Single cell level detection of Gadolinium-labeled stem cells using a clinical 3.0T MRI scanner

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Background

The ability to track transplanted cells in vivo is considered a crucial point in the development and validation of cell-based therapy. Following incorporation of iron-oxide particles, cells can be visualized by MRI in vivo, due to susceptibility artifacts caused by the iron-oxide particles resulting in hypo-intense contrast in MR images. The hypo-intense contrast thus obtained, is associated with some limitations. In order to obtain positive contrast from transplanted cells we have developed an effective labeling method for incorporation of Gadolinium (Gd) into cells.

Material and Methods

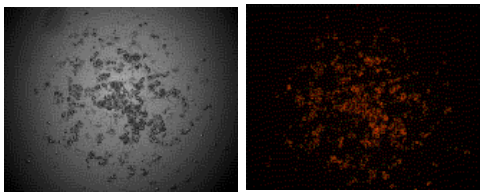
For labeling of cells with Gd, Gd-DTPA was incorporated into cationic, lipid-based, nano-particles (Gd-lipo). For validation purposes, a fluorescent dye (rhodamine-PE) was also incorporated into the nano-particles. Incorporation of Gd-lipo into cells was assessed by fluorescent microscopy or inductively coupled plasma optical emission spectroscopy. Toxicity of the labeling procedure was studied by assessing survival, proliferative capacity and tube forming capacity of labeled and non-labeled cells. 3D-T1-weighted imaging of cells in vitro and in vivo was performed on a clinical 3.0 T scanner using custom designed coils.

Results

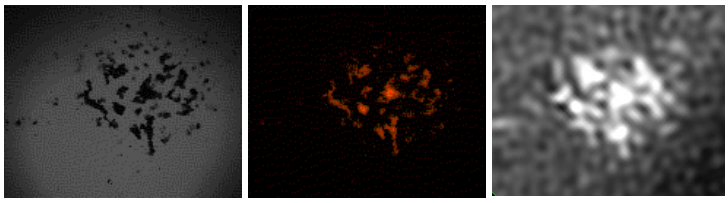
Labeling of cells using Gd-lipo nanoparticles resulted in a near 100% labeling efficiency with an average loading of 10-90 pg of Gadolinium per cell. Using a 1 cm loop custom surface coil, imaging of viable cells under in vitro conditions was possible at single cell level, at resolutions down to of 80 µm x 80 µm x 100 µm and acquisition times of less then 15 minutes. In vivo imaging of 10.000 Gd-labeled cells injected in the myocardium of syngenic rats was also achieved using a custum built quadrature birdcage coil with an inner diameter of 4.5 cm. Depending on the concentration of Gd-lipo and the cell type used, some toxic effects of the labeling procedure were observed.

Conclusions

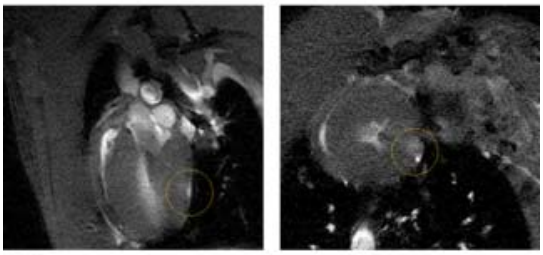
Efficient labeling of stem cells with Gd resulting in sensitive detection by MRI is feasible using cationic lipid carriers. Further studies regarding the potential toxic effects of the labeling procedure are necessary.



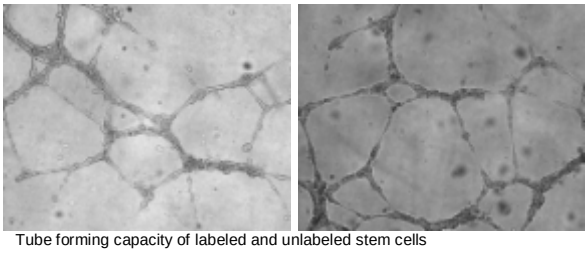
Matching light microscopy and fluorescent microscopy of Gd-lipo labeled stem cells.



Matching light microscopy, fluorescent microscopy and MR images of Gd-lipo labeled stem cells.



Gd-lipo labeled stem cells (yellow circle) injected in the myocardium of a living syngenic rat



Tube forming capacity of labeled and unlabeled stem cells