Manganese-enhanced MRI of acute cardiac ischemia and chronic infarction in pig hearts

V. V. Kupriyanov[1], Y. Yang[2], M. L. Gruwel[1], X. Yang[2], and J. Sun[1]
[1]Institute for Biodiagnostics, Winnipeg, Manitoba, Canada, [2]University of Manitoba, Winnipeg, Manitoba, Canada

Aim of the study: To assess infarction development in a large animal model using Mn-enhanced MRI and comparison with histological data.

Background: Mn^{2+} is a paramagnetic ion, which increases longitudinal relaxation rate (1/T1) of water protons thereby increasing signal intensity. It is an intracellular type of contrast agent, which accumulates inside viable cells being driven by sarcolemmal membrane potential, while damaged cells are unable to concentrate Mn^{2+} due to depolarization and leakiness of their cell membranes [1].

Methods: ***1. Animal model.*** In domestic pigs weighing 25-35 kg (n = 26) 1st and 2nd diagonal branches of the left anterior descending coronary artery (LAD) were ligated. Three, 7, and 21 days after ligation following sternotomy, hearts were excised and perfused *ex vivo* with a 50:50 mixture of blood and Krebs-Henseleit buffer. Acute ischemia was produced by permanent ligation of the same branches in vivo with subsequent excision of hearts 30 min thereafter. Cardiac function was recorded via the LV balloon. At the end hearts were sliced along the short axis and stained in 2% triphenyltetrazolium chloride (TTC) to determine infarct (IA) and normal (NA) areas, which were further analyzed using hematoxyline-eosin (H&E) and trichrome Masson (collagen) staining. ***2. MRI***. Ex vivo experiments on beating hearts were performed on a 7T magnet, interfaced to a Bruker Biospec console using spin-echo (2.0 ms SINC3 pulses, a FOV of 16x16 cm2, TE = 8 ms, data matrix a 128x128 points). The heart and 2 reference test tubes containing H_2O and H_2O + 10 mM $CuSO_4$ were placed into the perfusion chamber within the birdcage coil. The signal acquisition was gated by the LV dP/dt (TR=800 ms). Six 8-mm thick slices separated by 2 mm were obtained. Following the baseline image, 0.2 mM $MnCl_2$ was added and serial images were taken every 5 min over a 45-min period. Signal intensities for each slice were normalized to those of the H_2O reference.

Results: Intensity (I) time courses were fit by an exponential function: $I=I_0+\Delta I_{max}[1-\exp(-t/t1)]$ (Figs. 1 & 2). The rates of I increases ($\Delta I_{max}/t1$) and maximal increases (ΔI_{max}) were significantly lower in the ischemic/infarct areas (Table & Figs). These parameters showed trend to increase upon infarction progression, which is consistent with partial perfusion recovery in the IA. TTC staining revealed necrotic areas after all infarctions (3-21 days) and no necrosis after acute ischemia. Histological examination showed replacement of cellular material with collagen and some revascularization of the IA.

Conclusions: $MnCl_2$ highlights ischemic areas due to low perfusion (<5%) while in the infarct areas, in which perfusion was substantial, myocytes viability is a dominant factor governing contrast distribution.

Parameter	Area	Group (n)			
		Acute (5)	3-d (6)	7-d (7)	21-d (4)
ΔI_{max}, %	NA	137±16	100±12	101±2	148±6
	IA	40±0	39±6	51±5	57±3
$\Delta I_{max}/t1$,	NA	18±5.4	19.5±5.8	16±1.0	23.5±2.4
%/min	IA	2.1±0.3	6.6±2.8	6.9±2.0	12.1±1.9

Reference: 1. Wendland MF. *NMR Biomed,* **17**:581-594;2004.

Fig. 1. Acute ischemia

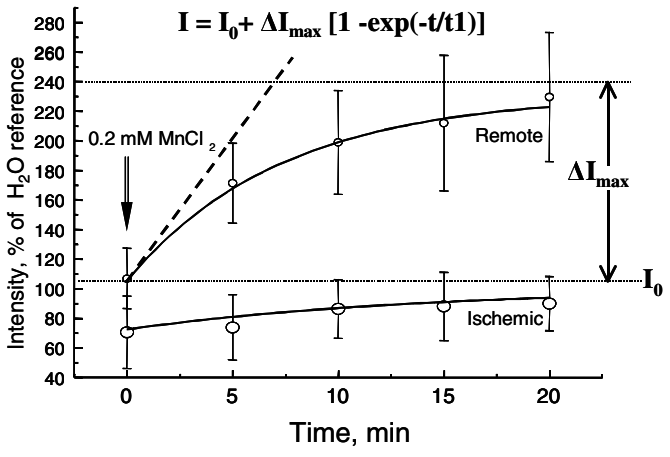

Fig. 2. Chronic infarction, 7 days