MR signal characteristics of viable and apoptotic human mesenchymal stem cells in matrix-associated stem cell implants for treatment of osteoarthritis.

Objective: To compare magnetic resonance (MR) signal characteristics of contrast agent-labeled apoptotic and viable human mesenchymal stem cells (hMSCs) in matrix-associated stem cell implants. Methods: hMSCs were labeled with Food and Drug Administration-approved ferumoxides nanoparticles. One group (A) remained untreated whereas a second group (B) underwent mitomycin C-induced apoptosis induction. Viability of group A and apoptosis of group B was confirmed by caspase-assays and terminal dUTP nick-end labeling (TUNEL) stains. Labeled viable hMSCs, unlabeled viable hMSCs, labeled apoptotic hMSCs, and unlabeled apoptotic hMSCs (n = 7 samples each) in an agarose scaffold were implanted into cartilage defects of porcine patellae specimens and underwent MR imaging at 7 T, using T1-weighted spin-echo sequences, T2-weighted spin-echo sequences, and T2*-weighted gradient-echo sequences. Signal-to-noise ratios (SNR) of the implants were calculated and compared between different experimental groups using linear mixed regression models. Results: Ferumoxides-labeled hMSCs provided a strong negative T2 and T2*-enhancement. Corresponding SNR data of labeled hMSCs were significantly lower compared with unlabeled controls (P< 0.05).
Apoptosis induction resulted in a significant signal decline of ferumoxides-labeled hMSC transplants on short echo time T2-weighted spinecho sequences. SNR data of labeled apoptotic hMSCs were significantly lower compared with labeled viable hMSCs (P< 0.05). CONCLUSION: Apoptosis of transplanted ferumoxides-labeled stem cells in cartilage defects can be visualized noninvasively by a significant signal decline on T2-weighted MR images. The described MR signal characteristics may serve as a noninvasive outcome measure for the assessment of matrix-associated stem cell implants in clinical practice. Additional studies are needed to further enhance the observed differences between viable and apoptotic cells, for example, by further optimizing the applied MR pulse sequence parameters or intracellular contrast agent concentration.