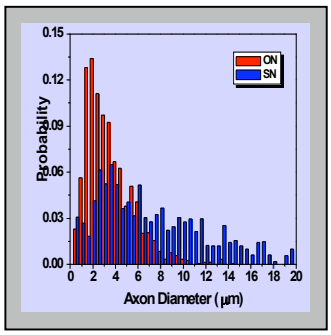
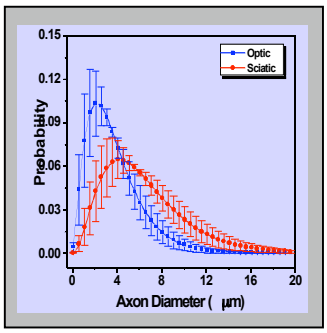
***AxCaliber*: An MRI Method to Measure the Diameter Distribution and Density of Axons in Neuronal Tissue**

P.J. Basser[a], T. Blumenfeld[b], G. Levin[b], Y. Yovel[b], Y. Assaf[b], [a]STBB/LIMB/NICHD, NIH; [b]Department of Neurobiochemistry, Tel Aviv University

The experimental determination of the diameter distribution, $p(d)$, of emulsions and droplets has long been studied using NMR methods (see (1,2)). In these experiments, $p(d)$ is estimated from PFG data by assuming a model of restricted diffusion within spheres. We have adapted this approach to estimate the diameter distribution within cylindrical nerve fascicles—a pack or array of nerve axons—by assuming that axons contain a restricted pool of water within their intracellular spaces. A composite hindered and restricted model of diffusion (*CHARMED*) within axons was first elaborated and tested in (3), and then applied clinically in (4).





The *AxCaliber* framework presented here extends *CHARMED* by providing an estimate of $p(d)$ directly from diffusion weighted (DW) MR data. In this implementation, a *Gamma* distribution is assumed to describe the axon diameter distribution. Parameters of this distribution are then estimated from the PFG data in optic nerve(ON) and sciatic nerve (SN) bundles. The estimated $p(d)$ using *AxCaliber* (above right) is compared with measurements obtained from histological analysis (above left).

MR experiments were performed using a 7T scanner (Bruker, Germany) on fixed porcine nerve tissue. High b-value DWIs were acquired with a stimulated echo DWI sequence with the following parameters: TR/TE=3000/166ms, δ=2.5ms, G_{max}=120 G/cm, # averages = 8, with the diffusion time, Δ, chosen from 20 to 150ms in 8 increments. Diffusion gradients were applied only perpendicular to the nerves' axes in 16 gradient amplitude increments for each Δ. The entire acquisition consisted of 128 DW spectra acquired in 51 min. Histological analysis was performed using conventional myelin basic protein (MBP) stains along with particle sizing software used on the histological sections.

Agreement between MR and histology data is excellent, suggesting the possibility for measuring $p(d)$ *in vivo* using DW-MRI data.

The marriage between MRI and porous media theory with biology and medicine is generating promising new applications. *AxCaliber* is one such example of a growing discipline of *virtual in vivo tissue biopsy*.

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