Endoscopic Endonasal Transclival Approach for Resection of a Pontine Glioma: Surgical Planning, Surgical Anatomy, and Technique

**BACKGROUND:** The endoscopic endonasal approach (EEA) has been proposed as a potential alternative for ventral brainstem lesions. The surgical anatomy, feasibility, and limitations of the EEA for intrinsic brainstem lesions are still poorly understood.

**OBJECTIVE:** To describe the surgical planning, anatomy, and technique of an intrinsic pontine glioma operated via EEA.

**METHODS:** Six human brainstems were prepared for white matter microdissection. Ten healthy subjects were studied with high-definition fiber tractography (HDFT). A 56-yr-old female with right-hemiparesis underwent EEA for an exophytic pontine glioma. Pre- and postoperative HDFTs were implemented.

**RESULTS:** The corticospinal tracts (CSTs) are the most eloquent fibers in the ventral brainstem. At the pons, CSTs run between the pontine nuclei and the middle cerebellar peduncle (MCP). At the lower medulla, the pyramidal decussation leaves no room for safe ventral access. In our illustrative case, preoperative HDFT showed left-CST displaced posteromedially and partially disrupted, right-CST posteriorly displaced, and MCP severely disrupted. A transclival exposure was performed achieving a complete resection of the exophytic component with residual intra-axial tumor. Immediately postop, patient developed new left-side abducens nerve palsy and worse right-hemiparesis. Ten days postop, her strength returned to baseline. HDFT showed preservation and trajectory restoration of the CSTs.

**CONCLUSION:** The EEA provides direct access to the ventral brainstem, overcoming the limitations of lateral approaches. For intrinsic pathology, HDFT helps choosing the most appropriate surgical route/boundaries for safer resection. Further experience is needed to determine the indications and limitations of this approach that should be performed by neurosurgeons with high-level expertise in EEA.

**KEY WORDS:** Pontine glioma, Endonasal approach, Endoscopy, Brainstem lesion, Oncology, Fiber tractography, Anatomy, Corticospinal tract, Middle cerebellar peduncle, Skull base, Transclival approach

ABBREVIATIONS: AF, arcuate fascicle; CN, cranial nerve; CST, corticospinal tract; DRTT, dorso-rubrothalamic tract; DSI, diffusion spectrum imaging; EEA, endoscopic endonasal approach; FA, fractional anisotropy; FOV, field-of-view; FPT, frontopontine tract; ML, medial lemniscus; MLF, medial longitudinal fasciculus; HDFT, high-definition fiber tractography; QA, quantitative anisotropy; RNu, red nuclei; STT, spinothalamic tract; TE, echo time; TPO-PT, temporo-parieto-occipital pontine tracts; TR, repetition time.
the anterior perspective on the anatomy, as well as the understanding of the clinical feasibility and limitations of the EEA in this context, is still lacking.5 In fact, just a few cases of endoscopic endonasal resection of brainstem cavernomas and only 1 previous intrinsic tumor, a recurrent pediatric pontine ependymoma, have been reported.6-10 Here, we review the surgical anatomy of ventral brainstem fiber tracts relevant to the EEA using white matter microdissection and fiber tractography techniques. Furthermore, we provide an anatomic and technical description of the endoscopic endonasal surgical resection of an intrinsic pontine glioma in an adult patient. We highlight the importance of preoperative high-definition fiber tractography (HDFT) in delineating the relationship of important fiber tracts to the lesion, thereby assisting in the selection of the least invasive surgical corridor and the boundaries of a safe resection.

