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*Research on cerebrovascular variational anatomy*

## ABSTRACT OF DOCTORAL THESIS

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|     |  |    |
|-----|--|----|
| 1   | Contents of the PhD thesis.....  | 2  |
| 2   | Personal research.....   | 5  |
| 2.1 | Anatomo-imaging investigations of the anterior cerebral artery.....          | 5  |
| 3   | Artera cerebrală posterioară de tip fetal.....                               | 11 |
| 4   | Modelele topografice ale venei lui Labbé (vena anastomotică inferioară)..... | 12 |
| 5   | PhD thesis conclusions and original contributions.....                       | 14 |
|     | Thesis Conclusions.....  | 14 |
|     | Original Contributions.....  | 15 |
|     | Selective Bibliography.....  | 16 |

## 1 Contents of the PhD thesis

|  |    |
|--|----|
| List of published scientific papers  | 4  |
| List of abbreviations  | 5  |
| Introduction   | 6  |
| General Part of the Doctoral Thesis  | 8  |
| 1 Elements of cerebral arterial anatomy  | 9  |
| 1.1 Anatomy of the internal carotid artery   | 9  |
| 1.1.1 Segments of the internal carotid artery  | 9  |
| 1.1.2 Branches of the internal carotid artery  | 12 |
| 1.1.2.1 Intrapyrarnidal branches of the internal carotid artery                                | 13 |
| 1.1.2.2 Intracranial collateral branches of the internal carotid artery                        | 14 |
| 1.1.2.2.1 Ophthalmic artery  | 14 |
| 1.1.2.2.2 Anterior choroidal artery  | 15 |
| 1.1.2.3 Terminal branches of the internal carotid artery                                       | 15 |
| 1.1.2.4 Middle cerebral artery   | 16 |
| 1.1.2.5 Anterior cerebral artery   | 18 |
| 1.1.2.6 Polygon of Willis  | 21 |
| 2 Elements of intracranial venous anatomy  | 23 |
| 2.1 Supratentorial cerebral veins  | 23 |
| 2.1.1 Superficial cerebral veins   | 23 |
| 2.1.2 Deep cerebral veins  | 23 |
| 2.1.2.1 Internal cerebral veins  | 23 |
| 2.1.2.2 Basal vein of Rosenthal  | 24 |
| 2.1.2.3 Large cerebral vein of Galen   | 24 |
| 2.2 Dural venous sinuses   | 24 |
| 2.2.1 Superior sagittal sinus  | 25 |
| 2.2.2 Inferior sagittal sinus  | 26 |
| 2.2.3 Right sinus  | 27 |
| 2.2.4 Occipital sinus  | 27 |
| 2.2.5 Marginal sinus   | 28 |
| 2.2.6 Transverse and sigmoid sinuses   | 29 |
| 2.2.7 Confluent venous sinuses   | 32 |
| 2.2.8 Superior stony sinus   | 33 |
| 2.2.9 Superior petrous veins   | 34 |
| 2.2.10 Inferior stony sinus  | 35 |
| 2.2.11 The stony sinus   | 35 |
| 2.2.12 Hyrtl's ophthalmopyretic sinus  | 36 |
| 2.2.13 Spheno-parietal sinus of Breschet (superior sphenoidal sinus, small wing sinus)         | 37 |
| 2.2.14 Suboccipital venous structures  | 37 |
| Personal Part of the PhD Thesis  | 39 |
| 3 Anatomico-imaging investigations of the anterior cerebral artery                             | 40 |
| 3.1 Infraoptic or infrachiasmatic A1 segment and dolichoectasia of the internal carotid artery | 40 |
| 3.1.1 Introduction   | 40 |
| 3.1.2 Material and method  | 41 |
| 3.1.3 Results  | 41 |
| 3.1.4 Discussion   | 46 |
| 3.1.4.1 Wong types of the infraoptic pathway of the A1 segment of the anterior cerebral artery | 47 |
| 3.1.4.2 Anterior carotid-cerebral anastomoses and infraoptic A1 segments                       | 48 |
| 3.1.4.3 Infraoptic or infrachiasmatic anterior cerebral artery                                 | 50 |

