

# Use of Cardiac MRI in Evaluating Acute Infarct Size and Ventricular Remodeling in an Animal Model of Heart Failure Subsequent to Reperfused Myocardial Infarction

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## Introduction

Animal models employing reperfused myocardial infarction (MI) are important in evaluating new pharmacologic and gene therapy treatments for heart failure (HF). Evaluation of these new methods of treating HF require determination of acute infarct size, as well as serially monitoring long-term ventricular remodeling. The objective of this study was to use cardiac MRI to evaluate a rat model of heart failure by: 1) determining acute infarct size using delayed hyperenhancement imaging after Gd-DTPA injection, and 2) evaluating ventricular remodeling using serial cine MRI measurements of left ventricular ejection fraction (LVEF) and left ventricular end-diastolic volume (LVEDV).

## Methods

Myocardial infarction (MI) was induced in 20 Lewis rats with a 2 hr (n=15) or 30 min (n=5) occlusion of the major left coronary artery, followed by reperfusion. Rats were imaged in a 1.5 Tesla MR scanner (Siemens Med Sys) using a quad-array wrist coil (Medical Advances) and an external cardiac gating system (In-Vivo Research).

Acute MI determination: In 10 rats (n=5, 2 hr and n=5 30 min occlusion), MRI scans were performed 48 ± 2.4 hours post-MI. An ECG-triggered, spin echo sequence with a non-selective inversion prepulse was used to obtain mid-ventricular short axis images at multiple time points following a 0.3 mmol/kg Gd-DTPA injection. Sequence parameters included; TE=20 msec, TD=225 msec, TR=2-3 beats, 0.35 x 0.35 mm in-plane resolution, 3 mm slice thickness, and acquisition timed to mid-diastole. The sizes of hyperenhanced regions at each time were obtained by threshold image analysis. Immediately after the MRI scan, animals were sacrificed, hearts were excised and sectioned to match the MRI slice positions, and sections were stained with TTC to determine infarct size. The size of the hyperenhanced zone and the size of the TTC stained zone were compared to determine the relation between hyperenhancement and infarct size.

Monitoring of Ventricular Remodeling: In 10 rats (n=10, 2 hr occlusion), MRI scans were performed at baseline (1 day before MI) and 1, 2, 4, 6, 8 and 10 weeks post-MI. An ECG-triggered 2D cine FLASH sequence yielded 6 images over the cardiac cycle with a pixel size of 0.4 mm x 0.4 mm and a slice thickness of 3 mm. Five contiguous slices covering the entire left ventricle were obtained in the short axis orientation and analyzed with ARGUS (Siemens Med Sys) or MedX (Sterling Sys) to calculate LVEF and LVEDV for each rat at each time point. Imaging was repeated at 8 sessions to evaluate repeatability.

## Results

Acute MI determination: Immediately after injection of Gd-DTPA, the hyperenhanced region overestimated infarct size 16-44%. The size of the hyperenhanced zone decreased after injection and accurately determined infarct size 22 ± 7 min after Gd-DTPA injection, figure 1.

Monitoring of Ventricular Remodeling: Seven rats survived the 10 week study. LVEF was reduced from 79 ± 4% at baseline to 35 ± 3% at week 1 (mean ± SEM, P < 0.01). LVEF remained low for the balance of the study (29 ± 5% at week 10), figure 1. LVEDV gradually increased over the first 4 weeks after from 0.15 ± 0.03 ml at baseline to 0.38 ± 0.03 ml at week 4, then remained elevated for the remainder of the study (0.37 ± 0.0 ml at 10 weeks), figure 2. Repeatability analysis indicated a standard error of 3.3%.

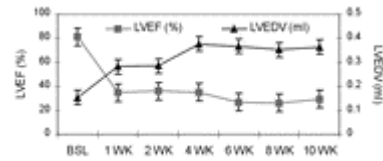


figure 2. LVEF and LVEDV

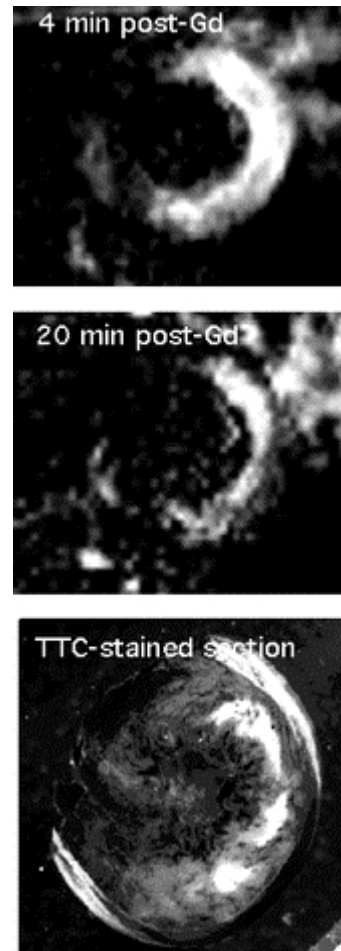


figure 1. MRI and TTC

## Discussion

Cardiac MRI is uniquely suited for the evaluation of animal models of heart failure, as it can both determine acute infarct size and monitor long-term ventricular remodeling. In this model of HF, the majority of LVEF reduction occurs immediately after MI without significant change over the next 10 weeks. Increases in LVEDV, on the other hand, take about four weeks before the majority of change occurs. One caveat found in this study was: in order to use MRI to accurately determine infarct size with delayed hyperenhancement, imaging should take place approximately 25 minutes after Gd-DTPA injection.