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

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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 used1,2. 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-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).

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