Standard and Probabilistic Models of Diffusion Tensor Imaging and Tractography in Patients with Brain Tumors

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Introduction:
It has been suggested that damage to white matter tracts by lesions, stroke, or surgical intervention may be a more significant predictor of speech recovery than the grey matter localization of putative language areas. Therefore, the localization of brain tumors in the context of major functional areas and axonal networks is crucial in diagnosis, surgical planning, and post-operative assessment. In addition to the usual fiber tracking challenges related to small fibers that may make sharp turns and/or encounter crossing fibers, tractography in patients with brain tumors may be compromised by the tumor and/or the associated edema. In patients with brain tumors near the arcuate fasciculus, we hypothesize that tractography based on a probabilistic model will perform better than tractography based on a standard deterministic model.

Materials and Methods:
We retrospectively identified 10 patients (mean age 52 years, range 30-76, 5 females and 5 males) with brain tumors (3 glioblastomas, 1 anaplastic oligodendroglioma, 3 low grade astrocytomas, 1 low grade oligoastrocytoma, 1 ependymoma, 1 breast metastasis) in the left hemisphere <2 cm from the expected location of the arcuate fasciculus. All 10 patients were left dominant for language by fMRI and had language deficits on the Boston Diagnostic Aphasia Examination. Patients were imaged on a 1.5 T (n=5) or 3.0 T (n=5) magnet (Signa HDx and Excite, GE Medical Systems, Milwaukee, WI) using a standard quadrature head coil. fMRI was performed using phonemic fluency, semantic fluency and verb generation paradigms with TR/TE=4000/35-40 ms, matrix 128×128, slice thickness 4.5 mm. DTI was acquired with a single shot spin-echo echo-planar imaging sequence using 25 noncollinear gradient directions, TR/TE=13,500/100 msec, matrix 128×128, in-plane resolution 1.88×1.88 mm, slice thickness 3 mm, b-value 1000 sec/mm^2 and NEX 1.The arcuate fasciculus was reconstructed using DTI&FiberTools (Medical Physics, Department of Diagnostic Radiology, University Hospital, Freiburg, Germany) implementing both deterministic and probabilistic algorithms. The deterministic model was based on the Fiber Assignment by Continuous Tracking (FACT) algorithm, and the probabilistic model on an extended Monte Carlo simulation of Random Walks using the Probabilistic Index of Connectivity (PICo) method. Tracking was controlled by the following input variables: two language fMRI defined regions of interest (ROIs) (diameter 8 mm) corresponding to fMRI localization of Broca's and Wernicke's areas and fractional anisotropy threshold of >0.15. The tracts were examined for their extension between Broca's and Wernicke's areas and their configuration near tumors or areas of edema. The fibers were scored in a similar way to Bernal et al 2009 for their rostral termination: 0 points if none, 1 if few, 2 if some, and 3 if all fibers spanned the expected course to Broca's area.

Results:
In 8 out of 10 cases, both probabilistic tracking and FACT tracking reconstructed tracts in the expected location of the arcuate fasciculus. Probabilistic tracts spanned the entire expected course of the arcuate fasciculus, with red voxels representing areas of highest connectivity and blue voxels lowest connectivity. FACT tracts did not show the anterior-most extent of the arcuate fasciculus. Consequently, only the probabilistic method was able to trace the entire tract to the inferior frontal gyrus (Broca's area). In one case, neither probabilistic nor FACT tracking could generate a tract through a region of extensive edema. In another case, probabilistic tracking generated a tract adjacent to a tumor whereas FACT tracking did not. The average score for the probabilistic tracts was 2, and the average for the FACT tracts was 0.

A. B. C. D.

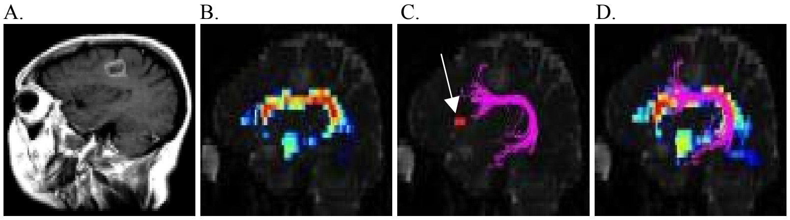

Fig 1. (A) Contrast sagittal T1 weighted image shows a glioblastoma in the fronto-parietal white matter near the dorsal portion of the arcuate fasciculus. (B) Probabilistic tracking demonstrates the entire course of the arcuate fasciculus. (C) FACT tracking (magenta) fails to reconstruct the anterior most fibers. Broca's area is highlighted in red (arrow). (D) Probabilistic and FACT tracts shown on the same sagittal slice confirms the absence of anterior fibers of the FACT tract.

A. B. C. D.

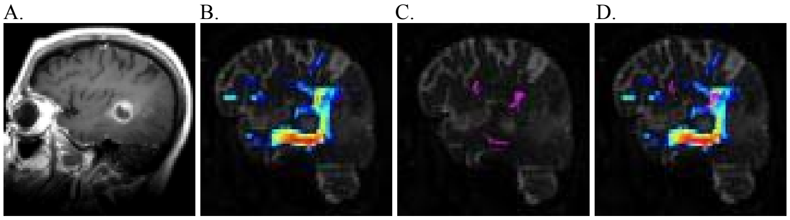

Fig 2. (A) Contrast sagittal T1 weighed image reveals an ependymoma in the posterior middle superior temporal lobe. (B) Probabilistic, (C) FACT and (D) combined probabilistic and FACT tracts show that the probabilistic method is able to reconstruct the tract around a tumor, whereas the FACT method is not.

A. B.

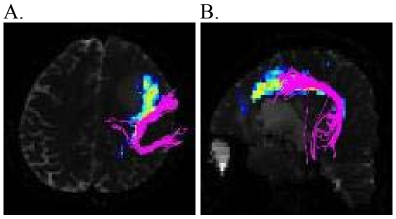

Fig 3. (A) Axial and (B) sagittal probabilistic and FACT (magenta) maps in a patient with a frontal glioblastoma reveal absence of FACT generated anterior arcuate fasciculus fibers, with termination in the region of crossing corticobulbar fibers. The probabilistic fibers have a more complete course to the fMRI-demonstrated Broca's area.

Discussion:
Probabilistic tractography reconstructs more complete courses of the arcuate fasciculus than deterministic tractography, and may perform better through areas of tumor and/or edema. The FACT method tends to underestimate the anterior most fibers of the arcuate fasciculus, where the fibers cross the larger intersecting corticobulbar (primary motor) fibers. The multiple pathways calculated by the probabilistic method appears to distinguish crossing fibers and true connecting fibers, and it may also help compensate for the decreased fractional anisotropy in areas near the tumor and/or edema. This process generates multiple pathways, some of which are extraneous, necessitating good anatomical knowledge to properly identify and isolate the tract of interest. Additional work is necessary to validate the reconstructed tracts with direct intraoperative stimulation to confirm the location and function of the arcuate fasciculus.

References: 1. Kreher et al. NeuroImage 2008; 43: 81-89. **2.** Mori et al. Ann. Neurol 1999; 45: 265-269. **3.** Saur et al. PNAS 2008; 105:18035-18040. **4.** Burgel et al. Cen Eur Neurosurg 2009; 70: 27-35. **5.** Bernal et al. Magnetic Resonance Imaging 2009. **5.** Jellison et al. AJNR 2004; 25:356-369. **6.** Naeser et al. Brain 1989;112:1-38.

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