T2 relaxation in ischemic and post-ischemic porcine myocardium in vivo

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Introduction: The evaluation and interpretation of MR relaxation times in viable and non-viable states of myocardium is a necessary step towards design of clinically-useful methodologies for myocardial characterization. It is accepted that myocardial T2 relaxation is prolonged in acute and chronic infarction due to elevation of the extracellular water content [(1,2)], and that T2* relaxation is accelerated distal to severe coronary disease [(3,4)], presumably due to an elevated open-capillary density. However, the application of state-of-the-art T2 measurement methodology to animal models of stunning, hibernation, and infarction has not yet been achieved.

We have developed a porcine model of transient ischemia and reperfusion injury via percutaneous balloon inflation/deflation in the left anterior descending coronary artery. The resulting tissue should demonstrate reversible myocardial dysfunction, corresponding to the phenotype of myocardial stunning, and thus it is a model of unstable angina, cardiopulmonary bypass, and exercise-induced ischemia in addition to other transient perturbations to coronary blood flow. The research goal is the characterization and interpretation of T2 signal fluctuation throughout the time course of the intervention.

Methods: Studies were conducted in three 40kg Yorkshire pigs by use of procedures and protocols approved of by the Research Ethics Board of Sunnybrook and Women's College Health Sciences Centre. Following standard anaesthesia and analgesia, animals were instrumented with a balloon catheter (Boston Scientific, Nadick, MA), placed distal to the second septal branch under guidance of x-ray angiography, and a coronary sinus catheter for blood sampling. Transient balloon inflation during iodinated contrast injection verified complete LAD occlusion. Amiodarone (150 mg bolus) and lidocaine (2 mg/min infusion) reduced risk of severe arrhythmia throughout the course of experimentation.

MRI scanning (1.5 Tesla GE Signa) was comprised of repetitive SSFP and T2 imaging under basal conditions, during an ischemic episode of 25 minutes duration, and following reperfusion to at least 30 minutes. Two short-axis slices, apical to the artifacts from instrumentation, were selected for monitoring. Bulk motion suppression was achieved using 6-fold averaging and peripheral cardiac gating from the pig's tail. A 5" surface coil placed on the pig's chest provided signal reception. As per Foltz's technique, T2 scanning used a robust magnetization-prepared spiral imaging technique with spectral-spatial excitation (6ms refocusing interval, 8 3072-point spiral interleaves over 22 cm providing 1.38mm in-plane resolution, slice thickness = 5 mm, cardiac gating to late diastole/early systole, 2 echo times of 11 and 55 ms, cardiac gating across 3 or 4 cardiac intervals) [(5)].

Wall motion analysis used the center-line technique (Mass plus software 5.1, MEDIS) [(7)], such that the entire perfusion bed of the LAD was included in one of the three sectors. T2 analysis used a single manually-drawn ROI placed in the middle 50% of the dysfunctional wall to minimize partial voluming from ventricular blood (xcinema, Stanford University)[(6)]. Statistical significance in parameter changes between the three animals was evaluated using Student's paired t-test.

Results: As expected for complete occlusion of the left anterior descending artery, a significant reduction in % wall thickening was observed in the anterior septum during ischemia (P=0.02), at 5 minutes post-reperfusion (P = 0.02), and at 30 minutes post-reperfusion (P=0.05). As expected for reversible contractile dysfunction, wall thickening increased significantly at 30 minutes post-reperfusion relative to that observed at 5 minutes post-reperfusion (P=0.04). T2 relaxation was equivalent during ischemia, increased significantly during early reperfusion (mean elevation of 16+/-1%), and tended to return to baseline within 15 minutes of reperfusion. Coronary sinus %O2 reduced during ischemia (Δ%O2 = -18%O2) and was at baseline at 10 minutes post-reperfusion (n = 1).

Summary and Conclusions: Post-ischemic and dysfunctional myocardium demonstrates near-normal resting blood flow and oxygen consumption, with a perfusion reserve which is constrained by the severity of arterial disease [(8)]. Thus one would expect similar T2 relaxation in normal and stunned regions. One might expect T2 modulations during ischemia however the variations were too slight for detectability within our experimental constraints. The T2 elevation post-reperfusion represents most likely an overcompensation of blood oxygen supply during reactive hyperemia, a prediction which is supported by the brevity and extent of the T2 response. Of particular note is the similarity between the T2 elevation of post-ischemic myocardium and the T2 elevation of normal myocardium during adenosine vasodilation [(5)]. Additional physiological instrumentation will clarify transient modulations in O2 supply and demand during early reperfusion.

References:

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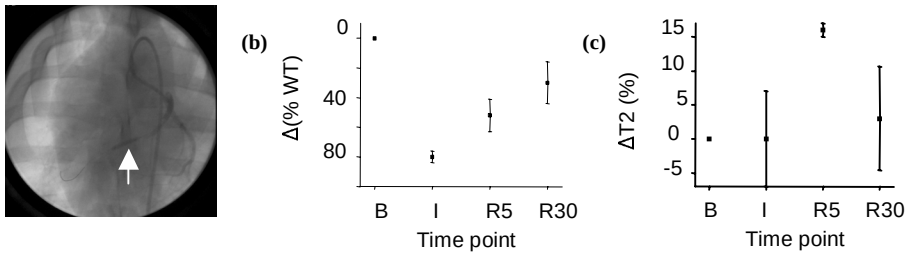

Figure 1: (a) X-ray angiography demonstrating absence of LAD filling distal to the inflated balloon (indicated by arrow) during contrast injection; (b) Relative Δ(% wall thickening) between functional states in; basal (B), ischemia (I), reperfusion at 5 minutes (R5), reperfusion at 30 minutes (R30) (mean and std.dev. across 3 animals); (c) Relative ΔT2 between functional states (mean and std across three animals).