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Reconstruction of the arcuate fasciculus for surgical planning in the setting of peritumoral edema using two-tensor unscented Kalman filter tractography

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ABSTRACT

Background: Diffusion imaging tractography is increasingly used to trace critical fiber tracts in brain tumor patients to reduce the risk of post-operative neurological deficit. However, the effects of peritumoral edema pose a challenge to conventional tractography using the standard diffusion tensor model. The aim of this study was to present a novel technique using a two-tensor unscented Kalman filter (UKF) algorithm to track the arcuate fasciculus (AF) in brain tumor patients with peritumoral edema.

Methods: Ten right-handed patients with left-sided brain tumors in the vicinity of language-related cortex and evidence of significant peritumoral edema were retrospectively selected for the study. All patients underwent 3-Tesla magnetic resonance imaging (MRI) including a diffusion-weighted dataset with 31 directions. Fiber tractography was performed using both single-tensor streamline and two-tensor UKF tractography. A two-regions-of-interest approach was applied to perform the delineation of the AF. Results from the two different tractography algorithms were compared visually and quantitatively.

Results: Using single-tensor streamline tractography, the AF appeared disrupted in four patients and contained few fibers in the remaining six patients. Two-tensor UKF tractography delineated an AF that traversed edematous brain areas in all patients. The volume of the AF was significantly larger on two-tensor UKF than on single-tensor streamline tractography ($p < 0.01$).

Conclusions: Two-tensor UKF tractography provides the ability to trace a larger volume AF than single-tensor streamline tractography in the setting of peritumoral edema in brain tumor patients.

1. Introduction

The purpose of brain tumor surgery is to achieve maximal lesion removal while maintaining or improving neurological function. For brain tumor resection, it is important to identify the key white matter tracts pre- or intra-operatively to avoid damaging them during surgery (Elhawary et al., 2011; Nimsky et al., 2007). Diffusion tensor imaging (DTI) tractography provides an innovative tool for investigating white matter architecture in vivo (Tournier et al., 2011). The use of this technique has been increasing in neurological surgery in recent years (Liu et al., 2011; Castellano et al., 2012). However, the effects of peritumoral edema pose a major challenge to conventional DTI tractography when tracing fiber tracts that are adjacent to malignant tumors (Zhang et al., 2013; Schonberg et al., 2006; Kinoshita et al., 2005). Peritumoral edema is usually related to dysfunction of the blood brain barrier that causes fluid to leak into the extracellular space, resulting in image voxels that contain part cerebral parenchyma and part extracellular water (Pasternak et al., 2009). DTI tractography (Basser et al., 2000), while robust, uses a single-tensor model that is inadequate in the case of partial volume, crossing fibers, and edema (Nimsky, 2014; Duffau, 2014).

In patients with brain tumors in the vicinity of language areas, definition of the relationship between language pathways and the surgical lesion becomes important. Classically thought to connect anterior

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(Broca's) and posterior (Wernicke's) language regions, the arcuate fasciculus (AF) is a C-shaped structure that connects temporal, parietal, and frontal lobes (Catani and Mesulam, 2008). The AF is arguably the most significant white matter fiber tract associated with language function, although there is some debate over the precise functional deficit that may accompany damage to it (Dick and Tremblay, 2012), as well as over the relationship of standard DTI tractography of the AF with functional areas. In a study using cortical stimulation for language mapping in focal epilepsy, DTI tractography of the AF colocalized well with Broca's areas but less so with Wernicke's areas (Diehl et al., 2010), while in another study, it was noted that DTI tractography connected to motor and premotor areas rather than to Broca's anterior language area (Bernal and Ardila, 2009). Thus in the clinical context, tracing of the AF poses a challenge.

To improve fiber tracking, it is becoming accepted that methods must move beyond the diffusion tensor (Nimsky, 2014; Farquharson et al., 2013; Fernandez-Miranda, 2013). Identifying a robust model to interpret the diffusion signal is thus of importance. In addition to modeling, the method chosen for tractography is still an open question in the diffusion neuroimaging analysis field (Jbabdi and Johansen-Berg, 2011), thus it is important to test tractography methods in clinical data, including in patients with brain tumors and edema. In this work, we evaluated the two-tensor unscented Kalman filter (UKF) tractography framework (Malcolm et al., 2010), where a two-tensor model is fit to the underlying data during the process of fiber tracking. The UKF tractography method was initially designed for neuroscientific studies, such as detection of abnormalities in first-episode schizophrenia (Rathi et al., 2011). In contrast to other methods that fit a model to the signal independently at each voxel (Qazi et al., 2009), in the UKF framework (Wan and Van Der Merwe, 2000) each tracking step employs prior information from the previous step to help fit and stabilize the model. The concept of employing information from the previous step during tracking (in an earlier DTI-based approach called tensor deflection; Lazar et al., 2003; Weinstein et al., 1999; Westin et al., 2002) has been shown to improve neurosurgical tractography (Feigl et al., 2014). In healthy subject data, it has been shown that for clinically typical diffusion data (b-value near 1000 s/mm^2), two-tensor UKF tractography outperforms other models such as spherical harmonics in terms of tractography coverage of expected connections (Baumgartner et al., 2012).