|           |   |    |
|-----------|---|----|
| 3.1.4.4   | Infraoptic A1 segment aneurysms   | 50 |
| 3.1.4.5   | Internal carotid artery dolichoectasia  | 51 |
| 3.1.4.6   | Optic nerve vascular decompressions   | 51 |
| 3.1.4.7   | Supracarotid and/or supraclinoid course of the A1 segment of the anterior cerebral artery modifies neurosurgical triangles of the skull base    | 52 |
| 3.1.4.7.1 | Optic-carotid triangle  | 52 |
| 3.1.4.7.2 | Clinoid triangle  | 52 |
| 3.1.4.7.3 | Supracarotid triangle   | 52 |
| 3.1.4.8   | Elements of surgical anatomy  | 53 |
| 3.2       | Pericalosal and transcalosal arteries arising from the anterior cerebral artery   | 53 |
| 3.2.1     | Introduction  | 53 |
| 3.2.2     | Material and method   | 54 |
| 3.2.2.1   | Pericalosal artery types  | 55 |
| 3.2.2.2   | Types of calosomarginal artery  | 55 |
| 3.2.3     | Results   | 55 |
| 3.2.3.1   | Anatomical types of pericalosal artery  | 55 |
| 3.2.3.2   | Anatomical types of the calosomarginal artery   | 61 |
| 3.2.3.3   | Unilateral combinations of pericalosal artery and calosomarginal artery types (A-P types)   | 62 |
| 3.2.3.4   | Bilateral combinations of A-P types   | 62 |
| 3.2.3.5   | Biemispheric anterior cerebral artery   | 63 |
| 3.2.3.6   | Wide fenestration of A2 segment   | 63 |
| 3.2.4     | Discussion  | 64 |
| 3.2.4.1   | Calosomarginal artery   | 65 |
| 3.2.4.2   | Pericalosal artery  | 65 |
| 3.2.4.3   | Absent pericalosal artery   | 65 |
| 3.2.4.4   | Azygos pericalosal artery   | 65 |
| 3.2.4.5   | Medial artery of corpus callosum  | 66 |
| 3.2.4.6   | Triple pericalosal artery   | 66 |
| 3.2.4.7   | Transcalosal arteries   | 66 |
| 3.2.4.8   | Twisted anterior cerebral arteries  | 67 |
| 3.2.4.9   | Fenestration of segment A2 ACA  | 67 |
| 3.2.4.10  | Elements of clinical anatomy of the distal portion of the anterior cerebral artery  | 67 |
| 3.2.4.11  | Endovascular approaches to the anterior cerebral artery   | 68 |
| 4         | Anatomical variants in the posterior portion of the polygon of Willis   | 69 |
| 4.1       | Fetal posterior cerebral artery - an anatomical-imaging study   | 69 |
| 4.1.1     | Introduction  | 69 |
| 4.1.2     | Material and method   | 70 |
| 4.1.3     | Results   | 71 |
| 4.1.4     | Discussion  | 74 |
| 4.2       | Bilateral asymmetric posterior communicating artery, fenestrated posterior cerebral artery, partially duplicated posterior communicating artery | 80 |
| 4.2.1     | Introduction  | 80 |
| 4.2.2     | Results   | 80 |
| 4.2.3     | Discussion  | 81 |
| 5         | Investigations of variational anatomy in the intracranial venous system   | 83 |
| 5.1       | Topographical patterns of Labbé's vein (inferior anastomotic vein)  | 83 |
| 5.1.1     | Introduction  | 83 |
| 5.1.2     | Material and method   | 84 |
| 5.1.2.1   | Lot studied   | 84 |
| 5.1.2.2   | Study method  | 84 |
| 5.1.2.3   | Anatomical variables determined   | 85 |

