Dynamic Distribution of Extracellular and Blood-Pool Contrast Agents in Acutely Infarcted Myocardium

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Introduction: Myocardial viability has been assessed mainly with delayed-enhanced MR imaging in conjunction with an extracellular-type (ET) contrast agent. Blood-pool (BP) contrast agents, on the other hand, are developed essentially for MR angiography. It would be clinically relevant if BP contrast agents could be used not only for assessment of vascular structure and integrity, but also for evaluation of myocardial viability. BP contrast agents have a much larger molecular weight than ET contrast agents. Thus, their distribution coefficients in normal and infarct myocardium may be very different compared to those of ET contrast agents. Since different distribution coefficients are fundamental mechanism for a MR contrast agent to distinguish infarct from normal myocardium, the present study was to compare dynamic distribution coefficients of BP and ET contrast agents in normal and damaged myocardium in the setting of acute myocardial infarction.

Materials and Methods: Ten pigs underwent 90 minutes of left anterior descending (LAD) coronary artery occlusion followed by 30 minutes of reperfusion. Then hearts were removed from animals and perfused in a Langendorff apparatus. Five pig hearts received a bolus injection of Vistarem (a representative of BP contrast agents, 1.9mmol/kg body wt) into the aorta, and another five received Gd-DTPA (a representative of ET contrast agents, 0.1 mmol/kg). First pass of the contrast agents through the heart was followed using a TurboFLASH T_2*-weighted imaging. Their dynamic distributions were monitored for 50 minutes using a Turbo-FLASH inversion-recovery T_1 imaging. Afterwards, 2 ml of colored microspheres (5-8 x 10^6, 15 µm diameter) was injected into the aortic perfusion line to measure regional myocardial blood flow. The hearts were then sectioned into 0.5 cm thick slices along the short cardiac axis and stained with triphenyl tetrazolium (TTC) to delineate infarct myocardium.

Results: It was found that during first pass of BP contrast agent, normal myocardium showed greatest reduction in T_2* signal intensity, followed by infarct rim (Fig. 1) whereas infarct core had a least decrease in T_2* signal (Fig. 1). T_2* signal reduction was found to be directly related to regional blood flow (Fig. 2). Since myocardial infarction is associated with decrease of blood flow, infarct region appeared hyper-enhanced on T_2* images acquired during first pass of the BP contrast agent (Fig. 3). Moreover, it was found that ΔR_1 ratio (myocardium ΔR_1/blood ΔR_1, a measurement of distribution co-efficient) in normal, infarct rim, and infarct core were not significantly different shortly after Vistarem injection (Fig. 4). However, ΔR_1 ratios in the three regions gradually increased and became statistically different at approximately 20 minutes after contrast injection with infarct rim having the largest ΔR_1 ratio. In contrast, Gd-DTPA-induced ΔR_1 ratios reached the maximum values at 5 minutes after GD-DTPA injection.

Discussions and Conclusions: Distribution coefficients of the BP contrast agent was significantly greater in infarct rim than in normal myocardium, indicating that the BP contrast agent was able to differentiate nonviable from viable myocardium. However, the BP contrast agent entered infarct and normal myocardium with a much slower rate than an ET contrast agent did. This suggests that a longer time should be allowed for delayed enhancement of BP contrast agent to reach maximum effect. In addition, because of reduction of blood flow, infarct myocardium could be delineated on T_2* images acquired during first pass of a BP contrast agent.

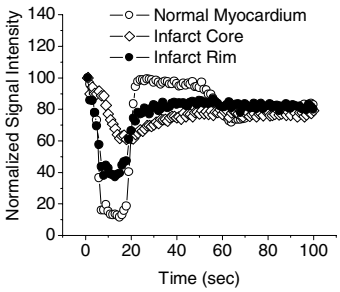


Fig.1. Representative T_2* intensity-time curves obtained from normal myocardium during the first pass of Vistarem. Wash-in of the contrast agent resulted in a significant reduction of T_2* signal intensity in normal myocardium and infarct rim as well as infarct core; however, extent of signal reduction was different among the three regions.

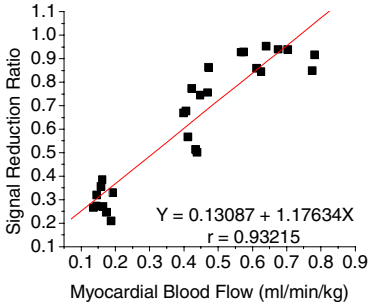


Fig. 2. Correlation between T_2* signal reduction and myocardial blood flow. It is clear that T_2* signal reduction during first pass of Vistarem was linearly related to regional blood flow.

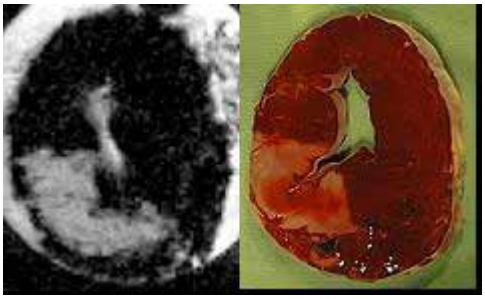
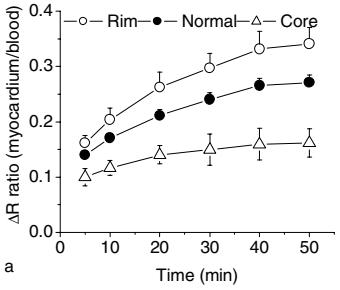


Fig. 3. TTC-stained picture of a pig heart (right panel) and T_2* image acquired when T_2* signal intensity was at minimum level (left panel). Infarct region appeared hyper-enhanced on T_2* perfusion imaging. The hyper-enhanced region matched well with the infarct zone determined by TTC-staining.



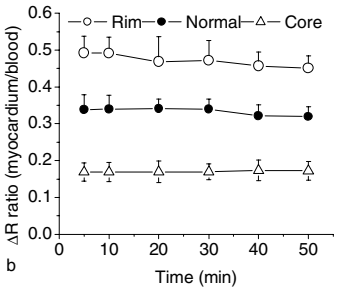


Fig. 4. Comparison of ΔR_1 ratios (myocardium ΔR_1/blood ΔR_1) obtained from infarct rim, infarct core, and normal myocardium following injection of Vistarem (a) and GD-DTPA (b). Note that it ook less than 5 minutes for GD-DTPA to reach its maximum ΔR_1, whereas difference in Vistarem-derived ΔR_1 ratios in the three regions became statistically different at 10 minutes after contrast injection.