In Vivo Magnetic Resonance Tracking of Endothelial Progenitor Cells Trafficking to Sites of Hepatoma Angiogenesis

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Purpose: The goal of this study was to use Micro-MR to track the migration and incorporation of intravenously injected, magnetically labeled rat peripheral blood endothelial progenitor cells (EPCs) into the blood vessels in a rapidly growing hepatoma model.

Materials and Methods: This study was approved by the Institutional Committee on Animal Research. Transplanted hepatoma in 18 BALB/c nude mice was induced with injected 1×10^6 cells from a H22 mouse hepatoma cell line into left hepatic lobe. Rat EPCs labeled (n=9) and unlabeled (n=9) with superparamagnetic particle Fe_2O_3 (Feraheme) -poly-L-lysine (PLL) complexes were injected intravenously 3 days' later, and MR imaging was obtained 3, 7, 10 and 14 days after transplantation. Hepatoma-to-muscle contrast-to-noise ratios (CNRs) on T_2^*WI were measured and compared to histomorphologic studies.

Results: Rat EPCs could be efficiently labeled. Migration and incorporation of transplanted labeled cells into tumor neovasculature were documented with in vivo MR as low signal intensity at the tumor periphery as early as 3 days after EPCs administration in preformed tumors. However, low signal intensities were not observed in tumors implanted at the time of EPC administration until tumor size reached 1 cm at 12 to 14 days. CNRs on T_2^*WI decreased significantly in the hepatoma 12 days after injected of EPCs. Prussian blue staining showed iron-positive cells at the sites corresponding to low signal intensity on MRI. The labeled cells initially localized in peripheral of the tumor. No free nano-particles were found in the interstitial substance or macrophage. Confocal microcopy showed incorporation into the neovasculature, and immunohistochemistry confirmed the transformation of the administered EPCs into endothelial cells.

Conclusion: Rat EPCs could be effectively labeled with Fe_2O_3-PLL. MRI demonstrated the incorporation of magnetic labeled rat EPCs into the neovasculature of implanted hepatoma.