Imaging intramyocardial hemorrhage following ischemia-reperfusion injury: A Translation Study

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Introduction – Intramyocardial hemorrhage is a common pathophysiological manifestation of ischemia-reperfusion (I-R) injury following reperfusion into severely ischemic myocardium. Although T2* [1,2] and T2-weighted [3,4] CMR are the commonly used techniques to detect hemorrhage, there is currently no general agreement on the most reliable technique. Here, we investigate the effectiveness of T2-STIR images, T2 and T2* maps in reliably detecting hemorrhage in an animal model and a pilot patient population.

Methods – *Animals:* Fourteen canines were subjected to I-R injury (3 hours of 100% LAD occlusion followed by reperfusion). Animals underwent CMR on day 7 following reperfusion (1.5T Siemens). Multi-GRE (T2*-weighted; TR = 220ms; 6 TEs from 3.4ms to 18.4ms with ΔTE = 3.0ms), T2-prepared SSFP (T2-weighted; TR/TE = 2.2/1.1ms; T2-prep times = 0, 24 and 55ms), T2-STIR (T2-weighted; TR = 2-3 R-R intervals; TE = 64ms; TI = 170ms) and Late Enhancement (LE; IR-prep SSFP; TR/TE = 1.75/3.5ms) images of contiguous short-axis slices covering the entire LV were acquired. Image resolution was 1.3 x 1.3 x 8.0mm^3 for all the scans. *Patients:* Fourteen patients (3 women; mean age = 58±8 years) with first ST-elevated myocardial infarction underwent CMR (1.5T Siemens) on day 3 post angioplasty. Multi-GRE (TR = 240ms, 6 TEs from 2.6ms to 13.6ms with ΔTE = 2.2ms), T2-STIR (TR = 2-3 R-R intervals; TE = 61ms; TI = 170ms) and LE (IR-prep FLASH; TR = 1 R-R interval; TE = 3.3ms) images of the whole LV were acquired along the short-axis. Image resolution was 1.4 x 1.4 x 10.0 mm^3 for all the scans. *Image Analysis:* T2* and T2 maps were constructed by fitting the multi-GRE and T2-prepared SSFP images respectively to monoexponential decay. Remote myocardium was defined as the region showing no hyperintensity on LE images. Hemorrhage (Hemo+) was defined on T2*-weighted images (TE = 18.4ms for animals and 13.6ms for patients) as the infarcted region with mean signal intensity (SI) at least 2 standard deviations (SD) below that of reference ROI drawn in Remote myocardium. Non-hemorrhagic infarcts (Hemo-) were defined as the infarcts not positive for hemorrhage on T2*-weighted images. T2-STIR SI, T2* and T2 values were measured from the Remote, Hemo+ and Hemo- myocardium and compared. A two-tailed p-value <0.05 was considered to be statistically significant.

Results – *Animals:* Ten dogs were positive for Hemo+ infarcts, while four dogs were negative (Hemo- infarcts). Representative T2* map, T2 map, T2-STIR and LE images obtained from a dog (day 7 post reperfusion) with Hemo+ infarct are shown in Figure 1A. Mean T2* of Hemo+ was significantly lower than those of Remote and Hemo- myocardium (-39%, p<0.001, Fig. 1B and C), but no significant differences were observed between mean T2* of Hemo- and Remote (p=0.27). Mean T2 and T2-STIR SI of both Hemo+ and Hemo- myocardium were significantly higher than that of Remote myocardium (T2: 17% and 29%; T2-STIR: 59% and 31%; p<0.001 for both cases). Also, T2 and T2-STIR SI of Hemo- were significantly higher than those of Hemo+ (p<0.001). *Patients:* Eight patients (2 women) sustained Hemo+ infarcts, while six patients sustained Hemo- infarcts. Representative T2* map, T2-STIR and LE images obtained from a patient with Hemo+ infarct are shown in Figure 2A. Consistent with the observations from animal studies, mean T2* of Hemo+ in patients was significantly lower than those of Remote and Hemo- myocardium (-46%, p<0.001, Fig. 2B and C), while mean T2* of Remote and Hemo- were not significantly different (p=0.61). Mean T2-STIR SI of both Hemo+ and Hemo- remained significantly elevated compared to Remote (78% and 33%, p<0.001). Also, mean T2-STIR SI of Hemo- was significantly higher than that of Hemo+ (p<0.001).