WHITE MATTER DISSECTION OF THE VENTRAL BRAINSTEM AND FIBER TRACKING CORRELATION

Midbrain

The corticospinal tract (CST) occupies the middle 3/5 of the transverse surface of the cerebral peduncles. Within the cerebral peduncles, it relates to the frontopontine tract (FPT) anteriorly, and to the temporoparieto-occipital pontine tracts (TPO-PT) posterolaterally (Figures 1 and 2). The cerebral peduncles have an oblique trajectory in the coronal plane, travelling from lateral to medial as they descend, and they are also oblique in the axial plane. When seen on an axial cut (Figure 2), the anterior portion is occupied by the FPT, followed by the CST, and finally the TPO-PT. The cerebral peduncles are separated by each other by the interpeduncular fossa. Here the third cranial nerves (CNs) are closely related to the FPT laterally. The substantia nigra separates the FPTs, CSTs, and TPO-PTs from the remaining midbrain structures. Posteriorly to the CST, TPO-PT, and substantia nigra runs 2 important tracts of the sensory system: The medial lemniscus (ML) located just postero-medial to the CST and the spinothalamic tract (STT) posteriorly to the ML and postero-medial to the TPO-PT. Just posterior to the nerve exit zones of CN III lay the red nuclei (RNu), which serve as relay stations of the dentato-rubro-thalamic tract (DRTT). Posterior to the RNu, the medial longitudinal fascicles (MLF) straddle the midline (Figure 2).

Pons

Once the CST reaches the pons, it runs between the pontine nuclei and the transverse fibers of the middle cerebellar peduncle (MCP; Figures 1 and 2). The whole bundle of white matter tracts involving the FPT, CST, and TPO-PT turns to adopt a more coronal orientation, which brings the CSTs in a more anterior location relative to the ventral surface of the brainstem. Here, the ventral aspect of the CST is covered by a thin layer of fibers of the MCP. At the lateral aspect of the pons, the MCP fibers divide into multiple groups travelling anterior, posterior, and through the fibers of the CST. The nerve entry zone of the trigeminal nerve lies posterolateral in the pons, which makes it less accessible through a purely ventral approach. To the contrary, the ventral course of CN VI is anterolateral and places it at risk for injury through such approaches. Important to note is that all the FPT and TPO-PT fibers, as well as the corticonuclear (CNT) fibers synapse within the pons, or upper medulla. Hence, the CSTs traversing the pontomedullary junction to the pyramids are significantly smaller.

Medulla Oblongata

Within the pyramids, the CSTs are smaller, and more compact, anterior, and medial. Corticonuclear fibers continue to provide innervation to the CN motor nuclei. At the upper 2/3 of the medulla, even though the medial pyramids are occupied by the arcuate nuclei, the CSTs are very close together to allow surgical access; lateral or medial displacement by an intrinsic lesion may widen this space and create a surgical corridor. Laterally, the multiple rootlets of CN XII at the preolivary sulcus demarcate the lateral limit of the ventral access to the upper medulla. At the lower third of the medulla, the pyramidal decussation leaves no room for safe ventral access regardless of potential tract displacement (Figures 1 and 2).

METHODS

The diffusion spectrum imaging (DSI Studio, Pittsburgh, Pennsylvania) data for the illustrative case presented herein (see Results section) were acquired using a 3-T Tim Trio System (Siemens AG, Munich, Germany) with a 32-channel coil. A head stabilizer was used to minimize head motion. Total scan time was 27 min and included a 15-min DSI scan (repetition time (TR) = 3439 ms, echo time (TE) = 150 ms, multiband acceleration factor = 3, voxel size = 2.4 mm3, field-of-view = 231 × 231 mm2) with 257 noncollinear gradient directions and maximum b-value of 7000 s/mm2, followed by a 4-min T1-weighted structural scan (TR = 2200 ms, TE = 3.58 ms, voxel size = 1.0 × 1.0 × 1.0 mm) and FLAIR sequence. In addition to the aforementioned reconstruction criteria, we placed a region of interest covering the pontine tumor in order to track any other intra or perilesional white matter pathways. White matter tracts were characterized as “displaced,” “infiltreated,” or “disrupted” as in previous publications.11-14 Following the qualitative assessment, mean quantitative anisotropy (QA) values were obtained for the whole and perilesional CSTs. Local QA index values were obtained from the DSI studio software to visually correlate the quantitative findings. Since both CST were affected by the lesion, there was no “healthy” side serving as a comparison. In order to overcome this issue, we apply an “internal corrector.” For this, we obtained the left arcuate fascicle (AF)15 to create an index that could allow us to better assess the quantitative changes in both CST. This index was performed dividing the QA of the affected tract by the QA of the AF in the pre- and postoperative scans (Table). The Institutional Review Board of our University approved this study and the patient was consented according to our protocol.
RESULTS

