In Vivo Tracking of Human Neural Progenitor Cells in the Rat Brain using Magnetic Resonance and Bioluminscence Imaging

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Recent advances in the field of stem cell research have generated a lot of therapeutic interest, especially in the treatment of neurodegenerative diseases. Human neural progenitor cells (hNPC) have been widely investigated since they differentiate into cells of the neural lineage and survive, thrive and migrate towards injured tissues. Molecular imaging modalities can be used to gain insight into cell location, migration and survival. Here, we describe multiple methods of tracking hNPC following rat brain transplants using magnetic resonance and bioluminescence imaging (MRI and BLI, respectively). Initially, we employed MRI, due to its excellent resolution and tissue-contrast, for tracking cells using three different methods. First, attempting to take advantage of its high contrast-to-noise ratio, we labeled hNPC with ^{19}F nanoparticles for detection using ^{19}F MRI. While we showed that *in vitro* these cells can be detected by ^{19}F MRI, we could not distinguish labeled hNPC *in vivo*. Next, we overexpressed ferritin, an iron storage protein, by hNPC (hNPC^{Fer}) and found that while hNPC^{Fer} induced hypointense T2*-weighted contrast in the accurate anatomical region, they could not be distinguished from negative control cells *in vivo*. Conversely, superparamagnetic iron oxide (SPIO) loading increased this hypointensity compared to all other conditions. Still, hNPC survival could not be estimated using any of the iron-based MRI methods explored *in vivo*. Finally, we employed a T1-weighted gadolinium [Gd(III)]-based approach, where hNPC expressed HaloTag7® protein (hNPC^{HT7}) and were able to bind Gd(III)-containing HaloTag® ligand. However, we found that hNPC^{HT7} could not be detected after labeling due to dual ligand's low longitudinal relaxivity. Finally, we utilized BLI, due to its high sensitivity, to track luciferase-expressing hNPC (hNPC^{Luc2}). We showed that surviving hNPC^{Luc2} can be detected in the rat striatum for up to 12 weeks while rejected hNPC^{Luc2} lose bioluminescence signal. Furthermore, we demonstrated that hNPC^{Luc2} contralateral migration can be discerned using this method *in vivo*. Through this work, we concluded that combining MRI and BLI may be the most promising method of tracking hNPC *in vivo* as luciferase-based BLI would provide information on cell survival and migration while iron-based MRI would provide understanding of cellular location in preclinical models.