

1 **Virtual Exploration of Safe Entry Zones in the Brainstem: Comprehensive Definition and**  
2 **Analysis of the Operative Approach**

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15

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18

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20 We have no conflicts of interest in regard to this research.

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23 **ABSTRACT**

24 **Background:** Detailed and accurate understanding of intrinsic brainstem anatomy and the inter-  
25 relationship between its internal tracts and nuclei and external landmarks is of paramount  
26 importance for safe and effective brainstem surgery. Using anatomical models can be an  
27 important step in sharpening such understanding.

28 **Objective:** To show the applicability of our developed virtual 3D model in depicting the safe  
29 entry zones (SEZs) to the brainstem.

30 **Methods:** Accurate 3D virtual models of brainstem elements were created using high-resolution  
31 magnetic resonance imaging and computed tomography to depict brainstem SEZs.

32 **Results:** All the described SEZs to different aspects of the brainstem were successfully depicted  
33 using our 3D virtual models.

34 **Conclusions:** The virtual models provide an immersive experience of brainstem anatomy,  
35 allowing users to understand the intricacies of the microdissection that is necessary to  
36 appropriately traverse the brainstem nuclei and tracts toward a particular target. The models  
37 provide an unparalleled learning environment for illustrating SEZs into the brainstem that can be  
38 used for training and research.

39

40

41 **INTRODUCTION**

42 Historically, intrinsic brainstem lesions have been considered inoperable.<sup>1</sup> In the 1980s, resecting  
43 brainstem lesions gained popularity with reports of favorable outcomes.<sup>2</sup> A more advanced  
44 understanding of the brainstem fiber tracts enabled establishment of the so-called safe entry  
45 zones (SEZs) (Figure 1).<sup>3-22</sup>

46

47 An in-depth understanding of the intrinsic structural anatomy of the brainstem is critical to  
48 brainstem surgery. Such knowledge can be gathered through spending countless hours in the  
49 laboratory working on cadaveric specimens that enable fiber tract dissection.<sup>3-22</sup> However,  
50 developing the fine art of white matter dissection can be extremely difficult and expensive.  
51 Therefore, using accurate virtual models is an indispensable tool for sharpening this  
52 understanding. The purpose of this study was to introduce the use of virtual reality 3D models as  
53 an ancillary tool for learning the surgical anatomy of the SEZs to different regions of the  
54 brainstem.

55

56 **METHODS**

57 These methods were described previously.<sup>13,23,24</sup> High-resolution computed tomography and  
58 magnetic resonance imaging, as well as both 2-dimensional (2D) and 3-dimensional (3D)  
59 reconstructed catheter-based angiograms, were used to create the models. The model was used to  
60 demonstrate the topography and relationships of 19 SEZs to the brainstem (Table 1).

61

62 As an anatomic study, the present work neither required nor received institutional review board  
63 or ethics committee approval. Similarly, no patient consent was required.

64

65 **Midbrain**

66

67 **I. Ventral and Lateral Midbrain SEZs**

68 *1. Anterior Mesencephalic Zone*

69 Topography

70 The anterior mesencephalic zone (AMZ) (also known as the periculomotor zone) is located on  
71 the medial one-fifth of the ventral aspect of the crus cerebri, just lateral to the root exit zone of

72 the oculomotor nerve (Figure 2A; Model 1 [showing the mesencephalic SEZs]).<sup>25</sup> The AMZ  
73 harbors the frontopontine fibers and is located medial to the middle three-fifths of the crus  
74 cerebri through which the corticospinal and corticonuclear tracts pass.<sup>13,14,26</sup> A relatively  
75 perforator-free zone lateral to the oculomotor nerve is located between the posterior cerebral  
76 artery (PCA) superiorly, and the superior cerebellar artery (SCA) inferiorly.

77

#### 78 Surgical Approach

79 The AMZ is adjacent to the medial crural cistern. The oculomotor-tentorial triangle (OTT) is the  
80 surgical window to access the AMZ.<sup>6,14</sup> This triangle is between the free tentorial edge and the  
81 cisternal oculomotor nerve. A pterional or orbitozygomatic craniotomy with the transsylvian  
82 pretemporal approach can be used.<sup>24,27</sup> The subtemporal approach with or without a tentorial  
83 incision may also be used.<sup>27</sup> An endoscopic endonasal transclival approach with pituitary  
84 transposition can also provide limited access to the AMZ.<sup>24,28,29</sup>

85

#### 86 *2. Lateral Mesencephalic Sulcus*

##### 87 Topography

88 The lateral mesencephalic sulcus (LMS) runs inferiorly on the lateral aspect of the midbrain  
89 between the cerebral peduncle anteriorly and the midbrain tegmentum posteriorly at the level of  
90 the inferior colliculus (surfaced by lateral lemniscus).<sup>30,31</sup> It extends in a rostral-caudal direction  
91 from the medial geniculate body superiorly, to join the pontomesencephalic sulcus inferiorly, and  
92 continues inferiorly between the middle and superior cerebellar peduncles as the interpeduncular  
93 sulcus. It has an average length of  $9.6 \pm 1.41$  mm (range, 13.3–7.4 mm).<sup>32</sup>

94

95 A perpendicular incision in the LMS would ideally enter the midbrain anterior to the medial  
96 lemniscus (ML) and posterior to the substantia nigra (Model 1; Figure 2B).<sup>15</sup> The anteromedial  
97 boundary for this approach is formed by the oculomotor fibers passing through the red nucleus.<sup>33</sup>  
98 Extreme ventral deviation of the axial incision trajectory would hit the substantia nigra and the  
99 ventrally located pyramidal tract. Extreme dorsal deviation of the incision trajectory would  
100 damage the ML, the mesencephalic superior cerebellar peduncle fibers (and their decussation,  
101 also known as the horseshoe-shaped commissure of Wernekinck<sup>6,14</sup>), red nucleus, oculomotor

102 nucleus, central tegmental tract (CTT), and the mesencephalic nucleus and tract of the trigeminal  
103 nerve.<sup>34</sup>

104

#### 105 Surgical Approach

106 The LMS is adjacent to the posterior ambient cistern.<sup>13,35</sup> Approaches used to access the LMS  
107 include the subtemporal, paramedian supracerebellar infratentorial (SCIT), extreme-lateral SCIT,  
108 retrosigmoid, and presigmoid approaches.<sup>36,37</sup> The cerebrovascular structures encountered during  
109 this approach include the P2-PCA superiorly, the distal s2- and proximal s3-SCA, and the medial  
110 posterior choroidal artery.

111

### 112 **II. Dorsal Midbrain SEZs**

113 All described SEZs through the dorsal aspect of the midbrain involve the quadrigeminal  
114 plate and are adjacent to the quadrigeminal cistern.

115

#### 116 *3. Supracollicular Approach*

##### 117 Topography

118 Bricolo<sup>14,38-42</sup> described an SEZ just above the superior colliculi. A transverse incision is made at  
119 the subpineal triangle (triangle of Obersteiner<sup>26</sup>) above the superior colliculi and below the  
120 posterior commissure (Figure 2C).<sup>43</sup> An incision kept behind the aqueduct causes minimal  
121 damage to the mesencephalic structures. However, incising beyond the cerebral aqueduct would  
122 damage the mesencephalic nucleus and tract of the trigeminal nerve, medial longitudinal  
123 fasciculus (MLF), and oculomotor nucleus.

124

#### 125 *4. Infracollicular Approach*

##### 126 Topography

127 A transverse incision inferior to the inferior colliculi is considered safe.<sup>24</sup> Similar to the  
128 supracollicular zone, the infracollicular incision will access the posterior tectal region behind the  
129 cerebral aqueduct (Model 1; Figure 2C). However, one should be aware of the decussation of the  
130 trochlear nerves just below the quadrigeminal plate within the superior medullary velum.<sup>26</sup> An  
131 incision surpassing the cerebral aqueduct violates the trochlear nucleus, mesencephalic nucleus,

132 and tract of the trigeminal nerve, then CTT, MLF, tectospinal tract, superior cerebral peduncle,  
133 and eventually the ML and anterolateral fasciculus.<sup>35</sup>

134

## 135 *5. Intercollicular Zone*

### 136 Topography

137 The scant intercollicular fibers between the bilateral superior and inferior colliculi enable access  
138 to lesions within the midbrain tectum dorsal to the aqueduct.<sup>35</sup> The main difference from the  
139 infracollicular and supracollicular approaches is the vertical trajectory of the midbrain incision in  
140 this approach (Figure 2C).<sup>6,35</sup>

141

### 142 Surgical Approach

143 The SCIT approach provides access to SEZs in the quadrigeminal plate.<sup>44</sup> Variants of the SCIT  
144 include the midline, paramedian, and extreme-lateral approaches, which have few differences  
145 regarding operative maneuverability.<sup>6,14,45</sup> We prefer the paramedian approach because of its  
146 less-invasive nature and the protection of the midline supracerebellar veins that it provides.

