Abstract: The purpose of this study was to (1) compare three different techniques for ferumoxide labeling of mesenchymal stem cells (MSCs), (2) evaluate if ferumoxide labeling allows in vivo tracking of matrix-associated stem cell implants (MASIs) in an animal model, and (3) compare the magnetic resonance imaging (MRI) characteristics of ferumoxide-labeled viable and apoptotic MSCs. MSCs labeled with ferumoxide by simple incubation, protamine transfection, or Lipofectin transfection were evaluated with MRI and histopathology. Ferumoxide-labeled and unlabeled viable and apoptotic MSCs in osteochondral defects of rat knee joints were evaluated over 12 weeks with MRI. Signal to noise ratios (SNRs) of viable and apoptotic labeled MASIs were tested for significant differences using t-tests. A simple incubation labeling protocol demonstrated the best compromise between significant magnetic resonance signal effects and preserved cell viability and potential for immediate clinical translation. Labeled viable and apoptotic MASIs did not show significant differences in SNR. Labeled viable but not apoptotic MSCs demonstrated an increasing area of T2 signal loss over time, which correlated to stem cell proliferation at the transplantation site. Histopathology confirmed successful
engraftment of viable MSCs. The engraftment of iron oxide-labeled MASIs by simple incubation can be monitored over several weeks with MRI. Viable and apoptotic MASIs can be distinguished via imaging signs of cell proliferation at the transplantation site.