Accurate Assessment of Myocardial Infarction in Mice Using 3D Inversion Recovery Gradient Echo MRI

S. Bohl[1,2], C. A. Lygate[1], H. Barnes[1], D. Medway[1], L-A. Stork[1], J. Schulz-Menger[2], S. Neubauer[3], and J. E. Schneider[1]

[1]Cardiovascular Medicine, BHF Experimental MR Unit, Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, United Kingdom, [2]Cardiology, Franz Volhard Klinik, Charite University Medicine, HELIOS Klinikum, Berlin, Berlin, Germany, [3]Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom

Introduction: Current methods to quantify infarct size after myocardial infarction (MI) in mice are not ideal, requiring either tissue destruction for histology, or relying on non-direct measurements such as wall motion. High field-strength cardiac MRI has the potential to provide non-invasive 'virtual histology' and could enable longitudinal studies of the same animal and, thereby, smaller group sizes. In initial reports only 2D multislice MR techniques have been used[1,2]. Furthermore, the pharmacokinetics of gadolinium (Gd) contrast agents have not been investigated systematically. Therefore, we aimed to implement high-resolution three-dimensional inversion recovery late Gd Enhancement MRI (3D-LGE), investigate Gd-kinetics after intravenous (i.v.) and intraperitoneal (i.p) injection and to correlate LGE findings to histology. **Methods**: All MR experiments were carried out on a 9.4Tesla horizontal bore system (Varian Inc.). Using continuous T1-measurements (SNAPSHOT-FLASH MRI, temporal resolution ~ 2 min/slice, see *Figure 1*) the myocardial pharmacokinetics after i.v. and i.p. injection of 0.5µmol/g Gd-dTPA were investigated over 60 minutes in 6 infarcted mice. From these data suitable latency after injection and inversion-time for double-gated segmented slice-selective inversion-recovery 3D-LGE (FA 10°, matrix 256 x 192 x 32, field-of-view 25.6 x 25.6 x 16 mm, 1 average, acquisition time 15-20 min) were then determined. Infarct size based on 3D-LGE was calculated using a threshold method, expressed as percentage of left ventricular mass (%LV) and related to histology (tetrazolium-chloride staining) in 5 mice. **Results:** T1-contrast between healthy and infarcted myocardium was higher after i.v. injection and peaked ~15 minutes earlier than after i.p. injection ($p<0.05$, see *Figure 2a/b*). Both injection techniques retained sufficient T1-contrast for LGE imaging over a full 60 minutes. Correlation between infarct sizes derived from 3D-LGE MRI and histology was high ($mean_{HISTO}$ 31.9 +/- 8%LV, $mean_{3D\text{-}LGE}$ 33.1 +/- 9%LV, r = 0.842, see *Figure* 3 for an example). **Discussion** & **Conclusions:** For the first time, three-dimensional inversion recovery LGE MRI was used to non-invasively quantify myocardial infarctions in mice. There was high agreement with the histological standard of reference. Optimal image contrast between necrotic and healthy myocardium was ensured through a) Inversion-Recovery preparation of the acquisition allowing for suppression of healthy myocardium and b) quantitative analysis of myocardial Gd-kinetics for i.v. and i.p. delivery of the contrast agent allowing for tailoring of latency after injection and inversion-time for both injection methods.

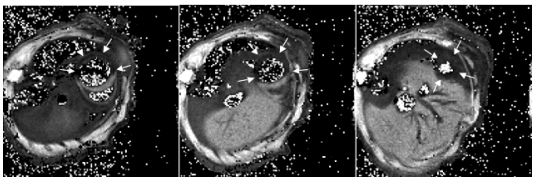
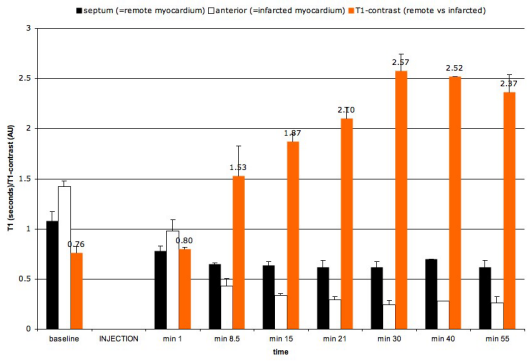


Figure 1: Post contrast cardiac T1map in short axis orientation (base, mid-cavity, apex) acquired 20 minutes after i.v. injection of 0.5µmol Gd-dTPA. The average T1 of infarcted myocardium was 217ms (hypointense, arrows) whereas $T1_{remote}$ was 490ms, resulting in high T1-contrast between the two compartments.



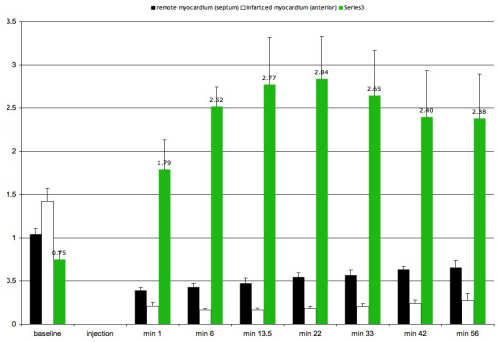


Figure 2a/b: Pharmacokinetics after i.p. (left) of and i.v. (right) injection of Gd-dTPA in MI-mice. T1-contrast (coloured bars) between infarcted (black bars) and healthy myocardium (white bars) peaked earlier and was higher after i.v. injection. The average starting time of continuous T1-measurements after Gd-administration is given on the x-axis.

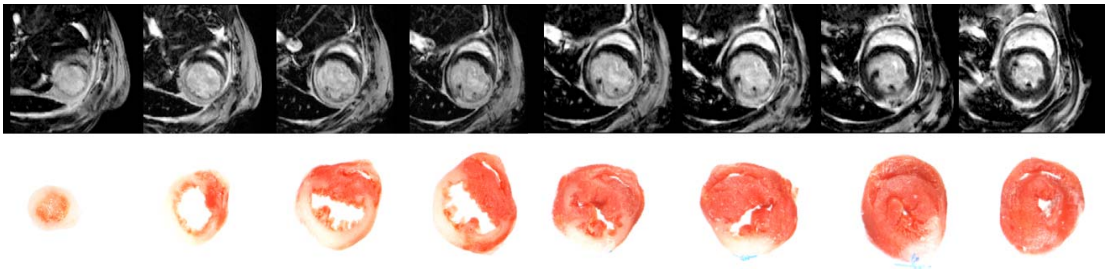


Figure 3. 3D-LGE (infarct: hyperintense; remote myocardium: hypointense) and corresponding TTC stained histological sections of a large anterior-inferior MI (infarct: pale; remote myocardium: brick red. Data obtained day 1 after surgical LCA-occlusion).

References: [1]Yang Z et al., 2004;109;1161-1167 *Circulation.* [2] Chapon C et al., 2008;*10(1):6 J Cardiovasc Magn Reson*

Acknowledgements: This project is supported by the German Cardiac Society, Else Kroener-Fresenius-Stiftung and the British Heart Foundation