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## Feasibility of Quantitative Diffusion MR Tractography of the Vestibulocochlear Nerve in Children with Unilateral Profound Sensorineural Hearing Loss

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### Synopsis

**Diffusion MR tractography modeling of the vestibulocochlear nerve (VCN) has clinical value for characterizing hearing loss and surgical planning for cochlear implants; however, the neuroanatomy of the VCN presents technical challenges to image-based modeling. We conducted a feasibility study to evaluate VCN tractography in children with unilateral sensorineural hearing loss using advanced diffusion MRI acquisitions and modeling techniques. The results indicate tractography of the VCN is clinically feasible and quantitative tractography metrics reflect lateralization of hearing loss. We further found significant improvements from a reverse-phase encoding acquisition and multi-shell multi-compartment diffusion modeling.**

### Introduction

MR imaging of vestibulocochlear nerve (VCN) is important for the characterization of hearing loss and surgical planning of cochlear implants<sup>3,14</sup>, and diffusion MR tractography is an emerging tool for VCN modeling<sup>6,7,13</sup>. Previous studies have shown that tractography can be useful for modeling the VCN; however, the neuroanatomy of the VCN presents technical challenges to its visualization and quantitation with MRI, due to its small size and the presence of susceptibility induced artifact<sup>1,2,5,8,9,10</sup>. We conducted a feasibility study of quantitative VCN tractography in children with unilateral severe to profound sensorineural hearing loss (SNHL) to evaluate advanced diffusion MR image acquisition and modeling techniques in this group. We specifically examined the relationship in laterality between tractography metrics and hearing loss, and evaluated multi-shell multi-compartment tractography compared to single-shell diffusion tensor tractography.

### Methods

MR imaging data was collected from four children with SNHL (mean age = 10 y.o, three females, average hearing loss = 102.5 dB HL, average unaffected ear = 12.5 dB HL) on a Siemens Prisma 3T scanner. T2-weighted SPACE scans at 0.5 mm isotropic resolution were acquired along with a multi-shell HCP-style diffusion-weighted imaging (DWI) at 1.5mm isotropic resolution with 14 scans at  $b=0$  s/mm<sup>2</sup>, 93 scans at  $b=1500$  s/mm<sup>2</sup>, 94 scans at  $b=2500$  s/mm<sup>2</sup>, and a complete repetition with reversed phase encoding in the anterior-posterior direction.

DWIs were denoised with a Rician non-local means filter and motion, susceptibility, and eddy current artifacts were corrected with FSL eddy<sup>4</sup>. Single diffusion tensor (SDT) models were fit using the  $b=1500$  data, and the multi-compartment models (MCM) were fit using both shells using FSL bedpostx<sup>4</sup>. Deterministic streamline tractography reconstructions of each VCN were created with SDT and MCM models using the Quantitative Imaging Toolkit<sup>12,15</sup>. 1000 seed points were sampled inside a 5mm radius sphere manually placed at the base of the pons in the brainstem. The study primarily focuses on the nerve, so tracking was stopped with manually placed box to exclude upstream connectivity. VCN tracks were selected by a 5mm radius sphere placed at the expected termination point of the VCN near the cochlea. Each tractography model was summarized by its track count, volume, average length, average density, and maximum density.

To compare imaging measures and SNHL, left and right metrics were combined to estimate a laterality index (LI) for each metric, which was defined by  $LI = 2.0 * (left - right) / (left + right)$ . This is a dimensionless measure of laterality, where a positive value indicates greater values on the left, while a negative value indicates greater values on the right. The measure is scaled by the average value, so that the LI can be more directly compared across imaging metrics with different units, such as length, volume, etc.

### Results

Tractography reconstructions of both left and right VCNs were found in all cases. A qualitative comparison showed shorter and smaller distribution of tracks consistent with the side with hearing loss (Fig 1). MCM revealed complex fiber architecture where the VCN enters the brainstem, while SDT modeling showed abrupt changes in fiber orientations (Fig 2). A quantitative analysis showed that the LI of track count, volume, length, and density reflected laterality consistent with subject's side of hearing loss (Fig 3). SDT tractography had a mean LI of 0.137 and MCM tractography had a mean LI of 0.317, and a paired t-test showed that MCM LI was significantly higher than DT ( $p=0.028$ ,  $t=-2.37$ ,  $df=19$ ). The improvements of MCM over SDT modeling were also present within each individual metric. We found that geometric distortion correction with FSL eddy was necessary to accurately co-register T2 and DWI datasets (Fig 4).

