Longitudinal assessment of T_2* changes in mouse myocardium following ischemia-reperfusion injury

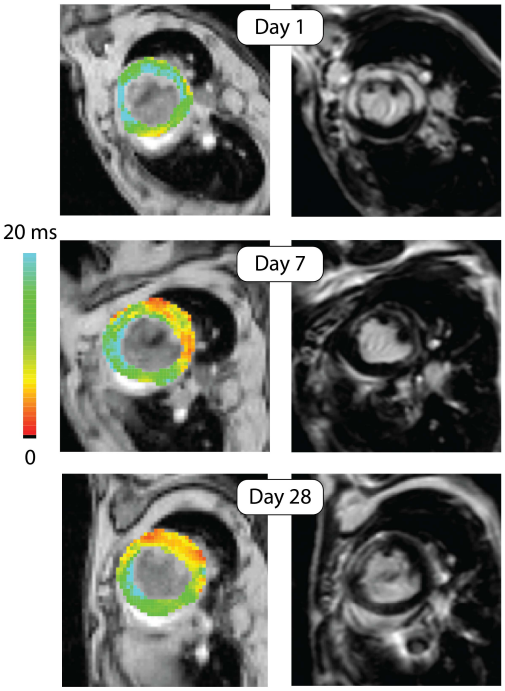
E. Aguor[1], F. Arslan[1], C. W. van de Kolk[1], M. G. Nederhoff[1], P. A. Doevendans[1], C. J. van Echteld[1], G. Pasterkamp[1], and G. J. Strijkers[2]
[1]Department of Cardiology, University Medical Center Utrecht, Utrecht, Netherlands, [2]Biomedical NMR, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands

Introduction: Ischemic injury triggers a cascade of histopathological changes in the myocardium, which may lead to a progressive decline in heart performance and heart failure. Noninvasive techniques to characterize the myocardium during infarct development are essential to assess efficacy of novel therapeutics. Late gadolinium enhancement (LGE) MRI is considered a suitable technique to quantify infarct size. However, LGE may overestimate acute infarct size due to the presence of edema and fails to distinguish acute from chronic infarction. Quantitative T_2*-mapping is hypothesized to provide additional information on infarct composition, such as the presence of edema, hemorrhage and fibrosis [1-3].

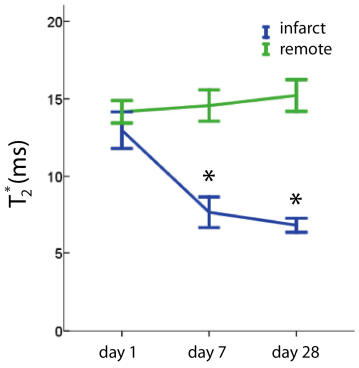
The **aim** of this study was to explore the utility of quantitative T_2*-mapping as a noninvasive technique to characterize the myocardium in the acute and chronic phases following ischemia/reperfusion (I/R) injury in the mouse.

Materials and Methods: *Mouse model* Myocardial I/R injury was surgically induced in C57BL/6 mice (N=10) by 30min transient ligation of the left coronary artery (LCA). A sham operated group of C57BL/6 mice (N=6) served as control. *MRI protocol* MRI measurements at 9.4T were performed at baseline, 1, 7 and 28 days after infarction. 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.

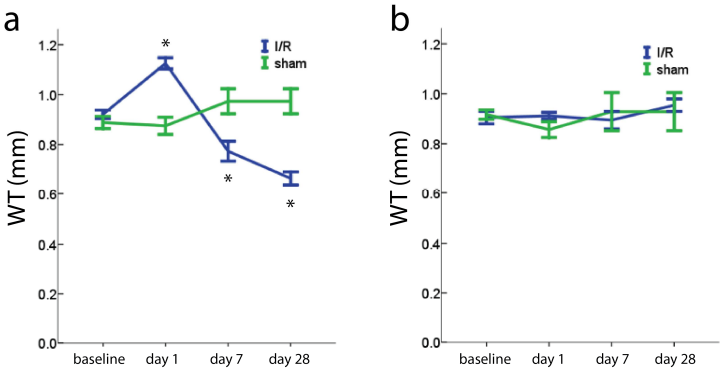
Results: Fig 1 shows a collection of representative T_2* maps in the myocardium and corresponding LGE images at 1, 7 and 28 days after myocardial infarction. At day 1, LGE displayed a homogeneous enhancement of the infarction. T_2* values (Fig 2) in the infarction were T_2*=13.0±3.7ms and T_2*=14.2±2.3ms in infarct and remote tissue, respectively. The diastolic myocardial wall thickness (WT) in the infarction was increased at day 1 as compared to baseline values and sham group (Fig 3a). Higher WT suggests presence of tissue edema at this early time point. On days 7 and 28, LGE area of enhancement was smaller and heterogeneous (Fig 1). The WT decreased (Fig 3a) as well as quantitative T_2* values (Fig 2) in the infarction (T_2*=7.7±2.4ms and T_2*=6.8±1.1ms, at days 7 and 28, respectively). Decreased wall thickness and lower T_2* values in the infarct area presumably can be understood in terms of tissue scar maturation. After long term follow up, the chronic matured infarctions were better identified on the T_2* maps than by LGE.



^ Figure 1: (left) Quantitative T_2* values in the mouse myocardium according to the pseudo color scale on the left. (right) Corresponding LGE images.



^ Figure 2: Quantitative T_2* values in infarction and remote myocardium as function of time. * significantly different from day 1 (p<0.05)



^ Figure 3: (**a**) Diastolic wall thickness (WT) for I/R group in infarct area and in the same myocardial location of the sham group, and (**b**) diastolic wall thickness in remote myocardium as function of time. * significantly different from baseline (p<0.05)

Conclusions: Quantitative T_2* values are dynamic during infarct development. In the acute phase, T_2* in infarct and remote areas were not significantly different. The infarction was best visualized by the LGE measurements in the acute phase. WT in the infarction at day 1 was higher than baseline, presumably associated with tissue edema, whereas at later stages WT and T_2* decreased during scar maturation. In the chronic phase the infarction was better distinguished on the T_2* maps than by LGE. Therefore, T_2* may enable distinction between acute and chronic myocardial infarctions, providing complementary information to LGE in the assessment of myocardial infarction.

References: [1] Yamamura et al. JMRI (2010) 32, 1104-9; [2] Kirk et al. JMRI (2010) 32,1095-8; [3] O'Regan et al. Heart (British Cardiac Society) (2010).