Title: Monitoring two cell populations using iron oxides and fluorine-19 MRI cell tracking at 3 Tesla

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Structured Abstract:

Introduction: Detecting the migration of cells is fundamental to understand biological processes and to develop cell therapies. Cellular MRI is an effective technique for non-invasive and longitudinal tracking of cells. Most cellular MRI has been performed with either iron oxides or perfluorocarbons (PFC) as cell labeling agents. In this study we explored the ability to label, detect, and quantify two cell types (stem cells and macrophages) simultaneously using dual iron (Fe) and fluorine-19 (19F) based MRI cell tracking in a model of stem cell rejection.

Methods: Mouse MSCs, labeled with 100µg Fe/mL ferumoxytol (n=5 mice) or unlabeled (n=3 mice), were implanted in the right hind limb muscle of C57Bl/6 mice. Immediately after, each mouse was administered 24mg PFC intravenously for in situ labeling of phagocytic immune cells (macrophages). 24 hours later, both 1H and 19F images were acquired on a 3T clinical scanner using a 4.31cm dual-tuned surface coil and a 3D balanced steady state free precession (bSSFP) sequence (day 1). Imaging was repeated on day 12 to investigate temporal changes in iron-associated signal voids and 19F signal.

Results: On day 1 regions of signal void were detected in 1H MRI of all mice that received iron-labeled MSCs. The signal void created by iron positive MSCs declines by 64% by day 12 (p < 0.01). PFC-labeled macrophages accumulate near both labeled and unlabeled MSCs within 24 hours. The 19F signal persists and rises by 25% over 12 days (p < 0.05).

Discussion: We have shown that it is possible to detect both implanted MSCs and infiltrating immune cells in the same mouse during the same imaging session. The decline in iron void volume is likely due to MSC death. This coincides with a rise in 19F signal that indicates increased infiltration of immune cells. This is the first study to demonstrate the ability to image macrophage infiltration in vivo using 19F on a clinical (3T) MRI system. We propose that this imaging technique could be used to identify immune rejection at cell transplant sites and contribute to other in vivo cell tracking applications.