Detection and Validation of Localized Chronic Iron Deposition within Non-Reperfused Myocardial Infarctions

Avinash Kali[1,2], Ivan Cokic[1], Hsin-Jung Yang[1,2], Richard Tang[1], and Rohan Dharmakumar[1,3]

[1]Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, United States, [2]Bioengineering, University of California, Los Angeles, CA, United States, [3]Department of Medicine, University of California, Los Angeles, CA, United States

Target Audience – Scientists and clinicians studying myocardial infarctions

Purpose – Chronic iron deposition has been shown to occur within reperfused hemorrhagic myocardial infarctions (MIs)[1,2], and could be a source of prolonged inflammatory activity within MI territories[1]. However, whether the stagnant blood within the permanently occluded vasculature in non-reperfused infarction also could lead to chronic iron deposition is unknown. In this study, using a controlled canine model, we have investigated whether chronic iron deposition could occur in non-reperfused MIs using T2* CMR and validated our findings with standard histological methods.

Methods – Canines (n=19) underwent permanent ligation of the left anterior descending artery and were recovered for 7 days. Breath-held, ECG-gated, 2D short axis T2* and late-gadolinium (LGE) images were acquired as contiguous slices with a clinical 3T system (Verio, Siemens Healthcare, Erlangen, Germany) at 7 days (acute) and 4 months (chronic) post-MI. T2* acquisitions were as follows: multi-gradient echo; TR=12ms; 6 TEs ranging from 2.4ms to 9.9ms with ΔTE=1.5ms; flip angle=10°; and LGE acquisition were as follows: IR-prepared FLASH; TI optimized to null remote myocardium; TR/TE=3.5/1.75ms; flip angle=25°. Commonly used imaging parameters were slice thickness = 6mm and in-plane resolution = 1.3x1.3mm^2. Presence of iron within MI territories was detected on T2*-weighted images using the Mean – 2 Standard Deviations criterion relative to a reference ROI drawn in the remote myocardium[1,3]. Following the chronic MI scan, animals were sacrificed and myocardial slices were stained with TTC to visualize gross histological evidence of chronic iron deposition. Subsequently, Perl's staining was performed for histopathological validation of iron deposition.

Results – Significant T2* losses were observed within the MI territories in 13 of the 19 canines at 7 days post-MI, and in all canines at 4 months post-MI. At day 7 post MI, mean T2* value of the infarcted myocardium was 42.6±10.5% lower than that of remote myocardium (16.7±3.4ms vs. 28.8±3.0ms, p<0.01); and at month 4 post MI, T2* value of the infarcted myocardium was 39.1±12.1% lower than that of remote myocardium (19.3±4.1ms vs. 31.7±1.8ms, p<0.01). Mean infarct and iron volumes (as percentage of total LV volume) were 14.7±8.7% and 2.1±1.6% respectively at 7 days post-MI, and 7.2±5.6% and 1.9±1.1% respectively at 4 months post-MI. Ex-vivo TTC staining at 4 months post-MI showed pale brown discoloration within the infarct core indicating chronic iron deposition. Perl's stain further confirmed iron deposition within chronic MI territories.

Conclusions – Chronic iron deposition can occur within non-reperfused MIs. The long-term effects of these depositions in the heart remain to be investigated.

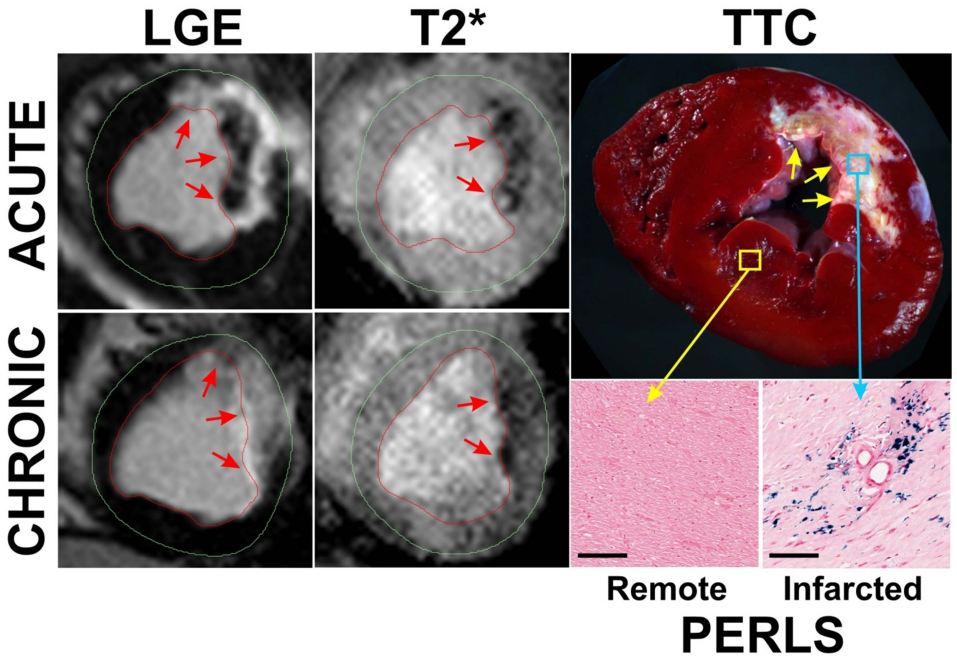

Figure 1: *Representative LGE images and T2*-weighted images (TE=6.9ms) acquired at 7 days (acute) and 4 months (chronic) post-MI from the same canine subjected to permanent ligation of LAD are shown. Arrows point to the site of infarction on LGE images and iron deposition on T2*-weighted images. T2* losses were observed within infarcted territories during both acute and chronic phases of MI indicating iron deposition. Ex-vivo TTC staining showed pale brown discoloration in the core of the infarcted territories. Microscopic histopathology using Perls staining (scale bars = 200μm) showed significant iron deposition within infarcted territories but not in remote myocardium.*

References: [1]Kali A et al, Circ Cardiovasc Imaging 2013; [2]Ye Y X et al, Circulation 2013; [3]Kumar A et al, JACC Cardiovasc Imaging 2011