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Histology of the Porous Oculomotorius: Relevance to Anterior Skull Base Approaches

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Abstract

Objective Mobilization of cranial nerve III (CNIII) at its dural entry site is commonly described to avoid damage from stretching during approaches to the parasellar, infrachiasmatic, posterior clinoid, and cavernous sinus regions. The histologic relationships of CNIII as it traverses the dura, and the associated surgical implications are nonetheless poorly described. We herein assess the histology of the CNIII–dura interface as it relates to surgical mobilization of the nerve.

Methods A fronto-orbitozygomatic temporopolar approach was performed on six adult cadaveric specimens. The CNIII–dural entry site was resected and histologically processed. The nerve–tissue planes were assessed by a neuropathologist.

Results Histologic analysis demonstrated that CNIII remained separate from the dura within the oculomotor cistern (porous oculomotorius up to the oculomotor foramen). Fusion of the epineurium of CNIII and the connective tissue of the dura was seen at the level of the foramen, with no clear histologic plane identified between these structures.

Conclusion CNIII may be directly mobilized within the oculomotor cistern, while dissections of CNIII distal to the oculomotor foramen should maintain a thin layer of connective tissue on the nerve.

Keywords
- oculomotor nerve
- cavernous sinus
- histology
- porous oculomotorius

Introduction

Surgical approaches to the parasellar, infrachiasmatic, posterior clinoid, and cavernous sinus regions, including the fronto-orbitozygomatic temporopolar (FOZT), transcavernous-transsellar, and pretemporal transcavernous approaches, often involve mobilization of cranial nerve III (CNIII; oculomotor nerve) to avoid damage from stretching and/or manipulation under tension.[1–7] This is achieved by sharply opening the oculomotor cistern, an invagination of the roof of the cavernous sinus that extends from the porous oculomotorius posteriorly (formed by the junction of the anterior petroclinoid, posterior petroclinoid, and interclinoid folds), to the incorporation of CNIII into the fibrous lateral wall of the cavernous sinus at the level of the inferior margin of the anterior clinoid process.[8–10]

Although prior cadaveric and radiologic studies have significantly advanced our understanding of the anatomy of this region,[8–13] a focused histologic description of the tissue relationships underlying the transition of CNIII from

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its cisternal to cavernous segments as it traverses the dura has not been previously reported. We herein assessed the histologic relationships of CNIII at its dural entry site within the oculomotor cistern using cadaveric specimens obtained after performance of a FOZT approach.

Materials and Methods

This work was performed in accordance with University and Department of Anatomy research policies. Preserved cadaveric heads were obtained from the University's Department of Anatomy. As no patients were utilized, institutional review board approval was not necessary.

FOZT approaches were performed on six preserved adult cadaveric heads (2 male, 4 female) as described below (►**Fig. 1**). CNIII from the interpeduncular cistern to the cavernous sinus was then resected, ensuring adequate circumferential margins around the dural entry site of the nerve, and longitudinally bisected (►**Fig. 2**). The specimens were fixed (formalin), embedded (paraffin),