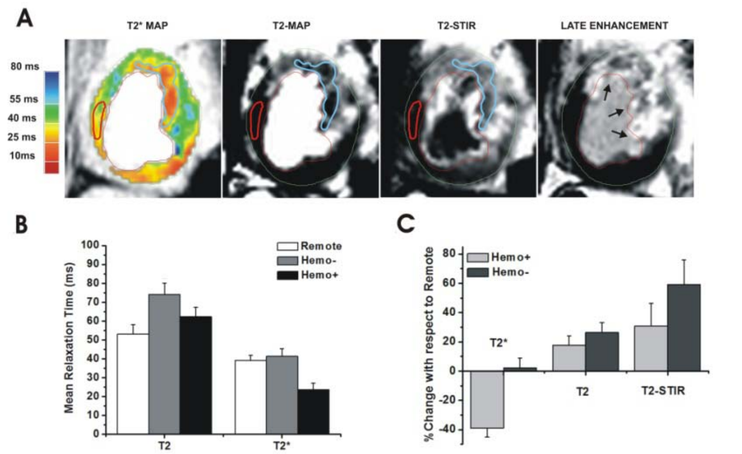

Figure 1: (A) Representative T2* map, T2 map, T2-STIR and LE images acquired from a canine with Hemo+ infarct on day 7 post reperfusion are shown. (B) Mean T2 and T2* values obtained from Remote, Hemo+ and Hemo- myocardium are shown. (C) Relative changes in T2, T2* and T2-STIR SI in Hemo- and Hemo+ myocardium with respect to Remote are shown

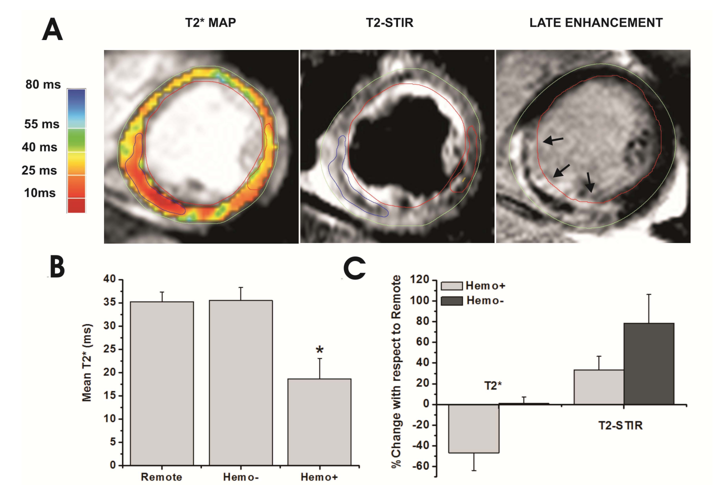

Figure 2: (A) Representative T2* map, T2-STIR and LE images acquired from a patient with Hemo+ infarct on day 3 post angioplasty are shown. (B) Mean T2* values obtained from Remote, Hemo- and Hemo+ myocardium are shown. (C) Relative changes in T2* and T2-STIR SI in Hemo+ and Hemo- myocardium with respect to Remote are shown.

Conclusions – This translational study showed that T2* decreases significantly in the presence of acute myocardial infarction with reperfusion hemorrhage. However, T2 and T2-STIR SI remain significantly elevated even in the presence of hemorrhage, likely due to their sensitivity to edema. We conclude that T2* is likely the most effective technique for reliably detecting reperfusion hemorrhage.

References – [1] O'Regan D P et al, *Heart*, 2010; [2] Kumar A et al, *13th Annual SCMR Scientific Sessions*, 2010 [3] Ganame J et al, *Eur Heart J*, 2009, [4] Payne A R et al, *Circ Cardiovasc Imaging*, 2011.