Quantitative MRI for characterising brain tissue

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Course organisers

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Course venue

Max Planck Institute for Human Cognitive and Brain Sciences,
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GOALS OF THE COURSE

The course on quantitative MRI for characterising brain tissue provides the basic foundation of the most frequently used quantitative MRI methods for imaging brain structure and composition. The emphasis will be on well-established approaches but also recent developments will be introduced. The course covers the data acquisition and processing methods, such as MR pulse sequences, fitting procedures and biophysical modelling. The course will discuss the biophysics and interpretation of the quantitative measures in conjunction with neuroanatomy and brain microstructure. Lectures will be complemented by MATLAB® or PHYTHON™ tutorials implementing different modelling, data-processing or fitting methods.

At the end of the course, attendees will understand the basic principles and implementation of relaxometry, magnetisation transfer mapping,

quantitative diffusion imaging and MR fingerprinting. Attendees will appreciate the relationship between the different quantitative measures and brain microstructure and composition based on basic biophysical models. The information will help them to understand current and future developments in the field of quantitative imaging.

The course will focus on:

1. Quantification of proton density.
2. Quantification of the longitudinal relaxation time, T_1.
3. Quantifying magnetisation transfer (MT).
4. Quantification of the transverse relaxation time T_2 and the effective transverse relaxation time T_2*.
5. Quantification of magnetic susceptibility.
6. Quantitative diffusion-weighted imaging including tensor and advanced diffusion models.
7. Fingerprinting for quantitative MRI.
8. Group analysis using quantitative MRI data.
9. Biophysical models and interpretation of quantitative MRI data.
10. Verification of qMRI measures.

EDUCATIONAL LEVELS

This course is intended for MR physicists, biomedical engineers or other scientists working with MRI, and early-stage researchers (PhD students), who already have initial experience in basic MR methods, image processing and data analysis, and who wish to extend their knowledge on quantitative MRI principles and techniques. Some knowledge of MATLAB® and/or or PHYTHON™ will be advantageous. All tutorials will be based around pre-existing code prepared for this course. Attendees without any MATLAB® or PHYTHON™ experience should have other programming experience and be willing to work with MATLAB® or PHYTHON™. This course runs from introductory to advanced methods over the three days. At the end of these three days, attendees will take with them the code that has been provided and developed by them. This code, in combination with notes taken at the course, will form a package, which will enable attendees to understand different and implement some basic methods and analysis packages discussed during the course.

Course description

This course is designed to provide a broad foundation of quantitative MRI of brain structure. Quantitative MRI is of increasing importance, since it is comparable across time points and imaging sites. It also offers a higher specificity for the underlying physical and biophysical contrast

mechanisms, facilitating its interpretation with respect to brain microstructure. Recently, these methods have been used to determine local myelin concentrations and different axonal properties. The access to information about structure much smaller than the nominal voxel size opens new possibilities for *in-vivo* biomarkers and may make "*in-vivo* histology" possible. This course is aimed at PhD students and scientists new to quantitative MRI, who wish to acquire theoretical knowledge and practical skills in this domain. The course will be split into two parts, with approximately half the time spent attending lectures and the other half doing practical MATLAB® or PHYTHON™ tutorial exercises. We will provide software licenses for the duration of the course.

For best experience, attendees are asked to bring their own laptop computer with a MATLAB® installation.

The course will cover the broad spectrum of quantification methods ranging from relaxometry of T_1, T_2 and T_2*, and proton density mapping to magnetisation transfer, diffusion and susceptibility mapping. The definition and basic models underlying the contrast parameters will be discussed. Biophysical models will be introduced for better interpretation and understanding of the relationship between contrast parameters and the underlying tissue microstructure. In order to place the physical models into the context of neuroscience studies, the appropriate treatment of quantitative data in group analyses will be discussed. Furthermore, an introduction into non-MRI methods suitable for a verification of results on tissue composition and microstructure derived with qMRI techniques will complement this.

An integral part of the course will be the MATLAB®/PHYTHON™ tutorials, where attendees will be able to work through example code provided for them. These examples will demonstrate and enhance their understanding of the concepts discussed throughout the course. Some previous exposure to MATLAB®/PHYTHON™ is preferable but not mandatory. Those participants, who have not used MATLAB®/PHYTHON™, should have some programming experience.

All participants will be expected to know basic MR physics, image processing and data analysis. A working knowledge of image acquisition methods is essential.

