Specialty area: Diffusion Goes Mad Course | Speaker Name: Yaniv Assaf, assafyan@post.tau.ac.il

HIGHLIGHTS:

- Diffusion MRI allows investigation of micron-scale features of white matter;
- Axonal Density and diameter distribution can be reliably extracted from diffusion MRI;
- Micro-structure is dynamic

# TITLE: q-Space and Micro-Structure

TARGET AUDIENCE: Students and researchers in the field of diffusion MRI. Students and researchers that seek to explore the fine micro-structure of the nervous system, its relation to neurophysiology and the CONNECTOME.

OBJECTIVE: To introduce axon diameter and axon density measurements with diffusion MRI and demonstrate their utility in exploring brain connectivity and neuro-physiology.

PURPOSE: There are no in-vivo probes that can quantify white matter's physiology (e.g. conduction velocity). These features of white matter are traditionally measured by invasive procedures on excised tissue samples. However, since white matter physiology is correlated with its micro-structure one can elucidate on the one by measuring the other. DTI provided the first unique measure of white matter's micro-structure: the diffusion anisotropy. Despite the fundamental new insights it provides, the DTI model [1] is not specific to any of the underlying tissue micro-structural features. Therefore, in this course we will introduce and demonstrate the utility of using micro-structural directed measures such as AxCaliber and CHARMED to study the white matter and its physiology.

METHODS: Recent geometrical models of diffusion offers a more direct measure of microstructural features [2, 3]. AxCaliber, is used to compute the axon diameter distribution (ADD) in each voxel through the measurement of diffusion weighted signals in various diffusion times. This model is based on the assumption that water diffusion within the axon is restricted while elsewhere it is only hindered. The idea behind AxCaliber is that each axon, depending on its diameter, will experience restricted diffusion at a different diffusion time.

RESULTS: The AxCaliber framework was verified on excised samples of optic and sciatic nerves and in-vivo on rat corpus callosum by comparison of the computed ADD with the histological analysis of the same samples (Fig. 1). Moreover, the relation of ADD measures to neurophysiology (conduction velocity) and white matter plasticity will be presented.

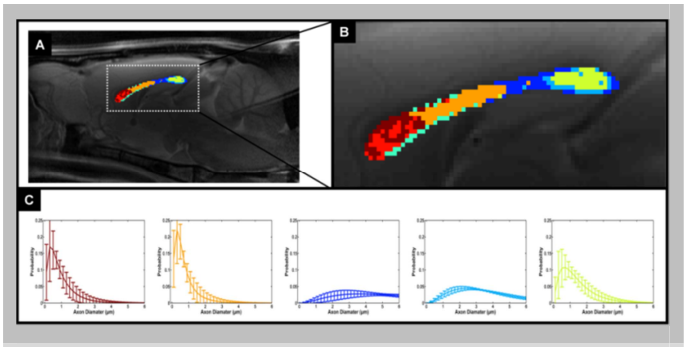


Fig. 1: Cluster analysis of the ADD along the corpus callosum: (A, B) A mid-saggital T2-weighted MRI with the AxCaliber clusters super-imposed (C) The AxCaliber averaged ADDs for the different clusters given in (A)

DISCUSSION & CONCLUSIONS: With the geometrical model approach (as in CHARMED and AxCaliber) it is possible to use diffusion MRI to extract compartment specific information and thus turning it into a microstructural probe that actually serves as a virtual histological tool. These kinds of measures represent white matter more directly and thus may infer accurately on the physiology of white matter.

REFERENCES: **1.** Basser, P.J. Inferring microstructural features and the physiological state of tissues from diffusion-weighted images. *NMR Biomed* **8**, 333-344 (1995). **2.** Assaf, Y. & Basser, P.J. Composite hindered and restricted model of diffusion (CHARMED) MR imaging of the human brain. *Neuroimage* **27**, 48-58 (2005). **3.** Barazany, D., Basser, P.J. & Assaf, Y. In vivo measurement of axon diameter distribution in the corpus callosum of rat brain. *Brain* **132**, 1210-1220 (2009).