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Preoperative tractography algorithm for safe resection of tumors located in the descending motor pathways zone

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ABSTRACT

Background: Diffusion tensor imaging (DTI) tractography facilitates maximal safe resection and optimizes planning to avoid injury during subcortical dissection along descending motor pathways (DMPs). We provide an affordable, safe, and timely algorithm for preoperative DTI motor reconstruction for gliomas adjacent to DMPs.

Methods: Preoperative DTI reconstructions were extracted from a prospectively acquired registry of glioma resections adjacent to DMPs. The surgeries were performed over a 7-year period. Demographic, clinical, and radiographic data were extracted from patients' electronic medical records.

Results: Nineteen patients (12 male) underwent preoperative tractography between January 1, 2013, and May 31, 2020. The average age was 44.5 years (range, 19–81 years). A complete radiological resection was achieved in nine patients, a subtotal resection in five, a partial resection in three, and a biopsy in two. Histopathological diagnoses included 10 patients with high-grade glioma and nine with low-grade glioma. A total of 16 perirolandic locations (10 frontal and six frontoparietal) were recorded, as well as two in the insula and one in the basal ganglia. In 9 patients (47.3%), the lesion was in the dominant hemisphere. The median preoperative and postoperative Karnofsky Performance Scores were 78 and 80, respectively. Motor function was unchanged or improved over time in 15 cases (78.9%).

Conclusion: This protocol of DTI reconstruction for glioma removal near the DMP shows good results in low-term neurological functional outcomes.

Keywords: Brain tumor surgery, Diffusion tensor imaging, Neuro-oncology, Tractography, White matter

INTRODUCTION

The operative goal for an eloquently located glioma is to perform a maximal safe resection,^[16,23,39] aiming to improve progression-free and overall survival for these patients while preserving functional

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cortex and subcortical tracts.^[18] Many different tools have been developed to achieve this goal, including advanced imaging and surgical techniques for brain mapping.^[10,16-18,23-25,27,29,32,35,38,41,50] Despite significant efforts, the overall survival rates have not changed significantly in the past decade.^[9]

Diffusion tensor imaging (DTI)-based tractography gives detailed information of the spatial relationship to functional boundaries of white matter connectivity between eloquent areas.^[15] However, the neurological function of the eloquent white matter can only be provided on a real-time fashion with an intraoperative guidance with direct subcortical stimulation (DSS), which remains the gold standard for this matter.^[10,35] Whereas some studies suggest that the central nervous system may have a high potential for plasticity.^[30,43] subcortical plasticity is limited and delayed.^[7] Identifying the motor tracts is paramount in surgical planning in all its extension, from the cortex to the deepest location according to the tumor site.

In the early era of DTI-based tractography studies, multiple technical limitations (limited fiber tracts detailing, erroneous definition of fiber endings, contamination of fiber crossings, etc.) were described.^[1,11-13,35,44] However, tractography is appropriate for confirming the location and integrity of fibers to determine the surgical risk of tract injury.^[7] The advent of new tractography algorithms in the past few years has improved the use of preoperative and intraoperative tractography.^[1,3,5,7,31,35,44] Only magnetic resonance imaging (MRI) tractography, of all preoperative imaging modalities, can reliably identify subcortical motor pathways.[46] This information can become inaccurate as a tumor is resected and brain shift increases.^[18,33] New software developments allow the performance of real-time updates on this information with ultrasound integration and reference intratumoral landmarks during resection, replacing the need for intraoperative MRI (fMRI). Unfortunately, these imaging techniques are time-taking and demand high costs to the health-care systems. In addition, the reconstruction of the eloquent subcortical pathways lacks a homogenization of the manual and automatic reconstruction protocols. We have elaborated new protocols for acquisitions and for processing aiming to manage the above limitations.^[34-36]

We propose a descending motor pathway (DMP) fibertracking algorithm with clinically available software. This work aims to provide a timely and accessible protocol for tractography reconstruction in surgical planning for glioma resections near the DMP in order to minimize postoperative motor disability, while allowing a maximal safe resection.

MATERIALS AND METHODS

Patients

The senior authors reviewed a prospectively acquired database of patients who had consecutively undergone resection of

gliomas adjacent to or involving the precentral gyrus (PrG) and/or the corticospinal tract (CST). Demographic, clinical, and imaging information were recorded for patients admitted to our two academic institutions between January 1, 2013, and May 31, 2020.

