VALUE OF FIRST PASS PERFUSION AND DELAYED CONTRAST ENHANCEMED MR IMAGING IN DETECTING MICROINFARCTION: HISTOPATHOLOGIC CONFIRMATION

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INTRODUCTION: Coronary microembolization is a significant and frequent complication of atherosclerotic plaque rupture in acute coronary syndromes and coronary interventions. Clinical studies have confirmed that microinfarction occurs in almost one fourth of patients undergoing coronary intervention. This experimental study was performed to simulate the clinical scenario, where different sizes of debris and thrombus scatter downstream from coronary plaques.
PURPOSE: Embolic agents with 100-300µm sizes were administered in a select segment of LAD coronary artery to create microinfarction. The potential of contrast enhanced MR imaging in assessing microinfarction and perfusion has been tested in acute (1hr) and subacute (7days) phases.
MATERIALS AND METHODS: The hybrid XMR suite (Philips Medical Systems) was used to deliver and assess the effect of the embolic agents. Under X-ray fluoroscopy, the catheter (3F) was placed in the LAD coronary artery distal to first diagonal branch. Under MR imaging, pigs (n=6) received the embolic agents ($n=10^4$, 100-300 µm) to induce microinfarction. One hour and one week after delivery of embolic agent, first pass perfusion and delayed contrast enhanced MRI were performed. MR perfusion imaging were obtained starting (5-6s) prior to injection of 0.1 mmol/kg Gd-DOTA and continuing for 70s using a saturation recovery GRE sequence. The imaging parameters were TR/TE=4.5/2.2 ms, FOV=26x26cm, matrix size=128x128, α=20°. Max upslope, peak signal intensity and time to the peak) will be used to determine regional myocardial perfusion. Delayed contrast enhanced imaging using a IR-GRE sequence, in short- and long-axis views encompassing the heart (18-20 slices). The extracellular agent 0.15mmol/kg Gd-DOTA or 0.026mmol/kg blood pool agent vistarem were administered to highlight microinfarction. The imaging parameters were: TR/TE=5.2/1.5 ms, slice thickness=3-5 mm, spacing=0, α=15°, FOV=26x26 cm and matrix size=256x162. Following the second imaging session, animals were euthanized and tissue samples were collected and stained to confirm the presence of embolic agents in myocardium and microinfarction.
RESULTS: First pass perfusion showed the embolized region as hypoenhanced region at 1 hr and 1 week. The extent of perfusion deficit was substantially smaller at 1week than 1 hr (**Fig. 1,2**). Perfusion parameters in acute and subacute microinfarction are shown in Table 1. Acute microinfarction was visulalized in 3 animals on delayed Gd-DOTA and 2 animals on vistarem enhanced MR imaging. In subacute phase, microinfarction was visualized in all animals using extracellular agent. The size of hyperenhanced microinfarction was 5±2% LV (SI mean + 2SD SI of remote myocardium) and confirmed on TTC. Microembolization resulted in a large variation in the size of microinfarction on delayed contrast enhanced MR imaging (**Fig. 2**). The underlying mechanisms for different hyperenhanced microinfarction sizes are: 1) clustering of injected embolic agents, 2) asymmetrical branching geometry of the coronary vessels and 3) adjacent arterioles occluded.

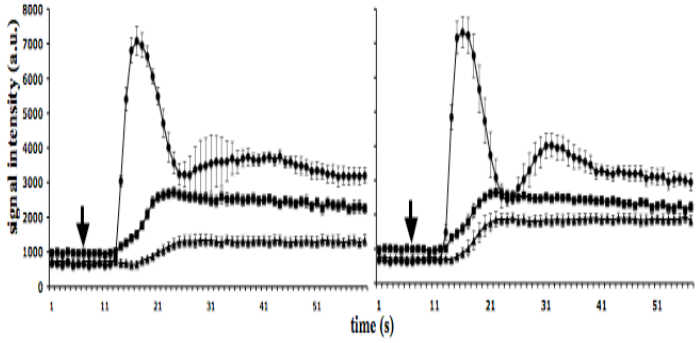

Fig. 1. Plots show the first passage of 0.1 mmol/kg Gd-DOTA (arrow) (in acute (left) and subacute (right) microinfarction. Top curves show the blood pool, middle curves the remote myocardium and lower curves the embolized region, all values are mean±SEM. The embolic agents caused a persistent decline in myocardial perfusion. Note the improvement in perfusion at 1 week after embolization.

