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Medial Pontine Area: A Safe Entry to the Brainstem as a Cut Above the Rest

Abdullah Emre TACYILDIZ[1,2], Ozan BARUT[2,3], Melih UCER[4], Yaser OZGUNDUZ[2,5], Necmettin TANRIOVER[6]

[1]Karabuk University, Faculty of Medicine, Department of Neurosurgery, Karabuk, Türkiye
[2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurosurgery, Microsurgical Neuroanatomy Laboratory, Istanbul, Türkiye
[3]Bingol State Hospital, Department of Neurosurgery, Bingol, Türkiye
[4]Biruni University, Faculty of Medicine, Department of Neurosurgery, Istanbul, Türkiye
[5]Aksaray Training and Research Hospital, Department of Neurosurgery, Aksaray, Türkiye
[6]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurosurgery, Istanbul, Türkiye

Corresponding author: Abdullah Emre TACYILDIZ ✉ abdullahemretacyildiz@gmail.com

ABSTRACT

AIM: To examine the fiber-based anatomy of the medial pontine area (MPA), one of the most commonly used brainstem (BS) safe entry zones in neurosurgery.

MATERIAL and METHODS: According to the protocol of Klingler and Ludwig, six BSs were kept in 10% formalin solution for at least 2 months. After removing the arachnoid mater, pia mater, and vascular structures, the samples were frozen at –16°C for at least 2 weeks. White matter (WM) pathways of the BS were gradually examined using fiber dissections under a surgical microscope.

RESULTS: Safe entry zones of the BS were defined and investigated, focusing on the ventral pontine region and pontomesencephalic junction. Because of the lack of fibers on the anterior surface of the pons, the MPA formed a safe surgical area. The MPA, strategically positioned between the descending corticospinal tracts and extending securely to the anterior limit of the medial lemniscus, serves as a protective pathway, creating a secure environment for accessing safe entry zones within the BS during surgery.

CONCLUSION: The position of the MPA has the potential to provide a combined surgical path with superiorly located BS entry zones, resulting in a larger surgical area. Entry to the BS via the MPA increases the accessible surface area in the ventral pons and can be combined with the other perioculomotor safe regions outlined. Our findings might lead to safer endoscopic endonasal transclival interventions for intrinsic pontine lesions.

KEYWORDS: Brainstem, Cerebellum, Endoscope, Entry zone, Microsurgical anatomy, Pons, Transclival approaches, White matter

INTRODUCTION

Safe entry paths to intrinsic brainstem (BS) lesions differ depending on lesion location and associated white matter pathways, whereas extrinsic BS tumors can form safe surgical corridors (3). The recommended entry locations for BS lesions should preferably be away from the cranial nerves (CN) and their nuclei, and the descending and ascending tracts and the zones should preferentially have few fibers (4,7,25). Until now, four safe entry zones on the ventral part of the pons have been proposed to access intrinsic BS lesions (1,5,7,8,12,23). The lateral pontine zone lies between the trigeminal and facial nerves (1,7). The peritrigeminal zone is superior to the trigeminal nerve and lateral to the corticospinal tract (CST), and it is anterior and medial to the trigeminal nerve and lateral to the CST (5,7,12).

Rhoton's group proposed the interpeduncular safe entry zones to the ventral parts of the mesencephalon and pons about a decade ago in the medial pontine area (MPA) (8). The

Abdullah Emre TACYILDIZ : 0000-0001-5806-243X
Ozan BARUT : 0000-0001-6572-9589
Melih UCER : 0000-0002-2004-2991
Yaser OZGUNDUZ : 0000-0001-7236-7766
Necmettin TANRIOVER : 0000-0001-7628-9443

supratrigeminal zone is medially located along the pons on the middle cerebellar peduncle, immediately superior to the origin of the trigeminal nerve (8,23). Because of the widespread use of endoscopic endonasal skull base surgery, recently, there has been a resurgence of surgical inquiry into MPA (5,7,12). Indeed, Serrato-Avila et al. recently characterized the microsurgical anatomy of the cerebellar interpeduncular entry zones, emphasizing the importance of the supratrigeminal safe entry zone along the medial side of the pons (23).

