MR-Imaging of the Coronary Arteries of Mice in Vivo

A. Nauerth[1], E. Treiber[1], C. Oerther[1], and U. Flögel[2]
[1]Bruker BioSpin MRI GmbH, Ettlingen, Germany, [2]Institut für Herz- und Kreislaufphysiologie, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany

INTRODUCTION:
Cardiac imaging is widely used in preclinical research. There is increasing interest in studying the coronary arteries in murine models of coronary heart disease. However, due to size and the motion of the coronary arteries, up to now it was difficult to visualize the coronary arteries of mice in vivo with MRI techniques. To visualize coronary vessels with a proximal diameter of 100–200 µm, high resolution must be realized not only in plane but in all three dimensions.
The development of self-gated MR imaging techniques in addition to cryogenically cooled RF-coil technology [1] for signal to noise increase, allows the acquisition of cardiac and respiratory movements of small rodents with high temporal and spatial resolution. Using this combination it became feasible to visualize the coronary arteries with full heart coverage of mice in vivo with unprecedented resolution in a reasonable acquisition time, which is especially relevant for studies of animals in labile hemodynamic conditions, such as myocardial infarction. However, processing the data with a standard maximum intensity projection (MIP) over the entire volume acquired hampers the visualization of the coronary arteries as they are covered by the blood-filled heart chambers and surrounding thicker vessels.

PURPOSE:
Purpose of this study was to develop a basis for studying coronary artery diseases in small rodents in vivo.

METHODS:
In order to acquire motion artifact free images the self-gated 2D-Time-Of-Flight (TOF) imaging technique IntraGateFLASH [2] was developed. Using the reconstruction tool IntraGate MIPs can be reconstructed in any cardiac phase.
To by-pass the mentioned display problems, special MIPs of sub-volumes (targeted MIP) were performed allowing stepwise movement through the imaged volume and in addition rotating the slab along the epicardium by defining a certain rotation axis for better visualization.
C57BL/6 mice were anesthetized with isoflurane and were freely breathing during data acquisition. The MRI experiments were performed in a Bruker BioSpec® 9.4 T system with a 20 cm bore and a transmit and receive MRI CryoProbe™ (Bruker BioSpin MRI GmbH). The MR scanner was equipped with a BGA12S gradient system.
Acquisition parameters: IntraGateFLASH, TR = 6 ms, TE = 1.5 ms, FA 55°, resolution = 117 µm x 78 µm, 11 overlapping slices thickness 0.5 mm, slice advance 0.2 mm, scan time = 34 min 15 s. No contrast agent was administered.
A navigator signal was used to assign each echo to its corresponding cardiac phase, respiratory phase, and k-space. A standard MIP and targeted MIPs were used to generate MR-cine-angiograms with 8 frames per heart cycle during exhalation.

RESULTS:
With the acquired data cine-MIPs were reconstructed (Fig 1a). For better visualization of the coronary arteries targeted MIPs were calculated (Fig. 1b and c) and clearly show the dynamic filling of these vessels in diastole due to the flow-dependent signal change in dynamic cine mode.

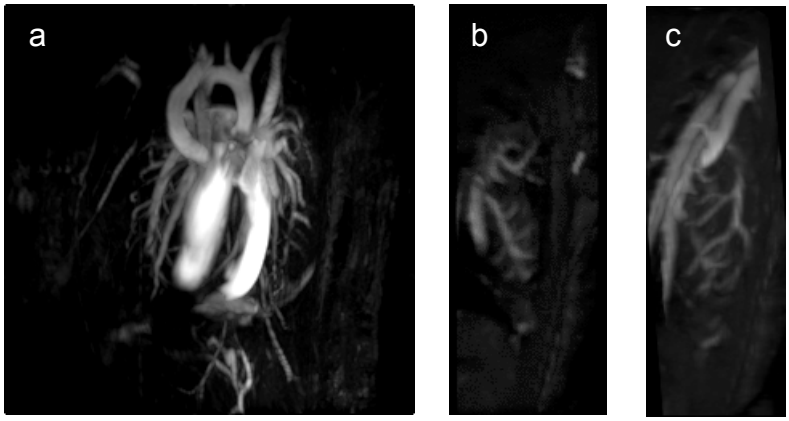

Fig. 1: MIPs in diastole
a) One selected frame showing MIP of the whole acquired volume
b) Targeted MIP of the left coronary artery in diastole derived by rotating a slab along the epicardium
c) Targeted MIP of the right coronary artery in diastole derived by rotating a slab along the epicardium

CONCLUSIONS:
The TOF angiography using self-gating technology, in combination with signal enhanced cryogenically cooled RF-coils opens up new possibilities in preclinical studies for coronary artery disease models in small rodents. This approach can be applied for visualization of collateral vessel formation after coronary artery occlusion or also to assess the outcome of therapeutically interventions for restoration of blood flow into the myocardium after infarction and allows by repetitive analysis of individual mice lacking or overexpressing relevant target genes to identify key factors involved in regulation of vascular remodeling.

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