

## Experience with q-ball language tracking in brain tumor patients

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### Target audience

Clinical practitioners and scientific investigators involved in language function and pre-surgical planning of brain tumor patients.

### Purpose

I) To evaluate the feasibility and reproducibility of our implementation of q-ball residual bootstrap probabilistic fiber tracking in pre-surgical planning of brain tumor patients; II) to explore the possibility of post surgical fiber tracking reconstruction to assess white matter connectivity status; III) to correlate fiber tracking results with language function pre and post surgery.

### Materials and methods

**Subjects** We reconstructed 280 fiber pathways in 35 individuals (46±15 ave±stdev) with diagnosed of brain tumor (14 WHO II; 11 WHO III; 10 WHO IV) who underwent awake left hemisphere surgical resection in eloquent regions with mapping techniques. **Clinical evaluation:** All patients underwent neurological evaluation at baseline prior to surgery, at discharge (within 3 days) and at follow up (6±5 months), in order to identify any language deficit. **MRI acquisition:** Subjects were scanned pre and post surgery with a 3T General Electric Medical Systems scanner (Discovery MR750). HARDI (TR/TE =6425/80 ms, 50 axial slices, 2.2 mm<sup>3</sup> isotropic voxel, b-value=2000 s/mm<sup>2</sup>, 55 diffusion gradients, 1 b0), FLAIR datasets were acquired pre and post surgery. 3D high-resolution T1-weighted IRSPGR (TR/TE/TI =7/2/400 ms, 180 axial slices 1 mm thickness, 0.94 x 0.94 mm<sup>3</sup> in plane resolution) was acquired only before surgery. **MRI data analysis:** HARDI datasets were corrected for movement and eddy-current distortions using FSL. The original gradient table was consequently rotated. <sup>1</sup> Dipy was used to fit diffusion tensors and for q-ball probabilistic fiber tracking.<sup>2</sup> **Tracking methods:** We have developed pre surgical mapping for eight language tracts. In-vivo diffusion MRI fiber tractography pre and post surgery were performed by a trained neuroradiologist in order to reconstruct white matter bundles belonging to either ventral or dorsal language streams. **Intraoperative use of tracking results:** Pre-surgical Fractional Anisotropy (FA) maps of each patient were co-registered to the anatomical images using FSL linear and non-linear transformations (FMRIB's FLIRT and FNIRT registration tools). By applying the direct transformation matrix we registered for each subject pre-surgical fiber tracking results (as binary mask) to the anatomical images. The data were imported into the BrainLab Navigation system and used by the surgeon in the operative room. **Tracking results rating scores:** Two operators independently evaluated the reconstructed tracts pre and post surgery and rated their involvement qualitatively (0: null; 1:mild; 2:moderate; 3: severe). Intra-operator concordance was assessed for the rating scale. Differences were resolved by consensus. **Volumetric Analyses:** Volumetric measures were calculated by segmenting hyperintense regions on axial T2 fluid-attenuated inversion-recovery (FLAIR) and T1-weighted contrast-enhanced MR images before and after surgery. **Reliability of fiber tracking reconstruction:** Two operators independently reconstructed several white matter pathways bilaterally in 10 healthy subjects (4 female; age 38±12). For each tract we evaluated: volume of binary density mask and percentage of overlap of the binary mask results by Sørensen-Dice index. The evaluation was performed at several threshold of the original density mask 0, >5, >10, >25, >50, >100 streamlines. **Statistical analysis:** Cross-sectional pre-surgical and long-term follow-up language deficits were used as response variables in separate partial least squares models with language tracts ratings and WHO grades as explanatory variables. In a longitudinal predictive model for long-term follow-up language deficits, pre-surgical tracts and language deficits along with WHO grade were used as explanatory variables.

### Results

**Reliability:** Pre and post surgical fiber tracking reconstruction was successful in all patients. Inter-operator agreement on tracts rating was 96 ± 3% (ave±stdev) for pre surgical data and 98 ± 2% for post surgical data. The language tract reconstruction spatial extent showed a high inter-operator reliability (78± 2% of Sørensen-Dice index, range between 74 to 85% depending on tract) for threshold of 10 streamlines. **Clinical data:** Eighty percent (28 of 35) of the patients did not show any clinical dysfunction at pre-surgical evaluation or at longer-term follow-up; however, 6 out of these 28 had some language deficits at discharge, which later resolved. Three out of 35 patients (9%) had a pre-surgical language dysfunction that persisted after surgery. Four out of 35 patients (11%) developed post-surgical language dysfunction. **Imaging results:** The average percentage of resection was 95±7% (ave±stdev). For the post-surgical tract evaluation, 80% (226 of 280) did not change, 16% got worse, and 4 % improved; significant worsening (null/mild to the moderate/severe changes) occurred for 9% (26 of 280). **Clinical and tracking correlation:** In the separate cross-sectional models 40% of the variability of the pre-surgical and 47% of the post-surgical language deficits were explained; the left arcuate (AF), temporo-parietal component of the superior longitudinal fascicle (SLF-tp), and middle longitudinal fascicles (Md-LF) significantly impacted the patients' language function and higher WHO grades showed worse language function. In the longitudinal model the pre-surgical data (pre-surgical deficits, AF, SLF-tp and Md-LF tract ratings) predicted 53% of the variability in the long-term language deficits. Of the 4 patients with new post-surgical language deficits, only one had significant worsening of tracts (the AF and SLF-tp).

### Discussion and conclusions

We show the successful application of q-ball tracking in pre-surgical planning for language pathways in brain tumor patients and for post-surgery white matter tracking in order to assess tract damages. The rating scales developed for fiber pathways damage were found to be highly reproducible and provided significant correlations with language deficits. The fiber tracking spatial inter-operator reliability was very high considering the intrinsic variability of this technique on a voxel-wise segmentation. Our results confirm the importance of preservation of dorsal stream tracts (AF and SLF-tp), in order to reduce language morbidity of brain tumor patients.<sup>3</sup>

### References

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