This study aimed to investigate the surgical fiber dissection–based anatomy of the MPA, which is considered one of the most commonly used BS entry zones in neurosurgery.

MATERIAL and METHODS

The study was conducted at the Department of Neurosurgery, Micro-Endo-Neurosurgery, and Neuroanatomy Research Laboratory of the Cerrahpasa Faculty of Medicine at Istanbul University between November 2017 and April 2018.

According to the protocol proposed by Ludwig and Klingler, six BSs were kept in a 10% formalin solution for at least 2 months. After removing the arachnoid mater, pia mater, and vascular structures, the samples were frozen at −16°C for at least 2 weeks (15). The brainstems were then thawed in tap water and prepared for dissections using the Rhoton microsurgery set (toothless tweezer, microhook, microscissors, scalpel, and dissector) under a surgical microscope (Carl Zeiss AG, Oberkochen, Germany) at 4x and 40x magnification.

All procedures were recorded using a professional digital camera (Canon EOS 600D, Japan), a macro 100-mm lens (Canon), a ring-flash bracket (Canon), and a professional tripod (Manfrotto 808 C4).

Magnetic resonance imaging (MRI) tractography derived from normal participants from the Human Connectome Project (HCP) was also used to assess the integrity of the fiber dissection results and show MPA. All tracts were generated using deterministic tractography on a template containing diffusion data from 1065 HCP controls, and the analysis was performed in DSI Studio (http://dsi-studio.labsolver.org) (27,28). Full descriptions of the imaging protocol and preprocessing steps are available on the HCP website (https://www.humanconnectome.org). Regions of interest for fibers were traced using the HCP1065 tractography atlas (26).

RESULTS

The pons is located between the pontomesencephalic and pontomedullary sulci. Transverse pontine fibers and the trigeminal nerve were found on the surface of the pons. Microdissection was initiated after the superficial transverse pontine fibers were removed from the anterior surface of the pons (Figure 1A). After removing the superficial transverse pontine fibers from the lower right half of the ventral pons, the deep, transverse pontine fibers; intrapontine trigeminal fibers; and CST were exposed (Figure 1B). After the superficial transverse pontine fibers were completely removed from the anterior surface of the ventral pons, the CST was exposed in both halves of the BS (Figure 1C). Before revealing the medial lemniscus and its arcuate fibers, the CST; pontine nuclei; and deep, transverse pontine fibers were removed (Figure 1D).

The CST was located in the center of the cerebral peduncle in the mesencephalon (Figure 1B). The CST was found in the anteromedial pons (Figure 1B), and it passed to the medulla as descending fibers toward the pyramids (Figures 1C, 2A, and 2D). The gracile and cuneate tubercles gave rise to the medial lemniscus, which ascended as a curved structure facing anteriorly and integrated into the substantia nigra (Figure 1D). The trigeminal, abducens, facial, and vestibulocochlear nerves were inside the pons (Figure 1C and 1D). Other fiber dissection results in this study were transcended by two significant findings: (a) typical clustering of descending CSTs in the midpons just at the level of an imaginary horizontal line intersecting the origins of both trigeminal nerves, and (b) sparsity of fibers along the MPA above this plane up to the level of the pontomesencephalic junction.

The transverse pontine fibers—formed by the middle cerebellar peduncle and wrapped around the frontopontine tracts, CSTs, and temporopontine tracts—make up a substantial portion of the ventral pons (Figure 3A). The medial lemniscus fibers posteriorly border the CSTs and transverse pontine fibers (Figure 3A and 3B). MPA can be separated into superior and inferior compartments by an imaginary horizontal line intersecting the origins of trigeminal nerves. The supratrigeminal MPA is characterized by a shortage of fibers on the anterior surface of the upper pons between the two CSTs (Figure 3B). Our fiber dissections and MRI tractography data indicated that the supratrigeminal MPA creates a rational BS entry location because of its secure depth back to the anterior limit of the medial lemniscus (Figures 1–3).