147

## 148 **Pons**

149 The pons is a common site for intrinsic brainstem lesions.<sup>45-47</sup> During resection of these lesions,  
150 the primary goal is to avoid the corticospinal, corticonuclear, and MLF tracts, as well as the  
151 nuclei and intrapontine segments of cranial nerves (CNs) V to VIII.

152

## 153 **III. Ventral Pontine SEZs**

154 The ventral pons is characterized by the root entry/exit zone (REZ) of CN V. Medial to CN V is  
155 the basis pontis, harboring the pyramidal tract and pontine nuclei. Lateral to trigeminal REZ, lies  
156 the middle cerebellar peduncle. Three SEZs through the region of the ventral pons have been  
157 described; they are based on 2 readily identifiable surface landmarks, CN V and CN VII to VIII  
158 REZs.<sup>3,26,48</sup>

159

## 160 *6. Peritrigeminal Zone*

### 161 Topography

162 The peritrigeminal zone (PTZ) provides access to the ventral pons via a longitudinal incision  
163 medial to a vertical line connecting the REZs of CNs V and VII to VIII with an average length of  
164  $8.9 \pm 1.3$  mm (range, 6.8–9.6 mm) (Figure 3A, [Model 2] showing the 3D reconstruction of  
165 pontine SEZs).<sup>14,24</sup> This trajectory transgresses the transverse pontine fibers and is lateral to the  
166 corticospinal tracts. It can extend as deeply as the trigeminal motor and sensory nuclei.<sup>5,6,30</sup> The  
167 longitudinal extent of dissection should not extend rostral to CN V or caudal to CN VII.<sup>5,16</sup>

168

169 The average distance between the most lateral fibers of the corticospinal tract and CN V is  $4.7 \pm$   
170  $0.7$  mm (range, 3.1–5.6 mm), which defines the medial extent of PTZ.<sup>6</sup> A no-fly zone of the  
171 ventral pons is described between the midline and a line connecting the lateral aspect of the  
172 cerebral peduncle and the pons.<sup>15,31</sup> The average distance from the lateral edge of the pyramidal  
173 tract to the CN V and VII REZs is  $9.2 \pm 1.2$  mm (range, 7.0–11.6 mm) and  $8.0 \pm 1.0$  mm (range,  
174 5.6–9.6 mm), respectively.<sup>13,15</sup>

175

176 In contrast, entering the pons lateral to the trigeminal nerve with an axially oblique trajectory  
177 jeopardizes the intrapontine segment of CN V and its nuclei, and the ventral cochlear nucleus.<sup>13</sup>  
178 The trigeminal nucleus is located, on average, 10 to 12 mm (range, 9.0–16.3 mm) from the  
179 pontine surface.<sup>13</sup>

180

### 181 Surgical Approach

182 The PTZ is accessed via the retrosigmoid and presigmoid retrolabyrinthine approaches.<sup>13,15,30</sup>  
183 Also, anterior petrosectomy provides such access.<sup>14,44</sup> The endoscopic endonasal transclival  
184 approach (preferably combined with an extradural anterior petrosectomy) can also provide  
185 access to the PTZ.<sup>13,14,44</sup>

186

## 187 *7. Supratrigeminal Zone*

### 188 Topography

189 Hebb and Spetzler<sup>30,31,49</sup> introduced the transpeduncular approach to intrinsic pontine lesions.

190 This zone is more accurately called the supratrigeminal zone (STZ), which is located above the  
191 CN V REZ lateral to the pyramidal tract (Figure 3B),<sup>50</sup> and is essentially the same zone  
192 described by Zenonos et al<sup>14</sup> as the epitrigeminal zone. To avoid the intrapontine segment of the

193 trigeminal nerve, a tangential trajectory is suggested parallel to the direction of middle cerebellar  
194 peduncle fibers.<sup>51</sup> The pons is entered lateral to the CN V. Marching superior to CN V REZ, a  
195 relatively superficial intrapontine lesion can be accessed. Extending the incision too medially or  
196 too deeply would risk the pyramidal tract and the superior cerebellar peduncle, respectively.  
197 Some have described another so-called STZ approximately 4 mm below the pontomesencephalic  
198 sulcus along the sagittal-level of CN III REZ, which is technically a continuation of the AMZ in  
199 the upper pontine area.<sup>19</sup>

200

#### 201 Surgical Approach

202 The STZ is located adjacent to the cerebellopontine cistern. Therefore, it is surgically accessed  
203 similar to PTZ. However, the STZ can also be accessed via a subtemporal transtentorial,<sup>27,50</sup> and  
204 the pretemporal transsylvian<sup>14,44</sup> approaches.

205

### 206 8. *Lateral Pontine Zone*

#### 207 Topography

208 The medial craniocaudal extent of the approach is from the CN V REZ to that of CN VII to VIII  
209 but narrows laterally over the surface of the middle cerebellar peduncle toward the medial end of  
210 the petrosal fissure (Figure 3C). In contrast to PTZ, the LPZ is accessed by entering the pons  
211 lateral to the trigeminal-facial line. Staying relatively superficial avoids the intrapontine  
212 trigeminal fibers and nuclei.<sup>9,15,27,35</sup>

213

#### 214 Surgical Approach

215 The LPZ is accessed through retrosigmoid and retrolabyrinthine approaches.

216

### 217 **IV. Dorsal Pontine SEZs**

218 Understanding dorsal pontine SEZs requires knowledge of the microanatomy of the fourth  
219 ventricular floor.<sup>4,5,50,52</sup>

220

### 221 9. *Suprafacial Approach*

#### 222 Topography



223 The suprafacial (SFZ) and infrafacial (IFZ) zones were defined on the basis of the location of the  
224 facial colliculus in the rhomboid fossa.<sup>13,20,24,35</sup> The facial colliculus is formed by the underlying  
225 abducens nucleus and the intrapontine fibers of the facial nerve.<sup>4,50,53,54</sup> The suprafacial triangle  
226 located rostral to the facial colliculus comprises the SFZ (Figure 3D). The boundaries of the  
227 suprafacial triangle include the superior cerebellar peduncle laterally, the MLF medially, and the  
228 facial colliculus inferiorly.<sup>13,35</sup> The facial colliculus might not be visible in more than one-third  
229 of the population.<sup>20</sup> In such cases, the average distance from the obex to the lower pole of the  
230 facial colliculus, which is 14 to 15 mm (range, 11.5–18.0 mm), can be used.<sup>11</sup> Mapping of the  
231 fourth ventricular floor to localize the facial nerve can be useful.<sup>21,55</sup> The apex of SFZ is located  
232 at the frenulum veli,<sup>4,56</sup> through which the trochlear nerves pass,<sup>11</sup> and the average height of this  
233 triangle is  $15.7 \pm 2.1$  mm (range, 10.8–19.2 mm).<sup>13</sup> The narrow base of this triangle runs between  
234 the lateral aspect of the MLF and the inferior end of the sulcus limitans at the upper border of the  
235 facial colliculus measuring  $7.4 \pm 0.5$  mm on average (range, 5.6–10.4 mm).<sup>11</sup>

236

237 The rationale of limiting the lateral extension of the SFZ to sulcus limitans (and not the  
238 cerebellar peduncle) is to avoid the trigeminal mesencephalic tract and the CTT located deep to  
239 the vestibular area or the trigeminal motor and main sensory nuclei deep to the superolateral  
240 edge of the superior fovea triangle (Model 2).<sup>11,13</sup>

241

242 A 1-cm longitudinal incision is started caudally from the edge of the superior cerebellar peduncle  
243 and 4 to 5 mm laterally from the median sulcus<sup>13</sup> (to avoid the MLF, with an average width of  $1$   
244  $\pm 0.4$  mm<sup>20</sup>). The deep limit of the SFZ is the ML, which is 4.5 mm from the ependymal  
245 surface.<sup>13</sup> Any lesion located deeper than 4 mm to the floor of the fourth ventricle would likely  
246 be anterior to the ML and would not be amenable to an SFZ approach. Any viable neuronal  
247 tissue overlying the lesion on magnetic resonance imaging on the floor of the fourth ventricle  
248 necessitates a peritrigeminal pathway, because even minor neuronal tissue on the floor can be  
249 highly functional.

250

251 *10. Infrafacial Approach*

252 Topography

253 The IFZ uses the interval between the intrapontine segment of the facial nerve superiorly, which  
254 is at the level of a transverse line passing through the upper edges of the lateral recesses of the  
255 fourth ventricle<sup>20,50,54,56</sup>, the MLF medially, and the hypoglossal and dorsal vagal nuclei  
256 inferiorly,<sup>13</sup> with an average rostrocaudal dimension of 6 to 9 mm (Figure 3D).<sup>53,55</sup> At the lower  
257 margin of the lateral recess, the facial and ambiguous nuclei are located just lateral to the medial-  
258 most point of the tela choroidea, and IFZ should be entered medial to this point.<sup>13,53</sup> The lower  
259 limit of IFZ corresponds to the lower edge of the lateral recess or the upper strands of the striae  
260 medullares.<sup>13</sup> When the striae medullares are not visible, the distance between the obex and the  
261 upper pole of the hypoglossal triangle can be used (range, 6.5–10.6 mm).<sup>11,13,20</sup> The ventral limit  
262 of IFZ is the CTT, which is reached at an average depth of 4.9 mm from the endymal  
263 surface.<sup>11,13,53</sup> Kyoshima et al<sup>13</sup> described an endymal incision just above the striae medullares,  
264 approximately 4 to 5 mm lateral to the median sulcus. The incision should be as small as possible  
265 ( $\leq 6$  mm) to avoid injuring the facial colliculus.