Case Presentation

A 56-yr-old female presented with gradual onset of right-side hemiparesis and left facial numbness. Physical examination revealed 4/5 strength on the right upper and 3/5 on the right lower extremity. MRI revealed a predominantly left sided minimally enhancing 3 cm intra-axial lesion in the pons with a large exophytic component, compatible with an intrinsic brainstem glioma (Figure 3). The lesion was partially encasing the basilar artery, and displacing it towards the right. CNs V and VII were displaced to the left.

Preoperative HDFT showed that the CST on the affected side was severely displaced posteromedially and partially disrupted (Figure 4A). The right CST was posteriorly displaced. The MCP was severely disrupted, predominantly its anterolateral segment, but still superficial to the CST (Figure 4B). Quantitative evaluation of the CST showed a decrease of 43% in the QA value in the perilesional segment when compared to the distal portion (Table and Figure 5). She was initially placed on dexamethasone.
6 mg/6 h for 10 d, with partial improvement of her hemiparesis, but on drug tapering her hemiparesis worsened to 3/5 on the right upper and 2/5 on the right lower extremity. A stereotactic frame-based needle biopsy was initially discussed as a first step. Given the progressive worsening and the evidence of significant compression of the CST, the possibility of biopsy plus surgical debulking was also offered to the patient, providing the intraoperative diagnosis confirmed the presumptive diagnosis of brainstem glioma. The...
risk of immediate postoperative worsening was quoted very high, and the patient was aware that the compressive component was only partly responsible for the hemiparesis, since there is also tract disruption (necrosis) and infiltration.

Description of Surgical Procedure

Details are shown in the Video, Supplemental Digital Content. Neuromonitoring of somatosensory evoked potentials, motor evoked potentials, brainstem auditory evoked potentials, and electromyography of CNs VI, VII, and IX-XII were performed. Image guidance was also used. A full middle transclival exposure was performed, extending from the sellar floor to the lower clivus, and including the left jugular tubercle (Figure 6A); a left transpterygoid approach to the petrous apex with vidian nerve transection was also completed; the internal carotid artery was skeletonized from the anterior wall of the cavernous sinus down to the foramen lacerum. Importantly, the left lingual process was removed to allow for lateral displacement of the paracalval and lacerum carotid segments providing a wider exposure of the petrous apex; the interdural segment of the abducens nerve was identified just behind the petroclival dural fold (Figure 6B). The dura was opened in a trap-door fashion and pedicled towards the left. The exophytic component of the tumor was initially debulked, while identifying and protecting the basilar, vertebral, and left anterior inferior cerebellar arteries, as well as the left abducens nerve, which was encased by the tumor and pushed towards the right side. Debulking was performed using teardrop suction and an ultrasonic aspirator with a modified
FIGURE 4. A. Preoperative HDFT showing severe displacement, infiltration over both CSTs. The left CST also has mild disruption. B. A close-up view of the preoperative status of the MCP (in red), which was severely disrupted by the tumor serving as a corridor to enter into the pons; in yellow the CST.

FIGURE 5. Preoperative segmentation and local QA index of the CST. A. The CST after the segmentation at the cerebral peduncles. B. The local QA index. Here, the red dashed lines show the affected segments in a slightly darker blue when comparing to the upper segments that shows a lighter blue and some yellow segments. The darker color in the lower segments represents a lower QA compared to the upper segments.

long tip. An angled endoscope was used to assist in resecting tumor extending towards the left cerebellopontine angle, where CNs V and VII-VIII were identified. The choroid plexus at the foramen of Luchska was identified along with the lower CNs (Figures 6C and 6D). A large intra-axial tumor component was removed until the necrotic component was reached; this was defined as the posterior limit of the resection; direct motor stimulation did not elicit any response here. Superiorly, normal appearing tissue was encountered at the upper pontine region; inferiorly, the pontomedullary sulcus was identified and the left CST was directly stimulated here. Left-sided motor evoked potentials were weak but present initially and remain preserved throughout the case. Right motor evoked potentials were present and remain preserved. The abducens nerve was structurally preserved but did not stimulate from the beginning of the case.