DISCUSSION

The recommended entry zones for intrinsic BS lesions should avoid the CN fibers, their nuclei, and the descending and ascending tracts. There should be a few fibers in the entry areas to any part of the BS (3,4,25). Literature shows that roughly 20 safe entry zones have these characteristics (3,4,7,16,19,25). Our study contributes to the literature by reviewing the ventral MPA, considered one of the most commonly used BS safe entry zones in neurosurgery.

Several studies have found that the distance between CSTs throughout the ventral pons decreases dramatically from the pontomesencephalic junction downward (10). Serrato-Avila et al. reported a distance of 4.1 mm from the midline to the CST in the upper part of the ventral midpons in a recent quantitative analysis of the BS safe entry zones. According to these authors, the supratrigeminal zone is limited inferiorly by the descending CSTs because these fibers follow a typical superolateral to inferomedial trajectory at this section of the pons (23). Notably, the safe working area along the upper half of the MPA is 33 mm^2, and it appears to decrease as the surgeon moves caudally (23). These findings are consistent with our fiber dissection results, indicating that using the lower pons for safe BS entry is challenging (Figure 2E). Indeed, it is almost impossible to use a midline pons entry below an imag-

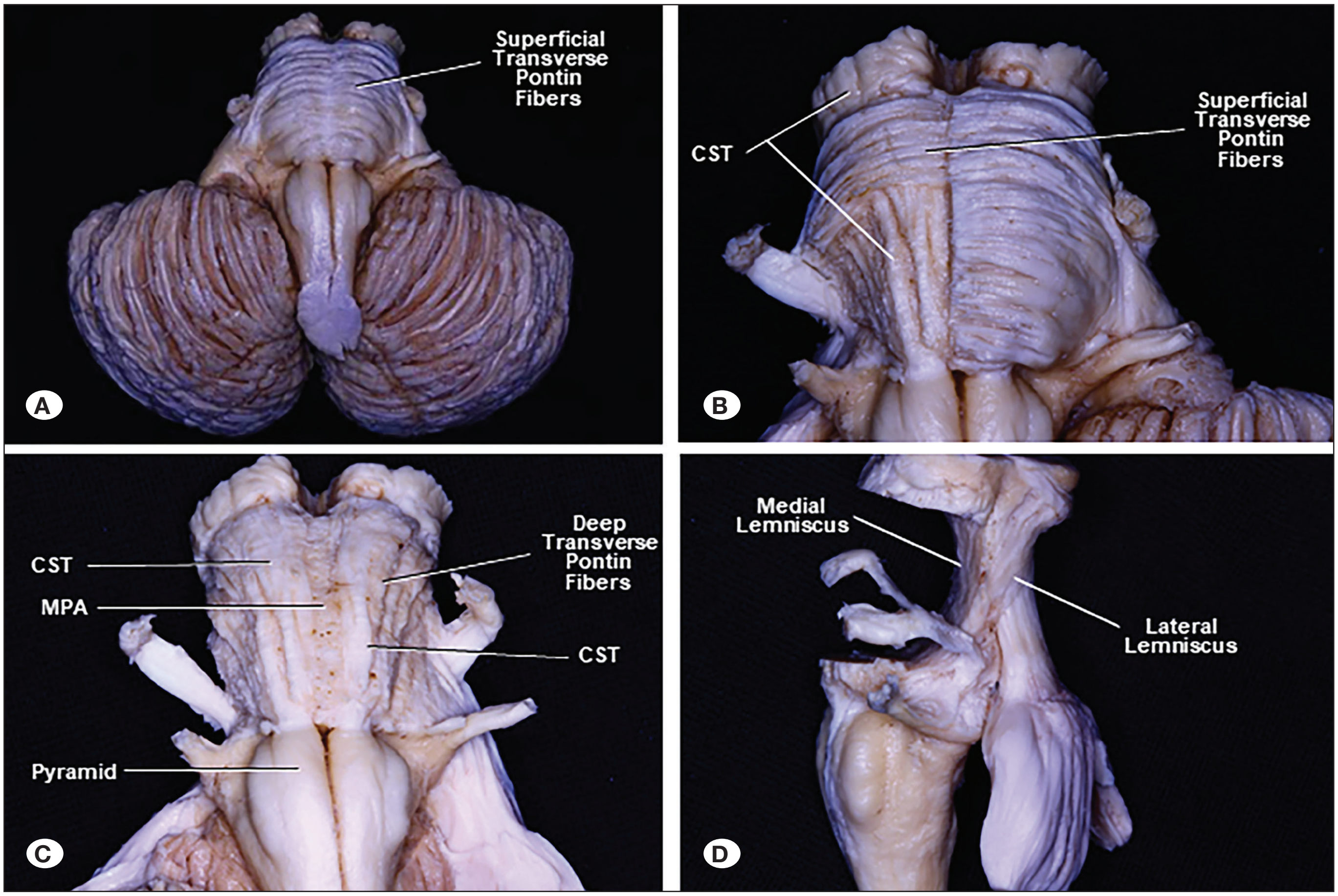

Figure 1: A) The pons is limited by the pontomesencephalic and pontomedullary sulcus. The trigeminal nerve and superficial transverse pontine fibers may be observed on the anterior surface of the pons. **B)** Deep, transverse pontine fibers; intrapontine trigeminal fibers; and CST were exposed after the superficial transverse pontine fibers were removed in the lower right half of the ventral pons. **C)** CST was found in both halves of the pons after the transverse pontine fibers in the anterior ventral pons were completely removed. Deep, transverse pontine fibers may be observed between the CST fibers. There are very few descending and ascending fibers and no CN nuclei in the MPA. **D)** The medial lemniscus and its anteriorly facing typical concavity were exposed after removing the CST; pontine nuclei; and deep, transverse pontine fibers. The region on the anterior surface of the pons between the two CSTs includes a wide area back to the medial lemniscus. Therefore, MPA can serve as a safe entry zone to the brainstem. **CST:** corticospinal tract; **MPA:** medial pontine area.

