Delivery and Tracking of Cardiovascular Stem Cells Using MRI

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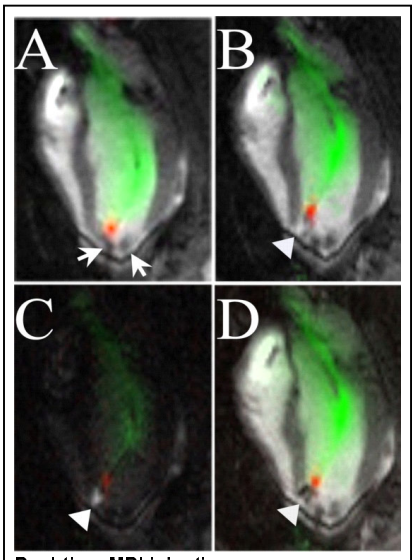
MRI is a good tool for tracking cardiovascular cell preparations because of the wide range of available tissue contrasts and because 3D imaging is possible even in moving structures. MRI might be useful to mark, confirm and guide delivery and to assess redistribution in time and space. Equally important, MRI is a promising guidance modality for minimally invasive delivery of therapeutic cell preparations to specific cardiovascular targets.

Exogenous cell labels can be added by co-cultivation, facilitated co-cultivation, or transfection. To date, T1- shortening agents have not successfully been used to label and track cardiovascular stem cell preparations. T2*-based tracking using iron is attractive in that the "blooming" artifact can be much larger than the particles themselves, increasing the detectability especially in moving tissues like the heart. Larger particles have proportionately greater T2* contrast than do smaller particles, but in vivo aggregation of USPIO mitigate this difference.

Most groups have labeled cell preparations using nanometer-(2,3) or micron-scale(4) iron particles. In vitro assays of proliferation or, in some cases, even lineage-specific differentiation are not necessarily impaired by cellular uptake of these relatively biocompatible particles(4). Particles appear to partition among dividing cells. Less clear is whether cellular tagging with these particles impairs cellular activity in vivo.

One promising report describes facilitated co-cultivation of a range of cell preparations using clinical grade reagents, ferumoxides and protamine(5). Another team(6) has visualized, albeit at high field, as few as 10^6 injected antibody-labeled cells wherein antibody-bound magnetic particles on the cell surface were used both for cell purification and for MRI.

Our group has used real-time MRI to guide catheter-base delivery of iron-labeled mesenchymal stromal cells to myocardial infarct border targets(1, Figure). These used a custom real-time MRI image reconstruction in a clinical-grade environment. Other groups also have conducted MRI-guided myocardial injections(7,8). Still others have reported accumulation of exogenous iron-labeled cells into freshly injured myocardium. The technique seems hampered by nonspecific accumulation of cell-free label.



Real-time MRI injection sequence. (A) Needle at infarct border. Needle tip is red, and catheter, green. Arrows indicate injections of iron-labeled MSCs, dark spots. (B) Gd-DTPA injection (arrowhead). (C) Sat-prep shows Gd-DTPA. (D) Iron-MSCs (1×10^6) injection extinguishes local signal. From Dick(1).

No team has yet convincingly demonstrated intramyocardial redistribution or migration ("tracking") of exogenous cell preparations using these techniques.

All of these reports of cell labeling with exogenous particles have important limitations. There is a degree of nonspecific accumulation of iron label in acutely injured myocardium. In addition, since label can be detected independently of the cells they are intended to identify, the presence of cells must be confirmed by an alternative modality.

That said, a variety of putative therapeutic cell preparations are easily labeled for detection after myocardial delivery using clinical MRI systems, in the beating heart, using as few as 10^5 cells, for intervals as long as one year.

Clinical-grade imaging, monitoring, and treatment environments are available today for targeted MRI-guided cardiovascular stem cell delivery. However, the field is hampered by the unavailability of clinical-grade catheters.

References

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