Vistarem Provides Prolonged and Reproducible Visualization of Microvascular Obstruction in Reperfused Myocardial Infarction

O. M. Weber[1], A. J. Martin[1,2], C. B. Higgins[1], M. Saeed[1]

[1]Department of Radiology, University of California, San Francisco, San Francisco, CA, United States, [2]Philips Medical Systems, Cleveland, OH, United States

Introduction: It has been shown that no-reflow zones (as determined 48-96 hours after reperfused coronary occlusion) denote irreversibly damaged tissue, the extent of which correlates well with infarct size [1]. Regions of microvascular obstruction can be seen briefly (90 seconds) in T1-sensitive perfusion sequences after bolus administration of extravascular contrast agents [2]. Due to requirements on imaging speed, spatial resolution in these images is usually moderate at best. The transient effect limits the time available for higher resolution MRI. Intravascular (blood-pool) agents show a different behavior and may offer an alternative opportunity for prolonged detection of microvascular obstruction and micro-embolization. It was thus the purpose of this study to investigate the potential of the intravascular contrast agent Vistarem (P792; currently in clinical trial phase II; Guerbet Group, Aulnay Sous Bois, France) in delineating and sizing microvascular obstruction in reperfused acute myocardial infarction.

Methods: Experiments were performed on six farm pigs (30-32 kg). To create a myocardial infarction, a midsternal thoracotomy was performed and the left anterior descending coronary artery was dissected and occluded for 2 hours, followed by reperfusion. The chest was closed and sutured, and the animals were allowed to recover. Three to four days after surgery, MRI was performed under anesthesia on a 1.5 T clinical MR imager (Philips Medical Systems, Best, the Netherlands). Steady-state free-precession (SSFP; TR, 3.6 ms; TE, 1.8 ms; FOV, 260 mm; matrix, 176) imaging was performed at baseline and within 2 minutes of contrast agent administration. T1-weighted turbo-spin echo imaging (TR, 1 heart beat; TE, 20 ms; FOV, 240 mm; matrix, 176) was performed at baseline; at 20 and 40 minutes after administration of 0.026 mmol/kg Vistarem; as well as 20 minutes after administration of 0.1 mmol/kg Dotarem (Gd-DOTA; extravascular contrast agent; Guerbet). Breath-held imaging was performed in short axis (SSFP and T1-TSE) and long axis views (T1-TSE) covering the entire heart. Before administration of Dotarem, at least one hour passed for the wash-out of Vistarem.

Images were processed in ImageJ (Research Services Branch, NIH, Bethesda, MD). Regions of interest were manually drawn in normal myocardium, at the rim of the infarct, and at the core of the infarct. Signal intensity (SI) and size of normal myocardium, rim, and infarct were determined in all slices. Two-sided Student's t-test and non-parametric repeated measures analysis of variance (Friedman test) with Dunn's multiple comparisons post-test were performed at a significance level of 5%.

Results: Immediately after bolus injection of Vistarem, all animals showed hypo-enhancement in the zone of microvascular obstruction on the SSFP images. SI was 20 ± 9% lower than in the normally enhancing myocardium (p=0.02). After Gd-DOTA, only three animals (50%) showed hypo-enhancement on the SSFP images. In these animals, a signal loss of 12±4% was observed (p=0.03), and the area of hypo-enhancement was smaller than after administration of Vistarem (132 ± 17 mm^3 vs. 173 ± 6 mm^3; p=0.02).

Table 1 summarizes the signal intensity values on the T1-TSE images over time, expressed as percentage of SI in normal myocardium. The size of Vistarem-enhanced region at 40 minutes was 18.8±5.1% of the total LV mass, and showed still a distinctive core region. Twenty minutes after administration of Gd-DOTA, the micro-vascular obstruction was visible in three animals (50%), even though the core region had started to fill in two of those animals.

SSFP and T1-weighted TSE showed similar hypo-enhanced areas (140 ± 40 mm^3 vs. 148 ± 42 mm^3; p=n.s.) 2-5 minutes after injection of Vistarem.

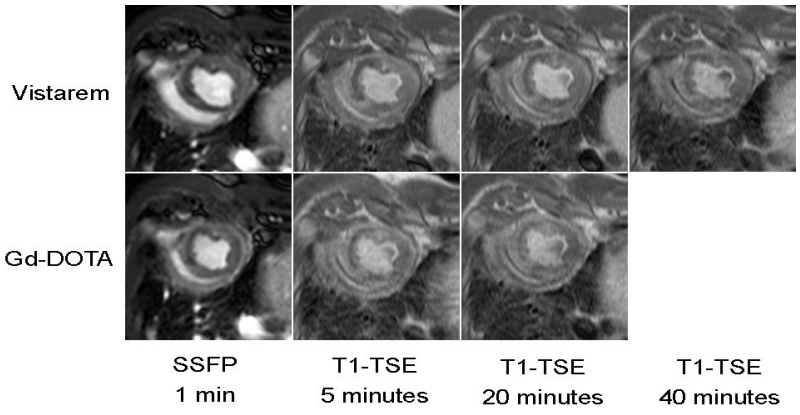

Figure 1: *SSFP and T1-TSE images show microvascular obstruction after administration of both intravascular and extravascular contrast agents. Note the better visibility and clearer delineation after administration of P792 (top row).*

Table 1: *Relative signal intensity in the core and in the rim of the infarcted zone. Values are normalized to normal myocardium (i.e., normal=100).*

	Core	Rim
Vistarem (5 minutes)	83±12	122±11 [a]
Vistarem (20 minutes)	90±11	133±16 [a]
Vsitarem (40 minutes)	99±12	145±13 [a,b]
Gd-DOTA (20 minutes)	130±44	153±34 [b]

a, p<0.05 vs core; b, p<0.05 vs normal

Discussion: After injection of Vistarem, both SSFP and T1-TSE showed microvascular obstruction as a hypo-enhanced region in all subjects. The delineation persisted for more than 40 minutes. After injection of Gd-DOTA, 50% showed underperfusion immediately after contrast agent injection. At 20 minutes, only one animal showed lower SI in the core than in the normal myocardium, and two others showed SI lower at the core than at the rim, but higher than in normal myocardium. The other 50% of animals showed normal enhancement at the core.

Conclusion: Vistarem provided prolonged delineation of microvascular obstruction. It also showed higher occurrence rate of microvascular obstruction compared to the extravascular contrast agent. Vistarem is therefore suitable for predicting left ventricular remodeling.

Acknowledgment: This study was supported by grants from NIH (RO1HL07295) and Guerbet Group, France.

References: [1] Kaul S, Ito H. Circulation 2004; 109:310. [2] Wu KC, Zerhouni EA, Judd RM, et al. Circulation 1998; 97:765.