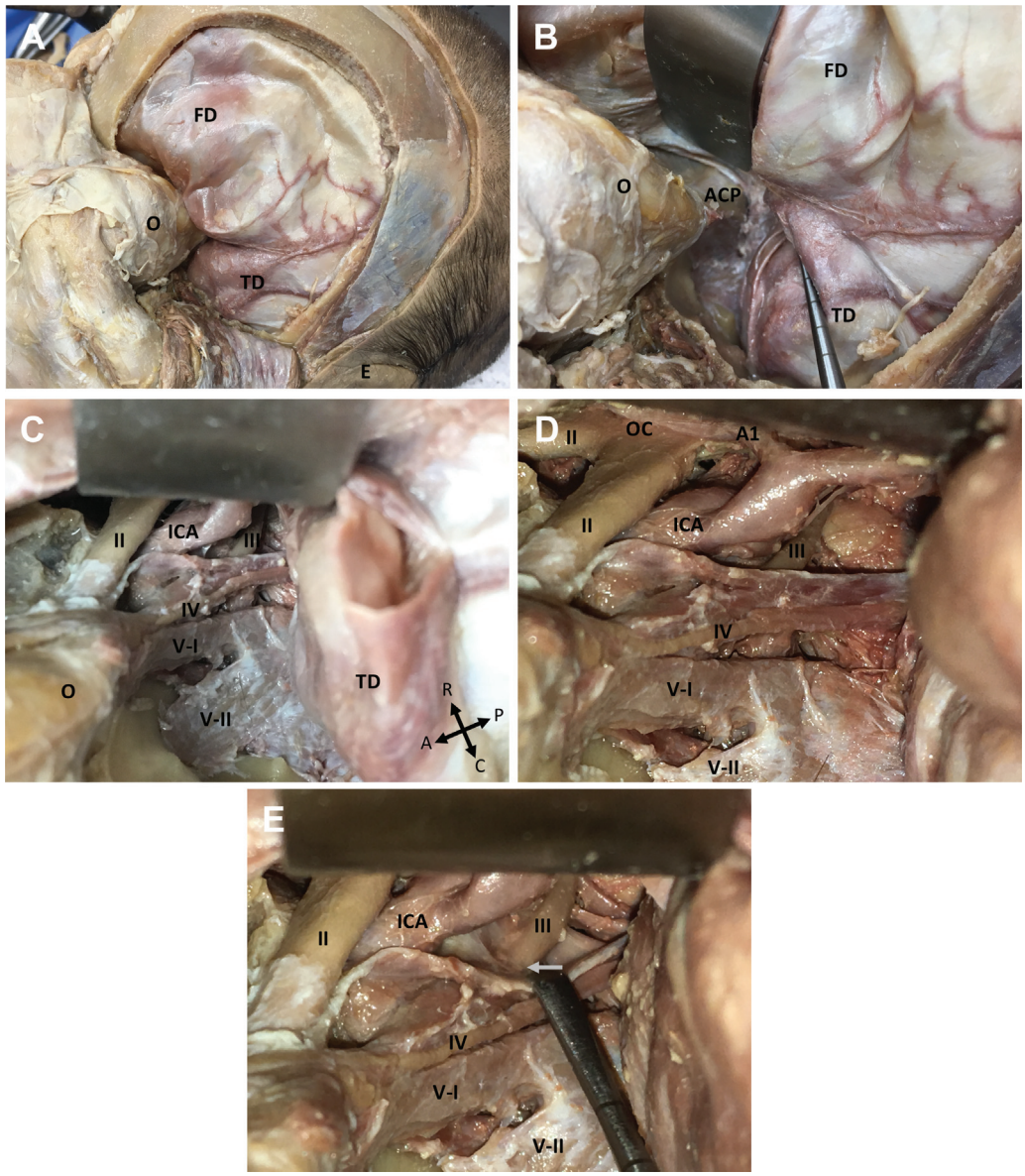

Fig. 1 FOZT cadaveric approach. The FOZT approach performed on six cadaveric specimens involved **(A)** a one-piece orbitozygomatic craniotomy, followed by removal of the sphenoid wing. **(B)** Peeling back the dura propria gained exposure of the superior orbital fissure and foramen rotundum, allowing for an extradural anterior clinoidectomy. **(C)** Dural opening allowed visualization of CNs II–V, the porous oculomotorius, and the proximal internal carotid artery. **(D)** Higher magnification views, including after mobilization of the anterior petroclinoidal fold **(E)**, further demonstrate the porous oculomotorius (*gray arrow*) in relation to other critical structures. Mobilization of the internal carotid artery by opening the distal dural ring and CNIII by opening the oculomotor cistern was not performed prior to harvesting the CNIII-dural entry site. Left-sided dissection shown. II, optic nerve; III, oculomotor nerve; IV, trochlear nerve; V-I, trigeminal nerve—ophthalmic division; V-II, trigeminal nerve—maxillary division; A, anterior; A1, first segment of the anterior cerebral artery; ACP, anterior clinoid process; C, caudal; CN, cranial nerve; E, ear; FD, frontal dura; FOZT, fronto-orbitozygomatic temporopolar; ICA, internal carotid artery; O, orbit; OC, optic chiasm; P, posterior; R, rostral; TD, temporal dura.

