Feasibility of the Combined Application of Navigated Probabilistic Fiber Tracking and Navigated Ultrasonography in Brain Tumor Surgery

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■ BACKGROUND: **Surgical resection of intra-axial tumors is a challenging procedure because of indistinct tumor margins, infiltration, and displacement of white matter tracts surrounding the lesion. Hence, gross total tumor resection without causing new neurologic deficits is demanding, especially in tumor sites adjoining eloquent structures. Feasibility of the combination of navigated probabilistic fiber tracking to identify eloquent fiber pathways and navigated ultrasonography to control brain shift was tested.**

■ METHODS: **Eleven patients with lesions adjacent to eloquent white matter structures (pyramidal tract, optic radiation and arcuate fascicle) were preoperatively subjected to magnetic resonance imaging including diffusion-weighted imaging on a 3-T magnetic resonance system (Trio [Siemens, Erlangen, Germany]). Probabilistic fiber tracking was performed using the tools of the FMRIB Software Library (FSL). Results of probabilistic fiber tracking and high-resolution anatomic images were integrated into the neuronavigation system Stealth Station (Medtronic, Minneapolis, Minnesota, USA) together with the navigated ultrasonography (SonoNav [Medtronic]).**

■ RESULTS: **FSL-based probabilistic fiber tracking depicted the pyramidal tract, the optic radiation, and arcuate fascicle anatomically plausibly. Integration of the probabilistic fiber tracking into neuronavigation was technically feasible and allowed visualization of the reconstructed fiber pathways. Navigated ultrasonography controlled brain shift.**

■ CONCLUSIONS: **Integration of probabilistic fiber tracking and navigated ultrasonography into intraoperative neuronavigation facilitated anatomic orientation during glioma resection. FSL-based probabilistic fiber tracking integrated sophisticated fiber tracking algorithms, including modeling of crossing fibers. Combination with navigated ultrasonography provided a three-dimensional estimation of intraoperative brain shift and, therefore, improved the reliability of neuronavigation.**

INTRODUCTION

Surgical resection of intra-axial brain tumors adjacent to eloquent fiber tracts like pyramidal tract, optic radiation, or language-associated fascicles is a challenging procedure because surgical damage of these functionally relevant structures may occur. Gliomas in particular present an infiltrative growth pattern, and the invasion of surrounding brain tissue leads to indistinct tumor margins. Furthermore, intraoperative microscopic appearance and consistency of low-grade gliomas (LGG) may resemble healthy brain tissue.[1-3] Conventional fluorescence microscopy is helpful in high-grade gliomas by optic marking of tumor tissue[4] but is usually futile for defining tumor margins in LGG. Only a few approaches using fluorescence confocal microscopy in LGG have been reported in the literature.[4,5] Gross total tumor resection

Key words
- Glioma surgery
- Navigated ultrasonography
- Neuronavigation
- Probabilistic fiber tracking

Abbreviations and Acronyms
3D: Three-dimensional
FACT: Fiber Assignment by Continuous Tracking
FSL: FMRIB Software Library
iMRI: Intraoperative magnetic resonance imaging
LGG: Low-grade gliomas
MR: Magnetic resonance
MRI: Magnetic resonance imaging
ROI: Region of interest

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should be achieved in both high-grade gliomas and LGG whenever possible, because the volume of tumor remnant is known to correlate with overall survival of the patients.[6,7] However, tumor resection without causing new or additional neurologic deficits is demanding, especially in tumor sites adjacent to eloquent cortical and subcortical structures. Intraoperative neuronavigation represents an important tool for defining safe tumor margins and is used in many departments routinely for glioma resection.[8] Still, identification of the pathways of eloquent fiber tracts within the white matter on conventional anatomic magnetic resonance (MR) imaging (MRI) is barely possible. Therefore, intraoperative use of fiber tracking based on MR diffusion tensor imaging, usually carried out with Fiber Assignment by Continuous Tracking (FACT), was recently progressively integrated into neuronavigation.[9-12] Although the usefulness of this technique for surgical planning has been confirmed by most studies, the validity of the visualized margins of the tracts has remained unsure and cannot be taken as a safety margin in clinical practice.[11,13-17]

The incapability to conceive crossing and kissing fibers within 1 voxel is an important limitation of tensor-based fiber tracking leading to false-negative tracking results. Deterministic diffusion tensor imaging—based tractography tends to image only a subset of the pyramidal tract medially to the vertex. Therefore, higher-order tractography models are needed to image the whole extent of the fiber tracts of interest in brain tumor surgery.[18,19]

Probabilistic fiber tracking algorithms address this problem and may constitute more reliable connectivity maps but have been seldom used in patients with intracerebral lesions undergoing surgery.[16,20]