LEARNING OBJECTIVES

Quantification of proton density (PD)

- Define proton density.
- Understand variable-flip-angle method for PD mapping.
- Identify confounds and pitfalls in PD mapping, including $B_1^{(+)}$ field inhomogeneities, acquisition at finite echo times.
- List typical PD values for brain tissue and appreciate their variability across the brain and across subjects.
- Understand the dependency of PD on myelination and free water, and its use for macromolecular tissue volume (MTV) mapping.

Quantification of the longitudinal relaxation time, T_1

- Define the longitudinal relaxation time T_1.
- Understand inversion recovery, variable flip angle methods for T_1 mapping.
- Identify confounds and pitfalls in T_1 mapping, including $B_1^{(+)}$ field inhomogeneities, slice-profile effects, inversion efficiency.
- List typical T_1 values for brain tissue and appreciate their variability across the brain and across subjects.
- Understand the dependency of T_1 on myelination and iron concentration.

Quantification of magnetisation transfer (MT)

- Define the magnetisation-transfer ratio (MTR) and the two-pool model and its parameters.
- Understand gradient-echo experiments with additional off-resonance saturation pulse for MT weighting.
- Identify confounds and pitfalls in MT mapping, including $B_1^{(+)}$ inhomogeneities, off-resonance effects.
- List typical two-pool-model parameters for brain tissue and appreciate their variability across the brain and across subjects.
- Understand the dependency of MT parameters on myelination.
- Introduce the so-called inhomogeneous MT and dipolar order.

Quantification of the transverse relaxation time, T_2 and the effective transverse relaxation time, T_2*

- Define the transverse relaxation time T_2 and the effective longitudinal relaxation time, T_2*.
- Understand multi echo methods for T_2 and T_2* mapping.
- Identify confounds and pitfalls in T_2 and T_2* mapping.

- List typical T_2 and T_2* values for brain tissue and appreciate their variability across the brain and across subjects.
- Understand the dependency of T_2 and T_2* on myelination and iron concentration.

Quantification of the magnetic susceptibility, χ

- Define the magnetic susceptibility, χ.
- Understand the multi-gradient-echo methods for susceptibility mapping.
- Identify confounds and pitfalls in susceptibility mapping, including the inversion problem and external sources.
- List typical susceptibility values for brain tissue and appreciate their variability across the brain and across subjects.
- Understand anisotropic susceptibility in white matter, e.g. via the hollow-cylinder model.
- Understand the dependency of susceptibility on myelination and iron concentration.

Diffusion-weighted imaging (DWI)

- Appreciate diffusion-weighted imaging (DWI) as a probe for microstructure.
- Understand the single and the twice-refocused spin echo experiments with diffusion-weighting gradients.
- Identify confounds and pitfalls in DWI, including eddy currents, Maxwell fields, susceptibility-related distortion.
- List typical DWI parameter values for brain tissue and appreciate their variability across the brain and across subjects.

Biophysical models and interpretation of quantitative relaxation data

- Summarize the main contrast mechanisms in quantitative MRI (PD, T_1, T_2, T_2*, MT).
- Understand basic relaxation mechanisms for water protons.
- Identify the specific sensitivity of quantitative parameters to certain brain microstructure differences and changes.
- Combination of different quantitative parameters to elucidate brain microstructure from different angles.

MR fingerprinting for accelerated acquisition of quantitative MRI data

- Understand how the signal evolution during randomized acquisitions may be modelled.
- Dictionaries for extracting the best-fitting response from all possible MR parameter combinations.
- Identify potential confounds and pitfalls and strategies for their mitigation.
- Review examples of MR fingerprinting-based qMRI.

Biophysical models and interpretation of DWI data

- Understand the dependency of DWI parameters on white and grey matter microstructure.
- Define the diffusion tensor and higher-order models including kurtosis and NODDI.
- Review examples of recent multi-modal biophysical models, such as axonal g-ratio maps.

Quantitative MRI in group analyses

- Describe spatial normalisation and shape analysis for multi-subject analyses.
- Challenges of spatial normalisation and registration of different individual brains.
- Correct treatment and transformation of quantitative MRI data in group-registration approaches; voxel-based quantification (VBQ).
- List possibilities how population studies can be used for understanding brain plasticity, development and validation of quantitative markers.

Verification of qMRI measures

- Classical 2D histological and immunohistochemical stains for myelin, neurons, glial cells or fibres.
- Clearing techniques for transforming brain tissue into optically transparent hydrogel polymers.
- Laser-scanning and light-sheet microscopy for 3D volumes.
- Physical methods for mapping tissue composition including proton-induced X-ray emission (PIXE) or mass spectrometry.