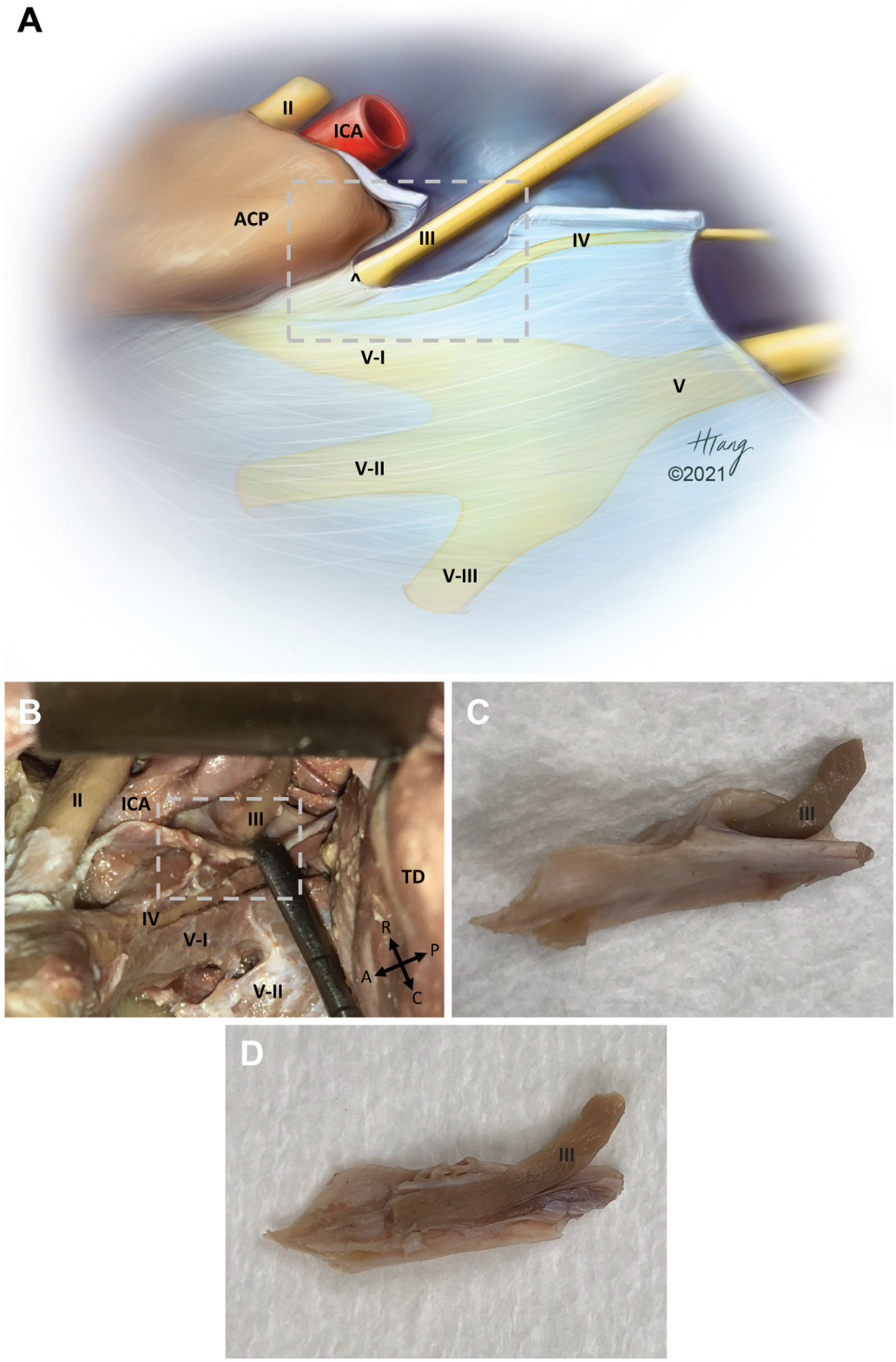

Fig. 2 CNIII–dural entry site harvest. **(A)** Illustration of the dural entry site of CNIII (highlighted by the *dashed gray rectangle*), with the dura of the oculomotor cistern opened and removed from the porous oculomotorius to the oculomotor foramen (marked with an ^). **(B)** After performance of the FOZT cadaveric approach, the CNIII–dural entry site (highlighted by the *dashed gray rectangle*) was resected from the interpeduncular cistern to the cavernous sinus, ensuring adequate circumferential margins around the dural entry site of the nerve. **(C)** The resected specimen was then bisected longitudinally **(D)**, processed, and histologically assessed. Left-sided illustration/dissection shown. II, optic nerve; III, oculomotor nerve; IV, trochlear nerve; V-I, trigeminal nerve–ophthalmic division; V-II, trigeminal nerve–maxillary division; V-III, trigeminal nerve–mandibular division; ACP, anterior clinoid process; C, caudal; CN, cranial nerve; FOZT, fronto-orbitozygomatic temporopolar; P, posterior; R, rostral; ICA, internal carotid artery; TD, temporal dura. Part (A) adapted with permission © 2021 Helen Tang.