|   |     |
|---|-----|
| 5.1.3 Results   | 85  |
| 5.1.4 Discussion  | 96  |
| 5.1.4.1 Classification of the middle superficial cerebral vein (SV) according to the persistence of the embryonic tentorial sinus                         | 96  |
| 5.1.4.2 Classification of superficial middle cerebral vein (SV) according to cortical tributaries   | 97  |
| 5.1.4.3 Adult tentorial sinuses   | 98  |
| 5.1.4.4 Inter- and intra-personal anatomical variations of Labbé's vein   | 99  |
| 5.1.4.5 Elements of neurosurgical anatomy   | 99  |
| 5.2 Absence and hypoplasia of the transverse sinuses compensated by drainage through the occipital sinus and marginal sinuses (occipitomarginal drainage) | 100 |
| 5.2.1 Introduction  | 100 |
| 5.2.2 Material and method   | 100 |
| 5.2.3 Anatomical variation  | 101 |
| 5.2.4 Discussion of bilateral absence of transverse sinuses and venous confluent drainage through the occipital sinus                                     | 103 |
| 5.3 Hyrtl's ophthalmopseal sinus  | 104 |
| 5.3.1 Introduction  | 104 |
| 5.3.2 Dissection of the ophthalmopleural sinus  | 104 |
| 5.3.3 Discussion  | 105 |
| Conclusions of the thesis and original contributions  | 108 |
| Conclusions of the PhD thesis   | 108 |
| Original contributions  | 110 |
| Bibliography  | 112 |
| Index of figures in the text  | 123 |
| Index of tables in the text   | 128 |
| Index of graphs in text   | 129 |

## 2 Personal research

I have performed anatomical-imaging investigations of the anterior cerebral arterial system - (a) anatomical variation of the A1 segment of the anterior cerebral artery and (b) studies of the trans- and pericalosal arteries.

I also studied the posterior portion of the Willis polygon: fetal posterior cerebral artery and posterior cerebral artery fenestration combined with posterior communicating deduplication.

Research on the intracranial venous system has been directed towards documenting anatomical patterns of Labbé's vein and anatomical areal variations of the dural sinuses.

### 2.1 Anatomico-imaging investigations of the anterior cerebral artery

#### Infraoptic or infrachiasmatic A1 segment and dolichoectasis of the internal carotid artery

Depending on its course, the ICA is described as consisting of 7 segments: C1 (cervical), C2 (stony), C3 (lacerum), C4 (cavernous), C5 (clinoid), C6 (ophthalmic) and C7 (terminal, communicating segment) [45]. Normally, the ICA terminates inferior to the anterior perforated substance, bifurcating into the ACA and ACM 3,12. Of the two terminal branches of the ACI, the ACA is the smaller [18]. The left ACA and the right ACA are joined by the AComA. At the base of the brain, the ACI system builds the circle of Willis (cW) with the ACP branching from the AB. AComP joins the ACI and the ACP. The nonagon of Willis is one of the best known eponyms in human anatomy [12]. Anatomical variations of the circle of Willis are the rule, not the exception [45].

As a rule, the precommunicating A1 segment of the ACA passes superior to the optic nerve on that side to reach anterior to the optic chiasm [40]. The anterior cerebral arteries continue distal to the AComA with the A2, postcommunicating segment [40].

Infraoptic A1 segments of the ACA have been identified originating from a low bifurcation of the ICA - the bifurcation of the proximal intradural segment of the ICA; such infraoptic A1 segments have a horizontal, medially directed path, passing beneath the optic nerve on that side, changing direction on the anterior aspect of the optic chiasm [7,8,17,25]. Such A1 segments of the ACA may even perforate the ipsilateral optic tract [37]. The infraoptic variant of the ACA A1 segment trajectory is rare [40]. Am avut ca scop al acestui studiu documentarea pe angiograme CT a incidenței segmentelor A1 infraoptice ale arterelor cerebrale anterioare [40].

