

Mouse myocardial first-pass perfusion imaging

B. F. Coolen¹, R. P. Moonen¹, L. E. Paulis¹, T. Geelen¹, L. de Graaf¹, K. Nicolay¹, and G. J. Strijkers¹

¹Biomedical NMR, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands

Introduction Myocardial perfusion is a key parameter in the characterization of cardiac pathology. Many cardiac diseases have their origin in reduced myocardial perfusion or the incapability of the heart to increase blood flow in stress conditions. Visualization and quantification of myocardial perfusion using MRI is possible by measuring the first-pass of an MRI contrast agent in the myocardium after intravenous injection.¹ While mouse models play an important role in studying cardiac disease and therapies, measurements of myocardial first-pass perfusion in mice using MRI have not been established so far.² In this study, we present a first-pass perfusion measurement method for mice.

Materials and Methods Sequence - The method was based on an ECG-triggered saturation-prepared FISP sequence (Fig. 1). Read-out was placed directly after detection of the R-wave. A combination of segmented acquisition and GRAPPA parallel imaging allowed for a temporal resolution of one image every three heart beats with an acquisition time (T_{ACQ}) of less than 16 ms. Saturation pulses were applied each R-R interval to generate strong T_1 -weighted contrast between normal and contrast-enhanced blood and myocardium. δ_{SAT} was based on the heart rate and chosen such that the effective saturation time T_{SAT} was approximately 60 ms. Other sequence parameters were: TR/TE = 1.18/0.51 ms; SW = 200 kHz; flip angle = 9°; FOV = 3×3 cm²; slice thickness = 1.5 mm; Matrix = 64×64 / centric k-space filling; Parallel acceleration = 1.64 (18 reference k-lines).

In vivo - Measurements were performed with a 9.4 T Bruker pre-clinical MRI scanner (Bruker BioSpin, Ettlingen, Germany). Healthy Swiss mice (n=3) were measured three times at different days to assess reproducibility of the method. Prior to MRI, mice were anesthetized with 1-2 % isoflurane in medical air (0.4 l/min). A catheter was inserted in the tail vein. Mice were positioned in prone position on a phased-array surface receiver coil and placed in the MRI scanner containing a 72 mm volume transmit coil. During 5 min, a time-series of 1000 short-axis images was made using the first-pass perfusion sequence. After a time period of 10 s, a 115 μ l bolus of Gd-DTPA in 0.9% NaCl (90 mM) was administered, while scanning continued. From the images, signal intensity-time curves of myocardium and left ventricle were extracted using semi-automatic segmentation software (CAAS MRV FARM 2.0, Pie Medical Imaging, Maastricht, the Netherlands). The upslope from baseline to the first-pass peak was fitted in both the left ventricle and myocardium and their ratio was used as a semi-quantitative measure for perfusion. The same procedure was repeated in a mouse with myocardial infarction induced by permanent occlusion of the LAD.

Results and Discussion For all experiments, the first-pass of the contrast agent was successfully visualized. The anatomical images in Fig. 2 clearly capture the bolus arrival in the right and left ventricles, followed by perfusion of the myocardium and finally the washout phase. High temporal resolution was achieved by a combination of parallel imaging, high sampling bandwidth and short acquisition time, resulting in high-quality motion-artifact-free images of the end-diastolic cardiac phase. A segmented acquisition over three heart periods provided the optimal trade-off between temporal resolution and image quality. The absence of respiratory gating in general only affected the global position of the heart in the image, but did not lead to movement artifacts. These global movements could easily be corrected for in the segmentation process.

Baseline normalized signal intensity-time curves of healthy mice were very reproducible when measured at three different days and did not vary significantly between the three mice (Fig. 2, bottom). The group averaged value for the normalized upslope (Myo/LV) was 0.20 ± 0.05 (95% CI, 0.10-0.31). In a next step to achieve absolute quantification of perfusion values we will use sophisticated analyses based on a deconvolution of the tissue response with the arterial input function.³ Such analysis is possible because the signal-intensity time curves are sampled with sufficient time resolution and our acquisition scheme allows for absolute quantification of blood and tissue contrast agent concentration with time.