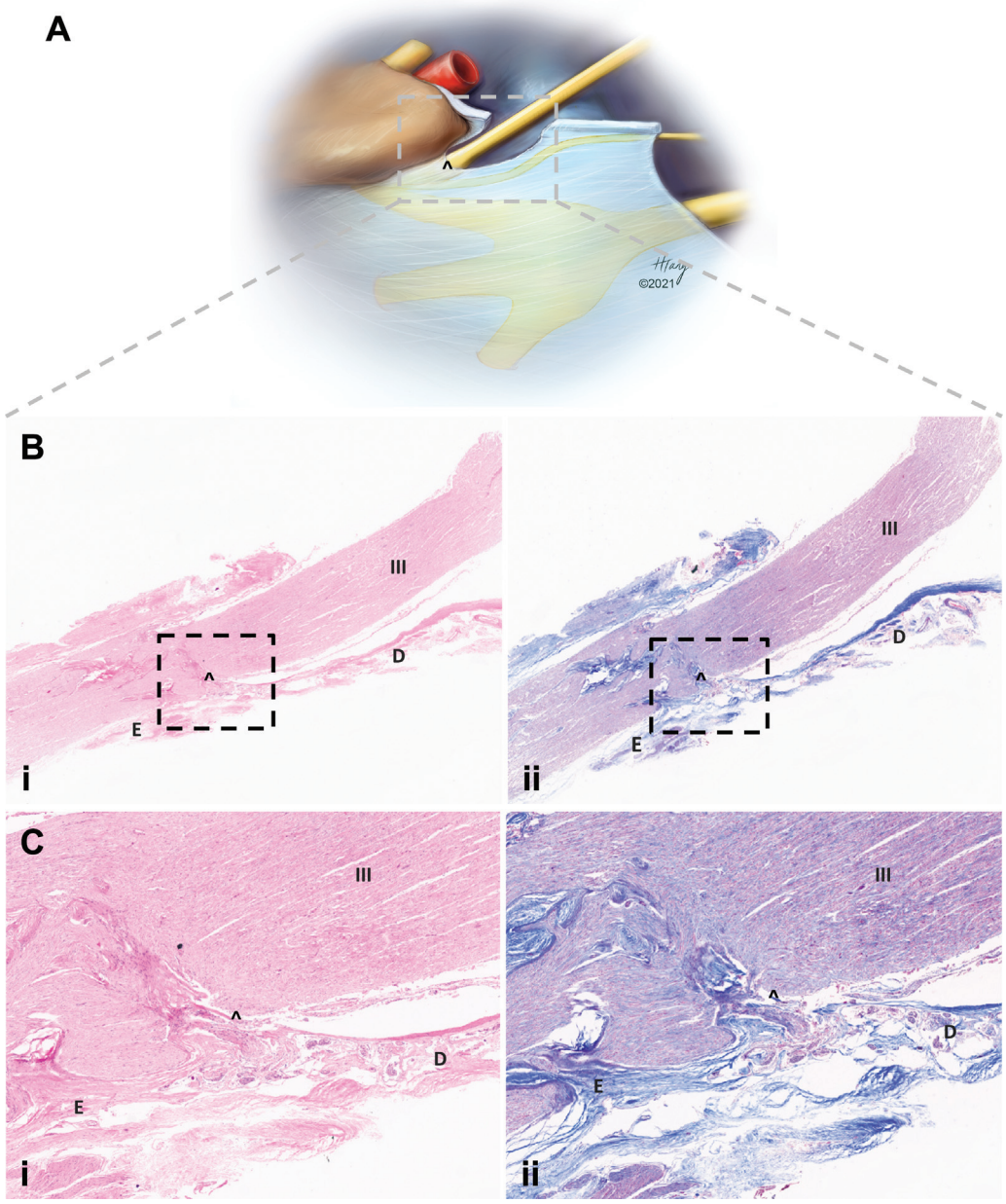

Fig. 3 Histologic analysis of the CNIII–dural junction. **(A)** Re-demonstration of the area of histologic assessment (highlighted by the *dashed gray rectangle*), with the dura of the oculomotor cistern opened from the porous oculomotorius to the oculomotor foramen (marked with an ^). **(B)** Representative 5× and **(C)** 20× photomicrographs of H&E (i) and Masson's Trichrome (ii) stains demonstrate that although CNIII remained separate from the dura within the oculomotor cistern, there was no clear histologic plane identified between these structures at the level of the oculomotor foramen (marked with an ^). These findings suggest that CNIII may be directly mobilized within the oculomotor cistern, while dissections of CNIII distal to the foramen should maintain a thin layer of connective tissue on the nerve. III, cranial nerve III/oculomotor nerve; CN, cranial nerve; D, dura; E, epineurium. *Dashed black boxes* in (B) indicate area of higher magnification in (C). Part (A) adapted with permission from © 2021 Helen Tang.

sectioned (4 microns), and stained (hematoxylin and eosin [H&E] or Masson's Trichrome stain) (►**Fig. 3**). Images of the nerve–dural interface (3 per specimen) were taken using an Aperio ImageScope (v12.3.3.508) after slides were scanned on a Leica Aperio AT2 digital whole slide scanner (Leica Biosystems, Wetzlar, Germany). The histologic relationship between the nerve and the dura was qualitatively assessed by a fellowship-trained neuropathologist. The mean ± standard deviation is reported for continuous variables.

Fronto-orbitozygomatic Temporopolar Approach

An FOZT approach was performed as previously described.[1,5] In brief, a curvilinear incision and interfascial dissection was performed to expose the orbital rim and zygoma, followed by performance of a one-piece orbitozygomatic craniotomy (►**Fig. 1A**). The sphenoid wing was then removed with rongeurs and a high-speed drill to expose the superior orbital fissure and foramen rotundum. An extradural anterior clinoidectomy was performed with a diamond drill bit on a high-speed drill to first core the inside of the bone, followed

by piecemeal removal with rongeurs (►**Fig. 1B**). The bone overlying the optic canal was removed with a high-speed drill, and the temporal tip was mobilized. The dura was opened in a t-shaped fashion, joining the intradural space with the extradural dissection and allowing visualization of the porous oculomotorius (►**Fig. 1D, E**). The next steps of an FOZT (mobilization of the carotid artery by opening the distal dural ring and mobilization of CNIII by opening the oculomotor cistern) were not performed to preserve the specimens for analysis. Harvest of the CNIII–dural interface was performed as described above.