A retrospective study was performed on 145 CT angiograms to assess the presence of infraoptic trajectory of ACA.

Cases were documented bilaterally for different topographic patterns of the A1 segment trajectory of the ACA in relation to the optic nerve (II): type 1 - supraoptic A1 segment trajectory or absent A1 segment; type 2 - infraoptic A1 segment trajectory; type 3 - infrachiasmatic A1 segment trajectory.

In 21/145 cases (14.48%) type 2 and 3 infraoptic tracts of the A1 segment of the ACA were found. These artery variants had horizontal medial inferior courses of the respective optic nerve. Infraoptic A1 segments were found in 12 male and 9 female cases. Type 2 was found bilaterally in 16/145 cases (11.03%), 9 males and 7 females. Unilateral evidence of type 2 was obtained in 3/145 cases (2.06%), 1 male and 2 female cases. Type 3 was found bilaterally in 2/145 cases (1.38%), both male.

All infraoptic or infrachiasmatic A1 segments were found to originate from long intradural ICAs, with horizontal tracts at or just above the level of the posterior clinoid processes, with low bifurcations of these ICAs. Except for one unilateral female case of type 2, all other ICAs giving rise to infraoptic A1 segments had a posterior instead of postero-superior tracts, to bifurcate at or just posterior to the posterior clinoid processes (low bifurcations). In the female unilateral type 2 case, the ICAs had high bifurcations. On the left side the ACI bifurcation was directed superiorly and the A1 segment of the ACA looped over the optic nerve. From the right ACI a fetal-type ACP started and then the ACI curved anteriorly above the anterior clinoid process; its bifurcation was straightened anteriorly and the A1 segment of the ACA crossed above the anterior clinoid process to continue between the optic nerve and the C6 segment of the ACI (supraclinoid, infraoptic and supracarotid path of the A1 segment). In one bilateral type 3 case, as well as in one bilateral type 2 female case, bilateral supracarotid tracts of these A1 segments were found. In one unilateral type 2 male case, as well as in one bilateral type 2 male case, the respective left A1 segments had supracarotid and infraoptic tracts. In the unilateral female type 2 case described above, the supraclinoid, infraoptic and supracarotid A1 segment was on the right side.

In a unilateral case of type 2 in a male subject, the left infraoptic A1 segment was hypoplastic. In two bilateral female type 2 cases, the respective right A1 segment was also hypoplastic.

In two bilateral female type 2 cases, the AB bifurcation was rotated so that the ACP almost came into contact with the A1 segment of the respective ACA.

The infraoptic course of the A1 segment of the ICA is an extremely rare but known anatomical variant, which was first found by Robinson in 1959 at dissection [41,51,53]. In that case, the left ICA bifurcated into the ICA and MCA immediately after perforating the dura mater, while the ophthalmic artery was replaced by an anastomosis of the lacrimal and middle meningeal arteries [51]. Thus, Robinson's identification was an early, low bifurcation of the proximal C6 segment of the ICA, and not the bifurcation of a C7 segment of the ICA with a low trajectory, like the cases presented in this paper. The infraoptic A1 segment of the ICA was found anteriorly originating from a low bifurcation of the C6 segment of the ICA, tracing inferiorly from the ipsilateral optic nerve, horizontally medially, then continuing superiorly from the anterior border of the optic chiasm [7,8,17,25]. An infraoptic A1 segment may even perforate the ipsilateral optic tract [37]. Thus, the infraoptic A1 segment of the ICA leaves the intradural ICA near the origin of the ophthalmic artery [28]. In such cases the bifurcation of the ICA is located at the level of the proximal dural ring, at or inferior to the level of the origin of the ophthalmic artery [7]. Bilateral infraoptic A1 segments have been identified originating below the optic pillar [7]. Infraoptic A1 segments originating from the extradural ICA have also been identified rarely. One case has been reported with an infraoptic A1 segment associated with an ipsilateral persistent trigeminal artery variant apparently unrelated to the basilar artery [59]. Another rare case has been reported recently: the left ICA was absent, being supplied intracranially via an interparaclinoid anastomosis from the contralateral ICA; an anastomosis between the left ICA (replaced) and the ACA, which had an infraoptic course, was also noted [67]. An infraoptic A1 segment could also be associated with, fused PCaA, abnormal origin of the ipsilateral ophthalmic artery, Moyamoya disease, as well as with symptoms of optic nerve compression, chiasm or cerebral arteriovenous malformations [17,66]. Robinson suggested that the infraoptic A1 ACA might represent the persistence of a small embryonic canal in the adult, an anastomosis between the superior pituitary branches of the ICA proximal to the AComP, and the ACA [51]. This anastomosis probably corresponds to the vessels surrounding the optic nerve [51]. To date, less than ten cases of bilateral infraoptic A1 segments of the ACA have