inary horizontal line joining two trigeminal nerve origin sites without inadvertently causing trauma to the pyramidal tracts.

Serrato-Avila et al. reported a safe depth of the supratrigeminal zone of 1 cm, and we have shown that the medial lemniscus defines the rear margin of the supratrigeminal safe entry zone, with its surgically favorable concavity facing anteriorly (23). This severely concave shape broadens the surgical field along the MPA and serves as the depth limit of the surgical route (Figure 2E). Based on our fiber dissection results, we believe that the MPA would be a solid alternative to other safe entry zones of the BS because of its different surgical approach from an anterior perspective.

Bricolo and Turazzi, and other researchers suggest that there should be few fibers in safe entry zones of the BS, which is also valid for the MPA (4,7). Histological findings reported by Nieuwenhuys et al. revealed that some pontocerebellar fibers and nuclei form the middle cerebellar peduncle in MPA (18). The ventral and dorsal parts of the MPA are typically covered by middle cerebellar fibers, which should be disrupted to reach the BS lesion (2). However, the pontocerebellar fibers are routinely sacrificed during surgical approaches into the BS via the lateral pontine and peritrigeminal zones, and most of these patients achieve favorable outcomes despite multiple transgressions during BS microneurosurgery (6). The lack of fibers in MPA distinguishes it as a viable option for a safe ventral BS entry zone (Figure 2E and 2F).

Meola et al. identified a region in the pons with few ascending and descending pathways between CSTs and showed that the frontopontine tract is medial to the CST (17). The findings of Meola et al. were consistent with our dissections, and few frontopontine tract distal fibers appeared vulnerable during any intervention along the MPA (Figure 2E and 2F).