The aim of this study was to determine whether two-tensor UKF tractography could improve the tracking of AF in brain tumor patients with peritumoral edema.

2. Materials and methods

2.1. Patient selection

We retrospectively evaluated all consecutive brain tumor patients who had undergone functional MRI and diffusion imaging through December 2008 and June 2012 at Brigham and Women's Hospital. Patients were selected for inclusion if they met the following criteria: (1) Brain tumor patients with peritumoral edema in the vicinity of the language cortex; (2) patients were native English speakers and right-handed as determined by the Edinburgh Handiness Inventory (Oldfield, 1971); (3) patients were left-hemisphere dominant for language according to functional MRI results. Exclusion criterion: The reconstructed AF did not pass through the peritumoral edema. In this study, a total of 126 brain tumor patients who had undergone functional and diffusion imaging were identified. 13 of these patients met the inclusion criteria, and after AF reconstruction 3 of the 13 met the exclusion criteria. After the exclusion of ineligible subjects, the study included 10 patients (4 male, 6 female; age range 37–77 years). We note that our initial goal was to include at least 10 subjects in the study; this goal was achieved by evaluating consecutive patients up to June 2012. Detailed patient demographics, including clinical presentation, tumor histology and tumor localization, are detailed in Table 1. The study was approved by the Partners Healthcare Institutional Review Board, and informed consent was obtained from all participants prior to scanning.

2.2. MRI acquisition

MR images were obtained using a 3-Tesla scanner (EXCITE Signa scanner, GE Medical System, Milwaukee, WI, USA) with Excite 14.0, using an 8-channel head coil and array spatial sensitivity encoding technique (ASSET). High resolution whole brain T1-weighted axial 3D spoiled gradient recalled structural images (TR = 7500 ms, TE = 30 ms, matrix = 512 × 512, FOV = 25.6 cm, flip angle = 20°, 176 slices, voxel size = 0.5 × 0.5 × 1 mm^3) were acquired. Diffusion weighted images were acquired using EPI with 8 channel head coil and ASSET (TR = 14,000 ms, TE = 75.4, 31 gradient directions evenly distributed on the sphere, b-value of 1000 s/mm^2, 1 baseline image, FOV = 25.6 cm, matrix = 128 × 128, 44 slices, voxel size = 2 × 2 × 3 mm^3). Acquisition of structural, diffusion, and functional imaging datasets took 45–60 min per patient.

2.3. Preprocessing of DTI data

3D Slicer (http://www.slicer.org, version 4) was used to convert the raw data from DICOM format into NRRD format (Gering et al., 2001). DTIPrep (http://www.nitrc.org/projects/dtiprep) was used to perform quality control (Liu et al., 2010), which included artifact correction/removal as well as eddy-current and head motion artifacts correction by registration to the baseline image. In 3D Slicer, fractional anisotropy (FA) maps were created and the standard color scheme was used to visualize the DTI eigenvector orientations (with blue indicating superior–inferior, red indicating transverse, and green indicating anterior–posterior) and brightness controlled by FA. Then, both single-tensor streamline and two-tensor UKF tractography were applied to each diffusion MRI dataset.

2.4. Single-tensor streamline tractography

For each dataset, a binary brain mask was computed in 3D Slicer from the diffusion images to restrict tractography (see below) to within

Table 1
Patient demographics.

Patient	Age (years)	Sex	Presentation	Pathology	Localization
1	54	F	Facial twitching, word-finding difficulties	Glioblastoma multiform, WHO IV	Fronto-parietal
2	37	M	Seizures, word-finding difficulties	Recurrent oligodendroglioma, WHO II	Frontal
3	77	M	Slurred speech, word-finding difficulties	Glioblastoma multiform, WHO IV	Temporo-parietal
4	56	F	Headaches, word-finding difficulties	Glioblastoma multiform, WHO IV	Temporal
5	48	F	Headaches, speech difficulties	Glioblastoma multiform, WHO IV	Parieto-occipital
6	44	M	Slurred speech, abnormal facial movement	Anaplastic oligodendroglioma, WHO III	Frontal
7	64	F	Sub-acute aphasia	Glioblastoma multiform, WHO IV	Temporal
8	41	F	Headaches, word-finding difficulties	Anaplastic oligodendroglioma, WHO III	Frontal
9	43	M	Seizures	Glioblastoma multiform, WHO IV	Temporal
10	60	F	Facial twitching, speech arrest	Atypical meningioma, WHO II	Frontal

WHO, World Health Organization.