High Resolution Imaging of Myocardial Infarction at 1.5T and 3.0T: Is it possible to track SPIO labeled cells?

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Introduction:

Delivery and tracking of cells in-vivo with MRI has a great potential. One particular application, the introduction of bone marrow cells to restore damaged or dysfunctional myocardium to functionality has been proposed and validated to certain extent. Nonetheless, tracking these cells in vivo to correlate cell presence with positive outcomes in cardiac function is difficult non-invasively and without the use appropriate markers that are safe, visible, durable and non-genomic. Superparamagnetic Iron Oxide particles (SPIOs) have appeared as potential cell tracers for MRI. Accumulated SPIOs in organelles inside the cells can cause a strong local disruption of the magnetic field homogeneity with a concomitant loss in MR signal, which makes labeled cells appear black. This effect can be as large as 50 times the size of the organelle, making the cells visible even with imaging voxel sizes that are far larger than a single cell. Single cell imaging of SPIO labeled pig and human myoblasts in culture has proven possible in our 1.5T and 3.0T clinical scanners at resolutions down to 20×20×50 μm^3 voxels.

Purpose:

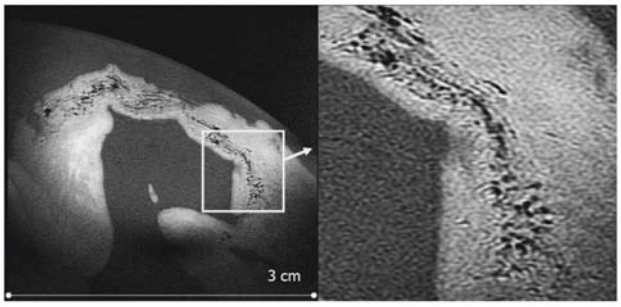
To explore pig excised heart specimens using high-resolution 1.5T and 3.0T MRI to detect SPIO labeled bone marrow cells introduced after intra-coronary injection to the feeding coronary artery of a previously infarcted region.

Methods:

Myocardial infarctions were created in seven pigs (weight 20-25 kg) by balloon occlusion of the left circumflex coronary artery for 2 hours followed by reperfusion. MRI was performed a week later on a GE 1.5T Signa CVi scanner (General Electric Medical Systems, Milwaukee, USA) with the standard clinical imaging gradient set (40 mT/m and SR150) and a phased array torso coil. A routine protocol was followed: cine FIESTA, T2*W GRE and delayed contrast enhanced IR-GRE scans. After the imaging session, SPIO labeled pig bone marrow cells where injected in the circumflex coronary artery in one pig. Two pigs received non-labeled cells and in four pigs only medium was injected. After four weeks the imaging protocol was repeated. The animal was sacrificed and the heart excised and scanned at higher resolution using the same phased array torso array. The hearts were then sliced into 1.4 cm thick sections and one section containing infarcted myocardium was placed in formaldehyde and scanned at much high resolution. Imaging was performed using the 1.5T or the 3.0T scanner with a 2 cm diameter loop coil for signal reception (the same imaging gradient sets in both). 3D SPGR sequences were chosen with a mildly T1W imaging parameters to provide good signal-to-noise in the infarcted region (still containing some of the 0.1 mmol/Kg Gd-DTPA injected 5 minutes prior to sacrificing the animal). Scan parameters were adjusted to suit different resolutions. For 60×60×100 μm^3 voxels, imaging parameters were TR/TE/flip angle = 34.0 ms/ 11.0 ms/ 24°/ (at 1.5T) and TR/TE/flip angle/ = 23.0 ms/ 7.2 ms/ 20° (at 3.0T). Histology was performed accordingly.

Results:

Infarcted regions in all hearts inspected (control pigs and those pigs that received unlabeled and labeled bone marrow cells) demonstrated regions of low signal intensity. In healthy myocardium, signal was homogeneous. The conspicuity of the low signal intensity was increased as smaller voxel sizes were achieved (Figure), depicting a pattern that could be interpreted as labeled cells. Histology confirmed the presence of iron after Prussian blue staining. The low signal intensity was associated to hemosiderin and collagen fibers.



Myocardial infarction in a pig model at 3T.

A 100 µm slice with an in-plane resolution of 60 µm x 60 µm collected at 3.0 Tesla from an infarction on a baseline pig without labeled myoblasts injected. The darker signal intensities detected in the infarcted myocardium reveal blood byproduct accumulation (hemosiderin). Hemosiderin causes signal loss from increased susceptibility effects similarly as SPIOs do, therefore, it is difficult to distinguish one from the other. Healthy myocardium shows with uniform signal intensity.

Conclusions:

Tracking SPIO labeled cells can prove difficult. The low signal intensity patterns that appear at high resolution scanning can be easily confused with that generated by SPIO labeled cells. A different infarct model may be necessary to demonstrate the fate of labeled cells for myocardial regeneration.