MRI was evaluated by the primary author (E.G.O.) in each patient to evaluate tumor location for study inclusion. Scans were reviewed by a dedicated neuroradiologist (J.M.J.) and one of the senior neurosurgeons for the confirmation of a location related to the DMPs. Fiber tracking was done by a dedicated neuroradiologist (J.M.J.) and assisted by a neurosurgeon (E.G.O.). The parameters that were quantified included a decrease in the volume of the tracts, displacement of fibers (fractional anisotropy [FA] values preserved), infiltration of the fibers (decreased FA values), and disruption of fibers (unable to detect continuity of the fibers), as we have described previously for language tracts.^[35]

The clinical charts were assessed for demographic and clinical data. Extent of resection was calculated using tumor volume measurements obtained from MRI in three dimensions divided by a factor of two (A × B × C/2). The extent of removal was classified as gross total resection (100%), subtotal resection (\geq 90%), or partial resection (<90%). This study was performed according to the Declaration of Helsinki ethical standards. The Local Institutional Ethics Committee approved this study, and the manuscript was approved by the Institutional Review Board. The Institutional Ethics Committee considered that the informed consent was not required given the retrospective nature of this study and the research involves no more than minimal risk to the patients.

Imaging acquisition

Study data were acquired with a General Electric Signa Excite HDXT (1.5 T GE Healthcare, Milwaukee, WI, USA) and a Siemens MAGNETOM® Aera (1.5T Siemens Healthcare, Erlangen, Germany). An axial T1-weighted structural/anatomical and an axial DTI were acquired for each patient. Each structural image in T1 has 140 slices (1 mm thick, without GAP [free space], matrix = 320×192 , repetition time [TR] = 650 ms, echo time [TE] = 22 ms, field of view [FOV] = 22, and acquisition time = 2 min and 35 s), covering the entire brain volume. For the isometric DTI sequence, a spin echo-planar imaging (EPI) sequence with 64 directions was used in an axial plane without angulation. Images were obtained from the base from the skull to the vertex. Each axial tensor sequence has 920 images, matrix = 100×100 , TR = 14000 to 17000 ms, TE = minimum, thickness = 2.5 mm, spacing = 0.0, number of excitations (NEX) = 1, pixel = 2.5, FOV = 250, b value = 1000, and acquisition time = 7 min.

DTI fiber tracking

The manual selection of each region of interest (ROI) and the fiber tracking was performed with *Functool* $9.4.04b^{TM}$ (by © *General Electric Medical Systems*) and *Syngo* DTITM (by *Siemens Healthcare*). Correction of EPI distortions (scaling + translation + shearing) was applied. Volume rendering was used to overlay streamlines on the anatomical T1. Brainlab Elements SmartBrush and Fiber Tracking software tools (version 2.6) were used for neuronavigation imaging fusion of tractography. The ROIs were manually determined by recognition in the tensors in the three planes and T1 structural sequences. We used a Brain White Matter Atlas to define these ROIs.^[8]

DMPs: CST and dorsal column-medial lemniscus (DCML)

For the reconstruction of the CST and the DCML, a single ROI was used in the anterior portion of the posterior limb of the internal capsule for each side. The posterior limb was chosen for this reconstruction as all DMPs are supposed to cross throughout this structure [Figure 1]. The DCML was included for this reconstruction since a reorganization of cortical motor representation may occur in patients with brain lesions, including a reorganization of motor neurons in the postcentral gyrus (PoG).^[6] An additional reconstruction was added using a cortical ROI that was placed in the PrG and PoG bilaterally [Figure 2]. Fiber tracking used a FA threshold of 0.15. Separated reconstructions based on fMRI were performed whenever possible to delineate limb-specific subcortical connections.