### Conclusions

Quantitative tractography is clinically feasible in SNHL and provides a variety of promising quantitative imaging biomarkers with potential prognostic and diagnostic value. Multi-compartment modeling and correction of susceptibility induced artifact are recommended for improving accuracy and sensitivity in tractography-based analysis of the VCN. Compared to previous work, we demonstrate the strengths of tractography metrics obtained using advanced image acquisition and modeling techniques, as they provide quantitative metrics and visualizations that are useful in characterizing SNHL. Several open problems remain, specifically to evaluate the subdivision of the VCN into cochlear and vestibular subcomponents and separation from the facial nerve. The results also demonstrated how multi-compartment diffusion modeling can reveal complex patterns of connectivity deeper into the brainstem; however, larger sample size is needed to investigate these in relation to SNHL.

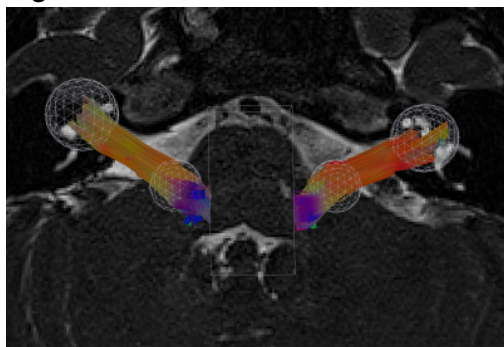
## Acknowledgements

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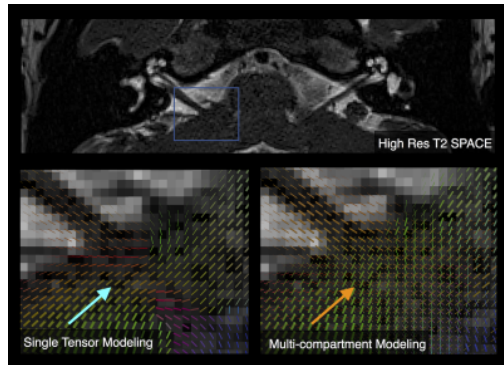
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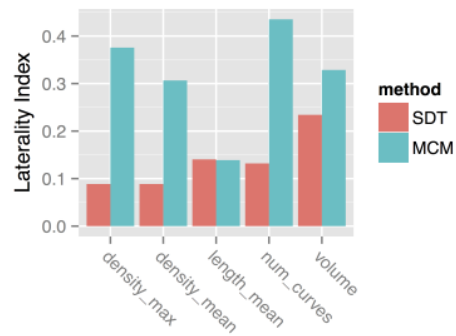
## Figures



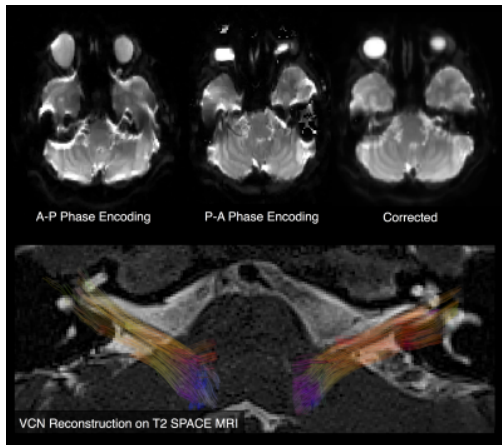
An illustration of the workflow used for VCN reconstruction. The spheres in the brainstem were used for seeding, and the spheres at the cochlea were used to selecting tracks. Boxes was used to terminate tractography to isolate the nerve. The tracks are superimposed with the T2 SPACE MRI, which showed good registration with the diffusion MRI.



An illustration of the differences between single diffusion tensor (SDT) modeling and multi-compartment modeling (MCM). Fiber orientations are shown in tube glyphs superimposed on the high resolution T2-weighted SPACE scan. The radius of the tube was modulated by the FA in SDT and volume fraction in MCM. The results show that MCM revealed complex crossing fibers in the region where the VCN enters the brainstem, which created artefactual changes in fiber orientations with SDT modeling (blue arrow) that is better represented as crossing fibers with MCM (orange arrow).



A comparison of quantitative tractography metrics obtained from single diffusion tensor (SDT) modeling and multi-compartment modeling (MCM). Each bar represents the mean laterality index, where higher values are likely to indicate greater sensitivity to differences in nerve integrity between the healthy and abnormal VCN. We found all metrics reflected hearing laterality to some degree, but MCM showed significantly higher laterality scores than SDT.



An illustration of susceptibility-induced artifact and corrections. The top row shows raw data in the left and middle panels, corresponding to the anterior-posterior (AP) and posterior-anterior (PA) phase encodings. The top right shows the result of FSL eddy correction of the spatial artifact. The bottom shows the resulting tractography reconstructions of the VCN superimposed on a slice of the T2 SPACE MRI, indicating the quality of the registration between the scans.