Results

Analysis at low ($5\times$), medium ($20\times$), and high-power ($100\times$) magnification of all nerve–dural interfaces (three views from six independent specimens) demonstrated that the epineurium of CNIII remained separate from the dura throughout its course within the oculomotor cistern (i.e., from the porous oculomotorius up to the oculomotor foramen). At the posterior aspect of the oculomotor cistern (at the level of the oculomotor foramen) there was fusion of the epineurium of CNIII and the connective tissue of the dura, with no clear histologic delineation between these structures identified (►**Fig. 3**). The mean length of CNIII within the oculomotor cistern (measured in five of six specimens) was 4.4 ± 0.5 mm.

These findings support the practice of opening the porous oculomotorius and oculomotor cistern to directly mobilize CNIII proximally, while preserving a thin layer of connective tissue on the nerve during dissections more distally within the cavernous sinus.

Discussion

Mobilization of CNIII is a commonly described maneuver to expand the working corridor of cavernous sinus triangles, while also limiting its manipulation under tension to avoid stretch injuries to the nerve.[1–7] The optimal technique for CNIII mobilization nonetheless requires an in-depth understanding of the histologic relationships of the nerve to surrounding structures throughout its course. Similar to dissections of other neurovascular structures as they traverse the dura, loose connections can be directly released while more dense adhesions may require leaving tissue on the mobilized structure to avoid injury. Examples of the latter situation are the dural entry sites of the vertebral artery in the posterior fossa and the internal carotid artery at the distal dural ring,[14,15] where fusion of the arterial adventitia with the dura requires maintenance of a dural cuff on the vessels to minimize risk of vascular injury with mobilization. CNIII's dural relationship is more nuanced than these arterial examples, however, with the histologic composition of the cavernous sinus itself remaining an active topic of debate.[16] Specifically, the question of whether the cavernous sinus is bounded on both the lateral and medial sides by a true dural layer or whether the medial wall of the cavernous sinus is composed of a loose, fibrous tissue that is not true dura remains unresolved.[16] Moreover, despite multiple histologic analyses of the cavernous sinus region,[17–24] to the best of our knowledge a dedicated study of the histology of the cisternal to cavernous course of CNIII has not been previously performed.