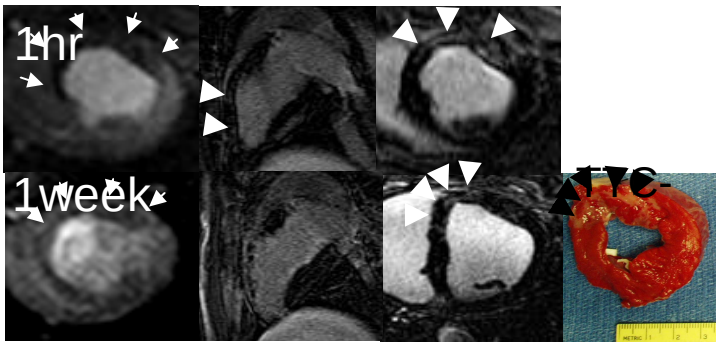

Fig. 2. MR images at 1hr (top) and 1week (bottom) show the heterogeneous embolized region on first pass of Gd-DOTA (left) and on delayed contrast enhancement in long (middle) and short (right) axis views. Note the perfusion deficit is greater at 1hr than at 1 week (left images, arrowheads). Corresponding TTC (right) slice shows discrete microinfarction in anteroseptal wall (arrows).

Table 1. Myocardial Perfusion in Acute and Subacute Microinfarction:

	Acute			Subacute		
Parameters	Blood	Remote	Infarct	Blood	Remote	Infarct
Max upslope (s^{-1})	1652±110	242±32	108±13	2198±119	289±25	208±16
Max SI (a.u.)	7507±695	2915±227	1511±153	7388±102	2753±102	2116±172
Time to peak (s)	5.3±0.7	14.3±1.3	23.7±2.5	5.1±0.7	12.0±0.8	18.4±2.5

Microscopic examination revealed presence of the embolic agents in various sizes of coronary arteries. The embolic agents are clustered within the vascular lumen. Adjacent myocytes show discrete early ischemic damage, denoted by dark purple discolorization, as shown on Masson's trichrome stain in the acute phase (9hr post delivery). Subacute microinfarction (7 days) was partially healed. The obstructed vessels showed evidence of inflammation and thrombi formation (**Fig. 3**). The core of the embolic territory showed necrotic myocytes and the margin granulation tissue.

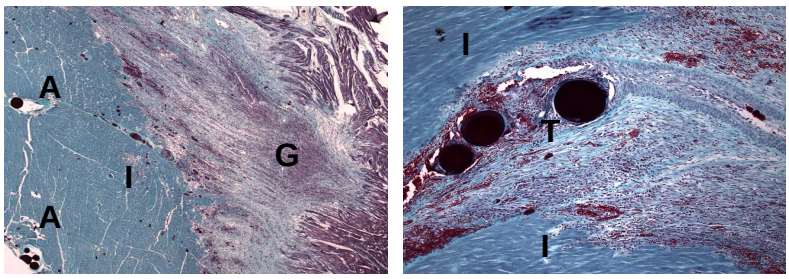

Fig. 3. Histological sections show partially healed microinfarction 7 days after delivery of the embolic agents (left panel, 40X). The center of the infarct is comprised of necrotic muscle (I) and the margin granulation tissue (G), indicating the start of the repair process. The embolic agents are shown occluding a vessel (right panel, 100X) and associated with organizing thrombus (T).

CONCLUSION*:* Acute and subacute microinfarction caused suppression in myocardial perfusion, most likely due to obstruction of microvessels. The embolic agents were visualized in the coronary tree. Perfusion imaging is a suitable technique for detecting microinfarction immediately after coronary intervention. Delayed contrast enhanced MR imaging partially discriminate acute discrete microinfarction, but all cases with subacute microinfarction due to the loss of membrane integrity of ischemic myocytes.
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