Feasibility of 3D Late Enhancement Imaging in Mice with Totally Occluded Left Anterior Ascending (LAD) artery on a Clinical 1.5T MR Scanner

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Introduction

Delayed enhancement cardiac magnetic resonance imaging is frequently used to detect and quantify the size of myocardial infarction. Mouse models have increasingly been used in cardiovascular research to investigate the mechanisms of myocardial infarction. Due to the small size and high heart rate of mice, MRI is usually performed at dedicated high field animal scanners (4.7T – 9.4T). For pre-clinical research, however, it is sometimes considered essential that myocardial infarction is assessed in a similar way as done for real clinical diagnosis. Thereby, for clinical late enhancement imaging usually 2D sequences with poor spatial resolution are used. Due to the small heart size of mice high resolution 3D scanning seems to be mandatory. In this study we demonstrate the feasibility of 3D late enhancement imaging in mice on a clinical 1.5T whole body MR scanner and compare the obtained results with 2D sequences as used for clinical applications.

Materials and Methods

Cardiac MR imaging in mice was performed on a clinical 1.5T whole body MR scanner (Magnetom Avanto, Siemens) equipped with a 40mT/m gradient system. Mice underwent a well-established in vivo procedure of LAD ligation as described elsewhere (1). Three days after the intervention MRI was performed. For MRI the mice were sedated with 250 mg/kg 222-tribromoethanol (2) and placed prone inside a small loop coil (standard finger coil) with an inner diameter of 30 mm. For ECG gating, the standard clinical ECG probe as provided by the MRI manufacturer was used. Three electrodes were attached to paws (right and left forepaw and left hind paw) with Skintact conductor pads for children (Leonhard Lang GmbH, Austria). After acquiring localizer images to determine heart axis, a segmented 2D phase-sensitive inversion recovery trueFISP sequence (PSIR)(3), as routinely used at our department for patient exams, with the following parameters was applied for late enhancement imaging: TR= 328ms; TE= 2.72ms; flip angle: 45°; TI= 320ms; slice thickness: 2.5mm; field of view: 80mmx72mm; acquisition matrix: 256x168. The parameters were chosen such that data acquisition during the R-R interval took place during diastasis in order to minimize artefacts caused by heart motion. The typical acquisition time was 60 sec. For infarct evaluation the obtained phase-sensitive image was used. In addition to the PSIR sequence an ECG gated 3D inversion recovery prepared single shot gradient echo sequence (turbo fast low angle shot, turboFLASH) was used covering the whole heart with a slice thickness of 0.8mm. Typical acquisition parameters were as follows: TR = 437ms, TE = 5,78ms , inversion time (TI) = 270ms, flip angle: 15°, acquisition matrix: 384x512, FOV: 56 mmx75mm. Fat saturation was used to suppress the fat signal and the typical acquisition time was 80 sec. As a contrast agent for late enhancement imaging Gd-DOTA (Dotarem, Guerbet) was used. We tested concentrations from 0.1 to 0.6 mmol/kg/bw Gd-DOTA measured 10, 15, 20 and 25 min after intravenous administration. Best results were obtained with a dose of 0.6 mmol/kg when measurements were done 20 min post administration. After MRI the hearts were excised and five 5-µm sections were cut in 0.6mm distance from the apex to the mid section of the left ventricle for hematoxylin-eosin staining. Infarct sizes measured as mean percentage of left ventricular (LV) area were compared between histologic sections and MRI scans.

Results and Discussion

Figure 1 shows a typical ECG trace as obtained with our "off the shelf" setup. No special amplification of the ECG signals was necessary for well defined cardiac gating. With both tested sequences the infracted areas could clearly be depicted as shown in figure 2 and figure 3. Due to the large slice thickness of the PSIR sequence it was difficult to obtain more than three representative slices of the whole mouse heart. In contrast, with the 3D-TFL sequence the mouse heart could easily be covered with up to 14 slices. Multi-slice coverage of the infracted heart is especially advantageous for detecting small infracted regions which can easily be missed by wrong placement of single slice late enhancement acquisitions. Although imaging was performed on a 1.5T scanner with standard equipment image quality was sufficient to quantify infarct area reproducibly. The mean histological infarct size was 50 ± 5% of LV area ; mean infarct size in the PSIR sequence was 60 ± 4% and infarct size in the 3D-TFL sequence was 54 ± 5%. Infarct sizes as measured by MRI tended to overestimate the histologic values by 20% for the PSIR sequence and 8% for the 3D-TFL sequence, whereby overestimation by the 3D-TFL is strongly reduced which can be attributed to the improvement in spatial resolution.

In conclusion, it is shown in this study that high resolution 3D late enhancement cardiac imaging in mice on a 1.5T MR scanner is feasible without the use of specialized equipment, making it an easily available tool for the non-invasive in-vivo quantification of infarct size in mice models.

References

[1] Metzler B, et al. Exp Physiol 2008;93:825-33. [2] Roth DM, et al. Am J Physiol Heart Circ Physiol 2002;282:H2134-40. [3] Kellman P, et al. MRM 2002;47:372-83.

Figure 1: Typical ECG trace as obtained with our "off the shelf" setup

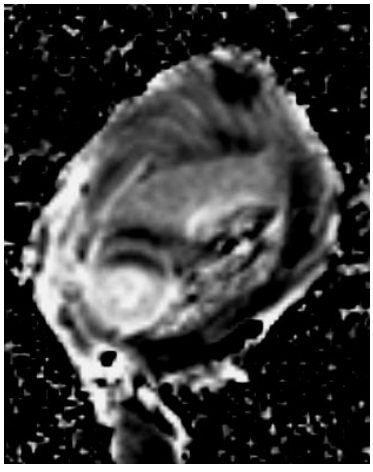

Figure 2: Phase sensitive late enhancement image obtained with the 2D-PSIR sequence (pixel size: 312 µm x 312µm x 2.5mm)

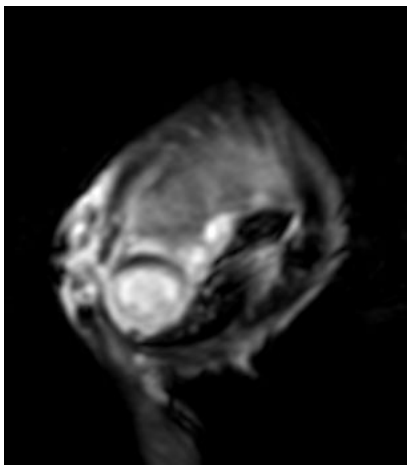

Figure 3: Late enhancement image obtained with the 3D-TurboFLASH sequence (pixel size: 180µm x 180µm x 800µm)

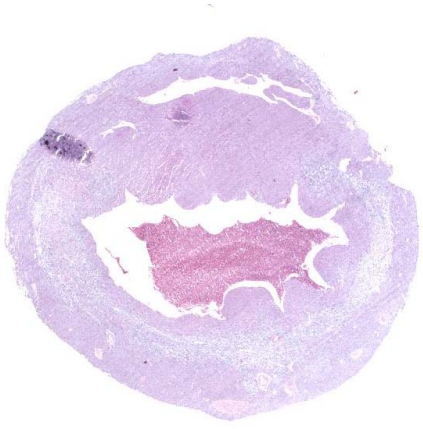

Figure 4: Hematoxylin-eosin stained histologic section showing the infracted region.