266

## 267 *11. Median Sulcus of the Fourth Ventricle*

### 268 Topography

269 Described by Bricolo,<sup>20</sup> the median sulcus (MS-IV) runs between the bilateral median eminences  
270 (also known as funiculi teres<sup>26</sup>) with underlying MLFs that do not have crossing fibers above the  
271 level of the facial colliculi.<sup>43</sup> Therefore, the MS is used above the facial colliculi (Figure 3D).  
272 The downside of this approach is that any lateral retraction would cause damage to the MLF.

273

### 274 Surgical Approach

275 Access to the SFZ, IFZ, and MS-IV requires a midline suboccipital transvermian or telovelar  
276 approach.<sup>13</sup>

277

## 278 *12. Area Acustica*

### 279 Topography

280 Bricolo<sup>4</sup> described the area acustica (AA) over the dorsal aspect of the lateral recess of the fourth  
281 ventricle. This zone corresponds to the inferior cerebellar peduncle fibers located underneath the  
282 lateral end of the dorsal acoustic striae (i.e., striae medullares) (Figure 3D). At this level, the  
283 peduncular fibers are ventral to the dorsal cochlear nucleus and dorsal to the spinal tract of the

284 trigeminal nerve. This area is a few millimeters superior to the lateral medullary zone (LMZ)  
285 (corresponding to a more inferiorly located part of the inferior cerebellar peduncle<sup>26</sup>; see “Lateral  
286 Medullary Zone”). The surgical corridor through the AA should be kept shallow, because deep to  
287 the inferior cerebellar peduncle, the following (from dorsal to ventral) will be reached: trigeminal  
288 spinal tract, nucleus ambiguus, and facial nucleus.<sup>7</sup> Evidently, the dorsal cochlear nucleus and  
289 the peduncular fibers would be breached after entering the AA.

290

### 291 *13. Floccular Peduncle*

#### 292 Topography

293 The floccular peduncle (FP) is a potential SEZ along the rostral wall of the lateral recess of the  
294 fourth ventricle, rostral to the floccular attachment of the inferior medullary velum (Figure  
295 3D).<sup>57,58</sup> The FP simply forms the roof of the lateral recess along the attachment of the inferior  
296 medullary velum. The approximate length of the FP is 8.0 mm (range, 5.2–9.3 mm).<sup>8</sup> No clinical  
297 correlate was provided by the authors.

298

#### 299 Surgical Approach

300 The AA and FP can be reached through exposure of the lateral end of the lateral recess from the  
301 ventricular side, which can be done by using a suboccipital telovelar approach. As an alternative,  
302 a trans-tonsillobiventral fissure or trans-tonsillouvular fissure approach can be used to reach the  
303 lateral recess of the fourth ventricle.<sup>13</sup>

304

## 305 **Medulla Oblongata**

### 306 **V. Ventral and Lateral Medullary SEZs**

#### 307 *14. Anterolateral Sulcus*

##### 308 Topography

309 The bilateral anterolateral sulci (ALS) form the lateral boundary of the medullary pyramids and  
310 reach the pontomedullary sulcus just anterior to the supraolivary fossette (Model 3; Figure 4A).  
311 It is continuous inferiorly with the ALS of the spinal cord. The ALS forms REZs for CN XII and  
312 motor roots of the spinal cord. At the level of the olive, the ALS is called the preolivary sulcus.  
313 The ALS approach requires an oblique trajectory through the preolivary sulcus between the  
314 caudal-most roots of CN XII and the rostral-most rootlets of the C1 nerve.<sup>8</sup> The tracts at risk are

315 the anterolateral fascicle, olivary amiculum and internal arcuate fibers laterally, and the ML and  
316 MLF medially.<sup>6,16</sup>

317

### 318 *15. Olivary Zone*

#### 319 Topography

320 The olivary zone (OZ) is approached similar to the ALS. The trajectory involves a neurotomy in  
321 the medullary olive (Figure 4A).<sup>30,31</sup> The olive has a craniocaudal length of 13.5 mm and a width  
322 of 7.0 mm.<sup>4,50</sup> The average distance from the pial surface on the olive to the point at which deep  
323 fiber groups enter its hilus is  $5.5 \pm 0.5$  mm (range, 4.7–6.9 mm).<sup>15</sup> Deeply, the intramedullary  
324 segment of CN XII is encountered.<sup>15</sup>

325

### 326 *16. Posterolateral Sulcus*

#### 327 Topography

328 The posterolateral sulcus (PLS) corresponds to the postolivary sulcus and marks the posterior  
329 limit of the olive on the anterolateral aspect of the medulla. The rootlets of CNs IX to X originate  
330 dorsolateral to this sulcus (Figure 4A). The spinal tract of the trigeminal nerve intersects with the  
331 intramedullary segment of CNs IX to X.<sup>35</sup>

332

#### 333 Surgical Approach

334 The ALS is appropriate for exophytic lesions that involve the caudal anterolateral medulla,  
335 adjacent to the lateral medullary cistern.<sup>35</sup> This region can be accessed using the far-lateral  
336 approach. The medullary olive and lower CNs serve as the landmarks.<sup>6</sup> An endoscopic endonasal  
337 approach to remove the lower third of the clivus and anterior part of the occipital condyle  
338 exposes the ALS.<sup>24</sup> The surgical exposure of OZ and PLS is similar to that of ALS, although  
339 endoscopic approaches provide limited exposure of the PLS.

340

### 341 *17. Lateral Medullary Zone*

#### 342 Topography

343 Deshmukh et al<sup>4,5</sup> described the approach through the lateral medullary zone (LMZ), to access  
344 the rostral dorsolateral medulla. The LMZ corresponds to the rostral part of the inferior  
345 cerebellar peduncle ventral to the foramen of Luschka and REZs of CNs IX to X (Figure 4B). At

346 the level of the rostral medulla, the floor of the fourth ventricle is lined by several nuclei and  
347 tracts. The nuclei include (medially to laterally) the hypoglossal, the dorsal vagal, the medial and  
348 vestibular, the lateral cuneate, and, more rostrally, dorsal cochlear nuclei.<sup>7</sup> Important tracts  
349 include (medially to laterally) the dorsal longitudinal fasciculus, the solitary fasciculus, and the  
350 lateral vestibulospinal tract.<sup>7,35</sup>

351

### 352 Surgical Approach

353 The LMZ can be accessed through a retrosigmoid craniotomy, although the far-lateral and  
354 presigmoid approaches can also be used. A vertical neurotomy is made on the inferior cerebellar  
355 peduncle, posterior to the origin of CNs IX to X.<sup>7</sup>

356

## 357 **VI. Dorsal Medullary SEZs**

### 358 *18. Posterior Median Sulcus*

#### 359 Topography

360 The posterior median sulcus (PMS) is entered along the midline below the level of the obex  
361 (Figure 4B).<sup>14</sup> The corridor is developed between the gracile fascicles/tubercles (clava) on the  
362 dorsal aspect of the medulla. The hypoglossal and dorsal vagal nuclei are located near the  
363 midline (average, 0.3 mm; range, 0.2–0.4 mm),<sup>4,5,16,26,50</sup> and lateral retraction of the neural tissue  
364 should be avoided when using PMS.

365

### 366 *19. Posterior Intermediate Sulcus*

#### 367 Topography

368 The posterior intermediate sulcus (PIS) runs between the gracile and cuneate tubercles/fascicles  
369 (Figure 4B).<sup>53</sup> Deepening the surgical corridor along the PIS puts the hypoglossal and dorsal  
370 vagal nuclei at risk.<sup>5,26</sup> These nuclei are reached even dorsal to the central canal and its most  
371 rostral dilatation just inferior to the obex (Arancio's ventricle).<sup>53</sup> The trigeminal spinal tract is  
372 located ventrolateral to the cuneate fascicle and descends down the upper spinal cord and might  
373 be at risk.<sup>43</sup>

374

### 375 Surgical Approach

376 The PMS and PIS can be approached via a median suboccipital craniotomy and C1 laminectomy.

377

378 **USE OF VIRTUAL REALITY MODELS IN UNDERSTANDING THE OPERATIVE**  
379 **ANATOMY OF THE BRAINSTEM**

380 We have shown the applicability of our 3D brainstem models in demonstrating the complex  
381 surgical anatomy of brainstem SEZs. Models are an integral part of teaching anatomy. They have  
382 been created and used since the 18th century, after publication of Morgagni's masterpiece *De*  
383 *Sedibus et Causis Morborum* in 1761.<sup>13,35</sup> Today, many medical educators use physical and/or  
384 digital 3D models to depict anatomical interrelationships that can be even more efficient and  
385 flexible than cadaver specimens while avoiding financial, institutional, ethical, and social  
386 limitations of cadaver use.<sup>59-62</sup>

387

388 **Importance of Digital 3D Models in Depicting Surgical Anatomy of the Brainstem**

389 When removing a symptomatic lesion that does not reach the pial surface, the surgeon should  
390 choose a port of entry with the minimal untoward complications. Achieving this goal requires  
391 knowledge of the internal structure of the brainstem as a see-through image that does not lose  
392 accuracy with perspective changes (i.e., different approaches). Extracted brains are usually used  
393 to study the external features of the brainstem. Further ahead, sectional anatomy of the brainstem  
394 should be analyzed. However, special tissue preparation is needed to reliably identify various  
395 tracts and nuclei. Even so, it is difficult to obtain a flawless mental see-through through sectional  
396 studies.

