High Contrast, Quantitative Stem Cell Tracking with Magnetic Particle Imaging

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Purpose: Stem cell therapy has enormous potential to heal damaged organs for diabetes, myocardial infarctions, and numerous other diseases. However, quantitative tracking of cells implanted into the body remains an imaging challenge, as the techniques used today are limited by tissue depth attenuation and blurring, nonlinear signal with cell number, poor contrast in certain tissue types, and low resolution [1]. Magnetic particle imaging (MPI) is a new technique that images superparamagnetic iron oxide (SPIO) nanoparticles [2-3]. MPI is well suited for cell tracking as it produces images with high contrast, zero tissue depth effects, high sensitivity, and the ability to accurately quantify cell number *in vivo*. This work is the *first* experimental demonstration of stem cell tracking with MPI.

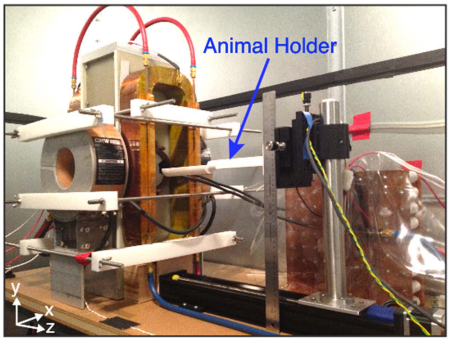
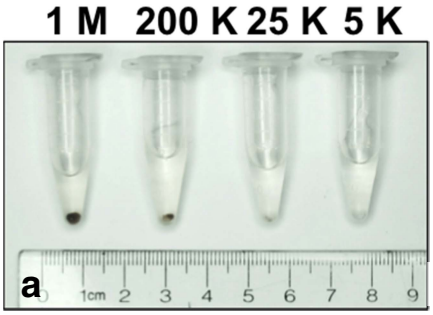
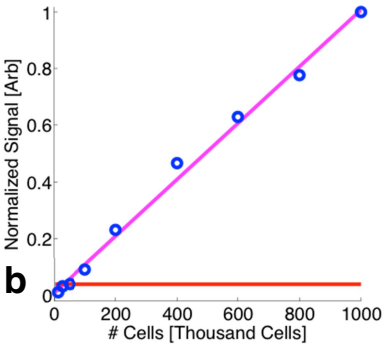
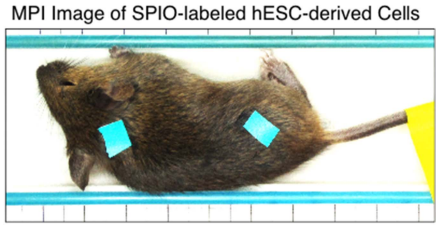


Figure 1. *Projection MPI scanner. A robot, attached to custom-built animal/sample holders, moves samples through the bore during imaging.*

Methods: *MPI image acquisition*: We constructed a projection-format MPI scanner (Fig. 1) with a 2.35 T/m magnetic field gradient and 5.5 cm free bore [4]. MPI scanning had a 5 cm X 10 cm FOV and 15 second acquisition time with 16 averages. *Cell labeling*: hESC-derived stem cells (Fig. 2a) were labeled with Resovist SPIO particles by transfection with protamine sulfate [5] and assessed for labeling efficiency through Prussian blue staining. *Postmortem mice imaging*: 200 µl PBS-suspended cell populations were subdermally injected at two dorsal sites (labeled in blue in Fig. 2c) of postmortem adult Sirt3 heterozygous mice, and allowed to diffuse *in situ* before imaging.







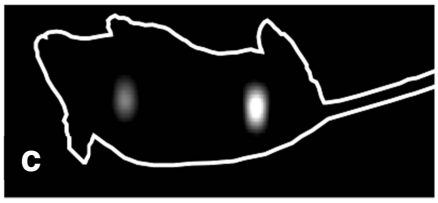


Figure 2. ***a)*** *Pelletized human embryonic stem cell-derived (hESC) populations ranging from five thousand to one million cells.* ***b)*** *Normalized MPI signal intensity linearly depends on number of labeled cells (R^2 = 0.99).* ***c)*** *MPI image of two hESC-derived cell injections (400K and 600K cells) subdermally in a postmortem mouse. Total scan time is 4 min, field of view is 5 by 10 cm.*

Results: *MPI stem cell imaging – sensitivity and linearity*: A series of 9 pelletized hESC-derived cell populations labeled with Resovist (Fig. 2a) were imaged successively in the projection MPI scanner. The maximum signal intensity from the MPI image of each cell pellet is shown as a function of cell number (Fig. 2b). We found a strong linear correlation between MPI signal intensity and cell number, with $R^2 >$ 0.99. The detection sensitivity of the projection MPI system was found to be slightly over 10K hESC-derived cells. *Mice imaging*: MPI image of postmortem cell injections containing 400K and 600K cells is shown in Fig. 2c. The MPI image shows excellent contrast with minimal tissue effects. Additionally, the ratio of total MPI signal between the 600K and 400K injection regions was found to be 1.5, as expected.

Discussion: This study is the first experimental demonstration of stem cell tracking with MPI. We expect image resolution to improve linearly with field gradient strengths and cubically with nanoparticle size, and the cell sensitivity to improve by more than two orders of magnitude with hardware improvements that enable coil noise dominance [6]. Our results show that MPI has great potential as a quantitative, high-contrast, high sensitivity method for *in vivo* cell tracking.

References: 1. Frangioni JV, Hajjar RJ. Circulation. 2004;110(21):3378–83. **2.** Gleich B., Weizenecker J. Nature 2005; (435):1214-17. **3.** Goodwill PW, Conolly SM. IEEE TMI. 2010;29(11):1851–9. **4.** Goodwill PW, et al. IEEE TMI. 2012;(c):11–13. **5.** Arbab AS, et al. Blood. 2004;104(4):1217–23. **6.** Zheng B, et al. Springer Proc. in Physics, 2012;(140):319-24.