Manganese Infusion During Acute Ischemia Delineates Myocardial Area at Risk up to 2 Hours After Reperfusion

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Introduction

It has been recently demonstrated in canines that $MnCl_2$ can be utilized as a contrast agent, which enhances the myocardium and delineates ischemic areas, without significant cardiac depressive effects. Manganese utilizes calcium channels to traverse the cell membrane and the tissue contrast generated by this intracellular agent can last for several hours. These properties can be potentially used for determining the myocardial area at risk with MRI after a patient has been stabilized following an ischemic episode, during which the agent is injected. The purpose of this study was to determine if $MnCl_2$ could accurately delineate the ischemic myocardial area at risk two hours after the end of an ischemic episode.

Methods

Nine anaesthetized beagles underwent a 90 minute total LAD occlusion followed by reperfusion. Five minutes into the occlusion period, $MnCl_2$ was infused for 12 minutes (total 150μM). The blood pressure and heart rate were continuously recorded. MR imaging was performed at 1.5T with CV/i scanner (GE Medical Systems, Milwaukee, WI) and the standard 4-element phased-array knee coil. During the $MnCl_2$ infusion and two hours post-reperfusion, T_1-weighted images were acquired with phase sensitive inversion recovery protocols similar to those demonstrated recently for gadolinium delayed enhancement imaging (TI 350ms, BW 32kHz, TE 3.4ms, TR 7.8ms, in-plane resolution 1.0x0.9mm, slice thickness 8mm). To mark the myocardial ischemic area at risk for comparing MRI against a gold standard, fluorescent microspheres (Duke Scientific Corporation, Palo Alto, CA) were injected in the left atrium immediately prior to sacrifice with the LAD re-occluded. Black light photography was used for visualizing the microspheres and manually segmenting the 4mm thick ex-vivo slices. TTC staining was performed for ex-vivo infarct imaging. Area at risk is reported as percent of the left ventricular myocardial region.

Results

Typical infarct histopathology (left), area at risk (middle) and in-vivo MRI (right) images are shown in Figure 1. Note that the infarcted area (white arrow, white area) is smaller than the area at risk (green arrow, area lacking fluorescent green microspheres), which in turn matches with the in-vivo manganese MRI (red arrow, light gray area). For the MRI image, gray scale was inverted to emphasize differences between blood (bright white), the area at risk (light gray), and the normal myocardium (dark gray). Summary comparison data between MRI and microspheres are shown in Figure 2 in the form of correlation (left) and Bland-Altman (right) plots. Blue squares depict data acquired during the occlusion and red triangles depict data acquired two hours post-reperfusion.

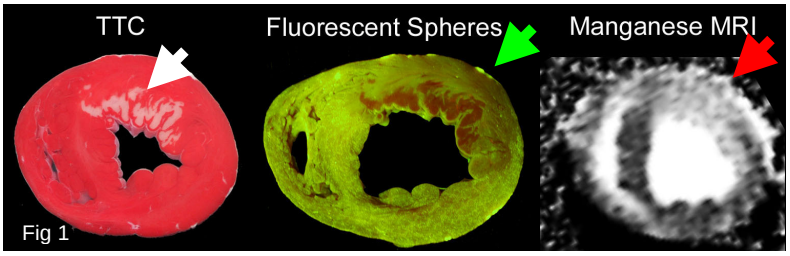

Fig 1

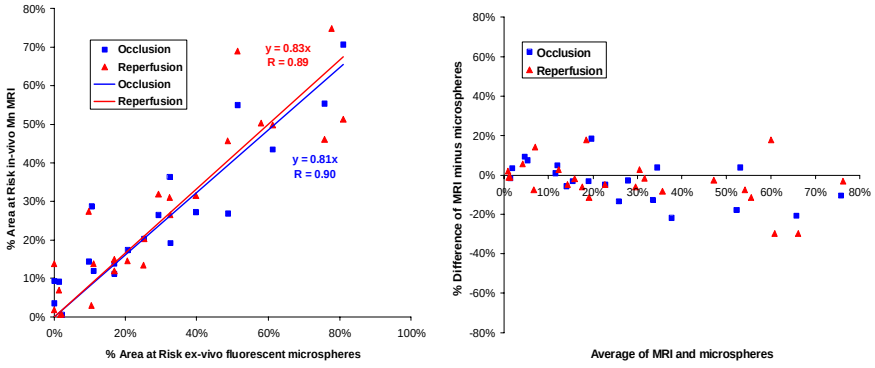

Fig 2

Conclusion

The area at risk in images acquired during the $MnCl_2$ infusion (concurrent to the occlusion) as well as in images acquired two hours post-reperfusion correlate well with the area at risk demarked ex-vivo by fluorescent microspheres. Marking the area at risk during the episode and performing the imaging at a later time could potentially allow MRI applications similar to those found in nuclear imaging methods.