Surgical procedure

Patients were positioned in skull pin fixation for neuronavigation (Kolibri or Kick, BrainLab, Feldkirchen, Germany or Aimnav, Micromar Ind. Com. Ltda., Sao Paolo, Brazil). All surgical supplies and equipment were rented and were transferred to our institution the day before surgery, including the neuronavigation system, the physiological neuromonitoring system (NIM-Eclipse 4 System, Medtronic, Minneapolis, MN, USA) for asleep brain double motor mapping with monopolar and bipolar stimulation, and the ultrasonic aspirator (Sonoca, Söring, Germany). Induction of anesthesia was performed with propofol, and an initial neuromuscular block was performed with vecuronium or rocuronium to facilitate intubation as preferred by the anesthesiologist. Anesthesia was maintained with nitrous oxide/oxygen, supplemented by isoflurane and fentanyl or remifentanil in the majority of cases. Light surgical anesthesia was maintained, relying on opioid agents to provide adequate analgesia while minimally suppressing cortical responsiveness for motor mapping. Subdermal electrodes were used for electromyographic recording, motor evoked potentials, and sensory evoked potentials.

Skin incision and craniotomy were planned according to neuronavigation. If brain shift was observed after dural opening, an additional dose of 8 mg of dexamethasone was administered to revert millimetric displacement. When the tumor could be visualized, the motor cortex was stimulated to find a safe entry point. When the tumor was not visible

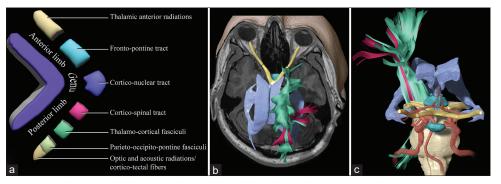


Figure 1: Schematic of the internal capsule and the descending motor pathways. (a) Fragmented illustration of the components of the anterior limb, the genu, and the posterior limb. Tracts coming from the prefrontal and the supplementary motor areas descend through the anterior limb and the genu, including the thalamic anterior radiations, the frontopontine tracts, and the corticobulbar tracts, and the corticonuclear tracts. (b) Superior view of a three-dimensional reconstruction of the ventricles, the optic pathways, and the motor tracts. The tracts (green) that were reconstructed from a region of interest are located in the posterior limb of the internal capsule bilaterally, including both the corticospinal tract and the dorsal column-medial lemniscus. In pink are shown the tracts reconstructed from a region of interest in the precentral gyri bilaterally. (c) Anterior view of a three-dimensional reconstruction shows the anatomical relationships of the descending motor pathways with the ventricles, the hypothalamus, and the intracranial arterial system.

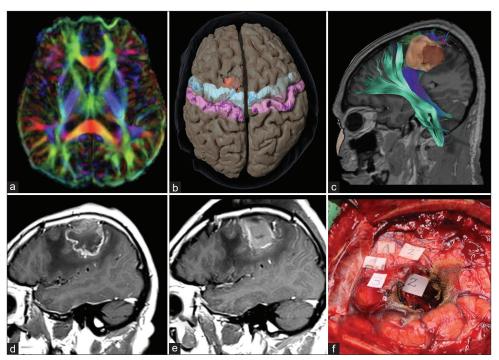


Figure 2: Regions of interest used for fiber tracking. (a) Diffusion tensor imaging demonstrating selection of region of interests (ROIs) in the posterior limb of the internal capsule bilaterally. (b) The selection of ROIs in the precentral and postcentral gyri bilaterally is demonstrated. (c) Tractography reconstruction of descending motor pathway and the corticospinal tract in relationship with a left frontal tumor is shown. Preoperative (d) and postoperative (e) T1 postcontrast sagittal magnetic resonance imaging demonstrate a gross total resection of the tumor. (f) The intraoperative visualization of cortical and subcortical mapping with direct stimulation demonstrates the corresponding areas of the left shoulder (3), arm (2), and hand (1).

at the cortical surface, a minimally invasive approach was performed after direct cortical stimulation (DCS). Total en bloc resection was performed when there was a subcortical cleavage plane; however, an internal debulking of the tumor was done in most patients. All efforts were made to preserve every cortical and subcortical vessel about the tumor to preserve adequate arterial supply and venous drainage of the primary motor cortex. Intermittent cortical and subcortical stimulations were used until achieving a maximal safe resection. At least two positive stimulations were required to consider an area as functional. High frequency stimulation was performed with a monopolar probe, with a train of 5 pulses, with 0.5 ms duration, and 1 Hz repetition rate. The intensity of the current used was 2-15 mA for the cortex, and 1-10 mA for the white matter. When a bipolar probe was used, the stimulus parameters were the same, but an increased current intensity was required. Threshold for stimulation was based on the electromyographic response to the electrical stimuli. Tumors were classified as low-grade glioma (LGG) (World Health Organization [WHO] Grade I or II glioma) and high-grade glioma (HGG) (WHO Grade III or IV glioma). Finally, closures were performed in a routine fashion.

