P846 and Gd-DOTA in Characterizing Occlusive and Reperfused (Reversible, Irreversible) Myocardial Infarcts

A. Jacquier[1], M. Bucknor[1], L. Do[1], P. Robert[2], C. Corot[2], C. Higgins[1], and M. Saeed[1]

[1]Radiology, University of California San Francisco, San Francisco, Ca, United States, [2]Radiology, Guerbet Group, Paris, France

Purpose: 1) To determine the potential of a new diffusion/convection MR contrast media P846 in defining viabile, non-viable, occlusive and reperfused myocardial infarcts and 2) To compare the wash-in and wash-out of P846 and Gd-DOTA in occlusive and reperfused infarcts using inversion recovery echo-planar imaging (IR-EPI),

Methods and Materials: 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. In this experimental study rats were subjected to:1) 15min LAD occlusion/2.5h reperfusion (n=8) to produce reversible injury, 2) 30min LAD occlusion/2.5h reperfusion (n=16) to produce non transmural injury, or 3) complete LAD occlusion (n=16). In reversible injury MR imaging was performed before and after administration of 0.1mmol/kg Gd-DOTA, 0.05mmol/kg P846 was injected 1.5h after Gd-DOTA in the same animals. In reperfused and occlusive infarcts MR imaging was performed before and after administration of 0.1mmol/kg Gd-DOTA (n=8) or 0.05mmol/kg P846 (n=8). IR-EPI and T1-SE sequences were repeatedly acquired to measure T_1 and injury extent during 60 min. Blue dye and TTC staining was performed to measure area at risk and true infarct size, respectively. Two sequences were used 1) A blipped inversion recovery EPI sequence (IR-EPI) was used with 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. 2) Multislice T1-weighted spin echo (T1-SE) images were acquired to cover the whole LV before and 15, 30, 60 and 90 minutes after injection of both 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 IR EPI images. R_1, ΔR_1, ΔR_1 ratio and contrast media concentration were calculated in LV blood normal and injured myocardium. On SE-T1 SI ratio and injury extent were measured during 90 min. TTC histochemical staining was used to measure true infarct size.

Results: Reversibly injured myocardium showed no differential changes in T1 and signal enhancement compared to normal myocardium on P846 enhanced IR-EPI and T1-SE images. Irreversible myocardial injury showed immediate enhancement on T1-SE images (Figure 1) and reduction in T1. In contrast, occlusive infarcts appeared as hypo-enhanced core surrounded by enhanced rim after contrast administration. P846 but not Gd-DOTA, provided persistent enhancement of irreversible injury during 60 min. This finding was confirmed by the persistent reduction in T1 of irreversible injured myocardium. ΔR_1 ratio values after injection of P846 and Gd-DOTA from rim and core of occlusive injury did not reach equilibrium during the 60min, suggesting poor delivery. The wash-in and wash-out of P846 and Gd-DOTA are different in this model (Figure 2). ΔR_1 ratio value from the rim and core of the occlusive injury were significantly different after injection of P846 (P=0.0001-0.02) than Gd-DOTA (P=0.0001-0.004).

Conclusion: P846 provides prolonged window of discrimination between occlusive and reperfused myocardial infarcts. The bright rim and dark core in occlusive infarcts persist for one hour after P846, but not after Gd-DOTA. Both MR contrast media differentiate viable (reversibly injured myocardium) from necrotic tissue. By using P846, the dose of MR contrast media can be reduced by half in cases of acute myocardial infarcts.

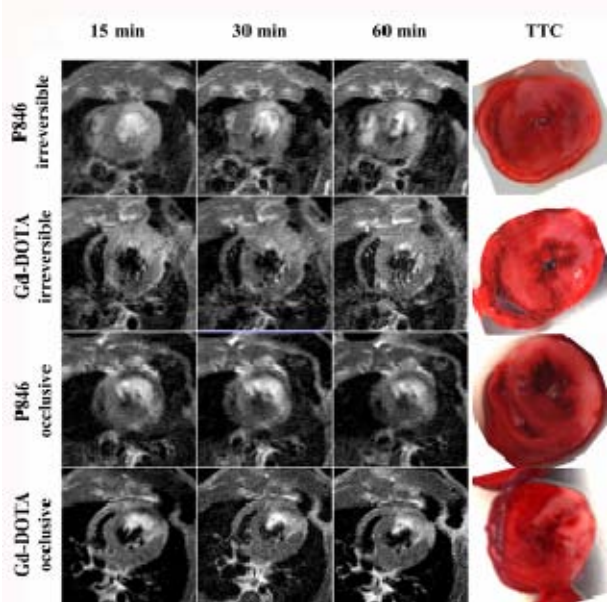

Figure 1: SE-T1 weighted images after injection of 0.05mol/kg P846 and 0.1mmol/kg Gd-DOTA. Reperfused infarcts appear bright immediately after administration of P846 (1st row images) and Gd-DOTA (2nd row images). In contrast, occlusive infarcts appear as hypo-enhanced regions surrounded by hyper-enhanced zones, compared to normal myocardium, after administration of P846 (3rd row images) and Gd-DOTA (4th row images). Gd-DOTA fills the infarcted territory faster than P846. The corresponding TTC slices are shown on the right side.

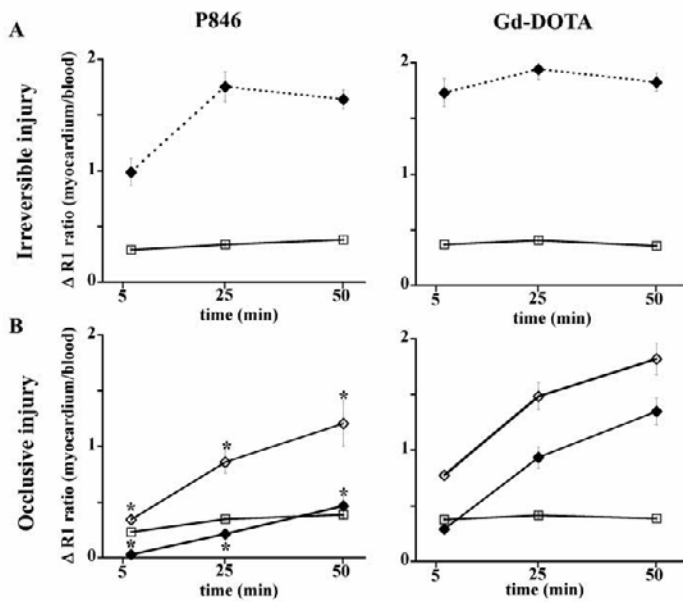

Figure 2 Changes in ΔR_1 ratio (ΔR_1myocardium/ΔR_1 blood) during the 50 min after administration of 0.05mmol/kg P846 (left) and 0.1mmol/kg Gd-DOTA (right) in reperfused (A) and occlusive infarcts (B). The slow wash-in and wash-out of P846 is clearly demonstrated by the increase in ΔR_1 ratio after injection of P846 in infarcted myocardium.