First-pass cardiac perfusion imaging of the infarcted rat heart

D. J. Stuckey[1], C. A. Carr[1], S. Meader[1], D. J. Tyler[1], and K. Clarke[1]
[1]Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, Oxon, United Kingdom

Background: Imaging the first-pass of a bolus infusion of Gadolinium-based contrast agent has become a standard clinical method for identifying under-perfused regions of the myocardium and can accurately predict severity of myocardial infarction in humans (1-2). Despite the clinical importance of this technique, it has never been used to study small animal models of disease, owing to the need for ultra-rapid and high-resolution imaging during first-pass (3). We have developed a method to acquire an image every cardiac cycle to identify perfusion deficits in infarcted rat hearts, *in vivo* and *ex vivo*.

Methods: ***Ex vivo study*****:** First-pass imaging was performed *ex vivo* in excised hearts, perfused retrogradely at 15 ml/min with Krebs-Henseleit buffer. Bolus infusions of between 10 and 200µl Gd-DTPA were performed during image acquisition in a vertical-bore, 500 MHz, 11.7 T MR system with a Bruker console running Paravision 2.1.1. First-pass perfusion was imaged in a 20 mm birdcage coil (Rapid), using a fast gradient echo sequence that acquired one mid-papillary short axis image in 128 ms (TE/TR, 0.8/2 ms; 60° pulse; field of view, 20 × 20 mm; slice thickness, 1 mm; matrix size, 64 × 64, zero filled to 256 × 256). ***In vivo study****:* Myocardial infarction was induced in 230 g female SD rats by ligation of the left anterior descending (LAD) coronary artery and MRI was performed within the first 7 days and at 42 days post infarction. Cardiac morphology and contraction was measured from a stack of contiguous 1.5-mm true short-axis ECG and respiration-gated cine-MR images using a 52 mm quadrature-driven birdcage coil (Rapid) and FLASH sequence (TE/TR, 1.43/4.6 ms; 17.5° pulse; field of view, 51.2 × 51.2 mm; matrix size, 256 × 256; voxel size, 200 × 200 × 1500 µm; 25 to 35 frames per cardiac cycle). First-pass perfusion was imaged using a fast gradient echo sequence that acquired one mid-papillary short axis image per heart beat during bolus injection of 0.5 mg/kg Gd-DTPA (TE/TR, 0.8/2 ms; 60° pulse; field of view, 40 × 40 mm; slice thickness, 1.5 mm; matrix size, 64 × 64, zero filled to 256 × 256). Signal intensity in the infarcted, peri infarcted and remote regions of the myocardium were measured using ImageJ. Perfusion deficit was calculated as the time delay in seconds between 90% max enhancement in infarcted regions compared with remote regions.

Results. Ex vivo study: Infusion of 25µl Gd-DTPA into the Langendorff perfused heart over a 3 second period resulted in uniform signal enhancement throughout the myocardium (*Figure 1A*), while 10 and 100 µl infusions lead to non-uniform enhancement and hypo-enhancement, respectively. Imaging was repeated after coronary occlusion and clear regions of no-flow were identified (*Figure 1B*).

