## **Trigeminal nerve tractography**

Currently, Trigeminal nerve imaging mostly rely on T2-weighted magnetic resonance imaging (MRI), which provides localization of the cisternal portion of the TGN where the contrast between nerve and cerebrospinal fluid (CSF) is high enough to allow differentiation. The course of the TGN within the brainstem as well as anterior to the cisternal portion, however, is more difficult to display on traditional imaging sequences. An advanced imaging technique, diffusion MRI (dMRI), enables tracking of the trajectory of TGN fibers and has the potential to visualize anatomical regions of the TGN not seen on T2-weighted imaging. This may allow a more comprehensive assessment of the nerve in the context of pathology. To date, most work in TGN tracking has used clinical dMRI acquisitions with a b-value of 1000 s/mm2 and conventional diffusion tensor MRI (DTI) tractography methods. Though higher b-value acquisitions and multi-tensor tractography methods are known to be beneficial for tracking brain white matter fiber tracts, there have been no studies conducted to evaluate the performance of these advanced approaches on nerve tracking of the TGN, in particular on tracking different anatomical regions of the TGN.

Xie et al. compared TGN tracking performance using dMRI data with different b-values, in combination with both single- and multi-tensor tractography methods. The goal was to assess the advantages and limitations of these different strategies for identifying the anatomical regions of the TGN.

They proposed seven anatomical rating criteria including true and false positive structures, and performed an expert rating study of over 1000 TGN visualizations, as follows. They tracked the TGN using high-quality dMRI data from 100 healthy adult subjects from the Human Connectome Project (HCP). TGN tracking performance was compared across dMRI acquisitions with b = 1000 s/mm2, b =2000 s/mm2 and b = 3000 s/mm2, using single-tensor (1T) and two-tensor (2T) unscented Kalman filter (UKF) tractography. This resulted in a total of six tracking strategies. The TGN was identified using an anatomical region-of-interest (ROI) selection approach. First, in a subset of the dataset, they identified ROIs that provided good TGN tracking performance across all tracking strategies. Using these ROIs, the TGN was then tracked in all subjects using the six tracking strategies. An expert rater (GX) visually assessed and scored each TGN based on seven anatomical judgment criteria. These criteria included the presence of multiple expected anatomical segments of the TGN (true positive structures), specifically branch-like structures, cisternal portion, mesencephalic trigeminal tract, and spinal cord tract of the TGN. False-positive criteria included the presence of any fibers entering the temporal lobe, the inferior cerebellar peduncle, or the middle cerebellar peduncle. Expert rating scores were analyzed to compare TGN tracking performance across the six tracking strategies. Intraand inter-rater validation was performed to assess the reliability of the expert TGN rating result.

The TGN was selected using two anatomical ROIs (Meckel's Cave and cisternal portion of the TGN). The two-tensor tractography method had significantly better performance on identifying true positive structures while generating more false-positive streamlines in comparison to the single-tensor tractography method. TGN tracking performance was significantly different across the three b-values for almost all structures studied. Tracking performance was reported in terms of the percentage of subjects achieving each anatomical rating criterion. Tracking of the cisternal portion and branching structure of the TGN was generally successful, with the highest performance of over 98% using two-tensor tractography and b = 1000 or b = 2000. However, tracking the smaller mesencephalic and spinal cord tracts of the TGN was quite challenging (highest performance of 37.5% and 57.07%, using two-tensor tractography with b = 1000 and b = 2000, respectively). False-positive connections to the temporal lobe (over 38% of subjects for all strategies) and cerebellar peduncles (100% of subjects for all strategies) were prevalent. High joint probability of agreement was obtained in the inter-rater (on average 83%) and intra-rater validation (on average 90%), showing a highly reliable expert rating

## result.

Overall, the results of the study suggest that researchers and clinicians may benefit from tailoring their acquisition and tracking methodology to the specific anatomical portion of the TGN that is of the greatest interest. For example, tracking of branching structures and TGN-T2 overlap can be best achieved with a two-tensor model and an acquisition using b = 1000 or b = 2000. In general, b = 1000 and b = 2000 acquisitions provided the best-rated tracking results. Further research is needed to improve both sensitivity and specificity of the depiction of the TGN anatomy using dMRI<sup>1</sup>.

## 1)

Xie G, Zhang F, Leung L, Mooney MA, Epprecht L, Norton I, Rathi Y, Kikinis R, Al-Mefty O, Makris N, Golby AJ, O'Donnell LJ. Anatomical assessment of trigeminal nerve tractography using diffusion MRI: A comparison of acquisition b-values and single- and multi-fiber tracking strategies. Neuroimage Clin. 2020 Jan 8;25:102160. doi: 10.1016/j.nicl.2019.102160. [Epub ahead of print] PubMed PMID: 31954337.

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