Quantitative changes in T2* reflect remodeling of both remote and ischemic myocardium in a murine heart failure model

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Introduction: Heart failure is an increasing burden to western societies due to aging and increased survival of patients suffering from myocardial infarction. Early identification of adverse structural changes in the myocardium may optimize clinical management. Late Gadolinium enhancement (LGE)-MRI is widely used to assess infarct size and myocardial fibrosis. We have recently shown that quantitative T_2^* mapping can provide additional information on infarct status and changes in the infarcted myocardium in relatively small murine infarctions after ischemia/reperfusion injury[1], In this study, we further explored quantitative changes in T_2^* in both infarcted and remote myocardium in a murine heart failure model induced by severe myocardial infarction.

Materials and Methods: *Mouse model* Myocardial infarction (MI) was surgically induced in C57Bl/6J mice (n=12) by permanent ligation of the left coronary artery. *MRI protocol* MRI at 9.4 T was performed at baseline, 1, 7 and 28 days after surgery. The protocol consisted of Cine-MRI, multi-gradient echo T_2^* mapping and LGE. A slice was positioned at the mid-ventricle lower papillary muscle level in mid-diastolic phase to include an area of remote viable tissue as well as a substantial infarct area. T_2^*-mapping was performed using a cardiac triggered multi gradient-echo sequence, with the following parameters: TR=1 R-R interval, TE=1.22, 3.45, 5.68, 7.91, 10.14, and 12.37ms, slice=1mm, matrix=128×128, FOV=3×3cm^2. In the same slice LGE measurements were performed with a cardiac triggered inversion-recovery segmented gradient echo sequence, with the following parameters: TI=160ms, TR=5.8ms, TE=2.2ms, 16 segments, slice=1mm, matrix=256×256, FOV=3×3cm^2. Cine imaging was performed with a retrospectively triggered gradient echo sequence, with the following parameters: TR=6.8ms, TE=1.9ms, number of movie frames=15, slice=1mm, matrix=256×256, FOV=3×3cm^2. Seven to 9 slices with inter slice distance of 1mm were measured to cover the heart from apex to base. *Analysis* Pixel-wise quantitative T_2^* values were calculated in Mathematica 7 (Wolfram). Cine images were used to compute end-diastolic volume (EDV), end-systolic volume (ESV) and diastolic wall thickness (WT). Ejection fraction (EF) was calculated as 100%(EDV-ESV)/EDV. Infarct location was determined on the basis of the LGE measurements and the akinetic area observed on Cine images on day 1.

Results: Fig 1 shows a collection of representative T_2^* maps in the myocardium and corresponding LGE images at 1, 7 and 28 days after myocardial infarction. as seen in Fig 2, baseline myocardial T_2^* was 15.0±1.1 ms in the remote myocardium (septal wall) and 14.6±1.0 ms in the free wall. At day 1, LGE displayed a homogeneous enhancement of the infarction. In addition, T_2^* values in the infarcts substantially decreased (5.7±0.4 ms), whereas a slight decrease was observed in the remote myocardium (13.0±1.5 ms). On days 7 and 28, LGE area of enhancement was smaller and heterogeneous compared to LGE at day 1. After 7 and 28 days, T_2^* values in the infarct remained low (5.5 ±0.5 ms and 5.0 ±0.5 ms, respectively). Interestingly, T_2^* values in the remote myocardium continued to decrease during follow-up (9.3±1.3 ms and 8.4±0.3 ms at day 7 and 28, respectively). Histological analysis revealed progressive deposition of collagen in the infarct and to a lesser degree in the remote myocardium, in parallel with decreased T_2^*.

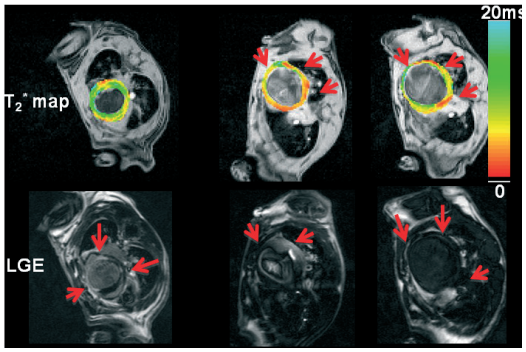

Figure 1: Mid-ventricle short-axis slice of a mouse heart at 1, 7, and 28 days, following permanent ligation of the left coronary artery. (bottom) LGE images. Red arrows point to the location of the infarct core (1) and peri-infarct regions (2). Corresponding T2* maps color-coded from 0 to 20 ms. Note the considerable T2* decrease in the free wall at day 7 and 28 (red arrows). (right) Corresponding Prussian blue staining at day 28.

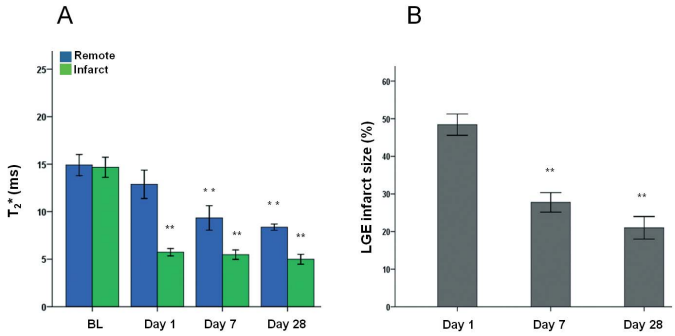

Figure 2: Quantitative T_2^* values and infarct size Quantitative T2 * values in the infarct and remote myocardium as function of days after surgery (A) and the infarct size from LGE-MRI (B). * = significantly different from baseline ($P < 0.05$), and ** = significantly different from baseline ($P < 0.005$).

Conclusions:

Quantitative T_2^* values changed dynamically in this murine heart failure model. T_2^* in infarcted areas exhibited a significant decrease starting from day 1, and further decreased with scar maturation. In contrast to our previous observations in relatively Quantitative changes in T_2^* reflect remodelling of both remote and ischemic myocardium in a murine heart failure model small murine infarctions, T_2^* in remote tissue also decreased significantly from baseline, most likely as ,a result of adverse ventricular remodeling of non-infarcted areas after MI. Serial LGE scans revealed merely changes in the infarct area, whereas the remote myocardium did not exhibit any dynamics in LGE assessments. In conclusion, quantitative T_2^* assessment may provide a valuable readout of both the infarct and remote areas in heart failure after MI.

References: [1] Aguor ENE et al. MAGMA (2012), [2] Kirk et al. JMRI (2010) 32,1095-8; [3] O'Regan et al. Heart (British Cardiac Society) (2010).