Our finding of a clear plane between CNIII and the dural sleeve comprising the oculomotor cistern throughout its course from the porous oculomotorius up to the oculomotor foramen is in line with prior cadaveric and radiologic assessments.[8,9,12,13] Additionally, while not the focus of this work, the length of the oculomotor nerve within the cistern as measured after histologic processing was 4.4 mm (range: 4–5 mm). This is similar to prior studies where the depth of the oculomotor cistern ranged from 3.0 to 6.5 mm, although it has been reported to be long as 13.1 mm.[8,9,13] Surgeon awareness of these anatomical features facilitates the sharp opening of the dura forming the roof of the oculomotor cistern, either over an angled dissector or with a blunt tip right-angle upgoing blade to protect the nerve below, and allows mobilization of this segment of CNIII away from the surrounding dural sleeve without expected dense connections between these structures.[1,8] This maneuver releases the first main tether point of CNIII, and allows for the potential expansion of the oculomotor, clinoidal, and supratrochlear cavernous sinus triangles.

The exact histologic relationship of CNIII to the dura at the depth of the oculomotor cistern at the level of the oculomotor foramen has been studied less, despite its significant surgical implications for mobilization of the distal nerve. Prior works have qualitatively described based on cadaveric dissections the continuation of a deep dural layer at the foramen with connective tissue investing the nerve within the lateral wall of the cavernous sinus.[8,12] This investing tissue, or endosteal layer, encasing the nerve in its cavernous segment is separate from a thicker outer meningeal layer, or dura propria.[5,8–10] A natural cleavage plane nonetheless exists between these two layers that facilitates their separation, for example during extradural exposure of the superior orbital fissure and foramen rotundum/ovale as part of a temporopolar or pretemporal approach.[1,5] With this maneuver, and subsequent mobilization of the carotid artery and CNIII within the oculomotor cistern as described above, significantly increased access to the parasellar, infrachiasmatic, and posterior clinoid regions can be gained.

In cases where dissection of CNIII at the level of or distal to the oculomotor foramen (within the cavernous sinus proper and including dissection from the carotidoculomotor membrane) is necessary; however, manipulation of the nerve within this more tightly invested endosteal tissue is required. Because, as demonstrated herein this tissue is histologically fused with the epineurium of CNIII, attempts to dissect the nerve completely free from the surrounding tissue should not be made. Rather, mobilization via sharp superomedial and/or superolateral release should be performed, with preservation of a layer of invested connective tissue lining the nerve. In contrast to the surgical technique used to open the oculomotor cistern, blunt dissection during mobilization