The MPA can be combined with relevant superior locations, such as the anterior mesencephalic zone, allowing the sur-

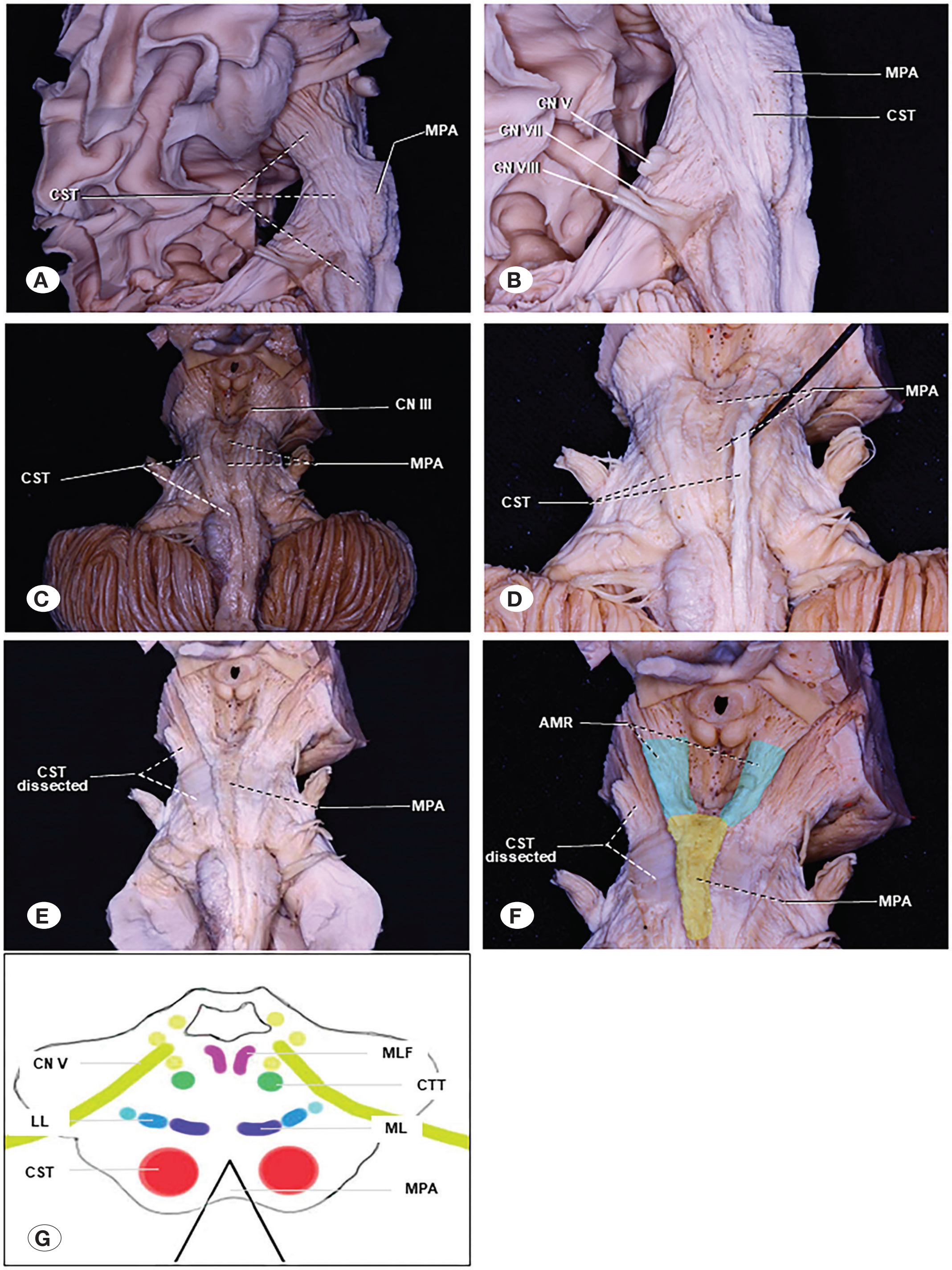

Figure 2: A) The mesencephalon was dissected to show the CST passing down the cerebral peduncle, and the superficial transverse pontine fibers at the pons were removed in another specimen. The dissection indicates that the CST runs from the cerebral peduncle to the medulla. **B)** The MPA is characterized by having fewer fibers and no descending or ascending white matter tracts. **C)** Both CSTs have been dissected in another hemisphere, revealing the fiber-loose MPA contained by the descending tracts. **D)** The left CST is lifted with a microhook in another specimen to show the width of the MPA at the trigeminal nerve origin level. **E)** Both CSTs were removed from the mesencephalon to the medulla to show the lateral limits of the MPA. Note that the distance between the two CSTs significantly decreases as the area descends toward the pontomedullary junction. **F)** The MPA could be combined with the upper perioculomotor areas to form a larger surgical entry zone providing surgical access to the brainstem. **G)** A schematic axial image of the brainstem and MPA (black arrow) at the trigeminal nerve level. **AMR:** Anterior mesencephalic region, **CN:** Cranial nerve, **CST:** Corticospinal tract, **CTT:** Central tegmental tract, **LL:** Lateral lemniscus, **ML:** Medial lemniscus, **MLF:** Medial longitudinal fasciculus, **MPA:** Medial pontine area.

