Monte Carlo simulations of diffusion-weighted MRI in breast cancer

Diffusion-weighted Magnetic Resonance Imaging (DW-MRI) reflects the microscopic cellular environment and is sensitive to tumor characteristics such as cell density, membrane integrity, viscosity, and microstructure. As such, it already plays an important role in characterizing tumors [1]. However, standard diffusion imaging methods rely on a Gaussian free diffusion model, which is usually not valid for vast majority of tissues.
At NTNU there is an ongoing research activity focusing on protocol development for a more complete diffusion characterization of breast tissue which combines advanced diffusion modelling techniques: IVIM (intra-voxel incoherent motion), RSI (restricted spectrum imaging), DKI (diffusion kurtosis imaging) and Td (mixing time) dependence imaging. All of these techniques may have a complementary role in lesion structure imaging: non-Gaussian modelling (RSI and DKI), tissue vascularity (IVIM), separation of different diffusion length scales (Td dependence).
In addition a new project recently started up at NTNU which focuses on detailed histological characterization of breast cancer tissue samples harvested from patients who before surgery performed the extensive DW-MRI protocol described above. This project will enable a direct comparison between actual tissue microstructure and the DW-MRI signal. A natural extension of this activity is to bridge the gap between microstructure and MRI-signal with the use of simulations. Such a project will add value to the existing activity by utilizing the unique experimental results produced by the other two projects.

Main aim of proposed project
The main component in this project is to perform Monte Carlo simulations to study in detail the link between tissue microstructure and DW-MRI signal, and to use such simulations to optimize DW-MRI acquisition methods.

Work-packages
We propose the following work-packages in the project:

1. To establish a workflow for generating tissue models based on input from histological characterization of tissue samples. This will require a process of systematization and simplification of the tissue microstructure.
2. To establish a workflow for Monte-Carlo simulations of diffusion and DW-MRI. "Diffusion Microscopist Simulator" is a possible framework, and our group has already contacted the developers of this simulation toolbox [2].
3. To compare the DW-MRI signal as predicted from tissue models with actual DW-MRI signal acquired in-vivo. This part will utilize the unique experimental data we have with tissue samples and MRI data from the same patients.

References

1. Guo, Y., et al., *Differentiation of clinically benign and malignant breast lesions using diffusion-weighted imaging.* J Magn Reson Imaging, 2002. **16**(2): p. 172-8.
2. Yeh, C.H., et al., *Diffusion microscopist simulator: a general Monte Carlo simulation system for diffusion magnetic resonance imaging.* PLoS One, 2013. **8**(10): p. e76626.