MR Tracking of Magnetically Labeled Cells: First Clinical Applications

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Cellular imaging is a new emerging application that aims to obtain a better understanding of cell migration and trafficking, including verification of accurate injection. The clinical use of novel experimental cell therapies calls for suitable methods that can monitor the cellular biodistribution non-invasively following administration. Positron emission tomography (PET), bioluminescent imaging (BLI), single photon emission compute tomography (SPECT), and magnetic resonance (MR) imaging have been succesfully used to track immune and hematopoietic cells in cancer, as well as neoplastic homing of stem cells. Some of these techniques rely on the use of reporter genes (i.e., luciferase or thymidine kinase), enzymes that convert substrates to detectable levels.

Among the above imaging techniques, MR imaging has superior resolution with excellent soft tissue contrast. In order for exogenous therapeutic cells to be detected, they need to have a different contrast from endogenous cells. The most sensitive MR label as of to date are so-called superparamagnetic iron oxide nanoparticles or SPIO particles. They create strong local magnetic field disturbances and spoil the MR signal leading to hypointensive contrast. We have developed several magnetic labeling techniques including magnetoelectroporation [1] that allow an effective cellular internalization of clinical SPIO formulations withhout affecting cell proliferation, differentiation, and function. Animal studies have shown that MR interrogation of cell migration is reliable when stem cells have limited cell division, as validated by conventional histological techniques.

Recently, a first clinical study was published [2] by investigators from the Catholic University of Nijmegen and the Johns Hopkins University, describing MR tracking of magnetically labeled dendritic cells in melanoma patients. One of the surprising findings, only observable by MR imaging, was the occurrence of misinjection (under ultrasound guidance) in half the patients. This may well explain why a significant proportion of cancer patients treated with cancer vaccines (dendritic cells primed with cancer antigenes) fail to show a boost of their immune response. It is generally believed that MR cell tracking will become an important technique that may become routine in standard radiological practice once cell therapy goes mainstream.

References

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