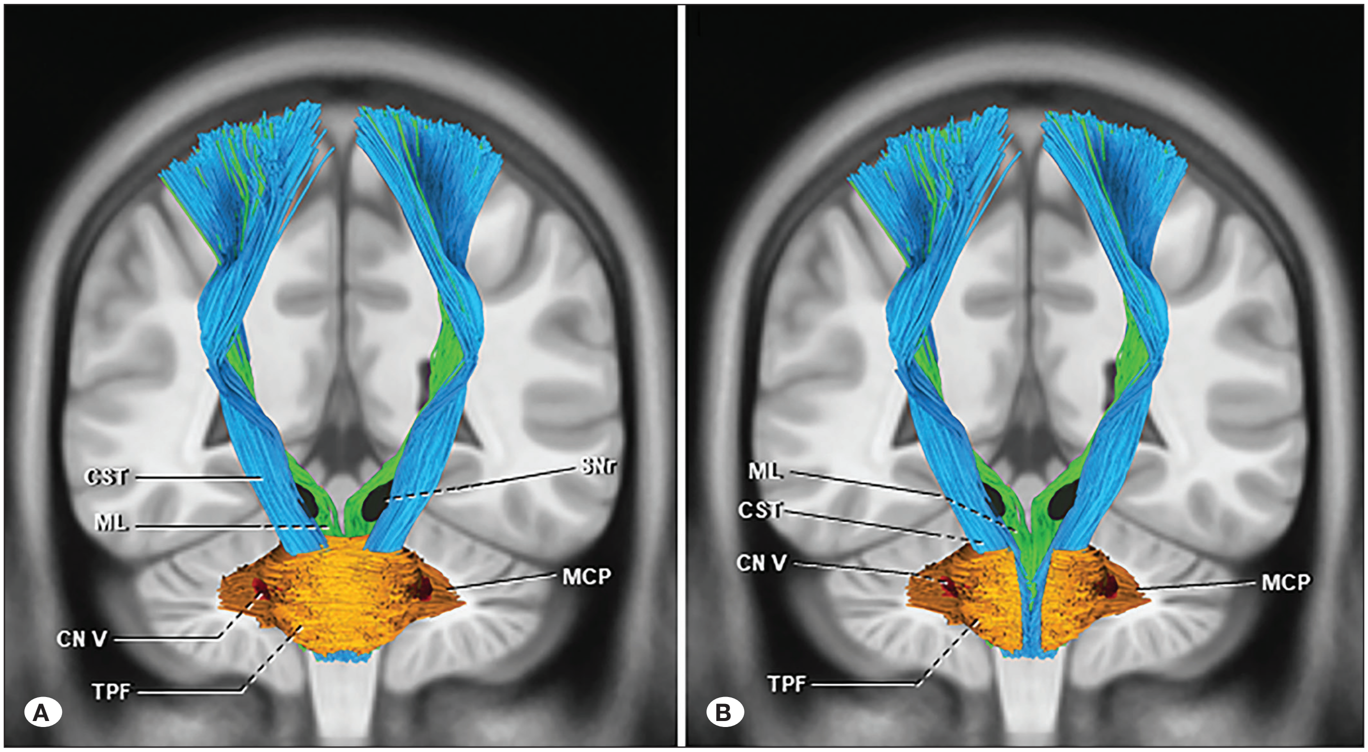

Figure 3: Magnetic resonance tractography images were derived from normal participants to assess the integrity of the fiber dissection results and show relevant ventral pontine fibers. All tracts were generated using deterministic tractography and analyzed in DSI Studio. **A)** A coronal view of the pons shows transverse pontine fibers (orange fibers) and the trigeminal nerve (red fibers). **B)** The CST (blue fibers) runs anterior to the deep, transverse pontine fibers; medial lemniscus (green fibers); and posterior to the superficial transverse pontine fibers. At the pons level, the distance between both CSTs widens at the upper part of the pons and decreases as the MPA approaches the horizontal plane along an imaginary line interconnecting the origins of the left and right trigeminal nerves. **AMR:** Anterior mesencephalic region, **CN:** Cranial nerve, **CST:** Corticospinal tract, **LL:** Lateral lemniscus, **ML:** Medial lemniscus, **MPA:** Medial pontine area, **SNr:** Substantia nigra, **TPF:** Transverse pontine fiber.

geon to reach a broader region (Figure 2E and 2F). The area between the origins of the third CN in the interpeduncular fossa at the most medial section of the cerebral peduncle is known as the anterior mesencephalic zone (4,7,19). According to Weiss et al., the perioculomotor region (anterior mesencephalic region) may be accessible in 60% of the specimens using an endoscopic endonasal approach and pituitary transposition (24). Indeed, He et al. performed an endoscopic endonasal excision of the cavernoma in the perioculomotor zone (14). Previous studies support our dissections and findings (14,24). The perioculomotor zone in conjunction with an incision along the MPA can access lesions within the ventral pons via the endoscopic endonasal transclival route. This modification can provide the surgeon a safe area for BS lesion resections.

Basilar artery perforating arteries that arise above and below the anterior inferior cerebellar artery exit zone can be considered an obstacle to accessing the MPA from the anterior (21). However, the basilar artery often has a complicated path and frequently deviates to one side at the aforementioned level, providing an advantage in managing the perforating artery barrier at the MPA (21).