397

398 Therefore, the application of accurate detailed digital 3D models that provide an interactive  
399 interface can be helpful in understanding this complexity. Our digital 3D models of the  
400 brainstem provide these features. The interactivity of our proposed models enables trainees to  
401 study the surgical anatomy of the brainstem and to understand the interrelationship between  
402 various internal structures, as well as the relationship between those structures and surface  
403 landmarks and vascular anatomy. Furthermore, the ability to turn and rotate the models enables  
404 trainees to visualize these relationships with the surgical positioning implemented. These  
405 features are extremely important in preparing neurosurgical trainees for complex surgical  
406 approaches to the brainstem for which patient positioning can disrupt the orthogonal  
407 understanding of anatomy. Indeed, the extent to which this model can enhance trainees'

408 understanding of brainstem anatomy is subject to further analysis. Another important potential  
409 advantage of digital 3D models of the brainstem (not yet present in our model) is the ability to  
410 add intrinsic lesions that could recapitulate tract distortions with lesional enlargement.

411

## 412 **CONCLUSION**

413 With detailed neuroanatomic evaluation, advancement in stereotactic neuronavigation and  
414 operative microscopic technology, safe neurosurgical procedures in the brainstem have become  
415 possible through SEZs. Using advanced computer modeling, we were able to illustrate these  
416 SEZs within a virtual 3D environment. This experience offers a superb learning environment for  
417 clinical, research, and educational purposes.

418

## 419 **ACKNOWLEDGMENTS**

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421

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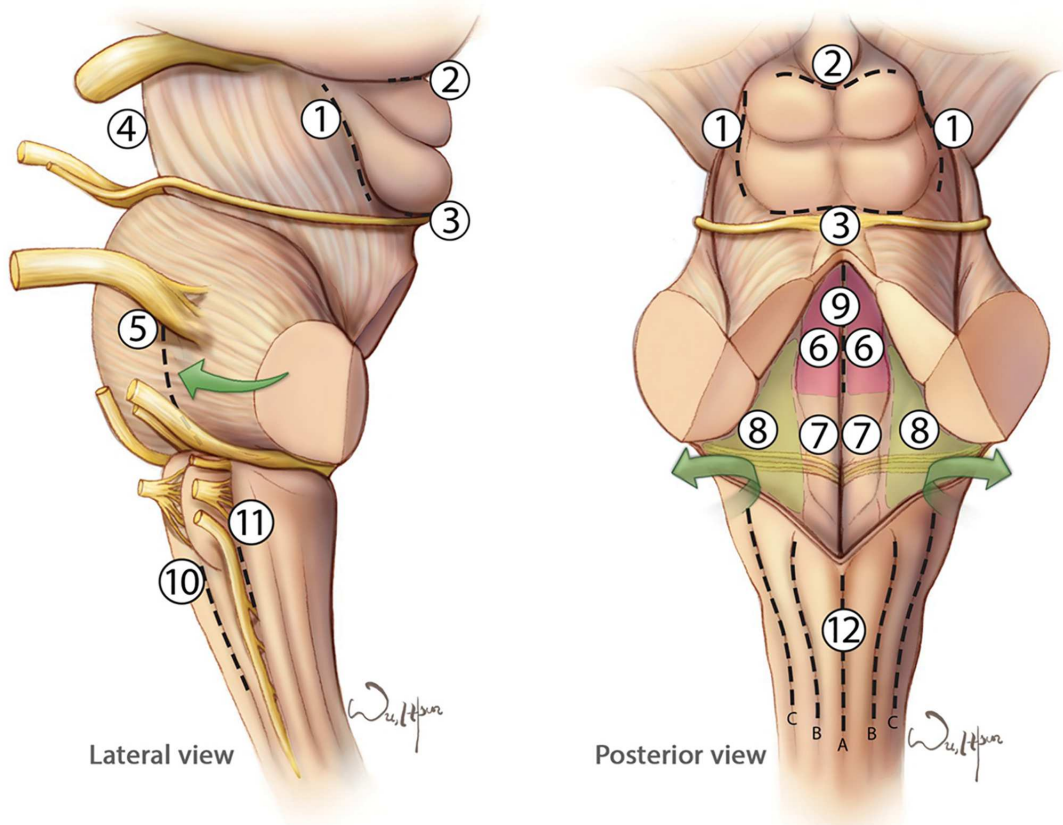
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584 **Figure 1.** Artist's illustration of the most commonly used safe entry zones to intrinsic brainstem  
 585 lesions. With permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.  
 586

### The Safe Entry Zones for Brainstem Lesions



#### The Midbrain:

- ① Lateral mesencephalic sulcus
- ② Supracollicular approach
- ③ Infracollicular approach
- ④ Periculomotor zone

#### The Pons:

*Ventral:*

- ⑤ Peritrigeminal zone
- Dorsal:*
- ⑥ Suprafacial approach
  - ⑦ Infracfacial approach
  - ⑧ Acoustic area
  - ⑨ Median sulcus above the facial colliculus

#### The Medulla:

- ⑩ Anterolateral sulcus
- ⑪ Postolivary sulcus
- ⑫ Dorsal medullary sulci:
  - A Posterior median sulcus
  - B Posterior intermediate sulcus
  - C Posterior lateral sulcus

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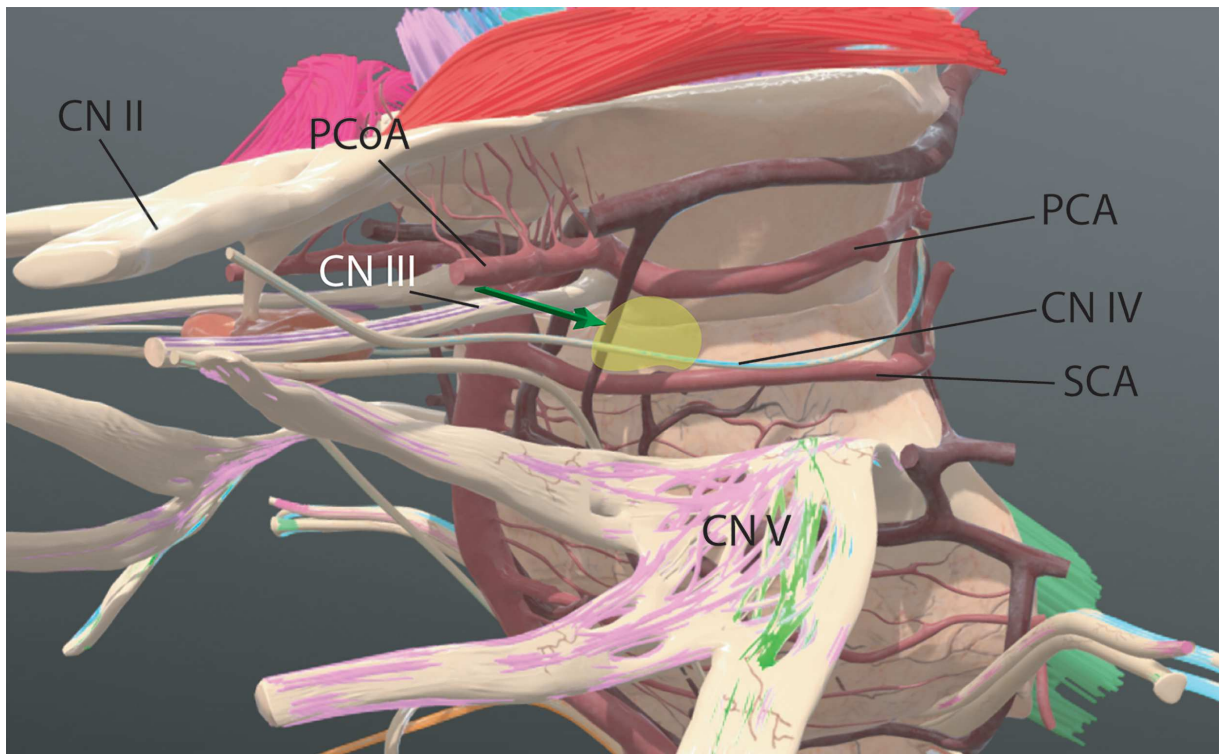
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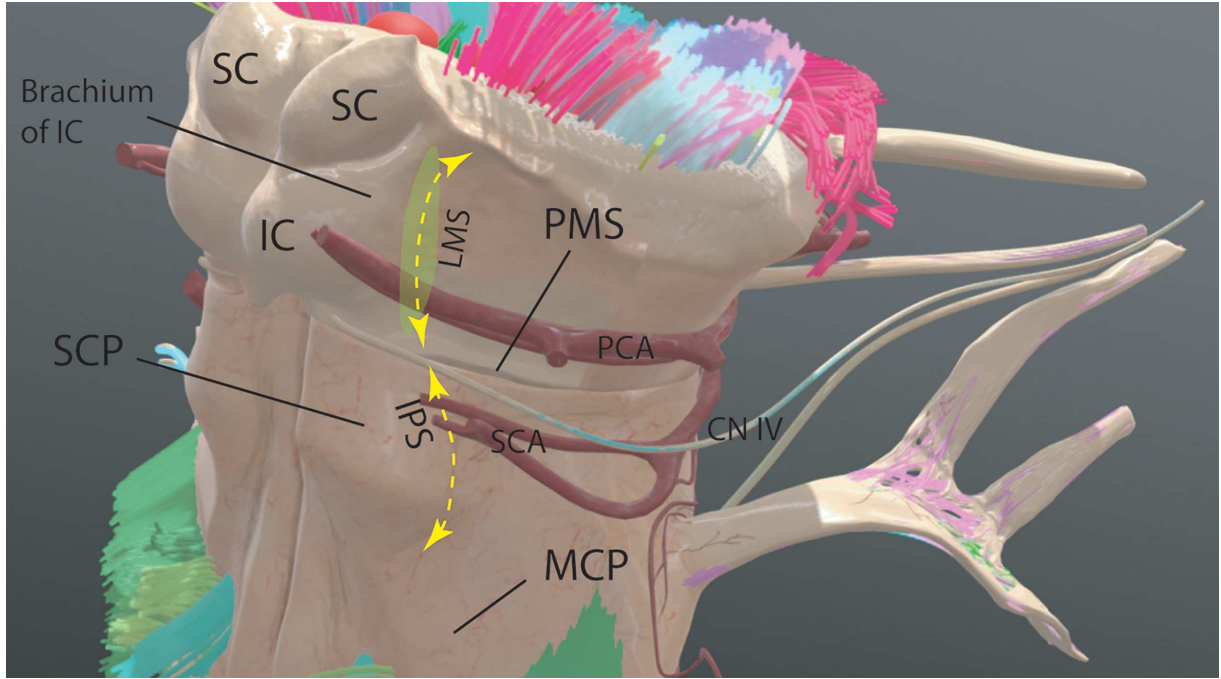