RESULTS

The DMPs were detected bilaterally in all patients. In each patient, we identified DMPs coming from the motor cortex, from both the PrG and PoG, and DMPs passing through the posterior limb of the internal capsule, demonstrating fibers descending from the supplementary motor cortex and the prefrontal cortex delineating the corona radiata [Figure 1].

Twenty-five patients with gliomas were identified in which DTI fiber tracking and neuronavigation were used for surgical resection. Nineteen patients (12 males) aged 19–81 years (average 44.5 years) underwent resection of a glioma with use of preoperative fiber tracking of DMPs. Among these, 10 cases (52.6%) were HGGs, and 9 (47.4%) were LGGs. In nine patients, the lesion was in the dominant hemisphere. Eight patients (42.1%) presented with seizures, 8 (42.1%) with a motor deficit, 4 (21.0%) with a sensorial deficit, 6 (31.6%) with behavioral deficits, and 3 (15.8%) with both motor and language deficits. In 10 cases (52.6%), the lesion was in the frontal lobe, in 6 cases (31.6%) between the frontal and parietal lobes, in 2 cases (10.5%) in the insula, and in 1 case (5.3%) in the basal ganglia. Complete radiological removal was achieved in 9 cases (47.4%), subtotal resection

in 5 (26.3%), partial resection in 3 (15.8%), and intended biopsies in 2 (10.5%). The fibers were infiltrated by the tumor in nine patients and displaced in 10 patients.

Assessment of motor function remained the same or improved in 15 cases (78.9%). A decline on the Karnofsky Performance Scale score directly associated with a postoperative motor deficit occurred in only two patients. One patient presented new-onset postoperative partial seizures, associated with an intended biopsy on an eloquent subcortical motor area after DCS. No other complications were observed. The mean follow-up time was 7 months (range, 1–12 months). Additional treatment with radiation only or radiation and chemotherapy was performed according to the indicated by the oncologist.

DISCUSSION

A new algorithm for DMPs reconstruction

Many authors have described preoperative reconstruction of DMP for resection of tumors associated with these tracts worldwide in the past 20 years, since the beginning of this technology.^[2,5,19,20,26,27,42,47] However, to the best of our knowledge, there is no consensus for the tractography reconstruction of DMP. Some authors have proposed automated whole-brain tractography.^[48,49] Others have proposed seeding of ROIs in the posterior limb of the internal capsule;^[45] others have included ROIs based on information obtained by fMRI with motor tasks;^[40] some have included only ROIs in the PrG and PoG including the complete or partial homunculus,^[21] whereas others have combined these seedings.^[37]

In this study, we propose to include information according to tumor location. If possible, primary motor cortex (perirolandic) tumors should be evaluated with both DTI and blood oxygen level-dependent acquisitions. Information from both should be explored and processed to be included in neuronavigation planning. For these tumors, the tractography reconstruction should be performed bilaterally including the following tracts separately: One ROI at the posterior limb of the internal capsule including both the CST and the DCML, an additional ROI starting from the activated areas with the motor fMRI and completing information with a cortical ROI including both PrG and PoG. It is important to note that for perirolandic tumors, DCS and DSS represent the gold standard, and this tractography protocol may serve as a road map for stimulation, giving information for the delineation of the most critical areas to be stimulated. In addition, the relation of the tracts (anterior, posterior, medial, or lateral) with the tumor confirms the correct position of the CST, preventing an unexpected injury. To avoid postoperative supplementary motor area syndrome in tumors located anteriorly in the supplementary motor area, we recommend

reconstructing additional peritumoral U fibers to prevent a postoperative supplementary motor area syndrome.^[4,14]

To incorporate the protocol discussed in this study for preoperative DTI reconstruction for glioma resection near the DMP, our goal is to simplify tools, including advanced preoperative imaging, which may be available but often neglected by surgeons, facilitating maximal safe resection. We present an easy way to reproduce all motor tracts with commercially and available software, using corresponding seeding points for ROIs to identify possible entry points and trajectories to motor areas related to gliomas. This surgical planning allows surgeons to identify routes without damaging motor tracts. We introduce a combination of ROIs to identify all DMPs, which could be represented as a combination of eloquent areas including the posterior limb of the internal capsule, peritumoral U fibers, the PrG, and the PoG, which can be used as anatomical landmarks. Displacement of the DMP makes a path for surgeons for a safe intraparenchymal corridor.

