Area at risk identified by T2 mapping is influenced by the severity of the initial ischemic insult in acute myocardial infarction

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Introduction: Knowledge of area at risk (AAR) in ischemia-related myocardial injury is important in determining the amount of salvageable myocardium following acute myocardial infarction (AMI). The true AAR is defined as the myocardial perfusion territory (MPT) associated with the concerned coronary artery at the level of the blood occlusion. Several studies have demonstrated that an elevated T2 signal can delineate the AAR (1-3). However, it has been questioned whether the T2 elevation simply identifies the infarcted myocardium rather than the true AAR and whether edema is indeed present in the salvageable region (4). To this end, the purpose of the study was two fold: 1) to assess the AAR with an MR-based method utilizing direct intracoronary injection of contrast media (representing MPT) as previously described (5); 2) to assess whether T2-based AAR is influenced by the severity of myocardial injury in which case presentation of microvascular obstruction (MVO) was considered as the marker of severity.

Methods: The study involved a porcine model of AMI (N=8), where the LAD was occluded for 45 min (N=1), 60 min (N=6) or 90 min (N=1) distal to second diagonal, followed by reperfusion. Imaging was performed on a 3T MRI scanner (MR 750, GE Healthcare) pre-occlusion (healthy baseline) and at day 2-3 post-infarction. T2 measurements were performed using a previously validated T2-prepared spiral imaging sequence (6) with the following parameters: 6 ms refocusing interval, twelve 12.3 ms spirals (3072 points), five TE's (2.9-184.2 ms). Infarct/MVO assessment was performed by early and late enhancement imaging (LGE) using a T1-weighed IR-GRE sequence (Gadolinium-DTPA 0.2 mmol/kg; Magnevist). Prior infarction, MPT maps were obtained under MRI via direct intracoronary injection of dilute Gadolinium-DTPA (at the site of balloon occlusion), using the IR-GRE sequence; this technique has been described earlier (5). T2 maps were obtained by fitting signal intensities at each pixel with an exponential model. AAR from T2 maps was identified by obtaining a threshold of two standard deviations above baseline T2 values, accounting for both inter- and intra-subject variability. In each animal, 3-4 anatomically registered slices were analyzed for MPT, T2-AAR and infarct areas.

Results: Animals were divided into two groups with (MVO+, N=5) and without MVO (MVO-, N=3). Infarct size was significantly larger in the MVO+ group (273±109 mm^2 vs. 150±46 mm^2, $p<0.001$). The edema threshold for T2-AAR was calculated as 46 ms from the baseline MRI. In the MVO+ group, T2-AAR was found to be in high agreement with MPT whereas no significant trend was observed in the MVO- group (Fig. 1). A paired t-test (per slice) revealed no significant difference between T2-AAR (322±94 mm^2) and MPT (340±70 mm^2) areas in the MVO+ group ($p=0.3$). In contrast, in the MVO- group, T2-AAR (261±102 mm^2) significantly underestimated MPT (485±154 mm^2, $p<0.005$). Fig. 2 demonstrates these observations via representative images. Both T2-AAR and MPT were significantly greater than the infarct area in the two groups ($p<0.006$).

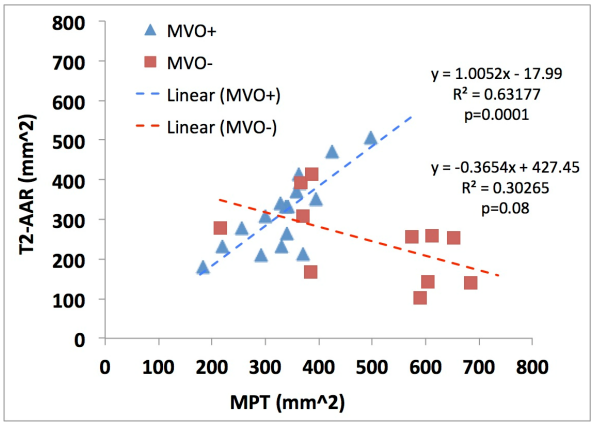

Figure 1: Plot of Area at risk computed from T2 maps vs. myocardial perfusion territory.

Discussion: The MRI-based MPT approach is identical to the microsphere technique and hence was considered as the reference measure for AAR. This method offers the advantage of all images being acquired within the same MRI reference as opposed to co-registration with gross pathology. Our study demonstrates that assessment of AAR by T2 is affected by the degree of myocardial damage, suggesting that edema extent may be related to infarct size. T2-AAR was always greater than the infarct area and thus offers value in identifying the extent of inflammation and predicting tissue progression towards necrosis or recovery. An understanding of these underlying effects will be critical in determining myocardial salvage, particularly to evaluate therapeutic interventions.

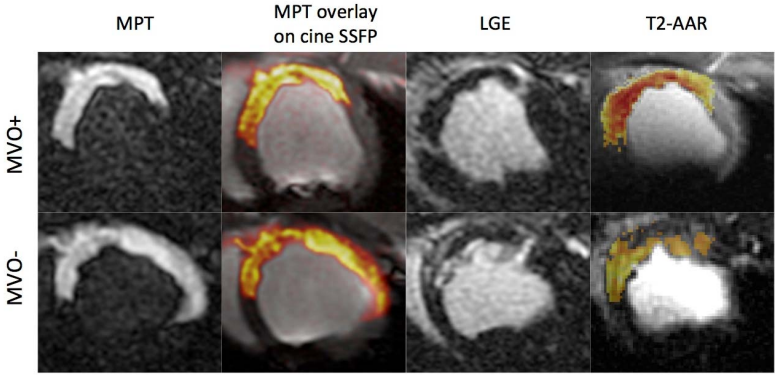

Figure 2: Representative images demonstrate that T2-based AAR highly correlated with the MPT in the MVO+ group that was characterized by large transmural infarction. In contrast, the MVO- group typically had heterogeneous infarction where the T2-AAR underestimated the true AAR represented by MPT.

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Acknowledgements: Support from the Ontario Research Fund, the Canadian Institutes of Health Research, Heart and Stroke Foundation and GE Healthcare.