590 **Figure 2.** Three-dimensional model snapshots of safe entry zones (SEZs) to the midbrain; the  
591 SEZs are shown as green-shaded areas. **A,** Approach trajectory to the anterior mesencephalic  
592 zone (between the PCA and SCA) is indicated by the green arrow. **B,** Lateral medullary sulcus  
593 (LMS). Note that the LMS is continuous inferiorly with the interpeduncular sulcus (IPS) between  
594 the middle cerebellar peduncle (MCP) and the superior cerebellar peduncle (SCP). **C,** Dashed  
595 lines show the SEZ in the pericolicular area in the tectal region. 1, supracolicular zone; 2,  
596 infracolicular zone; 3, intercollicular zone; CN, cranial nerve; IC, inferior colliculus; PCA,  
597 posterior cerebral artery; PCoA, posterior communicating artery; PMS, pontomesencephalic  
598 sulcus; SC, superior colliculus; SCA, superior cerebellar artery. With permission from *The*  
599 *Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.

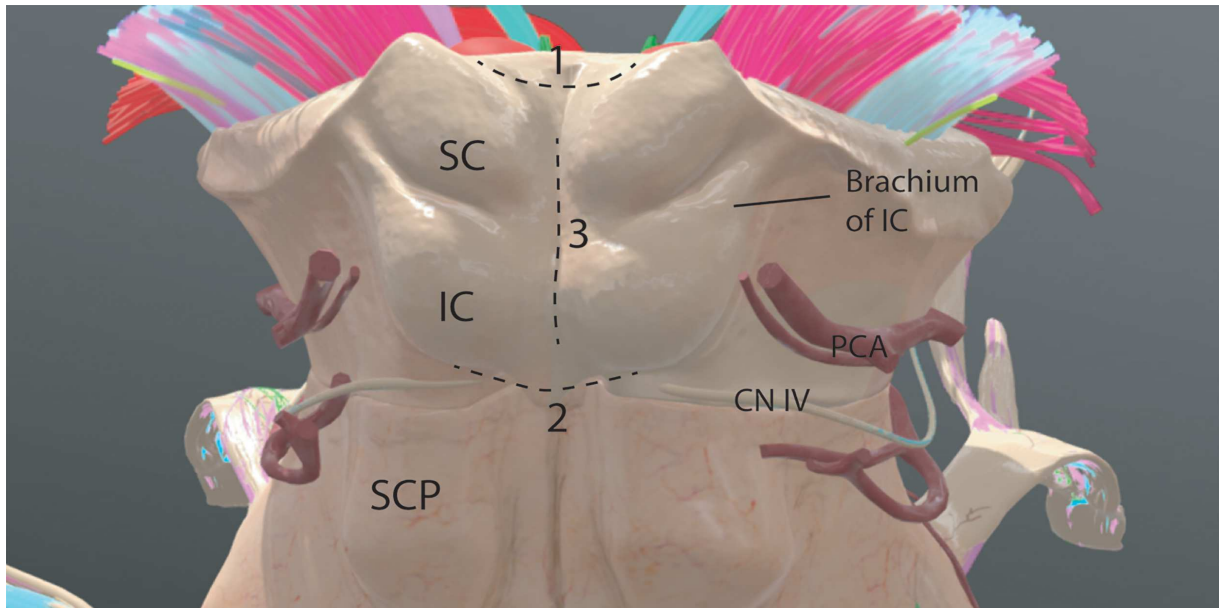
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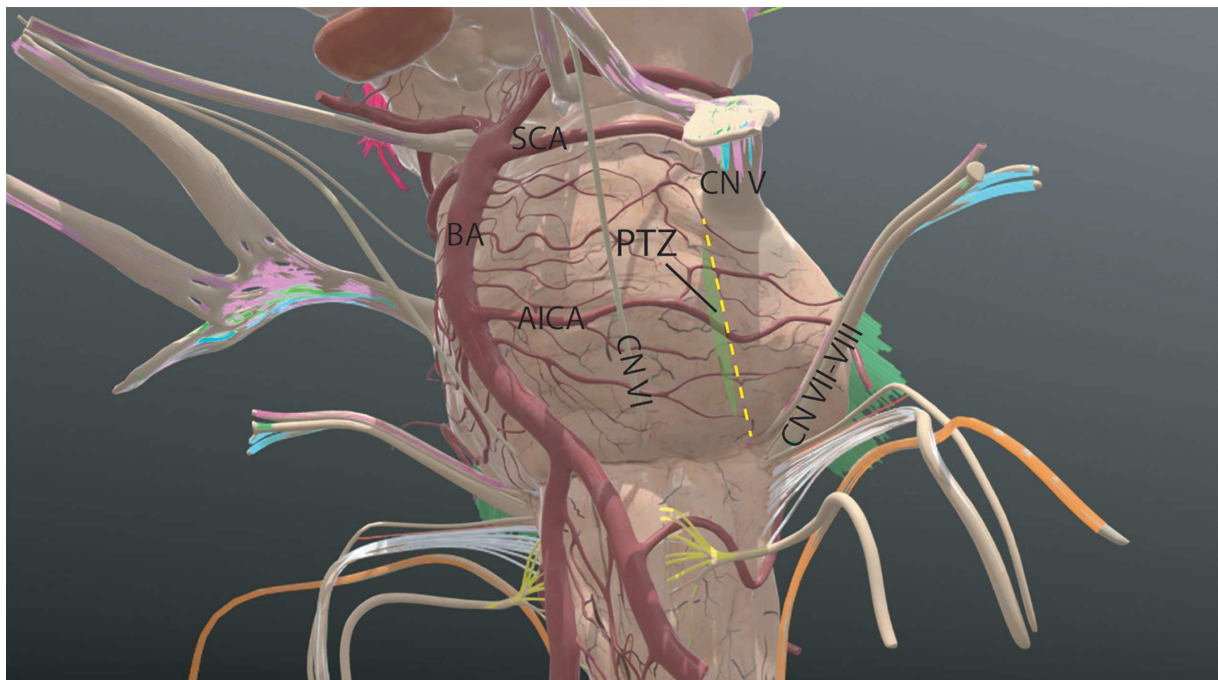
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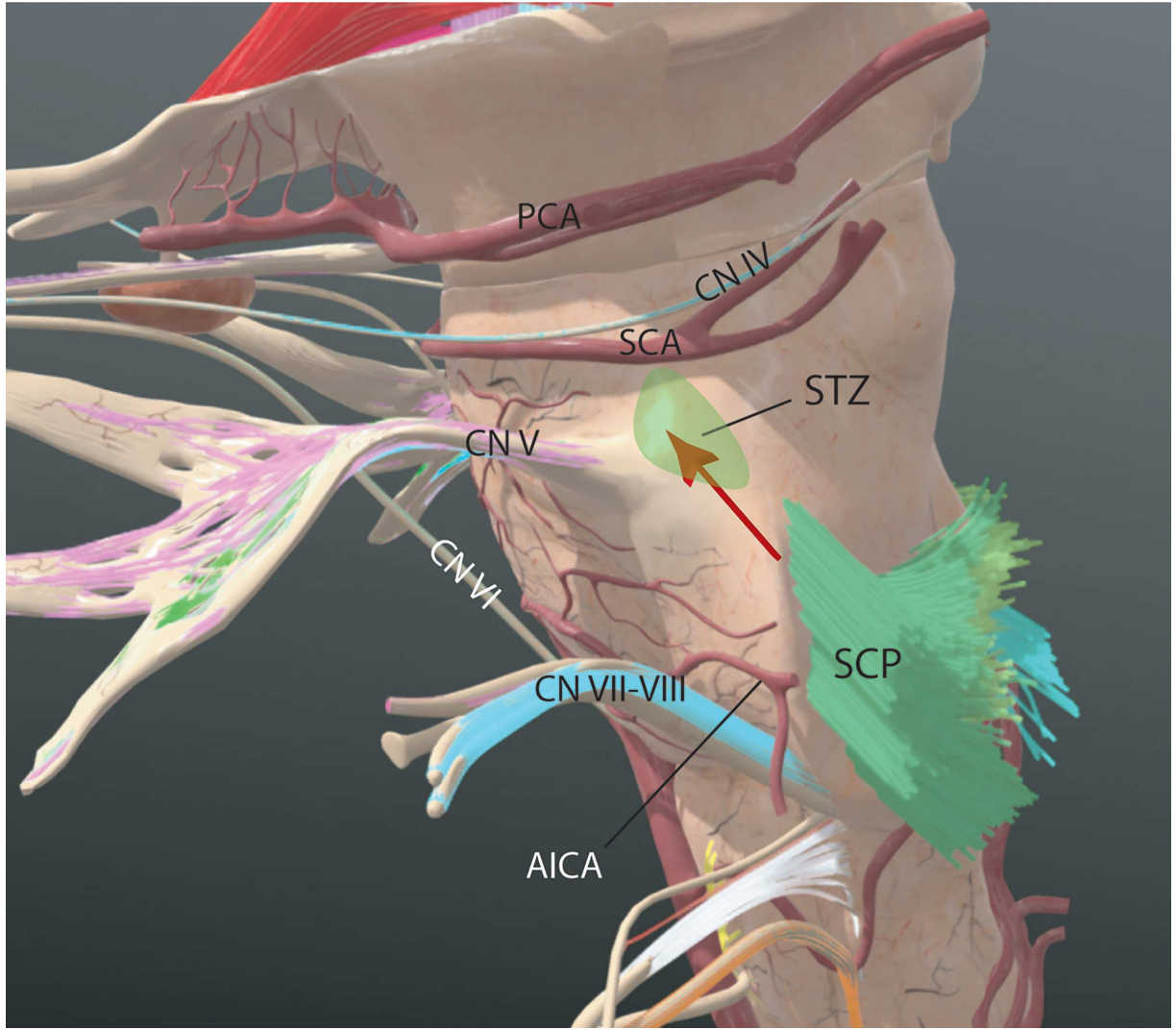
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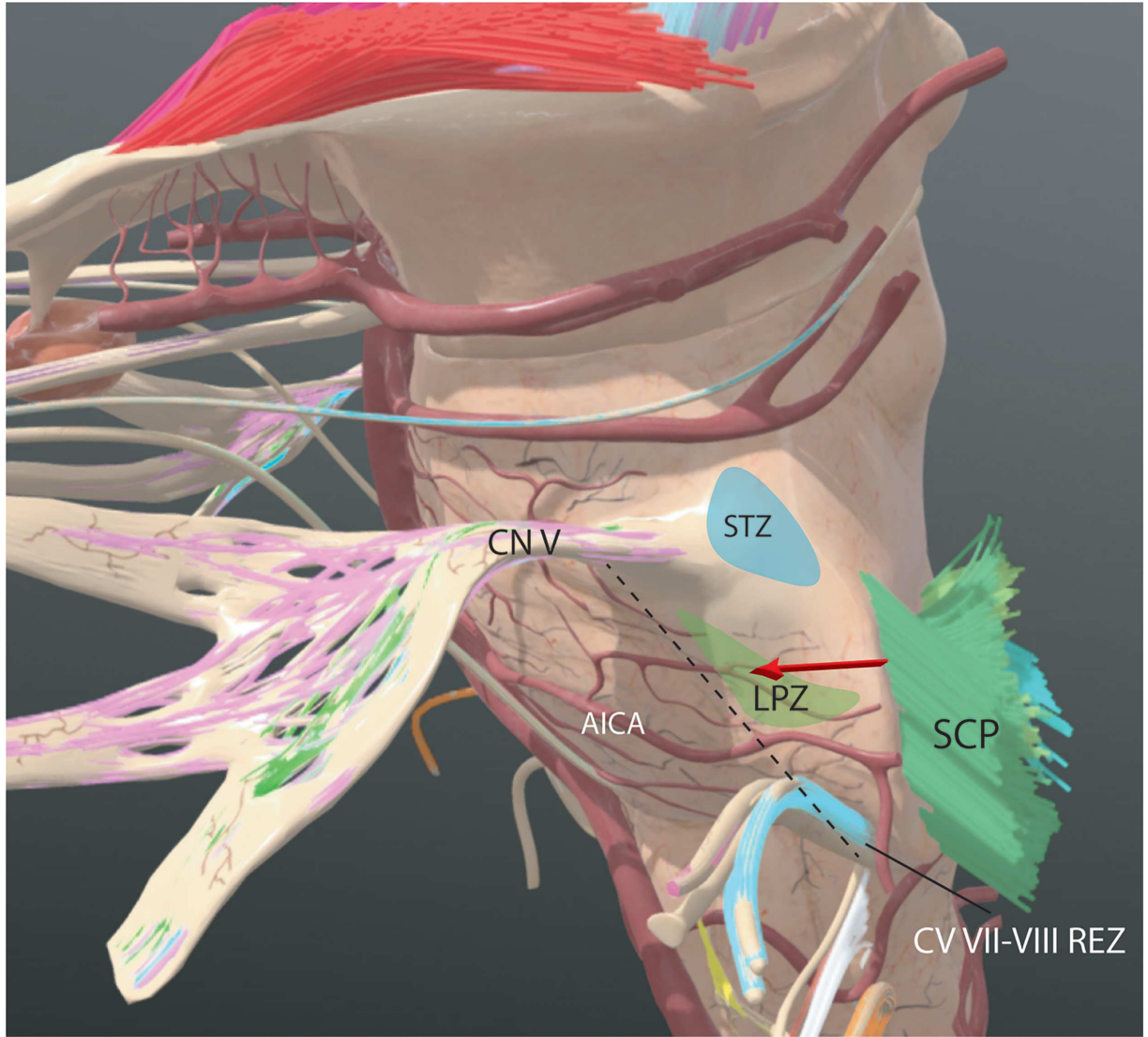