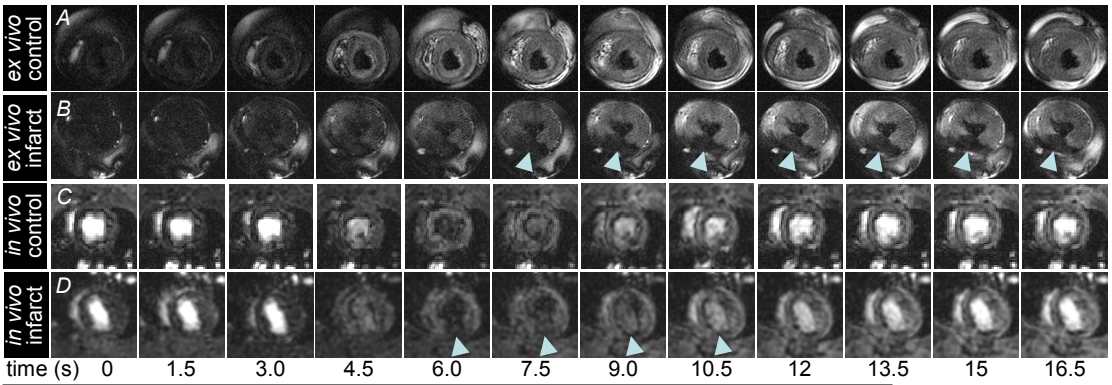

Figure 1: *ex vivo* (**A**&**B**) and *in vivo* (**C**&**D**) images of control (**A**&**C**) and infarcted (**B**&**D**) rat hearts during bolus infusion of Gd-DTPA. Arrows indicate region of perfusion deficit. Images shown are ~1 in every 10 of total number acquired.

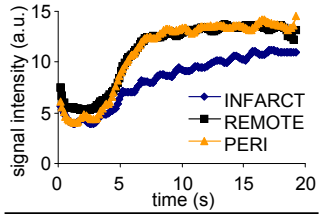

Figure 2: *Plot of signal intensity in infarct, peri-infarct and remote myocardium during an in vivo bolus infusion of Gd-DTPA into an infarcted rat.*

In vivo study: Imaging of first-pass perfusion in rat hearts performed 7 days post infarction identified areas of perfusion deficit in the region affected by LAD coronary artery occlusion (*Figure 1D* & *Figure* 2).

Perfusion deficits measured at 7 days post infarction strongly correlated with left ventricular ejection fractions and end systolic volumes measured at 42 days ($P < 0.0001$) (*Figure 3*), indicating that acute perfusion deficit resulted in greater chronic cardiac impairment. Importantly, these correlations were stronger than those between ejection fractions at 7 days and the resulting ejection fractions ($P < 0.05$) and end systolic volumes ($P < 0.01$) measured at 42 days.

Conclusions: We show that first-pass MRI can be used to identify regions of low perfusion in the infarcted rat heart *ex vivo* and *in vivo*. The extent of perfusion deficit was larger in rats that went on to develop greater cardiac impairment, demonstrating that first-pass MRI can be used as an early indicator of the extent of myocardial infarction in rats. Further, first-pass MRI performed up to 7 days post infarction was a better predictor of outcome than the commonly used measures of cardiac function, ejection fraction and end systolic volume (2). First pass MRI can be used to evaluate rodent models of human disease and experimental therapies, including cytokine and stem-cell mediated angiogenesis in the infarcted heart.

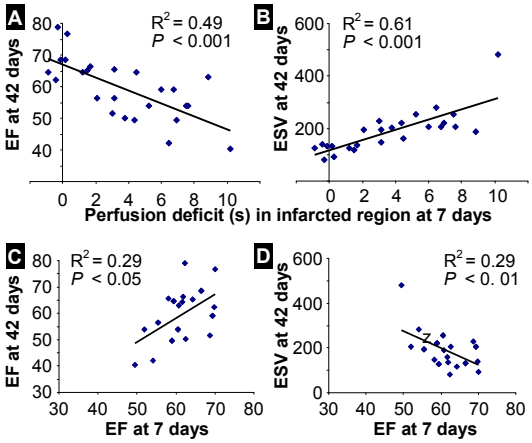

Figure 3: Correlations between perfusion deficit (**A**&**B**) or ejection fraction (**C**&**D**) measured at 7 days with resulting ejection fraction (**A**&**C**) or end systolic volume (**B**&**D**) measured at 42 days post infarction.

1) Wu KC, *et al*. **Circulation**. 1998;**97**:765. 2) Gerber BL, *et al*. **Circulation**. 2000;**101**:2734. 3) Kober F, *et al*. **MRM**. 2004, **51** :62