Real-Time In Vivo MPI Cytometry

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Magnetic particle imaging (MPI) has emerged as non-invasive imaging modality that can be applied for in vivo (stem) cell tracking[1]. It can use the same SPIO nanoparticles as those used with MRI, but instead of MRI contrast agents these formulations act as MPI tracer agents to provide "hot spot" signal without tissue background signal and true cell quantification[2], enabling "in vivo cytometry" on a time scale of minutes. Examples will be shown for mesenchymal stem cells (MSCs) and neural precursor cells (NPCs) after intra-arterial injection in mouse models. Using fiducials with known cell concentrations, the cytometric ratio of the number of cells localizing in the liver/lung vs. the brain differed 10-fold between the two cell types, representing the different cellular volumes which is a critical parameter for passage through the cerebral capillary network.

By virtue of their tumor-tropism, MSCs can also be applied as cellular theranostics to deliver and retain theranostic gold-containing SPIOs to tumors. Using in vivo MPI cytometry of intratumoral vs. systemic distribution of gold-SPIO-loaded MSCs, we found that the total amount of tumor-associated particles different 10-fold between labeled hMSCs and "naked" nanoparticles, which correlated with the efficacy of laser irradiation-mediated photothermal therapy (PTT) for eradication of tumors.

Finally, we are developing an all-in-one nanotheranostic plastform that can be visualized with MRI, MPI, CT, and photoacoustic imaging. The formulation contains albumin, bismuth sulfide, and SPIO and can act as a radiosensitizer and activator for PTT and magnetic hyperthermia. Examples of in vivo MPI cytometry will be shown for stem cells directly implanted in the brain, and how MPI cytometry compares to cell quantification with CT and MRI.

1. Bulte, JWM et al., *Tomography* **2015**, 1, 91-97.
2. Bulte, JWM et al., *Adv. Drug Del. Rev*. **2019**, 138, 293-301.