606 **Figure 3.** Three-dimensional model snapshots of safe entry zones (SEZs) to the pons. **A,**  
607 Peritrigeminal zone (PTZ), located just anteromedial to a line connecting the root entry/exit zone  
608 (REZs) of cranial nerves (CNs) V and VII through VIII. **B,** Supratrigeminal zone (STZ), located  
609 just superolateral to the REZ of CN V, with the approach trajectory almost tangential to the  
610 surface parallel to superior cerebellar peduncle (SCP) fibers (red arrow). **C,** Lateral trigeminal  
611 zone (LPZ), located just lateral to the line connecting the REZs of CNs V and VII through VIII.  
612 The approach trajectory is shown with a red arrow. **D,** Dorsal pontine SEZ with the fourth  
613 ventricle unroofed to facilitate visualization of the floor. The blue arrow shows the directionality  
614 of the lateral recess of the fourth ventricle. AA, area acoustica; AICA, anterior inferior cerebellar  
615 artery; BA, basilar artery; FC, facial colliculus; FP, floccular peduncle; HT, hypoglossal triangle;  
616 ICP, inferior cerebellar peduncle; IFZ, infrafacial zone; MCP, middle cerebellar peduncle; PCA,  
617 posterior cerebral artery; SCA, superior cerebellar artery; SFT, superior fovea triangle; SFZ,  
618 suprafacial zone; VT, vagal triangle. With permission from *The Neurosurgical Atlas* by Aaron  
619 Cohen-Gadol, MD.

