

Tracking edema, hemorrhage and microvascular obstruction by MRI after acute myocardial infarction

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Introduction: In acute myocardial infarction (AMI), the no-reflow phenomenon is caused by ischemia-induced microvascular injury/obstruction and has been correlated with adverse remodeling and poor patient outcome (1). The severity of the initial ischemic insult may also lead to intramyocardial hemorrhage (2). Alongside, intracellular and interstitial edema is a consistent feature of AMI and has been associated with the salvageable area-at-risk (3). The *in vivo* evolution of these processes throughout infarct healing is not well-characterized but is important in grading severity and evaluating treatment strategies, potentially improving clinical outcome. The purpose of the study was to characterize the time course of edema (T2), hemorrhage (T2*) and microvascular obstruction (MVO) in porcine myocardium following AMI and to observe the relative resolution of these pathophysiological mechanisms.

Methods: 7 pigs underwent MRI before LAD infarction (control) with subgroups studied at 2,7,14, and 28-42 days post-infarction. Histology was performed upon sacrifice at either Day 14 (N=3) or Day 30-42 (N=4). Imaging was performed on a 3T MRI scanner (MR 750, GE Healthcare). T2 measurements were performed using a previously validated T2-prepared spiral imaging sequence (4) with the following parameters: 6 ms refocusing interval, sixteen 12.3 ms spirals (3072 points), five TE's (2.9-184.2 ms). The T2* sequence was a multi-echo gradient echo acquisition with 8 echoes (between 1.4 and 12.7 ms) and TR=16.8 ms. An early (~3min) contrast-enhanced (CE) IR-GRE sequence was used for infarct/MVO delineation. Diastolic-wall-thickness (DWT) was measured from CINE-SSFP imaging. Finally, T2 and T2* maps were generated by fitting signal intensities at each pixel with an exponential model.

Results: Figure 1 demonstrates T2 and T2* maps and early CE images for an antero-septal infarct in a short-axis slice for a representative animal at three time points. T2 maps indicate edematous changes (bright regions); T2* maps indicate hemorrhage (dark regions); and CE images delineate MVO (signal voids within infarct). Figure 2 shows the cumulative time course of T2, T2* and DWT within infarct and remote myocardium. T2 was indistinguishable from control at day 2 (p=0.38) while the T2 elevation beyond week 1 was statistically significant (p<0.05). T2* was reduced up to week 2 as a result of hemorrhage, and its normalization at week 4 coincided with resolution of MVO. DWT was significantly increased at day 2 (7.5 vs 5.3mm, p=0.06) suggesting increased tissue water content while it fell below control values at week 6 (4.3mm, p=0.003) indicating scar formation.

Discussion: Post-infarct remodeling is a complex process with inter-dependent mechanisms occurring simultaneously, where assessing remote myocardium is equally important (5,6). In this respect quantitative T2 and T2* mapping techniques are potentially more specific than intensity measures in single images, allowing regional, serial and cross-subject comparisons. Edema and hemorrhage have counter-acting effects on T2, hence care should be taken while evaluating day 2. Our study demonstrates that multi-factorial MR-based parameters, acquired in a longitudinal fashion, can be employed to assess the state of myocardial tissue following AMI. Furthermore, tissue histology obtained at various time points of healing will provide ground truth for understanding MRI signal fluctuations.

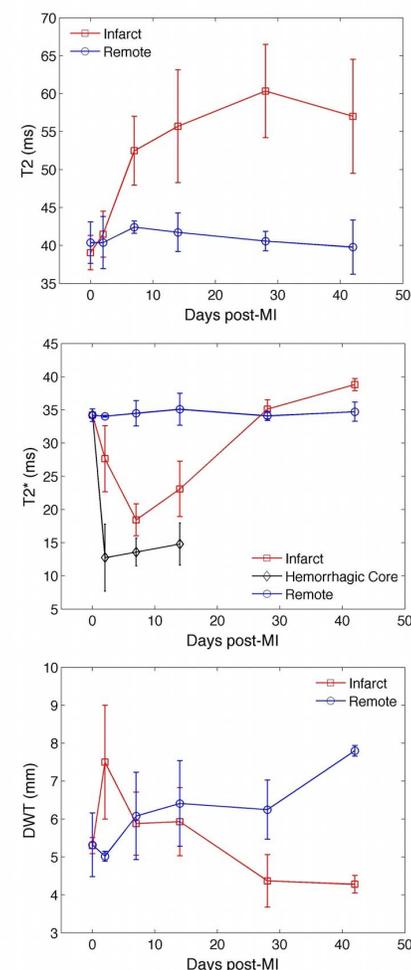


Figure 2: Plots demonstrate longitudinal fluctuations in T2, T2* and DWT in infarct zone compared to remote myocardium averaged over all animals; error bars represent standard deviations. Remote zones were selected from a basal slice not having an infarct. Day 0 represents control scans.

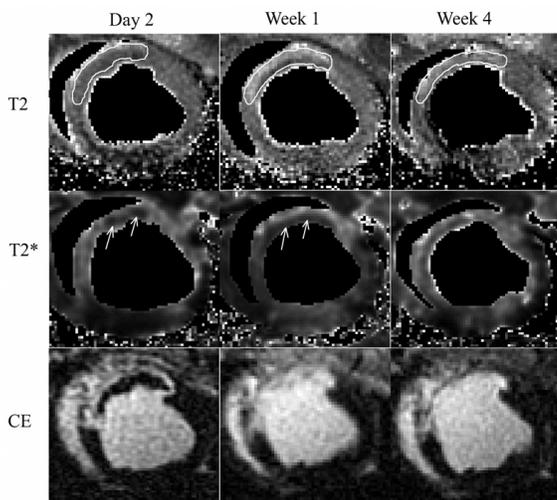


Figure 1: At day 2 in this animal, T2 elevation usually associated with edema was not apparent in the infarct zone (39.2 ms vs 39.1 ms control); however DWT was increased by 34% suggesting edematous swelling. Lower T2* (arrows) indicated presence of hemorrhage (18.5 ms vs 34.2 ms) while the CE image showed a large MVO. At Week 1, T2 was elevated in most of the infarct (51.1 ms) with reduced T2* (20.5 ms) indicating diffuse hemorrhagic by-products. CE image showed only a slight MVO. By week 4, antero-septal region was thin (scar) with reduced edema and hemorrhage/MVO were resolved.

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