Interleaved Magnetic Steering and MR imaging of USPIO Particles in One Dimension: Early Results

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Introduction Retention of therapeutic cells within regions of interest following their delivery is a known obstacle in the field of regenerative medicine. Recent studies have demonstrated that magnetic field gradient of bar magnets can be used to couple with the dipole moment of the cells labeled with iron oxide can be used to enhance retention and therapeutic regeneration.[1] However, this approach is typically taken under invasive conditions so that the magnetic field gradients of the bar magnets are sufficiently close to the proximity of the labeled cells. Moreover, such an approach is not conducive to the immediate assessment of the effectiveness of gradient fields in retaining the cells once the magnetic force is removed. In this work, we investigated whether (a) a Maxwell coil, which can be positioned within the MR scanner, would be able to deliver sufficient one-dimensional force on USPIO particles; and (b) the effect of this resultant force can be captured on the basis of T2* MR images.

Theory The magnetic force generated by a particle with dipole moment (m) in a magnetic field gradient (∇B) can be written as, $F_{magnetic} = m \cdot \nabla B = V_{fe} \cdot p \cdot (c \cdot m_0 \cdot B_0) \cdot \nabla B$, where V=volume of the magnetic dipole, p=density of magnetic dipoles, cm_0=permeability and B_0=magnetic field. Hence the two major factors that determine the magnetic force on an object are the magnetic moment of the object and the magnetic field gradient in the environment around the object. In the case of manipulating magnetic force with bar magnet, B_0 and ∇B both drop dramatically ($B_0 \propto d^2$ and $\nabla B \propto d^3$) as one moves away from the surface of the magnet. This rapid decrease in B_0 and ∇B only permits one to impose sufficient force over short distances and nearly impossible to impart magnetic force in deeper tissues. Alternatively, if the particles are inside the bore of the MR scanner, they will be strongly magnetized (generate a large magnetic moment) in the static magnetic field (B_0) of the MR system. When additional field gradients are imposed on these particles, the particles may be attracted in the direction of the gradient permitting generation of force that is effective in deeper tissue.

Method Gradient Coil Design We designed a Maxwell coil to introduce additional gradients within the MR system that are capable of generating sufficient force to guide or retain USPIO loaded cells in deep tissues. The Maxwell coil was composed of a pair of 6 inches wide spools, which are coiled with 200 turns of the wire. A 3T MRI system (Verio, Siemens Healthcare, Erlangen, Germany) was used throughout the study and a 30A DC current was supplied to the coil for generating the field gradient. Phantom experiments Two proof-of-concept phantom experiments were conducted. In the first experiment, a tube of USPIO particles in gelatin solution were used and in the second experiment, rodent cardiac stem cells loaded with USPIOs were used. In both cases the tubes containing USPIOs were horizontally placed within the coil inside the MR scanner as shown in Figure 1. Optical and MR images (T2*-weighted acquisitions with GRE readout, TR/TE =4/2 ms, flip angle = 15°, resolution= 1x1x3mm^3 resolution) were both acquired before and after applying magnetic gradient for 3 minutes.

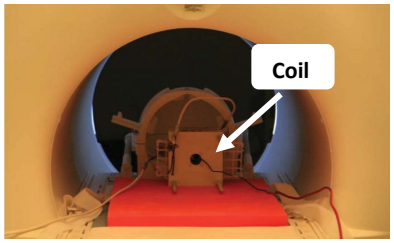

Figure 1 Experimental setup of phantom studies. USPIO containing tubes were placed within the Maxwell coil positioned inside the MR scanner. The coil is connected to a DC power supply. 30A current was supplied to generate ∇B.

Results Our calculations confirmed that such a setup can generate a magnetic gradient up to 3 T/m when 30A of DC current is delivered. Figure 2 shows the effect of magnetic force on USPIO particles in gelatin solution. After turning on the magnetic field gradient for 3 minutes, most of the particles were pushed toward the left side of the tube. Both MR images and optical images show obvious aggregation of the particles. T2* blooming effect caused by highly concentrated USPIOs can also be observed in the distal end of the tube. Figure 3 shows similar effect from stem cells loaded with USPIO. Cell aggregation is highlighted with red circle in the optical and T2*-weighted MR image.

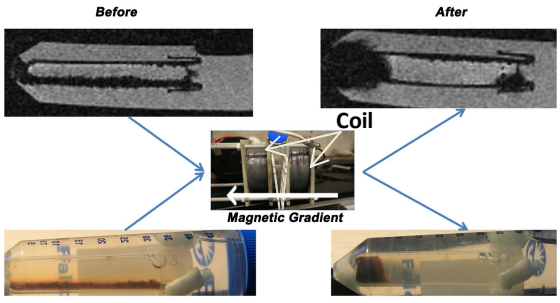

Figure 2 Shows the experimental set up and the optical and T2*-weighted MR images pre and post delivery of the magnetic force (direction shown in the central image) within side the MR system containing the Maxwell coil. Note that the aggregation of USPIO in the distal (left) end of the tubes following the application of the field gradient.

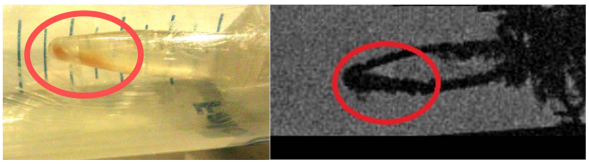

Figure 3 Shows the effect of magnetic field gradient on USPIO loaded cells. Cell aggregation can be readily observed at the left end of the tube (red).

Conclusions The proposed system has the capability to steer USPIO loaded cells in one dimension inside a MR scanner with immediate imaging validation of displacement. Additional studies are required to demonstrate the feasibility in vivo.

Ref: [1] Ke Circ. Res. 2010;