
Magnetic Resonance Imaging of Iron Oxide-Labeled Human Embryonic Stem Cell-Derived Cardiac Progenitors.

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Public Summary:

In this study, we describe a method to label human embryonic stem cells with iron particles. When differentiated to heart lineage, these cells were transplanted into pigs' hearts and the signal was detected by MRI. Imaging by MRI allowed us to precisely locate and track the transplanted cells in the pig's heart.

Scientific Abstract:

: Given the limited regenerative capacity of the heart, cellular therapy with stem cell-derived cardiac cells could be a potential treatment for patients with heart disease. However, reliable imaging techniques to longitudinally assess engraftment of the transplanted cells are scant. To address this issue, we used ferumoxytol as a labeling agent of human embryonic stem cell-derived cardiac progenitor cells (hESC-CPCs) to facilitate tracking by magnetic resonance imaging (MRI) in a large animal model. Differentiating hESCs were exposed to ferumoxytol at different time points and varying concentrations. We determined that treatment with ferumoxytol at 300 µg/ml on day 0 of cardiac differentiation offered adequate cell viability and signal intensity for MRI detection without compromising further differentiation into definitive cardiac lineages. Labeled hESC-CPCs were transplanted by open surgical methods into the left ventricular free wall of uninjured pig hearts and imaged both ex vivo and in vivo. Comprehensive T2^{*}-weighted images were obtained immediately after transplantation and 40 days later before termination. The localization and dispersion of labeled cells could be effectively imaged and tracked at days 0 and 40 by MRI. Thus, under the described conditions, ferumoxytol can be used as a long-term, differentiation-neutral cell-labeling agent to track transplanted hESC-CPCs in vivo using MRI. SIGNIFICANCE: The development of a safe and reproducible in vivo imaging technique to track the fate of transplanted human embryonic stem cell-derived cardiac progenitor cells (hESC-CPCs) is a necessary step to clinical translation. An iron oxide nanoparticle (ferumoxytol)-based approach was used for cell labeling and subsequent in vivo magnetic resonance imaging monitoring of hESC-CPCs transplanted into uninjured pig hearts. The present results demonstrate the use of ferumoxytol labeling and imaging techniques in tracking the location and dispersion of cell grafts, highlighting its utility in future cardiac stem cell therapy trials.

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