A COMPARISON OF HARDI AND RESTRICTED DIFFUSION Q-SPACE IMAGING FOR ASSESSMENT OF AUDITORY NERVE INTEGRITY

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INTRODUCTION: Since the introduction of the bionic ear over 30 years ago, cochlear implants have been remarkably successful in providing hearing to the profoundly deaf. There is great variability, however, in the benefit that individual cochlear implant users experience. One of the main factors in performance is the duration of deafness prior to implantation; it is assumed that auditory depravation leads to deterioration of the auditory nerve, including death of spiral ganglion cells and loss of myelin [1,2]. This has not been able to be verified, however, other than through indirect measures because of the invasiveness of direct measurement of auditory nerve condition. Although structural MRI has been used to investigate cochlear nerve cross-sectional area in normal and postlingually deafened patients [3], microstructural white matter measures using diffusion imaging techniques have yet to be applied to the auditory nerve itself. Diffusion imaging studies have instead focused on the integrity of the subcortical auditory tracts, for example, in patients with auditory nerve deficiencies [4]. The lack of non-invasive direct assessment of the auditory nerve via diffusion MRI motivated this study. In particular, we compare high angular resolution diffusion imaging (HARDI) and AxCaliber-type q-space approaches from which axon diameter densities can be inferred [5,6]. We assess both techniques in ex vivo rat cochlea, with the aim of developing a clinical tool to predict the viability of cochlea implantation prior to surgery. Our results prompt us to conjecture that AxCaliber-type approaches will prove more efficacious than HARDI for in vivo assessment of the auditory nerve.

METHODS: An intact cochlea, auditory nerve and surrounding tissue were sectioned from a perfusion fixed (4%PFA) Sprague Dawley rat. The sample was imaged by 4.7 T Brüker Biospec system using a cryogenically cooled surface coil suspended within a BGA12S-HP gradient set. **Structural dataset:** 3D RARE, rare factor=8, TR/TE_{eff}=1000/30ms, NEX=2, NR=2, FOV = 1.28x1.28x0.48cm^3,matrix size=256x256x96 for $50^3\mu m^3$ resolution. **HARDI dataset:** 8-shot dw-EPI, TR/TE=4000/33.08ms, NEX=5, FOV=1.92x1.92cm^2, matrix size=192x192, 126 directions, b=3000s/mm^2, δ=6ms, Δ=14ms, 14 slices each 100µm, spaced at 200µm intervals. A second acquisition was acquired with the same parameters and slice interval shifted 100µm to cover the region of interest. The protocol was repeated three times. Data were analysed using FSL-FDT software. **q-space dataset:** 16-shot dw-EPI, single 1mm slice perpendicular to the auditory nerve, TR/TE=3000/23ms, FOV=1x1cm^2, matrix size=128x128, g={5,10,…,50,75,100,…,400}mT/m, δ=5ms, Δ={20,40}ms. A single region of interest within the auditory nerve was manually delineated. The distribution of axon diameters was estimated using our recent method [6] that provides a simple closed-form model of restricted diffusion on the micron-level scale of axons.

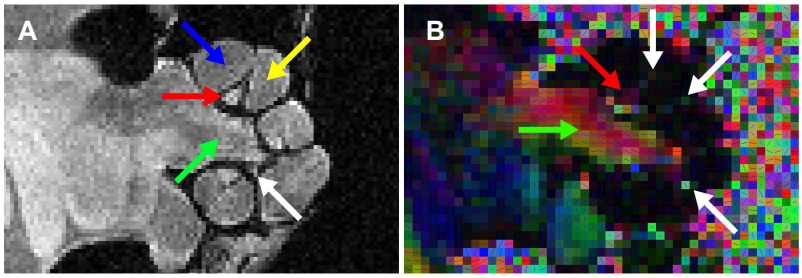

Figure 1 A. 50x50x50μm^3 T2-weighted image of the rat cochlea showing scala vestibuli (yellow arrow), scala tympani (blue arrow), auditory nerve (green arrow), spiral ganglion (red arrow) and small connecting fibres (white arrow). **B.** Corresponding HARDI data showing the auditory nerve (green arrow) and spiral ganglion (red arrow), colour-encoded by principle eigenvector modulated by fractional anisotropy, overlaid with distributional mean of fibre orientations (thin blue lines). Note the apparent small connecting fibres running to and from the spiral ganglion. Each square is a 100x100x100μm^3 voxel.

RESULTS: High-resolution structural T2-weighted images clearly show the cochlea anatomy including the perilymph filled scala vestibuli, scala tympani, auditory nerve, spiral ganglion and connecting fibres (Fig 1A). It was of interest to determine the level of this information able to be assessed using a HARDI acquisition. The standard colour-encoded diffusion information is shown in Fig.1B, overlaid by the distributional mean of fibre orientations (FSL-BedpostX output). The anisotropic and colinear fibres of the auditory nerve are clearly visible, with the suggestion of visible fibres branching outward from the auditory nerve to the spiral ganglia. In comparison, the q-space imaging assessment of the auditory nerve (Fig.2A) produced a normalised diffusion decay curve, $E(q)$, that was well-fit by a two-compartment hindered/restricted model (Fig.2B). The resultant estimated axon diameter distribution with mean 1.7µm (Fig.1C) closely agrees with histology (1.7 +/- 0.5µm [7]).

CONCLUSION: We have presented HARDI data of the rat cochlea suggestive of being able to resolve the fibres of the auditory nerve branching out to the spiral ganglia. Despite the wealth of information obtained within such images, the scan times involved and technical difficulties with in vivo subjects greatly limit the viability for human auditory nerve studies. In contrast, obtaining the distribution of auditory nerve axon diameters can be determined from images requiring a fraction of the imaging time, and when used in combination with lower resolution DWI can provide a comprehensive assessment of the condition of the auditory nerve. Future work will use apply these techniques in normal and deafened animals.

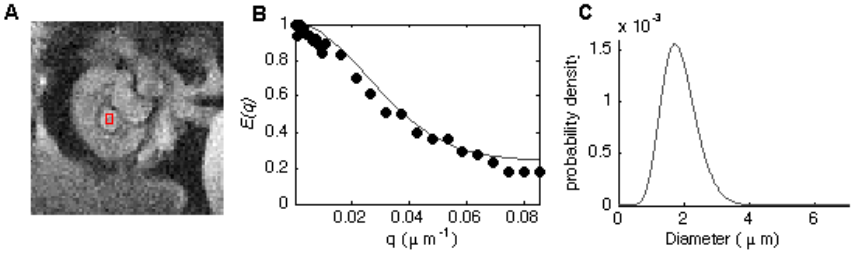

Fig.2 A. Auditory nerve ROI (red square) in ex vivo rat cochlea. **B.** Signal decay, $E(q)$, experimental (dots), and estimated (line). **C.** Inferred axon diameter distribution.

References: [1] Blamey *et al* (1996) *Audiology & Neurotology* 1:293-306. [2] Sarant *et al* (2001) *Ear Hear* 22:18-28. [3] Herman & Angeli (2011) *Otolaryngology Head and Neck Surgery* 144(1):64–66. [4] Wu et al (2009) AJNR Am J Neuroradiol 30:1773-77 [5] Assaf *et al* (2008) *MRM* 59:1347-1354. [6] _____ [7] Barbary (1991) *Hearing Res* 54:75-90.