MR Imaging of Perfusion Defects in Mice

A. Bashir, J. Bao, M. Simons, M. Post, D. Burstein
Beth Israel Deaconess Medical Center. Harvard Medical School. Boston, MA

Introduction
Advances in technology to manipulate mice at the genetic level have enabled models with which to study angiogenesis. In order to evaluate these models, an imaging system capable of resolving serial changes in myocardial status in mice is needed. Several reports have previously demonstrated the use of MRI system for anatomic and functional imaging on adult and neonatal mice (1-3). However, myocardial perfusion MR imaging in mice has not yet been demonstrated. The goal of this work was to demonstrate perfusion defects in mice using MRI. Due to difficulties of injecting contrast agent within the bore of the magnet, first pass imaging techniques are not practical for mice perfusion imaging. In this work, we demonstrated myocardial perfusion defects in a mouse model using a blood pool contrast agent “MS325” (4).

Methods
A mouse cardiac model involving ligation of the left anterior descending (LAD) artery was used for these studies. Surgery (n=11) was done 3-6 days prior to MR imaging. The mice were anesthetized using isoflurane for MR imaging. T1 weighted MR images were acquired with a 2T BRUKER BIOSPEC using a fast gradient echo pulse sequence and a dual triggered inversion recovery sequence. Mice were imaged prior to contrast agent administration. Contrast agent (up to 110μl) was then injected via a tail vein and the mice were repositioned in the magnet and reimaged. After MR imaging, Evan’s blue dye was injected through the femoral vein and the mice were sacrificed. The heart was excised and cut into thin sections.

Results
Normal mice (n = 2) showed significant signal intensity (SI) enhancement after contrast agent administration. There was no further significant change in SI up to an hour after injection (Fig 1 and 2). Four of the operated mice showed significant SI differences in the myocardium after contrast administration indicating perfusion defects. These SI differences were not found before contrast injection. The Evan’s stained pathology sections of these hearts showed myocardial infarcts and the infarct region correlated very well with the MR observed perfusion defects (Fig 3). One heart showed very subtle SI differences on MR image that were at first not attributed to infarct. Pathology revealed a very small region of infarct in this heart. Another heart showed a very small region of infarct on pathology but no SI differences on MR images. This was possibly due to volume averaging in the MR image.

The remaining five hearts did not show any perfusion defects on MR images and no infarcts on the pathology section. Previous experiments have shown that an infarct may not develop in all mice after ligation of LAD.

Discussion
These initial results demonstrate that MR perfusion defects can be observed in mouse hearts using an intravascular contrast agent. The image data represent qualitative maps of contrast agent. Further experiments are underway to determine the time course of perfusion defects with the infarct development and quantitative grading of myocardial perfusion defects.

References
1. F. Wiesmann et. al. Proceedings ISMRM 1999 (27)