After meticulous hemostasis, a multilayered reconstruction was performed using inlay collagen matrix, onlay epidural layer of fascia lata, followed by a fat graft to fill up the clival defect, and a nasoseptal flap covering all the reconstruction. CSF lumbar drainage was employed for 3 d.

Postoperative Course

Postoperative imaging showed complete resection of the exophytic component of the tumor, with residual infiltrating tumor within the brainstem (Figure 7). HDFT was done 10 d after surgery and showed preservation and recovery of the normal right CST trajectory. The left CST was also preserved, but some of the fibers appeared to be infiltrated by tumor (Figure 8A). We did not appreciate any changes in the MCP, which was disrupted preoperatively (Figure 8B). Quantitative evaluation showed an
improvement of 4% in the left CST and 18% on the right CST (Table and Figure 9). Immediately postop, the patient developed new abducens nerve palsy and worse right hemiparesis with no strength in the upper, and 2/5 in the lower extremity. At 10 d postop, her strength had improved to 2/5 and 3/5, respectively. At 6 wk postop, her upper extremity was 3/5 but still 2/5 distally, and the lower extremity has improved to 4/5 proximally, and 3/5 distally, being able to ambulate with assistance and off steroids. The pathology was consistent with high-grade pontine glioma, Ki67 of 20%, and no MGMT promoter methylation identified. The patient received chemoradiation therapy, and succumbed to her progressive disease 6 mo later.
FIGURE 7. Postoperative FIESTA MRI sequence. A and B, Complete resection of the exophytic component and subtotal resection of the intraxial lesion.

DISCUSSION

Brainstem gliomas are extremely uncommon in adults, accounting for only 1% to 2% of the intracranial gliomas in this patient population.16,17 Two main groups have been described in the literature: low-grade tumors, which show no contrast enhancement on MRI, represent 46% of these lesions, typically affect patients younger than 30 yr-old, and are associated with a better overall survival18; and high-grade tumors, which are usually contrast enhancing with an area of central necrosis, represent 31% of adult brainstem gliomas, affect patients older than 40 yr, and are associated with a worse prognosis.17,19,20

Although surgical treatment for intra-axial brainstem tumors remains controversial, resection of lesions with large exophytic component has been recommended.16 Previously reported cases on resection of exophytic lesions have been performed through lateral surgical approaches.21-24 Here we present a unique case of an adult high-grade pontine glioma with a large exophytic component operated through an endoscopic endonasal transcervical transpterygoid approach. The nuances of this approach for intrinsic brainstem lesions, as well as the role of presurgical planning using HDFT, are discussed herein.

Endoscopic Endonasal Surgery for Ventral Brainstem Lesions

Traditional open approaches to the brainstem do not provide direct access to its ventral surface.1,25,26 Indeed, limitations such as an indirect working angle and excessive retraction of neurovascular structures made ventral brainstem lesions nearly “inoperable” via transcranial approaches.2 Thus, the importance of fiber tractography in guiding surgical resection of ventral brainstem lesions has been emphasized.2,3,24,25 Recently, Essayed et al.3 described the potential indications and limitations of the EEA for such lesions. Their report provided a first step towards the application of this route for ventral brainstem lesions, but their anatomic study did not include detailed fiber microdissection and/or fiber tractography of ventral brainstem tracts, and they did not present any clinical examples. Although surgical resection for brainstem gliomas is controversial, the presence of a large exophytic component potentially causing compressive symptoms may serve as an indication for surgery.16 In addition, cytoreductive surgery is recommended for high-grade gliomas because, as long as surgical complications and side effects are minimized, it improves clinical outcomes.27-31 An honest discussion with the patient regarding the different treatment options, potential for postoperative worsening, and the surgery’s goals should be performed.

