Real-time in vivo MRI tracking of single cells and nanoparticles

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Non-invasive imaging of defined population or even individual cells is gaining increasing attention in basic biomedical research and also in the context of cellular therapies in patients. Labeling cells with super paramagnetic iron oxide nanoparticles (ION) provides strong contrasts and excellent detection sensitivity for the tracking of individual cells in vivo. Real-time tracking of slowly moving or migrating cells, however, requires sufficient temporal resolution to perform time-lapse MRI. We have shown that it is feasible to detect single cells in sequential acquisitions with an effective temporal resolution of one minute for the whole mouse brain in vivo. Simulations of image contrast showed that cells with velocities of roughly 1 µm/s can be detected, while faster moving cells did not give rise to sufficient image contrast. This velocity range is perfectly suitable to differentiate between slowly patrolling immune cells in healthy mice from faster moving cell after an immune response has been triggered. In different animal models we have triggered an immune response, which can be detected with high sensitivity before disease symptoms become evident. However, a quantitative assessment of ION-labelled cells in the body is not straight forward, due to processing of nanoparticles in vivo. For this purpose, we have employed ^{57}Fe-ION and combined MRI with ex vivo elemental mass spectrometric imaging by LA-ICP-MS. This approach allows to unambiguously identify labelled cells, follow their migration, assess biodistribution of the administered iron and study metabolization of ION. A different contribution to relaxivity depending on the physiological processing of ION was revealed, confirming both relaxation theories and models of iron metabolization.