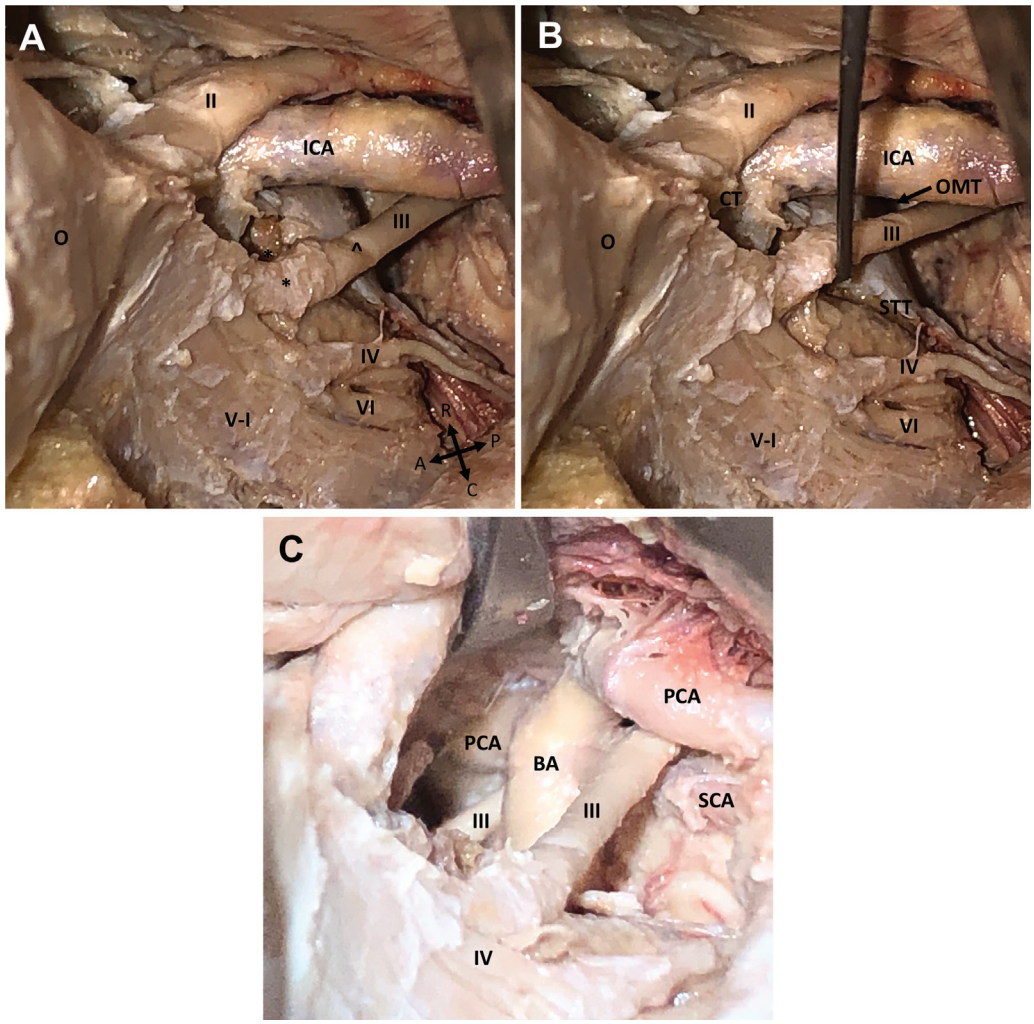

Fig. 4 Mobilization of CNIII distal to the oculomotor foramen. **(A)** When mobilizing CNIII distal to the oculomotor foramen a thin layer of connective tissue (marked with an *) should be left on the nerve due to fusion of the epineurium and the connective tissue of the dura at this level (indentation on CNIII marked with an ^ indicates the level of the porous oculomotorius). **(B)** This dissection further mobilizes the nerve to increase the operative corridors within the oculomotor, clinoidal, and supratrochlear triangles, allowing increased access to the parasellar, infrachiasmatic, and posterior clinoid regions **(C)**. Left-sided dissection shown. II, optic nerve; III, oculomotor nerve; IV, trochlear nerve; VI, abducens nerve; V-I, trigeminal nerve—ophthalmic division; A, anterior; BA, basilar artery; C, caudal; CN, cranial nerve; CT, clinoidal triangle; ICA, internal carotid artery; O, orbit; OMT, oculomotor triangle; P, posterior; PCA, posterior cerebral artery; R, rostral; SCA, superior cerebellar artery; STT, supratrochlear triangle.

of the cavernous segment of CNIII is most effective after a plane has been sharply developed. Moreover, while the fusion point of the dura/epineurium appears to be at the level of the oculomotor foramen itself, mobilization at this point is still possible in our experience, as long as a thin layer of the investing tissue is preserved on the nerve (►**Fig. 4**). This is notably different from the operative technique required for mobilization of the internal carotid and vertebral arteries at their dural entry points, where thick attachments from the dura to the arterial adventitia require maintenance of a healthy dural cuff on the artery to avoid vascular injury.[14,15]

Despite the relatively small *n* of 6 utilized in this study, each sample was obtained from a separate cadaver and three sites per specimen were assessed. Histologic analysis by a specialty-trained neuropathologist demonstrated consistency across all samples (18 sites total), supporting the fidelity of our data.

Conclusion

While CNIII is separate from the dura within the oculomotor cistern, the epineurium fuses with the connective tissue of the dura at the level of the oculomotor foramen. Mobilization of CNIII distal to the foramen should maintain a thin layer of connective tissue on the nerve.

Conflict of Interest
None declared.

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