The endoscopic endonasal surgery field has dramatically evolved during the past decades being now commonly used worldwide. The approach proposed here, however, should only be performed by neurosurgeons with high-level expertise in this field. The microsurgical dissection technique must be applied when addressing a brainstem lesion via EEA in order to decrease the incidence of neurovascular injury and damage to brainstem tracts or nuclei; the use of image-guidance and intraoperative neuromonitoring is mandatory to prevent complications. Specific of the EEA, the risk of postoperative CSF leak can be minimized with the use of multilayer vascularized reconstruction and placement of a lumbar drain.

Applications of HDFT for Intra-Axial Brainstem Lesions

The principal tract running ventrally in the brainstem is the CST. As such, lesions located in between the CSTs or anterior to them might be best approached ventrally. Although fiber tract anatomy may help in defining the so-called safe entry zones to the ventral brainstem, the reality is that relevant tracts may be
displaced in a way that are mistakenly included in the selected surgical corridors. Abla et al. reported up to 36% rate of permanent new deficits when following the 2-point methods for brainstem cavernous malformation resection. As previously reported for brainstem lesions, DTI-based fiber tracking serves as an important tool to preoperatively assess the integrity and status of the white matter tracts. Here we used an advanced diffusion-based fiber tracking technique, HDFT, that has shown to have the best valid connections, with over 90% accuracy as examined in an open competition. As illustrated in our case, HDFT was able to accurately depict the anatomy of important fiber tracts within the brainstem, and helped in constructing a surgical plan. The disruption of the MCP as well as the postero-medial displacement of the CST provided a safe entry zone for resection of this intra-axial lesion through a ventral corridor. In cases where HDFT shows lesions completely infiltrating the CST or lesions located posteriorly to these tracts making the CST anterior to them; the EEA route for the ventral brainstem lesions

FIGURE 8. Postoperative HDFT. A. Preservation of the CST as well as restoration of the trajectory. B. Close-up view of the postoperative preservation of the MCP fibers (in red), which was severely disrupted by the tumor serving as a corridor to enter the pons; in yellow the CST.

FIGURE 9. Postoperative segmentation and local QA index of the CST. A. The CST after the segmentation at the cerebral peduncles. B. The local QA index. Here, the red dashed lines show the affected segments in a slightly darker blue when comparing to the upper segments that shows a lighter blue and some yellow segments. The darker color in the lower segments represents a lower QA compared to the upper segments.
should not be indicated. Each case should be studied individually and exhaustively before making any decision regarding the most appropriate surgical corridor.

In cases involving noninfiltrative lesions (eg cavernous malformations), surgical resection is facilitated by the fact that the white matter tracts are typically displaced to the periphery of the lesion, while no tracts run within the lesion itself. In contrast, in cases of diffuse pathology, such as the glioma presented here, important fiber tracts may be infiltrated in addition to displaced, and located within the confines of the lesion instead of the periphery. In such cases, HDFT not only can help defining the anatomy of the displaced fiber tracts around the lesion but can depict the location of infiltrated fiber tracts that could be placed at risk during the resection and therefore can also help defining the boundaries of a safe resection within the lesion. HDFT may also be useful in the postoperative setting, because preservation of fiber tracts can increase confidence in that any immediate clinical deterioration may be partially related to tract neuroapraxia, rather than complete and permanent disruption (neurotmesis). Moreover, it is possible to complement the qualitative analysis with QA, which has shown to be a reliable and superior method when assessing white matter integrity on diffusion MRI. QA bypasses the limitations of fractional anisotropy (FA) and general- ized FA on the areas of crossing fibers, such as the centrum semiovale and the brainstem, and the areas of mass effect originated by a lesion. In the case presented here, the quantitative results showed a correlation with the qualitative data of trajectory restoration and tract preservation and with the partial improvement on patient’s motor strength.

