MRI of myocardial infarction with Vasovist: A potential marker for permeability in MI

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Introduction. MRI plays an increasingly important role in cardiac imaging for the non-invasive assessment of myocardial infarction (1). Contrast agent uptake and distribution have shown high sensitivity and specificity to many pathological changes that are not detectable by anatomical imaging (2,3). Gd-DTPA is one of the most used clinical MR contrast agents because allows visualizing ischemic and necrotic myocardium on late gadolinium enhancement MRI. Although Gd-DTPA has been shown to be excellent to delineate the extent of ischemic and infarcted areas, it does not provide any insight of the remodeling processes. For this reason, we sought to investigate gadofosveset, an albumin binding contrast agent (Ablavar, Lantheus Medical Imaging, USA) (4), for the assessment of permeability in an MI mouse model at 7T. MRI R1 mapping was use for myocardial tissue characterization. This technique provides highly accurate measurements of the extension and strength of enhancement area and this lends itself for the comparison of Gd-DTPA and gadofosveset. In this study, using similar concentrations of Gd-DTPA and gadofosveset, the latter revealed higher relaxation rates but comparable areas of enhancement. Also, in contrast to Gd-DTPA, there was a decline in R1 values within the enhanced area with gadofosveset, suggesting recovery of the endothelial cells.

Method. 8 C57Bl6 mice underwent permanent left coronary artery ligation. Gd-DTPA and gadofosveset were administrated intra-peritoneal (IP) at a dose of 0.75 mmol/kg at time points of 3 days, 1 week and 3 weeks after MI. Gadofosveset was administered 24 hours after Gd-DTPA to allow for complete blood clearance. MRI images were obtained on a 7T horizontal bore MR scanner (Agilent, Inc., Palo Alto, CA). An inversion recovery (Look-Locker) LGE sequence was used to study the area of enhancement and the related R1 values. At each time point of the study and for each agent, R1 values were obtained at 30, 45, 60, 75 and 90 minutes after injection. Imaging parameters included: FOV of 20x25mm^2, 1mm thickness, 30 phases, matrix size 128x128, 1 slice, flip angle=10°, IR = 2500ms, cardiac cycle ≈ 120ms, acquisition time ≈ 13min. R1 values were estimated for blood, remote myocardium and infarcted myocardium.

Results. The extension of enhanced infarcted areas by MRI was not significant different (P>0.05) between Gd-DTPA and gadofosveset at 3, 10 and 21 days post MI. At 10 and 21 days post MI, however, areas resulted in higher variability than at 3 days. The average percentage difference resulted -1±3.6% at 3 days, 0.8±5,8% at 1week and 3.1±5.9% at 3weeks. The associated R1 values for the 3 time points and from 30min to 90min are reported in figure 1 for infarct myocardium A), blood B) and remote myocardium C). Higher R1 values were found for gadofosveset for all measured parameters and time points and enhancement was maintained for longer compared to Gd-DTPA. Also, R1 values were significantly decreased from 3 to 10 days and from 3 to 21 days (P<0.05) in infarcted regions enhanced with Vasovist at all time points. In blood and remote myocardium gadofosveset did not present such drop. When using Magnevist no significant differences were found between R1 values at any time points in any tissues. Figure 1 shows typical enhancement at 3, 10 and 21 days in an infarcted mouse model using the two agents.

Discussion and Conclusions. The study is assessing the albumin contrast agent gadofosveset as a way of investigating myocardial infarction mice model. The agent is bounded to albumin while in blood and transported into infarcted areas with similar diffusion mechanisms to that used by Magnevist. The drop in R1 from 3 to 10 and 21 days experienced with Vasovist is suggesting a recovery of endothelial cells at late stage of MI leading to a decrease of permeability. Such endorsement reflects Vasovist unique permeability properties. Also, R1 values are always higher than that of Magnevist for the three investigated tissues thus making Vasovist a valuable candidate to replacement Gd-DTPA in MI investigations. The properties of gadofosveset are only recently emerging making the albumin agent increasingly applicable to different medical fields.

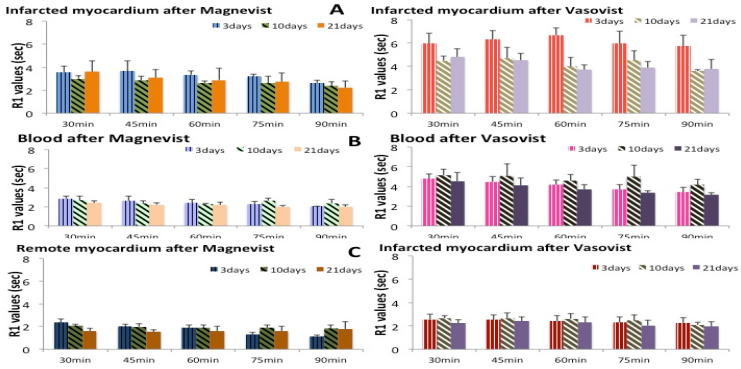

Fig1: R1 values for infarcted myocardium A), blood B) and remote myocardium C) after IP injection of similar concentration of Magnevist and Vasovist.

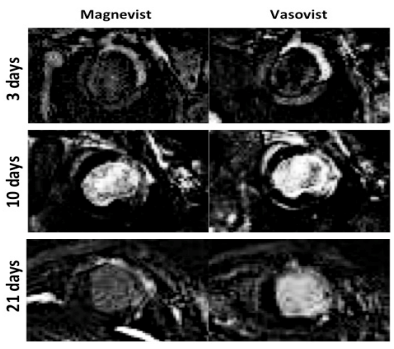

Fig2: MRI images of an infarcted mouse model at 3, 10 and 21 days after Magnevist and Vasovist injection.

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