

# Contrast agents and MR protocols for molecular imaging of murine myocardial infarction

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## Purpose

Mouse models of (temporary) coronary artery occlusion are widely used to study specific processes after myocardial infarction, for instance cell death, inflammation and scar tissue formation. An emerging field is the application of molecular magnetic resonance imaging (MRI) for visualization of these molecular processes *in vivo*. The application of (target-specific) contrast agents provides new insights in disease progression and enables evaluation of emerging therapies. This adds to measurements of global and regional cardiac function, for which MRI is considered the gold standard. In this educational poster, we will give an overview on current applications of contrast agents in molecular imaging of myocardial infarction, as well as on the development of dedicated protocols for contrast-enhanced MRI of the mouse heart. To conclude, we will reflect on some future perspectives of molecular MRI of myocardial infarction.

## Outline of contents

### 1. Introduction

An overview on mouse models of myocardial infarction and subsequent left ventricular (LV) remodeling processes will be given. Furthermore, the basic principles of molecular MRI will be discussed.

### 2. Molecular imaging of myocardial infarction

**Cell death:** Cell death of cardiomyocytes occurs in the acute phase after myocardial infarction. Imaging of different parameters has been explored: infarct size with small Gd-chelates [1], cell viability with manganese [2], and apoptotic cells with annexin A5-conjugated contrast agents [3].

**Inflammation:** In response to cell death, inflammatory cells migrate to infarcted myocardium. Besides the phagocytosis of dead cells, they promote LV remodeling. Macrophages have been visualized with iron oxides [4] and emulsions of perfluorocarbons [5]. Moreover, myeloperoxidases, which are secreted by neutrophils, have been imaged with an activatable Gd-probe [6].

**Reparative processes:** collagen-targeted Gd-based contrast agents [7] and paramagnetic quantum dots targeted against angiogenic vessels [8] have been used for the evaluation of LV remodeling.

### 3. MR protocols

**Sequence characteristics:** Several studies have dealt with the use of prospective versus retrospective triggering approaches, black-blood versus bright-blood imaging and parallel imaging.

**$T_1$  and  $T_2$ -weighted imaging:** Paramagnetic contrast agents are routinely visualized with  $T_1$ -weighted sequences. The application of inversion recovery (IR) and steady-state gradient echo (GE) sequences has been evaluated [9]. Furthermore, the optimal sequence parameters, timing after contrast agent injection and nulling mechanisms for healthy myocardium have been explored [10]. Iron oxides are imaged with  $T_2/T_2^*$ -weighted scans, which have been particularly optimized in terms of image quality and imaging time windows [3, 11].

**$T_1$  and  $T_2$  mapping:** Although  $T_1$ - and  $T_2$ -weighted imaging can visualize the accumulation of contrast agent,  $T_1$  and  $T_2$  mapping are more powerful in terms of quantification. Lately,  $T_1$  and  $T_2$  mapping for mouse myocardium has been introduced [12, 13].

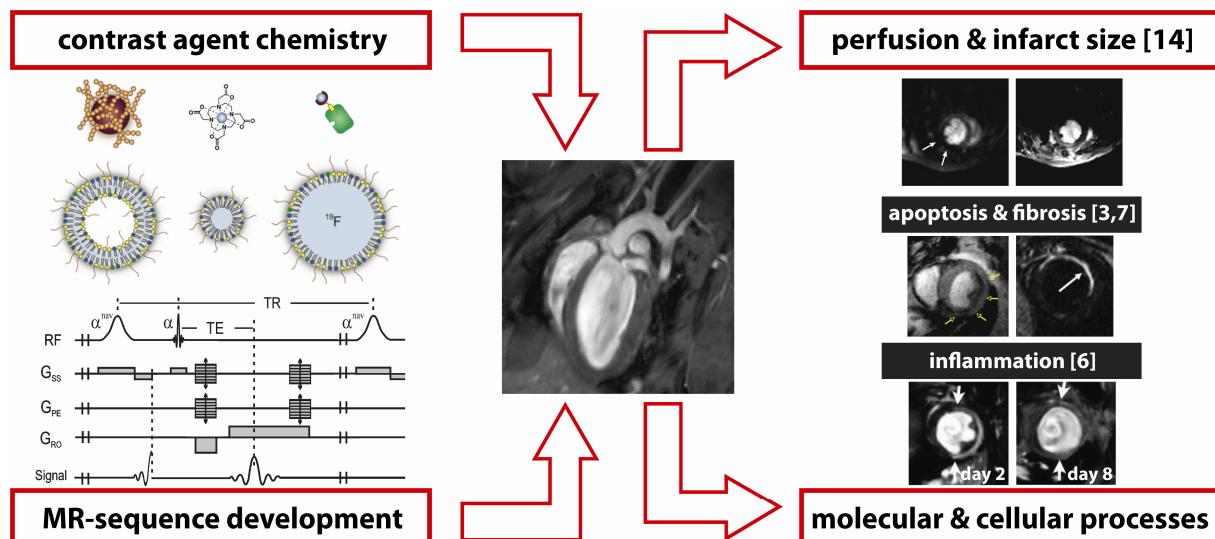
**First-pass perfusion:** Imaging of the first-pass of a bolus of contrast agent is a clinically used protocol to measure the perfusion status of the heart. Recently, this protocol has been implemented in mice using fast MR methods [14, 15].

### 4. Future perspectives

New or improved MRI protocols for mouse myocardial infarction imaging are still under development. Examples are UTE sequences for  $T_1$ -weighted visualization of iron oxides or the application of diffusion tensor imaging (DTI) in the mouse heart to study cardiac remodeling.

## Summary

Recently, major progress has been made in the field of molecular MRI of mouse myocardial infarction. Contrast agents have been designed and successfully applied to image cell death, inflammation and LV remodeling. To visualize these contrast agents, dedicated MRI sequences are required. Specifically,  $T_1$ - and  $T_2$ -weighted sequences have been optimized, quantitative  $T_1$  and  $T_2$  mapping protocols have been developed and first-pass perfusion measurements have been implemented. This has led to improved evaluation of biological processes after myocardial infarction.



## Key references

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