In a mouse with myocardial infarction (Fig. 3), the infarcted area could clearly be identified during the first-pass of the contrast agent. Signal intensity in the remote area increased rapidly after injection of the contrast agent, while the infarcted region remained dark in the image, because of reduced perfusion. At about 60 s after injection, intensity in the infarcted myocardium became higher than the intensity in the remote myocardium (red-green crossing in Fig.3). Here the delayed-enhancement time-window was entered. The normalized upslope for remote and infarcted regions were 0.14 and 0.04, respectively. The latter was outside the CI and therefore significantly different from healthy control mice.

Conclusions We presented for the first time an MRI method enabling myocardial first-pass perfusion measurements in mouse models. Determination of semi-quantitative perfusion values discriminated between healthy and infarcted mice. This new method is a valuable addition to diagnostic techniques in experimental studies on cardiac disease. Future studies using this approach will focus on the absolute quantification of myocardial perfusion.

References ¹Gebker, R. et al. *J Cardiovasc Magn Reson* 2007; 9(3):539-547 ²Epstein, FH. *NMR Biomed.* 2007; 20:238-255. ³Jerosh-Herold, M. *Semin UltraSound CT MRI* 2006; 27:2-10.

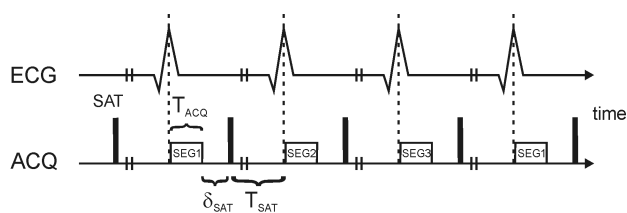


Figure 1: Mouse myocardial first-pass perfusion sequence.

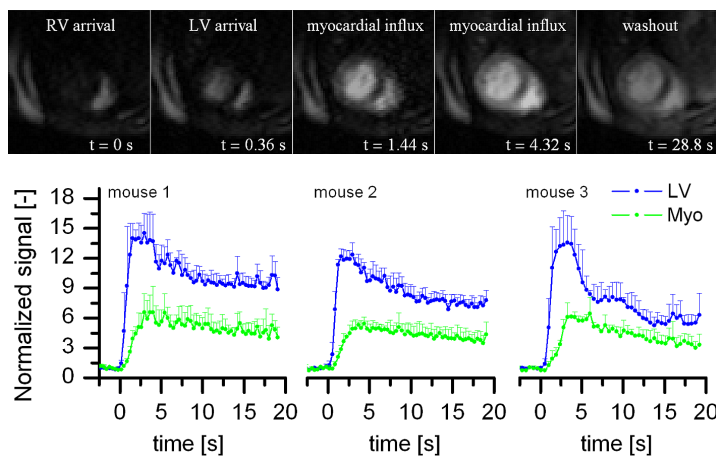


Figure 2: (top) Typical first-pass perfusion images in a healthy mouse. (bottom) Signal intensity-time curves (mean \pm SD) in left ventricle and myocardium of three different mice. At $t = 0$ s contrast agent arrived in the right ventricle.

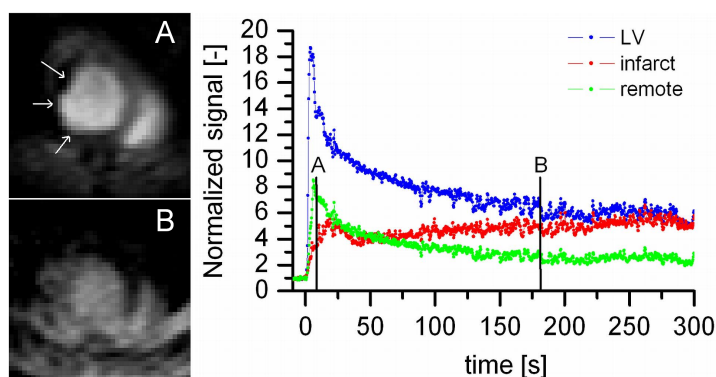


Figure 3: (left) First-pass perfusion images in a mouse with myocardial infarction. (right) Signal intensity-time curves extracted from three different ROIs. At time 'A', a lower rate of contrast agent uptake was seen in the infarcted myocardium, followed by a period of delayed-enhancement 'B'.