INVERSION RECOVERY ECHO PLANAR AND SPIN ECHO MR IMAGING IN ASSESSMENT OF THE KINETICS OF A NEW MR CONTRAST MEDIUM (P846) IN ISCHEMICALLY INJURED MYOCARDIUM

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Purpose: The purpose of this study was to 1) determine the kinetics of a new diffusion/convection (medium size) MR contrast medium, P846, in LV blood, normal, ischemically injured myocardium using inversion recovery echo-planar imaging (IR-EPI), 2) compare the kinetics of P846 with the extracellular MR contrast medium Gd-DOTA and 3) chronologically measure the extent of myocardial injury after P846, using T1-weighted spin-echo imaging (T1-SE).

Materials and Methods: The new macrocyclic gadolinium chelate, P846, represents medium size compounds that diffuse/convect through the vascular endothelium and myocardial matrix at a slower rate than extracellular contrast media. The r1 and r2 relaxivities of P846 are 32 $s^{-1}mM^{-1}$ and 41 $s^{-1}mM^{-1}$, respectively, at 1.5 T, 37 °C in 4% human serum albumin. Rats were subjected to myocardial injury by occluding LAD for 30 min/reperfusion. This occlusion time was designed to obtain non-transmural infarcts. MRI was performed before and after 0.05 mmol/kg P846 (n=8) or 0.1 mmol/kg Gd-DOTA (n=8) administration. A blipped inversion recovery IR-EPI was used to measure regional T1 using the following acquisition parameters: 20 sequential images with: TI=20 to 1100ms, TR≥7.0 s, TE=10 ms, matrix=64X64, FOV=50X50 mm and BW=125 kHz. IR-EPI was performed before and 5, 25, 50, 75 min after injection. Multi-slice T1-weighted spin echo (T1-SE) images were acquired to measure infarct size and regional signal intensity (SI). SI were measure before and 15, 30, 60 and 90 minutes after injection of contrast media. The following parameters were used: TR= 400-550 ms, TE: 12 ms, slice thickness=2 mm, field of view 48x48 mm, data matrix 256x256, number of acquisitions=2. T_1 values were derived from measurement of the inversion recovery null point by fitting regional SI on 20 IR EPI images. R_1, ΔR_1, ΔR_1 ratio and contrast media concentration were calculated in LV blood, normal and injured myocardium. The extent of the injury was measured over 90 min. TTC histochemical staining was used to measure true infarct size.

Results: Changes in ΔR_1 were greater after administration of 0.05 mmol/kg P846 than after 0.1 mmol/kg Gd-DOTA in LV blood (6.3±0.9 s^{-1} versus 0.9±0.1 s^{-1}, P<0.0001), normal (1.7±0.2 s^{-1} versus 0.34±0.03 s^{-1}, P<0.0001) and ischemically injured myocardium (5.4±0.4 s^{-1} versus 1.6±0.1 s^{-1}, P<0.0001). For instance, the greatest change in ΔR_1 occurred in LV blood (6.3±0.9 s^{-1}) 5 min after injecting P846. The change in concentration of Gd-DOTA in LV blood was mono-exponential, while the change in concentration of P846 showed poor fitting to mono-exponential decay, consistent with bi-exponential decay (Figure 1). ΔR_1 ratio of ischemically injured myocardium exhibited an initial increase in value from 1±0.1 at 5 min, 1.7±0.1 at 25 min and 1.67±0.01 at 75 min (P=0.005), suggesting a slow wash-in and wash-out of P846 into injured myocardium. On contrast enhanced T1-SE, ischemically injured myocardium was visualized as a bright region compared to normal myocardium (Figure 2). The differential enhancement was visualized for 90 min on P846, but not on GD-DOTA enhanced images.

Conclusion: The kinetics of P846 and Gd-DOTA are different in myocardium. The wash-in and wash-out of P846 from myocardium was slower than Gd-DOTA, providing longer imaging window (90 min) to measure the extent of injury. The effects of P846 on ΔR_1 of LV blood, normal and ischemically injured myocardium were greater than Gd-DOTA in spite of the difference in the dose between Gd-DOTA (0.1 mmol/kg) and P846 (0.05 mmol/kg) on a molar gadolinium basis. This difference can be attributed to the difference in relaxivity of the agents and/or binding of P846 to proteins.

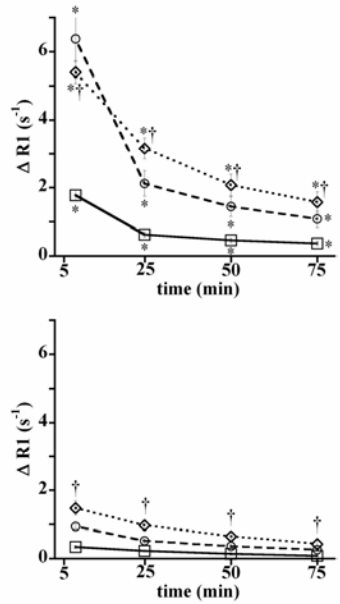

Figure 1. The kinetics of P846 (top) and Gd-DOTA (bottom) are reflected by the regional changes in ΔR_1 ($1/T_{1\text{postcontrast}} - 1/T_{1\text{precontrast}}$) of LV blood (open circle), normal myocardium (open square) and ischemically injured myocardium (open diamond). Data were obtained for 75 min after administration of 0.05 mmol/kg P846 and 0.1 mmol/kg of Gd-DOTA. ΔR_1 was greater in each region of interest after administration of P846 compared with Gd-DOTA. * P=0.01-0.0001 in comparison with values obtained with Gd-DOTA using unpaired Student's t-test. † P=0.01-0.0001 in comparison with normal myocardium using paired student's t-test.

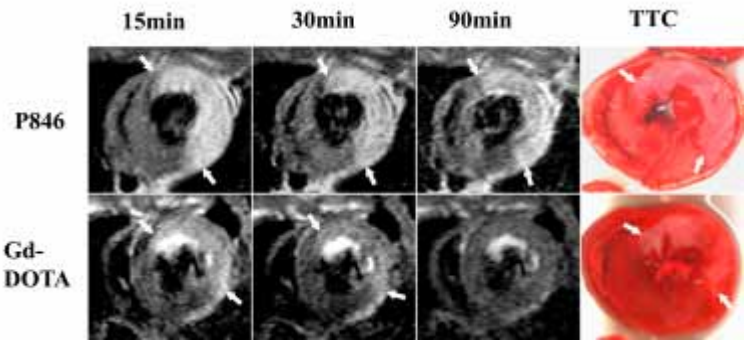

Figure 2. Time-course changes in the extent of the enhanced region on SE-T1 acquired at 15, 30 and 90 min after injection of 0.05 mmol/kg P846 (top images) and 0.1 mmol/kg Gd-DOTA (bottom images). A corresponding slice of triphenyltetrazolium chloride (TTC) histochemical staining is shown on the right side. P846, but not Gd-DOTA, provided high and persistent enhancement of the ischemically injured myocardium over 90 min.