Intraoperative mapping with direct cortical and subcortical stimulation cannot be substituted with preoperative tractography and remains the gold standard for determining motor function in glioma resection.^[18,28] However, DMP tractography may serve as a road map for surgeons to perform DCS and DSS.^[22] Even though, intraoperative mapping requires surgeons with experience in the field and multidisciplinary collaboration, especially of anesthesiologists and neuropsychologists.^[35]

Illustrative case

A 36-year-old woman presented with complex seizures. Her antecedents and physical examination were unremarkable. Preoperative contrast-enhanced MRI demonstrated a right frontal tumor, with minimal enhancement, most consistent with an LGG. The patient participated in a preoperative discussion and agreed that if the tumor could not be resected without producing a permanent motor deficit, then only a biopsy would be performed. Intraoperatively, multiple responses were obtained from the majority of the tumor area [Figure 3]. Given this situation, a decision was made to preserve all eloquent motor areas and do an intentional biopsy, with postoperative preservation of all motor functions. Histopathologic analysis demonstrated an LGG, and further radiation therapy was performed.

Study limitations

This retrospective study was limited by the quality of data collected within the medical charts and by the small number of cases in whom the tractography was performed. Examination by an independent examiner may have revealed subtle deficits that could be missed during follow-up, and

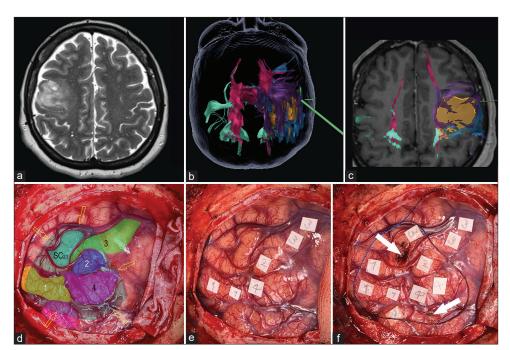


Figure 3: Preoperative magnetic resonance imaging, neuronavigation fused tractography, and intraoperative images of an intentional biopsy. (a) Axial T2 image reveals a right frontal heterogeneous hyperintense intra-axial lesion. (b and c) Neuronavigation images of tractography of descending motor pathways. The volumetric reconstruction of the tumor is shown in yellow. Also shown are the motor tracts coming from the posterior limb of the internal capsule (pink), from the supplementary area (purple), and from the medial (green) and lateral (blue) precentral gyrus. (d-f) Intraoperative images of brain mapping with direct cortical stimulation. Numbers 1 (yellow), 2 (dark blue), 3 (green), and 4 (pink) show the motor areas of the tongue, eye, upper limb, and mouth, respectively. Yellow arrows show the borders of the tumor area verified with the neuronavigation system; white arrows show the safest areas of the cortex from which the biopsy was taken. The aquamarine area (SC2,3) shows where a subcortical response from the eye and the upper limb was noted during subcortical mapping during the biopsy.

documentation of motor outcome could be biased. Whereas the tractography is a unique tool that permits an individual analysis of the white matter for each patient, the DTI reconstruction also remains with the limitations mentioned above. This study lacks information comparing tractography and DSS; however, fiber tracking was used to improve subcortical stimulation.

CONCLUSION

Separate reconstructions of tracts from all DMPs can be performed preoperatively in a timely and accurate manner to improve brain mapping for resection of tumors associated with motor areas, consequently helping surgeons preserve the patients' motor function. In addition, this reconstruction, when fused with neuronavigation, may serve as a road map during resection for subcortical stimulation. However, additional studies are needed to compare the accuracy of information between pre and postoperative tractography as well as between tractography and DSS.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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