

Quantitative MRI can distinguish remodeling mechanisms after acute myocardial infarction based on the severity of ischemic insult

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Introduction: In acute myocardial infarction (AMI), the aim of any therapeutic intervention is to reduce the infarct size and attenuate adverse remodeling (1). The type and extent of infarction encountered clinically [transmural, hemorrhagic, heterogeneous, with microvascular obstruction (MVO)] is primarily determined by the severity of the initial ischemic insult (2). Understanding the *in vivo* pathophysiological mechanisms after AMI as a function of severity will be key in predicting functional recovery and assessing the efficacy of novel therapies. The purpose of our study was to evaluate longitudinal fluctuations in edema, hemorrhage and vasodilatory function in infarcted and remote territories of porcine myocardium following different ischemic insult durations.

Methods: The study involved two groups of animals that were subjected to balloon occlusion of the LAD [90 min (N=4) and 45 min (N=3)], followed by reperfusion. Imaging was performed on a 3T MRI scanner (MR 750, GE Healthcare) pre-LAD occlusion (day 0), at day 2, and at weeks 1,2,4 and 6 post-LAD occlusion. Edema was evaluated by T2 quantification using a T2-prepared spiral sequence and hemorrhage was identified by T2* determined using a multi-echo gradient-echo acquisition. Vasodilatory function was assessed at rest and following Dipyridamole administration (stress), noting BOLD-induced T2 alterations. Non-infarcted basal myocardium was also analyzed to study remote zone remodeling. A contrast-enhanced IR-GRE sequence was used for infarct assessment.

Results: Figure 1 demonstrates contrast-enhanced short-axis slices from representative animals subjected to 90 and 45 min occlusion shown at day-2 and week-4 post-AMI. In the infarct zone, the 90 min group demonstrated significant elevation in resting T2 (Fig. 2a), persisting at week-6 (p<0.005) that was unchanged by stress. In the 45 min group, T2 values in the infarct zone had normalized by week-6 (Fig. 2d) with non-significant elevation under stress. Vasodilatory function in the remote zone normalized after week-2 in the 45 min group (Fig. 2e) whereas it demonstrated prolonged impairment beyond week-2 in the 90 min animals (Fig. 2b). In the infarct zone of the 90 min group, T2* was significantly depressed between day-2 and week-2 (p<0.05) while it remained unaffected throughout infarct healing in the 45 min group.

Discussion: Current therapies have been successful in limiting infarct size in animal models; however their benefit in humans has been inconclusive (3). Hence, to understand the underlying effects of novel therapies, quantitative *in vivo* characterization will be key. The utility of quantitative MRI in serial evaluation of edema, hemorrhage, MVO and vasodilatory function after AMI has been demonstrated previously in both infarcted and remote myocardium (4,5). Our study further demonstrated that such an evaluation could also distinguish serial patterns of tissue injury based on severity of the initial ischemic insult. MRI parameters revealed faster resolution of edema and earlier restoration of vasodilatory function in less severe infarcts potentially indicating reduced adverse remodeling. Furthermore, preliminary studies in our laboratory involving ischemic preconditioning (6) have revealed non-hemorrhagic and non-MVO infarction along with a substantially reduced inflammatory response at 6 weeks in a 90 min occlusion model. Thus, this type of characterization may allow determination of the optimal timing and duration of novel therapies in the clinical setting that are targeted to alleviate ischemia-reperfusion injury.

References:

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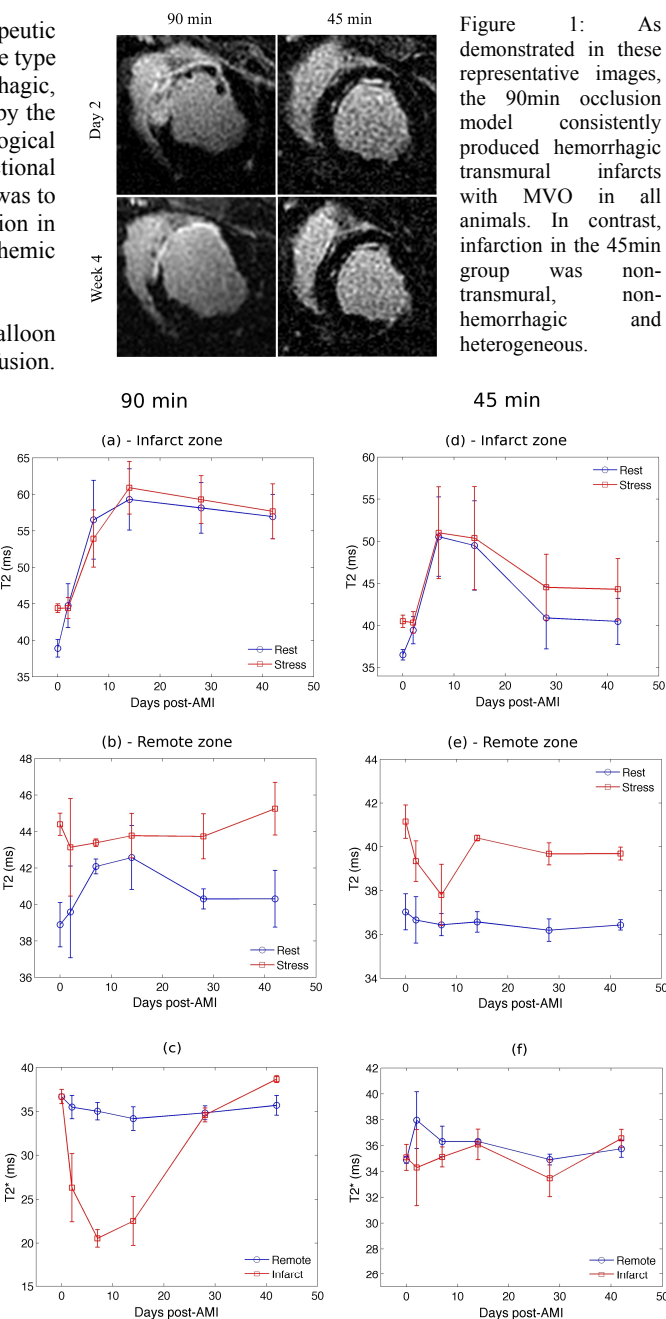


Figure 2: Cumulative time course of T2 and T2* parameters post-AMI pooled across all animals in the 90 (a-c) and 45 (d-f) min sub-groups; error bars show standard error and day 0 indicates control MRI. (a), (d) represent fluctuations in T2 within infarct zone while (b), (e) represent remote zone under rest and stress states. (c), (f) demonstrate T2* alterations in infarct and remote zones. At week 6, edema was apparent in the 90 min group whereas it was significantly reduced in the 45min group suggesting a quicker resolution of inflammatory response.

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