Data Acquisition & Modeling Strategies

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Most of the changes in tissue microstructure caused by pathology result in altering physical and chemical environment of water protons and therefore affect MR properties of tissue. This phenomenon is a basis of successful use of MRI in diagnosis of variety of diseases and pathological disorders. Routine, clinical imaging protocols are often optimized to maximize tissue contrast and their analysis is based on morphological patterns of intensity images. In the recent years, parametric maps representing MR parameters such as average tissue relaxation times, diffusion parameters or magnetization transfer ratio have become increasingly utilized and provide more useful information that allow for direct comparison between different clinical sessions or clinical studies. They are however, often insufficient to provide more detailed structural information. The reason for lack of parametric maps specificity is related to the fact that there is no one to one relationship between given aspect of tissue microstructure and given MR parameter. For example, T1 relaxation increase can be caused by inflammation, edema or cellular shrinkage – therefore, on the basis on T1 changes alone it is generally not possible to distinguish between these processes. Multi-parametric imaging that combines different MR parameters, to some extent, improves specificity, but it still has significant limitations. It is generally used in cases of well defined clinical problems such as in tissue classification of normal and cancerous tissue [1] or certain brain pathologies [2]. Using MRI to reveal structural characteristics of tissue microstructure generally requires more complex methods of data acquisition and analysis.

Structural aspects	MR measurements
Cellular/vascular volume fractions	Relaxation (T1, T2, T2*)
Cell dimensions and organization	Magnetization Transfer
Cell membrane/vascular permeability	Diffusion
Lipid & Protein Content	Dynamic Contrast
Water density	Spin's Motion
Vascular Flow …	Spectroscopy …

Feasibility of using MRI to assess certain aspects of tissue micro structure relies on the fact that there are several MR measurements sensitive to different structural aspects of tissue (right). However, what is also required is a physical model that links measured MR signal with tissue microstructure. Given complex water environment such models typically are quite simplistic representation of water environment. The simplest theoretical representation of tissue, yet in most cases sufficient, is the two compartmental model presented in Fig.1.

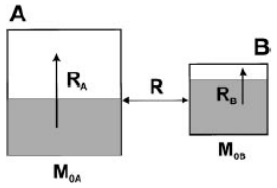

Figure 1. Tissue model consists of two compartments/pools (A-intra &B-extracellular) with the relative population of spins M_{0A}=1- M_{0B}. The un-shaded regions in each compartment represent magnetization that contributes to overall signal. R_A and R_B denote relaxation. Permeable membranes result in exchange of magnetization between compartments that can be described by exchange rate, R. Similar models can be constructed for diffusion, magnetization transfer or chemical exchange or consequently include more compartments/pools. Measured MR signal is therefore, a function of four model parameters which can be determined from carefully designed experiments.

Accurate evaluation of tissue parameters requires experimental data with sufficient number of independent features (i.e. larger than the number of model parameters). In the case of relaxation measurements that means acquiring data at multiple time points to reveal non-monoexponential behaviour and use of contrast agents at different concentrations to alter relaxation in extracellular compartment [3]. Diffusion measurements collected at different gradient strength and diffusion times generally provides sufficient data to estimate mobility of water in different compartments, their relative sizes, cell membrane permeability and cellular dimensions [4,5]. Magnetization or saturation transfer experiments with varying RF amplitudes and powers are useful to probe tissue chemical environment. Finally, combined experiments, such as diffusion-T2 or MT-T2, offer more robust evaluation of tissue microstructure [6,7]. Although, most researchers use specially developed imaging sequences to probe tissue microstructure, it is also possible to use standard imaging sequences, such as SPGR, or DTI-EPI for data acquisition. However, such sequences need to be rigorously calibrated in order to provide meaningful, physical parameters. Quantitative data fitting additionally requires substantial signal to noise and elimination of any systematic errors caused by B0 or B1 inhomogeneities. Therefore, structural assessment experiments are typically time consuming. Evaluation of tissue microstructure has been more successful in tissues with relatively simple structure but also exhibiting complex MR behaviour such as blood [4], cartilage [8] and white matter [5]. In the recent years, there is however some moderate success in evaluating tissue microstructure in more biologically complex systems. It has to be noted however, that such studies require independent validation of applied methodology using quantitative histopathology.

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