CONCLUSION

The EEA provides direct access to the ventral brainstem surface overcoming the limitations of lateral surgical approaches. When facing an intraaxial lesion, HDFT is an accurate noninvasive tool to characterize the brainstem anatomy, and its implementation in preoperative planning helps defining the safest working corridor and surgical resection boundaries based on the location of major brainstem tracts. Further studies are warranted to better define indications, limitations, and outcomes of the proposed approach for ventral brainstem lesions. Finally, the approach proposed herein must be performed only by neurosurgeons with high-level expertise in endoscopic endonasal surgery.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

The authors described a case report of partial resection of an exophytic pontine glioma in a 56-year-old patient. They present the case report along with fiber dissection of 6 cadavers (although data are scant on cadaveric study) and also evaluate the fiber tracking imaging in healthy individuals. Because of the location of this lesion, the corticospinal tracts (CST) are pushed posteromedially and technically a more ventral approach seems more desirable as advocated and done here. The authors justify their indication based on the exophytic aspect of the lesion guided by high definition tractography. Endoscopic endonasal approach to ventral pons, and DTI as the outcome in this single case does not justify a partial decompression and worse neurological status.

The clinical results do not seem to have improved by the use of high-definition fiber tracking. Maintaining a stable neurological function is crucial for a patient with known limited survival. Is it worth it to offer a limited longer survival by causing new neurological deficit and decreased quality of life?

These are important questions that need to be addressed on a case by case basis and with a thorough discussion with patient and the family. The authors’ contribution to operative neurosurgery is important in this regard and incites a scientific debate on the rational for indication and treatment in these complex and incurable diseases.

Amir R. Dehdashti
Manhasset, New York


Using cadaveric dissections, and High-Definition Fiber Tractography (HDFT) acquired with MRI imaging of normal subjects, the authors review the relevant anatomy for an endoscopic endonasal transclival surgical approach guided by HDFT for partial resection of an exophytic brainstem glioma. A surgical video demonstrates the surgery performed. The authors indicate that the HDFT was performed using quantitative anisotropy, which overcomes some of the limitations of the fractional anisotropy used in other techniques such as fiber tracking with diffusion-tensor imaging (DTI). The authors indicate that this is the first surgical case of a brainstem glioma operated through an endoscopic endonasal approach (EEA) to be reported in the literature. This technique is controversial in that the surgery has relatively high risk of neurological morbidity with unproven therapeutic benefit, and therefore, if this strategy it is to be considered at all, only surgeons with high-level endoscopic endonasal expertise should consider this. Because of these risks, even in the hands of best and most experienced endoscopic endonasal surgeons, the "risk/reward ratio" of this surgery may be too high. In no way should the feasibility of this technique "open the door" to a trend towards more of as yet unproven surgeries such as this for brainstem gliomas until there is more clear evidence as to when this approach might be advisable.

Nonetheless, the authors have presented their technique in a balanced fashion with careful thought and discussion with the patient of the inherent risks. Regardless of the controversial nature of this strategy, it is well established that the condition of brainstem gliomas has a very poor prognosis, does not respond necessarily favorably to most any other surgical, radiation, or chemotheraphy treatments, and improved therapeutic modalities with surgery, targeted therapies, or otherwise are desperately needed. Certainly, one would have to weigh very carefully the pros and cons of whether to ever consider such an EEA for a brainstem glioma, always bearing in mind our Hippocratic Oath, “to do no harm”. If there ever is a case in which to utilize an EEA for a brainstem glioma, a case as presented with an anterior exophytic tumor component with posterior displacement of the corticospinal tracts and other critical structures might be that rare exception when it is considered.

Michael R. Chicoine
St. Louis, Missouri


Supplemental digital content is available for this article at www.operativeneurosurgery-online.com.

Supplemental Digital Content 1. Video. EEA Pontine Glioma. This video shows a brief introduction of the case presented herein as well as the key aspects of the endoscopic endonasal technique for brainstem lesions.