

Detection of inflammatory cell migration using MRI

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MRI is capable of image resolution below 0.1 mm pixel size. However, for cellular MRI, this dimension is not sufficient to directly resolve individual cells *in vivo*. Indirect imaging strategies are therefore required to detect individual immune cells and visualise their migration in the body. Successful strategies involve labelling target cells with either directly detected imaging agents, such as ¹⁹F-containing compounds, or indirectly detected contrast agents, such as iron oxide nanoparticles (IONPs). The latter allow the detection of single cells and the use of time-lapse MRI for real-time tracking of immune cells in the healthy animal as well as during the onset and progression of inflammation. We have applied time-lapse MRI to several mouse models of disease and have shown that time-lapse MRI of immune cells in the brain can indicate the immune status of the body. We have further developed methods to perform accelerated time-lapse MRI to capture the migration of faster (than patrolling) moving cells within the vasculature.

In more severe inflammation, and also in the tumour microenvironment (TME), massive immune cell infiltration occurs and single cell tracking is not required. MRI techniques that are sensitive to microstructural changes are well suited to resolve cellular infiltration. We have used time-dependent diffusion MRI with oscillating gradients to characterise cellular microstructure in the TME. Our approach is able to distinguish between macrophage and T-cell infiltration. It is therefore suitable for differentiating tumours of different malignancy and also allows characterisation of tumour response as early as three days after initiation of therapy, before any changes in tumour size can be detected.

Literature:

1. Masthoff M, Gran S, Zhang X, Wachsmuth L, Bietenbeck M, Helfen A, Heindel W, Sorokin L, Roth J, Eisenblatter M, Wildgruber M, Faber C. Temporal window for detection of inflammatory disease using dynamic cell tracking with time-lapse MRI. *Sci Rep* 2018;8: 9563.
2. Masthoff M, Freppon FN, Zondler L, Wilken E, Wachsmuth L, Niemann S, Schwarz C, Fredrich I, Havlas A, Block H, Gerwing M, Helfen A, Heindel W, Zarbock A, Wildgruber M, Faber C. Resolving immune cells with patrolling behaviour by magnetic resonance time-lapse single cell tracking. *EBioMedicine* 2021;73: 103670.
3. Armstrong M, Wilken E, Freppon F, Masthoff M, Faber C, Xiao D. Dynamic cell tracking using time-lapse MRI with variable temporal resolution Cartesian sampling. *Magn Reson Med* 2023;90: 2443-2453.
4. Hoffmann E, Gerwing M, Niland S, Niehoff R, Masthoff M, Geyer C, Wachsmuth L, Wilken E, Höltnke C, Heindel WL, Hörr V, Schinner R, Berger P, Vogl T, Eble JA, Maus B, Helfen A, Wildgruber M, Faber C. Profiling specific cell populations within the inflammatory tumor microenvironment by oscillating-gradient diffusion-weighted MRI. *J Immunother Canc* 2023;11: e006092.