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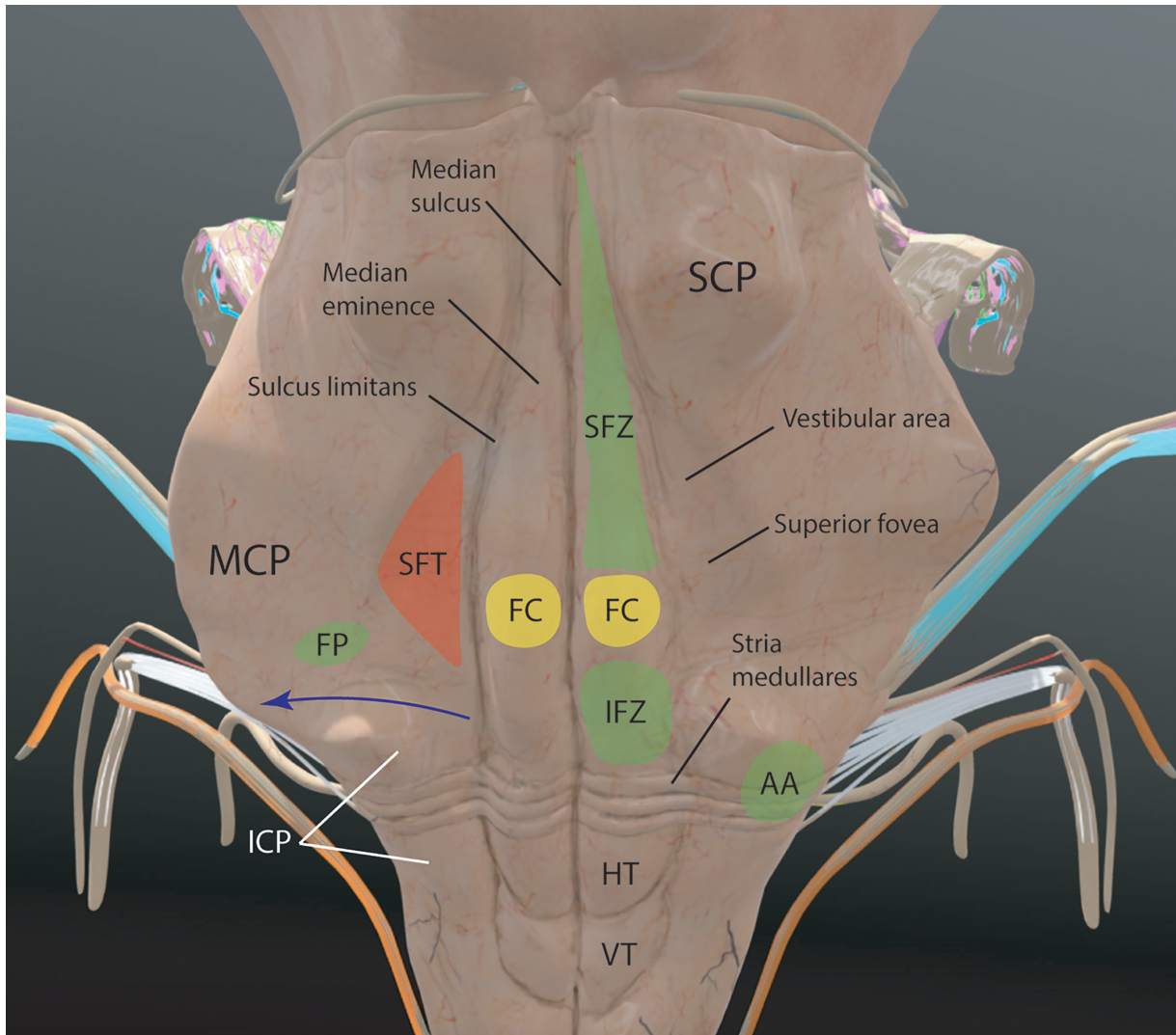


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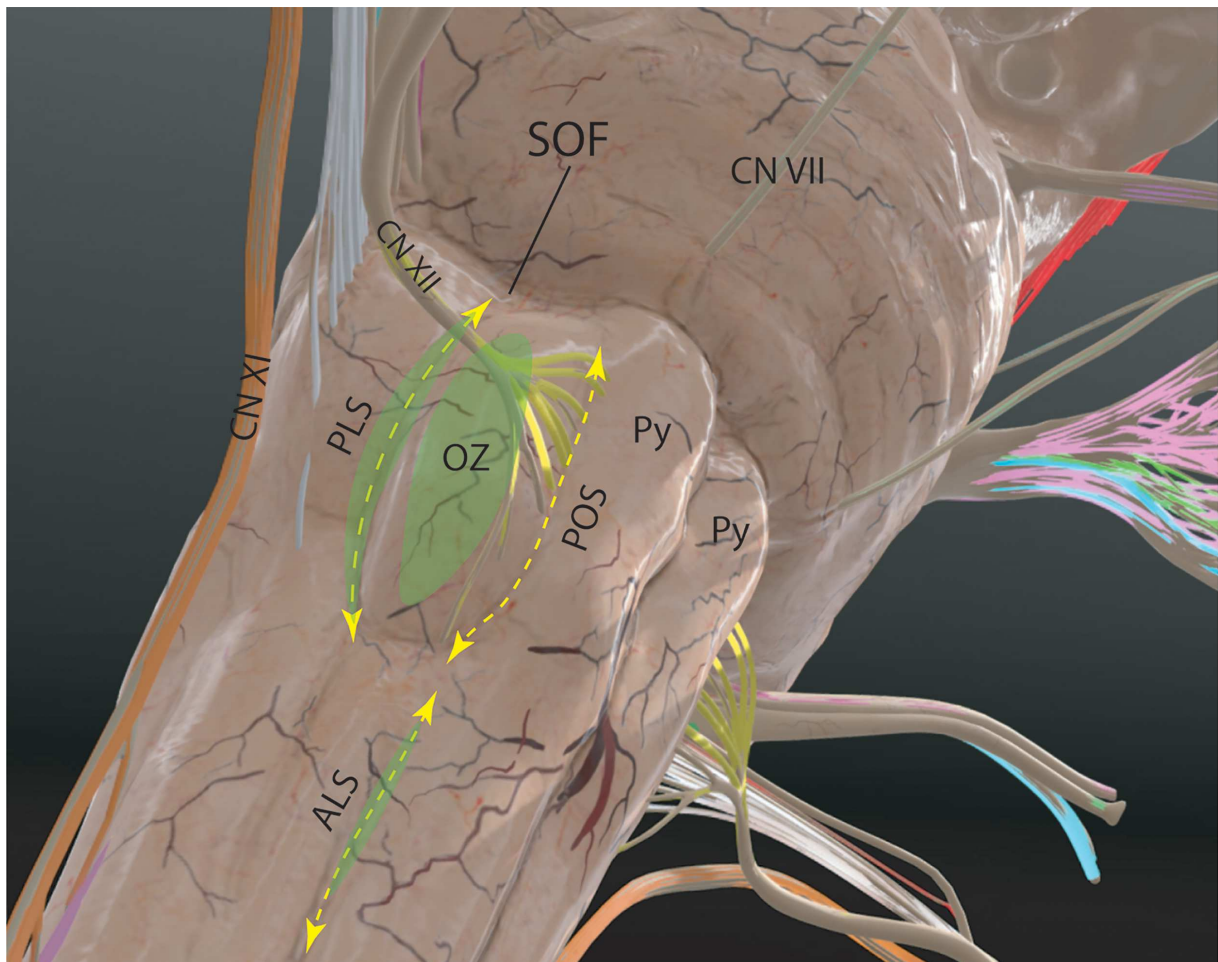
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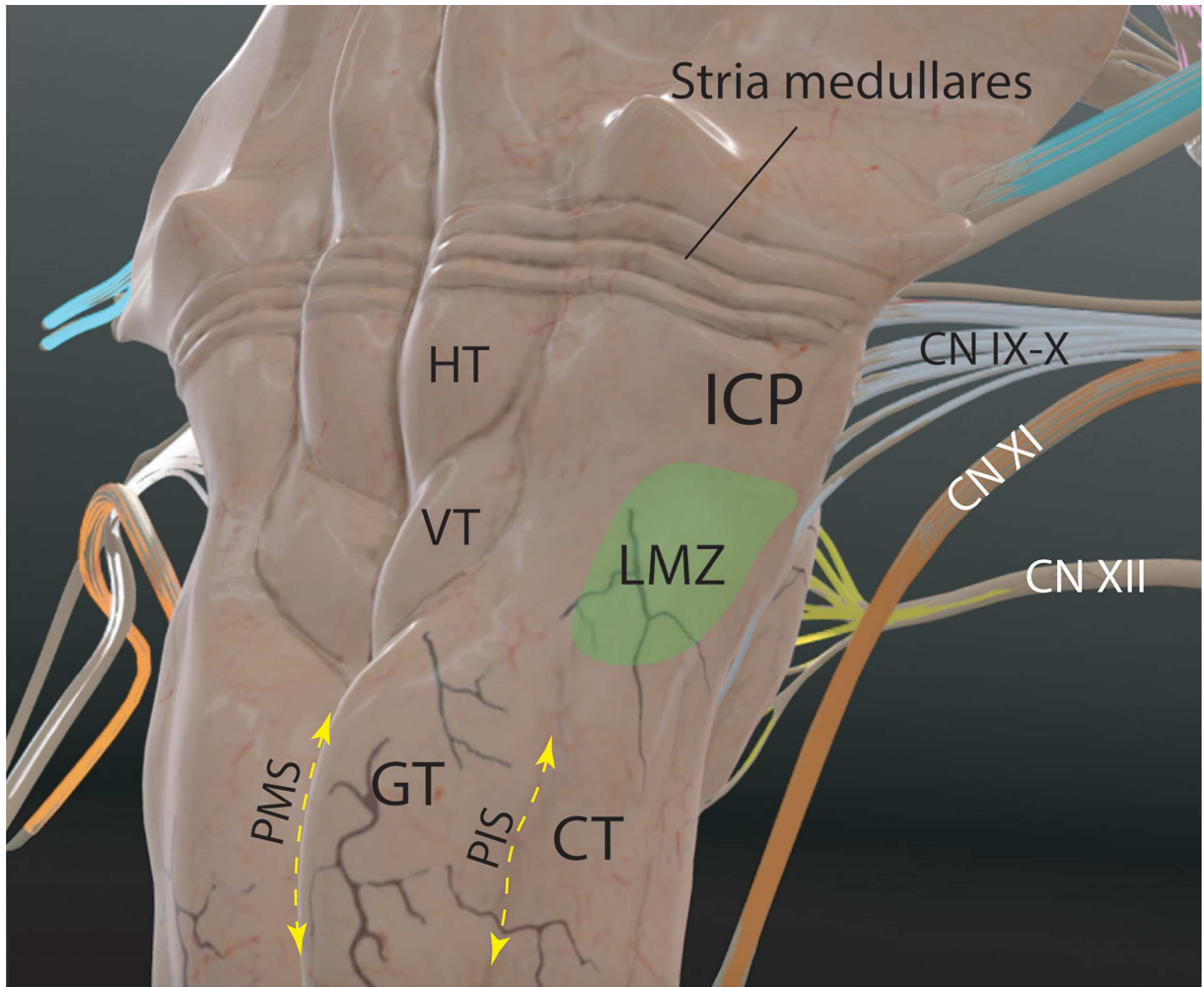
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626 **Figure 4.** Three-dimensional model snapshots of safe entry zones (SEZs) to the medulla. **A,**  
627 Right ventrolateral perspective of the lower brainstem showing the following ventral and lateral  
628 SEZs of the medulla: olivary zone (OZ), anterolateral sulcus (ALS), and posterolateral sulcus  
629 (PLS). Note that the preolivary sulcus (POS) is continuous with the ALS inferiorly. The PLS is a  
630 few millimeters anterior to the root entry/exit zone of cranial nerves (CNs) IX and X. **B,** Right  
631 dorsolateral perspective of the medulla showing the lateral medullary zone (LMZ), posterior  
632 median sulcus (PMS), and posterior intermediate zone (PIS). CT, cuneate tubercle; GT, gracile  
633 tubercle; HT, hypoglossal triangle; ICP, inferior cerebellar peduncle; OZ, olivary zone; Py,  
634 pyramid; SOF, supraolivary fossette; VT, vagal triangle. With permission from *The*  
635 *Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.