Endoscopic endonasal skull base surgery has been widely used in recent years, resulting in several studies indicating safe resection of ventral BS lesions using endoscopic endonasal skull base approaches (10,11,22,24). Endoscopic endonasal transclival surgery has been used to treat cavernous malformations and resections of ependymomas and high-grade pontine gliomas (9,11,13,20). High-definition fiber tractography is recommended to treat intrinsic BS lesions and ensure surgical safety (11). A thorough understanding of the connectional anatomy of the ventral pons and the relationships of the major fiber tracts is essential for safely accessing intrinsic pontine lesions by endoscopic endonasal skull base interventions. The Pittsburgh group reported a case of an exophytic pontine glioma accessed between both CSTs (11).

All the findings in previous studies on safe surgery along the ventral pons support our findings on the potential use of MPA as a reliable, safe entry zone. Similarly, Essayed et al. showed the entryway to ventral BS via the interpyramidal pathway in their schematic representations (10). The MPA entry into the BS increases the surface area accessed in the ventral pons. Our findings might lead to safer endoscopic endonasal transclival interventions for intrinsic pontine lesions.

CONCLUSION

The MPA is a safe and physically appropriate surgical option for ventral pontine lesions because of the lack of functional fibers in the surgical field. Using the MPA as the entry zone to the ventral pons increases the surface area for access, and the MPA can also be combined with other perioculomotor safe entry zones. MPA has the potential to become one of the most dominant surgical routes to pontine lesions because of its anatomically reliable and safe composition and apparent evidence that the use of endoscopic skull base surgery is increasing over time.

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Declarations

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Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no conflicts of interest.

AUTHORSHIP CONTRIBUTION

Study conception and design: AET
Data collection: AET, OB
Analysis and interpretation of results: AET, OB, MU, YO
Draft manuscript preparation: AET, YO
Critical revision of the article: NT
Other (study supervision, fundings, materials, etc...): NT
All authors (AET, OB, MU, YO, NT) reviewed the results and approved the final version of the manuscript.

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