From Bench to Bed-side: Quantifying brain microstructure using multi-parameter MRI

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Symposium

Computational anatomy using T1-weighted MRI data has provided many fundamental insights into the changes in brain architecture occurring in health and disease. However, understanding the biological basis underpinning these observations is far more challenging, often reliant on indirect comparisons between unrelated studies. Quantitative MRI (qMRI) allows to directly link in vivo MR contrast measures to tissue property changes and provides a powerful suite of non-invasive tools to advance the study of brain anatomy. qMRI maps have been successfully used to study development, plasticity, aging and disease. Whilst, compared to conventional anatomical imaging approaches, qMRI provides more stable measurements across sites and greater insight at the biological level, it is not without limitations. Differences remain across scanners limiting the potential of the technology, necessitating the underlying variability in proprietary hardware and software used by MR vendors to be addressed.
This symposium will bring together advances in qMRI at the level of physics, processing, analysis and applications. Dr. Keenan (U.S. National Institute of Standards and Technology) will introduce the qMR basics and resources for standardizing the field. Dr. Phillips (University of Liège) will discuss qMR analysis tools and how to interpret the results. Dr. Huang (Massachusetts General Hospital) will present clinical applications and opportunities for qMR in studying neuroinflammatory disease. Finally, Dr. Lambert (UCL) will discuss advances and applications in the study of early and pre-clinical neurodegeneration. Attendees will gain a comprehensive grounding in science of qMRI, an overview of state-of-the-art developments, and the opportunities to apply these techniques to their own research.

Objective

- Recognise that even in qMRI the choice of hardware and imaging protocol will affect quality and comparability within and across sites. This will allow the user to describe the challenges related to reproducibility in the field.
- Learn the specificity of qMRI data processing and hear about available open access dedicated analysis tools.
- Discover neuro-scientific applications of qMRI in fundamental and translational research.

Target Audience

We target a wide audience spanning from clinical and fundamental neuroscientists, MR physicists up to computational scientists to convey the paradigm shift in computational anatomy using qMRI. Additionally, we will engage the OHBM open science community by addressing issues of data transparency and reproducibility depending on MRI hardware and protocol design.

Presentations

Getting Started with Quantitative MRI

Quantitative MRI can be defined as any measurement derived from an MR image that can be assigned a unit. This definition encompases distance and volume, meaning that the community's structural MRI work is quantitative. Quantitative MRI also includes T1, T2 and T2* relaxation times, susceptibility, diffusion, magnetization transfer, etc. There are challenges of comparing quantitative data, even simple distance or contrast measurements, across sites or over time, as discovered by early work on the ADNI trial and, separately, with the fBIRN phantom (Friedman and Glover, 2006). The origin of these discrepancies is the acquisition platform, including both hardware and software, and we should be aware of the steps leading to the images (not just the analysis after the image is created). Recent studies documented challenges in acquiring quantitative data across platforms and over time (such as scanner upgrades Lee et al., 2019; Keenan et al., 2019). Steps can be taken in the acquisition process to both limit and quantify these variations. In this talk, I will discuss the physics behind certain quantitative methods and present some tools to address these challenges: phantoms for quality assurance (e.g. for distance, T1, T2, susceptibility, and isotropic diffusion) and methods to improve repeatability and reproducibility across sites (e.g. tools like the HeartVista platform RTHawk, which can be used to implement the same pulse sequence across scanners regardless of vendor and software version).

Presenter

Kathryn Keenan, National Institute of Standards and Technology Boulder, CO, United States

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Going Beyond Morphometry with Quantitative MRI, Benefits, and Challenges

The signal in quantitative structural MR images has a physical interpretation, which informs us about the brain tissue microstructure properties such as macromolecular, iron, and water content. Moreover this information is available for both grey and white matter tissues. Therefore there is more than the shape of the brain to explore: morphometric analysis (e.g. "voxel-based morphometry" of grey matter volume or cortical thickness) are still possible but "voxel-based quantification" (VBQ) analysis can complement these and provide new insights. Nevertheless the quantitative nature of the images and their improved contrast, especially in subcortical areas, calls for specific processing steps. The aim of this presentation is thus to highlight, as compared to standard structural MRI, potential pitfalls and solutions for the handling of qMRI data, at the individual and group level. For a VBQ approach I will cover issues related to segmentation and normalization, requiring updated "tissue probability maps" (Lorio et al., 2016) and the difficulty of handling the noise component amplified by the map creation. Smoothing should also be applied separately for grey and white matter, in order to avoid mixing tissue properties at the interfaces and introducing partial volume effect. The multiplicity of maps and tissue classes to analyze also brings in new statistical challenges. Finally I will introduce existing tools, like qMRLab and hMRI, that can help end-users make sense of qMRI data and encourage tool developers to tackle new challenges.

Presenter

Christophe Phillips, Ir. PhD, University of Liège, GIGA Institute, Liège, Belgium

Translating Quantitative MRI Techniques from Research Applications to Clinical Trials and Practice

I will discuss the opportunities and challenges of translating quantitative MRI techniques from research applications to clinical trials and practice, with an emphasis on measuring white matter inflammatory injury and damage in the context of multiple sclerosis and other neuroinflammatory conditions. Quantitative multi-parametric mapping of tissue properties dates to the early days of MRI, yet diagnosis in neurological disease still relies on subjective assessments of non-quantitative, contrast-weighted images. I will provide an overview of how the understanding of neuroinflammatory tissue injury has progressed beyond characterizing the burden of T2 hyperintense lesions and cerebral atrophy to quantifying the amount of myelin damage and axonal damage using quantitative T2 mapping, magnetization transfer and advanced multi-compartment diffusion MRI models. Continued progress within the field will require improved harmonization, reliability, and efficiency in the acquisition of quantitative MRI markers, and significant logistical and practical issues continue to surround adoption beyond research scenarios. I will describe some techniques that have already been successfully used as biomarkers in clinical trials, and approaches to overcoming the barriers to their translation into clinical practice.

Presenter

Susie Huang, MD, PhD, Massachusetts General Hospital, Harvard Medical School, Department of Radiology Boston, MA, United States

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Mapping Subcortical Nuclei using qMRI: Applications for neurodegenerative disorders

Conventional structural MRI techniques, such as those provided using T1 and/or T2-weighted MRI, have been widely adopted by a number of large initiatives (e.g. ADNI, PPMI) yet are completely unable to accurately map brainstem or subcortical nuclei at an individual subject level. This represents a major problem: First, it will implicitly bias any derived results to areas that can be more easily aligned using T1w MRI (i.e. the cortex). Second, in many neurodegenerative disorders, including Parkinson's and Alzheimer's disease, these deep cortical structures are affected many years before overt clinical symptoms develop, and therefore represent key targets for potential prodromal biomarkers. In this talk, I will use MRI meta-analytical techniques to highlight the major discrepancies between current structural imaging results, and the canonical, disease-defining, pathological damage seen ex vivo. I will show how qMRI based methods can be used to improve imaging of these subcortical and brainstem structures at an individual subject level, including the hypothalamus, locus coeruleus, thalamic and medullary nuclei. I will then demonstrate proof of concept using the most common subcortical neurodegenerative condition worldwide, Parkinson's disease.

Presenter

Christian Lambert, Wellcome Centre for Human Neuroimaging London, United Kingdom