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641 **Model 1:** Three-dimensional (3D) model showing the reconstructed anatomy of the external and  
642 internal structure of the midbrain with relevant safe entry zones. (The instructions for use of this  
643 model are as follows: Please use the full-screen function for optimal visualization [by clicking on  
644 the arrows on the right lower corner of the model]. To move the model in 3D space, use your  
645 mouse's left click and drag; to enlarge or decrease the size of the object, use the mouse's wheel.  
646 The right click and drag function moves the model across the plane.) Please click on "Select an  
647 annotation" link at the bottom of the window and "Show annotations" so that the anatomical  
648 labels become visible. With permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol,  
649 MD. (<https://sketchfab.com/3d-models/midbrain-labeled-cda12a620a7c4b65b7067d55d4e79294>)  
650  
651

652 **Model 2:** Three-dimensional model showing the reconstructed anatomy of the external and  
653 internal structure of the pons with relevant safe entry zones. Please click on “Select an  
654 annotation” link at the bottom of the window and “Show annotations” so that the anatomical  
655 labels become visible. With permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol,  
656 MD. (<https://sketchfab.com/3d-models/pons-labeled-d876bd93e3134c18a1edb981e270e2e2>)  
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659 **Model 3:** Three-dimensional model showing the reconstructed anatomy of the external and  
660 internal structures of the medulla oblongata with relevant safe entry zones. Please click on  
661 “Select an annotation” link at the bottom of the window and “Show annotations” so that the  
662 anatomical labels become visible. With permission from *The Neurosurgical Atlas* by Aaron  
663 Cohen-Gadol, MD. ([https://sketchfab.com/3d-models/medulla-labeled-  
664 4f405fd9dc2b4074aeec2c04ae50a814](https://sketchfab.com/3d-models/medulla-labeled-4f405fd9dc2b4074aeec2c04ae50a814))  
665  
666

667 Table 1. Summary of safe entry zones to the brainstem and surgical approaches used to access  
 668 them  
 669

SEZ	Definition/Boundaries	Cisternal Relationship	Surgical Approach(es)
<b>Midbrain</b>			
AMZ	Medial one-fifth of the ventral aspect of the crus cerebri lateral to the root exit zone of the oculomotor nerve, between the superior cerebellar and posterior cerebral arteries	Crural	PTTS, ST, ETC and PT
LMS	Between the cerebral peduncle anteriorly and the midbrain tegmentum posteriorly	Ambient (posterior)	ST, SCIT (paramedian, extreme-lateral), RS, PS
Supra-CZ	Above the superior colliculi at the subpineal triangle (of Obersteiner)	Quadrigeminal	SCIT
Infra-CZ	Below the inferior colliculi	Quadrigeminal	SCIT
Inter-CZ	Vertical cleft between the left and right colliculi	Quadrigeminal	SCIT
<b>Pons</b>			
PTZ	Ventral aspect of pons, medial to the trigeminal-facial line and lateral to the pyramidal fibers	Prepontine	RS, PS, ST and AP, ETC and EDAP
STZ	Superior to the CN V REZ lateral to the pyramidal tract	Cerebellopontine, prepontine	RS, PS, ST and AP, ETC and EDAP, ST, PTTS
LPZ	Ventrolateral aspect of pons, lateral to the trigeminal-facial line	Cerebellopontine	RS, PS
SFZ	Suprafacial triangle delimited by the superior cerebellar peduncle laterally, the MLF medially, and the facial colliculus inferiorly	Fourth ventricle	TV, TeV
IFZ	Between the facial colliculus superiorly and the hypoglossal and vagal triangles inferiorly	Fourth ventricle	TV, TeV
MS-IV	Between the bilateral median eminences above the level of facial colliculi	Fourth ventricle	TV, TeV
AA	Inferior cerebellar peduncle fibers located underneath the lateral end of the striae medullares at the region of the lateral recess of the fourth ventricle	Lateral recess of the fourth ventricle	TBF, TeV, TUT
FP	Rostral wall of the lateral recess of the fourth ventricle just rostral to the	Lateral recess of the fourth ventricle	TBF, TeV, TUT

	attachment of the inferior medullary velum to the flocculus		
<b>Medulla</b>			
ALS	Preolivary sulcus between the caudal-most roots of the hypoglossal nerve and the rostral-most rootlets of the C1 nerve	Cerebellomedullary	FL, ETC and pC
PLS	Postolivary sulcus, anterior to the rootlets of CN IX–X	Cerebellomedullary	FL
LMZ	Rostrolateral part of the inferior cerebellar peduncle dorsal to the foramen of Luschka and REZs of CN IX–X	Cerebellomedullary (rostral part), cerebellopontine	RS, PS, FL
PMS	Between the gracile fascicles	Magna	MSO and C1 laminectomy
PLS	Between the gracile and cuneate tubercles/fascicles	Magna	MSO and C1 laminectomy

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671 AA, area acustica; ALS, anterolateral sulcus; AMZ, anterior mesencephalic zone; AP, anterior  
672 petrosectomy; CN, cranial nerve; CZ, collicular zone; EDAP, extradural anterior petrosectomy;  
673 ETC, endoscopic transclival; FL, far lateral; FP, floccular peduncle; IFZ, Infracial zone; LMS,  
674 lateral mesencephalic zone; LMZ, lateral medullary zone; LPZ, lateral pontine zone; MLF,  
675 medial longitudinal fasciculus; MS-IV, median sulcus of fourth ventricle; MSO, midline  
676 suboccipital approach; pC, partial condylectomy; PLS, posterolateral sulcus; PMS, posterior  
677 median sulcus; PS, presigmoid; PT, pituitary transposition; PTTS, pretemporal trans-Sylvian;  
678 PTZ, peritrigeminal zone; REZ, root entry/exit zone; RS, retrosigmoid; SCIT, supracerebellar  
679 infratentorial; SFZ, suprafacial zone; ST, subtemporal; STZ, supratrigeminal zone; TBF,  
680 tonsillobiventral fissure; TeV, telovelar; TUT, trans-uvulotonsillar; TV, transversian.