Validation of Infarct Measurements by Inversion Recovery Delayed-Enhancement MRI during the Hyper-Acute Phase of Myocardial Infarction in Rats

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INTRODUCTION — Infarct size is an important measurement for assessing disease progression and treatment efficacy in myocardial infarction (MI), where *ex vivo* staining with tetrazolium salts such as triphenyltetrazolium chloride (TTC) is regarded as the gold standard[1]. Recently, delayed-enhancement (DE)-MRI with gadolinium (Gd)-DTPA has been established as an accurate method for assessing *in vivo* infarct size in humans following MI, and has become increasingly popular in pre-clinical studies of chronic and sub-chronic MI where its accuracy has been validated against TTC staining[2]. However, the feasibility and accuracy of DE-MRI in measuring infarct size during the very early phases (i.e. hours) following MI is less well understood. In addition, while inversion recovery (IR) is clinically the MR sequence of choice for DE-MRI as it offers optimal contrast between normal and infarcted myocardium, this technique has not been fully explored in small animal models with dedicated high-field experimental systems. Here we present a comparison between infarct measurements by IR-based DE-MRI and TTC staining during the hyper-acute phase of MI in a rat model.

METHODS — Male Wistar rats (n=13) were anaesthetised and underwent 30 minutes of myocardial ischaemia by ligation of the left anterior descending coronary artery followed by 2 hours of reperfusion. At this point, subjects were imaged using a 9.4T Varian experimental system while breathing spontaneously under general anaesthesia. Short-axis images of the infarcted heart were acquired *in vivo* using Gd-DTPA (0.6mmol/kg) DE-MRI with a modified dual ECG/respiratory-gated IR sequence[3] (α=90°, TE=1.5ms, TR=3.6ms, TI~400ms, FOV=40x40mm^2, 192x192, ΔZ=1mm, 10-15 slices, single time frame). Hearts were extracted following MR imaging for *ex vivo* infarct measurements by TTC staining and planimetry. DE-MRI and TTC infarct measurements were quantified semi-automatically using ImageJ software. Infarct size was normalised to the size of left ventricle and expressed as a ratio (In/LV). Linear regression and Bland-Altman analysis were performed using SPSS software to assess the accuracy and variation of infarct measurements by the two methods.

RESULTS AND DISCUSSION — Figure 1 shows representative DE-MRI and TTC image slices of an infarcted rat heart 2 hours after myocardial ischaemia-reperfusion. DE-MRI using an IR sequence with dual ECG/respiratory gating generated images with excellent contrast between normal and infarcted myocardium. DE-MRI of infarcted myocardium was clearly visible within approximately 10 minutes after injection of Gd-DTPA. DE-MRI measurement of absolute LV and infarct sizes was systemically larger than TTC planimetry, and is most likely due to tissue shrinkage from TTC staining and subsequent tissue preparation. Analysis of normalised infarct size (as a percentage of LV, In/LV) demonstrated a strong correlation between DE-MRI and TTC planimetry (TTC vs DE-MRI: R^2=0.893, F=108.7, p<0.0001; see Figure 2a). Bland Altman analysis revealed negligible bias (0.4%; 95% limits of agreement = -6.6 to 7.4%; see Figure 2b).

CONCLUSION — DE-MRI using Gd-DTPA offers a non-invasive approach for assessing infarct size *in vivo*. However, its application in small animals has mainly been in chronic and sub-chronic MI models using lower field clinical systems (1.5-3T) [4,5]. In this study, we have achieved excellent image contrast between normal and infarcted myocardium by employing a dual-ECG/respiratory-gated IR sequence at 9.4T. In addition, we have demonstrated that DE-MRI with Gd-DTPA can provide accurate infarct measurements during the hyper-acute phase of MI as validated by TTC planimetry. Together with its non-invasive nature, DE-MRI infarct measurement in the hyper-acute phase of MI may serve as a valuable early surrogate marker for prognostic evaluation and assessing outcome of therapeutic interventions.

REFERENCES — [1] Fishbein M.C. et al, *Am Heart J* 1981;101(5):593-600. [2] Kim R.J. et al, *Circulation* 1999;100(19):1992-2002. [3] Price A.N. et al, *Proc ISMRM* 2007; #2528. [4] Flacke S. et al, *Radiology* 2003;226:731-738. [5] Gilson W.D. et al, *Methods* 2007;43(1):35-45.

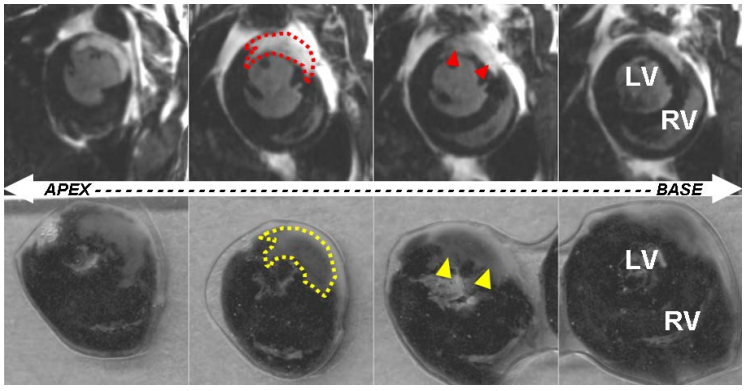
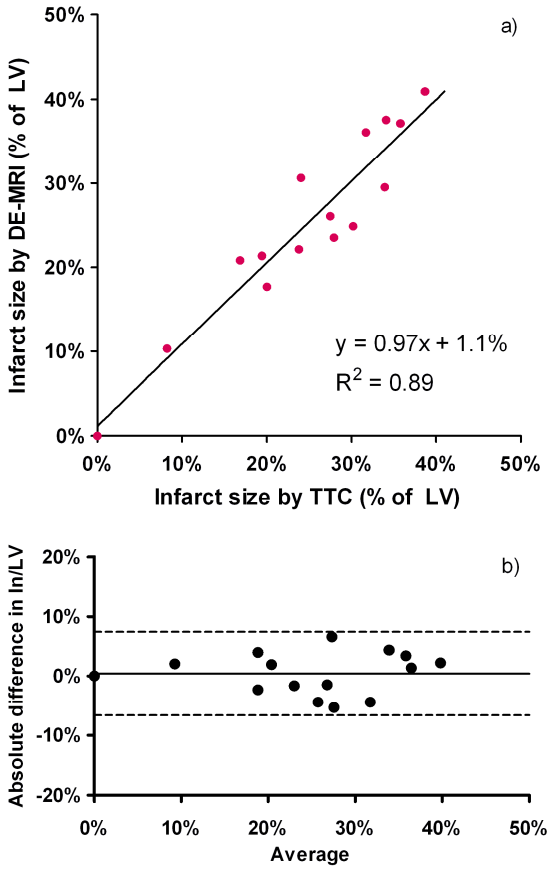


Figure 1: Infarct imaged by *in vivo* DE-MRI with Gd-DTPA (top row) and *ex vivo* TTC staining (bottom row). This series of images was obtained from the same animal. Note the similar sizes and borders of the infarct area, and the collapsed heart chambers due to tissue contracture and shrinkage from TTC staining.



Figures 2a & b: Correlation of infarct size as a percentage of LV (In/LV) measured by DE-MRI and TTC planimetry, represented here as linear regression (2a) and Bland-Altman plot (2b).