Objectives Currently, magnetic resonance imaging (MRI) are adopted to evaluate the outcomes of cardiac cell therapy such as on left ventricular (LV) contractile function and LV remodelling. While the ability of MRI for in vivo stem cell tracking remains controversial. Here we tested the hypothesis that MRI can track the long-term fate of the superparamagnetic iron oxide (SPIO) nanoparticles labelled mesenchymal stem cells (MSCs) following intramyocardially injection in the experimental acute myocardial infarction in rats.

Methods Myocardial infarction was experimentally induced in adult female Lewis rats by permanent ligation of the left anterior descending coronary artery. MSCs (2×10^6) from male Lewis rats doubly labelled with SPIO and 4′-6-diamidino-2-phenylindole dihydrochloride (DAPI) were injected into the peri-infarct region 2 weeks after myocardial infarction. The control group received cell-free media injection. In vivo serial MRI was performed using a 7.0 T horizontal-bore animal scanner (Varian, Palo Alto, California, USA) supplied with an actively-shielded gradient of 400 mT/m and a 70-mm transmit/receive birdcage radio frequency (RF) coil, at 24 h before cell delivery (baseline), 3 days, 1, 2, and 4 weeks after cell delivery, respectively. Electrocardiography-gated T2*WI gradient echo sequence and cine MRI were performed for in vivo cell tracking and assessing cardiac function using left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV); left ventricular end-systolic volume (LVESV), respectively. The survival, migration and apoptosis of grafted MSCs were assessed by polymerase chain reaction analysis for the rat Y-chromosome-specific SRY gene, histopathological examination and terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL) staining, respectively.

Results Serial follow-up MRI demonstrated large persistent intramyocardial signal-voids as large black spots representing SPIO during the follow-up of 4 weeks, and MSCs moderate the left ventricular dilatation and dysfunction compared with controls at 3 days, 1 and 2 weeks after cell transplantation, respectively. The TUNEL analysis confirmed that MSCs engrafted in infarcted hearts underwent apoptosis. The histopathological studies (at 2, 4 weeks) revealed that the site of cell injection was infiltrated by inflammatory cells and the iron-positive cells were macrophages identified by CD68 staining, but very few or no DAPI-positive stem cells in the animals after cells transplantation, respectively. The presence of engrafted cells was confirmed by real-time polymerase chain reaction on postmortem specimens, which showed that the expression of Y-chromosome-specific SRY gene of MSCs from male donors in infarcted hearts of female recipients was consistent with the results of the histopathological assessment.

Conclusions MRI enables in vivo evaluation of the long-term therapeutic potential of MSCs for myocardial infarction, while does not reliably track the long-term fate of SPIO-labelled MSCs engraftment in the heart.

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MAGNETIC RESONANCE IMAGING WITH SUPERPARAMAGNETIC IRON OXIDE FAILS TO TRACK THE LONG-TERM FATE OF MESENCHYMAL STEM CELLS AFTER TRANSPLANTATION IN THE HEART

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