The most important drawback of intraoperative neuronavigation is the frequent occurrence of brain shift during surgery, leading to incongruency between the preoperative imaging and the anatomic situation. Brain shift occurs nonlinearly and is not foreseeable, because various causes such as loss of cerebrospinal fluid, brain swelling, shift toward the resection cavity, and retractors contribute to the distortion. Because of brain shift, neuronavigation may become inaccurate after opening of the dura mater and even more during tumor resection. Therefore, some groups use intraoperative MRI (iMRI) to address this drawback. iMRI facilitates an assessment of the resection radicality and the estimation of brain shift after tumor removal.[21,22] It provides an update of brain shift usually only at 1 time point during surgery and diffusion-weighted imaging in particular is prone to artifacts caused by air and blood layers in the resection cavity. Furthermore, it is cost and time intensive, and available only in a few neurosurgical centers.

Navigated ultrasonography may constitute an effective substitute for iMRI to control brain shift.[23] The intraoperative overlay of landmarks like ventricles or falx by navigated ultrasonography and neuronavigation allows the immediate and repetitive control of the accuracy of initial patient reference and of the ongoing brain shift during resection.[24,25] The combination of neuronavigated probabilistic fiber tracking and navigated ultrasonography is a promising time- and cost-effective approach of intraoperative imaging to reduce morbidity in resection of gliomas adjoining eloquent fiber tracts.[26]

We report on 11 patients with intracerebral lesions adjacent to eloquent white matter who were operated on using navigated ultrasonography combined with the integration of FMRIB Software Library (FSL; http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/)-based probabilistic fiber tracking into neuronavigation to identify eloquent fiber pathways and potentially enhance the safety of the resection. The aim of this retrospective analysis was to assess whether the combined use of these techniques is technically feasible and achievable in the preoperative and intraoperative workflow.

METHODS

Eleven patients with intra-axial lesions adjacent to the eloquent white matter pathways of the pyramidal tract, optic radiation, or arcuate fascicle were preoperatively subjected to MRI. Patients' characteristics are displayed in **Table 1**. MR diffusion-weighted imaging was performed on a 3.0-T MRI system with a 12-channel headcoil (MAGNETOM Trio [Siemens Healthcare, Erlangen, Germany]) using 32 diffusion encoding directions at an in-plane resolution of 1.8 mm with slice thickness of 3.6 mm and averaging 2 preprocessed datasets. T1-weighted magnetization prepared rapid gradient echo images were recorded with and without contrast enhancement. Further anatomic imaging was performed with three-dimensional (3D) T2-weighted high-resolution imaging. Postprocessing was carried out using a computer with a 2 × 6 core CPU (2.3 GHz) and 64 GB RAM. Probabilistic fiber tracking was performed using the freely available FMRIB Diffusion Toolbox (bedpostx and probtrackx), part of FSL version 5.0.6,[3] after eddy current correction. The ball-and-stick-model was used as a diffusion model. The bedpostx algorithm ascertains a distribution of main eigenvectors (stick, ie, orientation) with specific background isotropy (ball, ie, uncertainty) for each voxel. The probabilistic tractography algorithm based on this diffusion model iterates streamlines from the seed regions of interest (ROIs). For each propagation step, an orientation is chosen randomly from the distribution and is thereby able to model crossing fibers. For the tracking of the pyramidal tract, 2 seed ROIs were defined at the primary motor cortex and the posterior limb of the internal capsule of the lesion side. For the tracking of the optic radiation, 2 seed ROIs were marked at the lateral geniculate body and the primary visual cortex of the lesion side. For the tracking of the arcuate fascicle, 2 seed ROIs were manually defined at the cortices of Broca and Wernicke areas using a conservative anatomic definition of these areas. The connectivity distribution map was thresholded by excluding voxels with low connectivity values. Threshold level was chosen individually to exclude implausible voxels localized distant from the pyramidal tract, optic radiation, and arcuate fascicle. This volume was rescaled and added to a T1-weighted magnetization prepared rapid gradient echo image to allow accurate fusion with other image modalities on the neuronavigation system using the FSL tool fslmaths. Results of probabilistic fiber tracking were then reconverted from NIFTI (Neuroimaging Informatics Technology Initiative) into DICOM (Digital Imaging and Communications in Medicine) format (using a customized in-house algorithm, written by A.J.B. and G.A.H., based on Nifti2Dicom, primarily written by Daniele E. Domenichelli and Gabriele Arnulfo) and integrated into the neuronavigation system Stealth Station (Medtronic, Minneapolis, Minnesota, USA) together with fractional anisotropy images and T1-and T2-weighted high-resolution anatomic images. Intraoperative ultrasonography (Hitachi Aloka Medical, Tokyo,