM, 1 DBA) with CIC>550µg/g (R2*>130 s^{-1}) did show cardiac failure and had periodically elevated NTpro-BNP levels. In all patients other than TM and DBA, we observed elevated R2*-relaxation rates only in one patient with severe aplastic anemia post-SCT (R2*: 98s^{-1}, LIC: 5382µg/g) and in one patient with plasmocytoma (R2*: 56s^{-1}, LIC: 7681µg/g).



Discussion

In summary, for R2*<100 s^{-1}, a free fit of the signal level offset usually fails and lung tissue within the shim box could be used as a surrogate measure. This is especially important for following chelation treatment effects in the heart, where simple mono-exponential fit procedures will underestimate R2* at higher cardiac iron load. There is now sufficient data available to convert R2*-relaxation rates into CIC values if the signal level offset is taken into account. From the limited number of patients with iron overload other than thalassemia major and DBA, one may conclude that a relatively high iron burden is needed until increased cardiac iron will be observed.

Conclusion

The measurement of MRI-R2* in the ventricular septum can detect patients with iron overload at risk of developing heart failure from cardiac iron toxicity due to chronic blood transfusions. Early detection may induce intensive iron chelation with the benefit of avoiding heart failure. To do so, however, the mean SI+SD of lung tissue within the shim-box should be taken in consideration in order to achieve more precise results.

References

[1] He et al; 2006, [2] Ghugre et al; 2006, [3] Westwood et al; 2004, [4] Pennell et al; 2005