been reported [5,7,8,24,25,32,34,53,66]; in the present study, 16 more such cases were identified, but with a different anatomical pattern: the infraoptic A1 segments resulted from the late bifurcation of the ICA. Apparently, when the ACI bifurcates posteriorly, at the level of the posterior clinoid processes, an infraoptic A1 segment trajectory will invariably occur, because the upward angle of the optic nerve of 45°, on average, would cause it to cross superior to the ACA. Various authors have documented three embryogenetic theories: (1) persistence of an embryonic anastomotic loop between the dorsal and ventral primitive ophthalmic arteries; (2) persistence of an embryonic anastomosis of the ACA and the primitive maxillary artery; and (3) widening of a prechiasmatic arterial anastomosis [22,68]. The authors adhered to the first hypothesis because all of the infraoptic ACA origins they documented were found in the ophthalmic artery [68]. However, in the present study, late bifurcations of the ICA, or ectatic ICAs, were found to originate infraoptic ICAs from the C7 segment of the ICA, which could not fit into either of these embryogenetic hypotheses.

Various authors have reported cases of aneurysms associated with infraoptic ACA [50]. These have been found at the level of the AComA or on the A1 or A2 segments of the ACA [7,8,25,29,30,34,36,37,44,50,53,57,59]. An aneurysm on an infraoptic A1 segment of an azygos ACA has also been reported [28]. Approximately 44% of patients with an infraoptic A1 are associated with AComA aneurysms [7,53]. Therefore, it is important to recognize such anatomical variants.

Progressive visual loss is commonly seen in pituitary adenomas and associated lesions of the sella turcica [33]. The infraoptic A1 segment of the ACA, or an ICA-ACA anastomosis, could anatomically cause visual alterations, but to our knowledge has been commonly overlooked in previous studies as a potential etiology of these visual alterations.

In a patient with open-angle glaucoma, bilateral ICA ectacy was demonstrated, prolonged in the ACM; the authors discussed that nerve imaging investigations should be considered if the presentation is not typical for a chronic bilateral optic neuropathy [14]. The authors' three-dimensional rendering evidence demonstrates good supracarotid and infraoptic tracts of the A1 segments of the ACM, as in my study. The infraoptic or infrachiasmatic trajectories of the A1 segments of these ACAs were overlooked, this despite the authors explicitly detailing that the ACAs "invaded the inferior surface of the optic chiasm" [14].

For a vascular or skull base neurosurgeon understanding the anatomy of the skull base is crucial. This is especially true in the anterior cranial fossa because a wide variety of vascular and tumour pathology develops in this region. This is a strong reason for knowing the vascular anatomy and accurately identifying anatomical variants preoperatively. The appearance of unexpected vascular variants can pose intraoperative problems even for experienced neurosurgeons. In the middle region of the skull base, at the level of the sphenoid body and small wings, thus anatomically related to the anterior portion of the cW, significant tumor pathology may be present: (a) meningiomas: of the sphenoid small wing, anterior clinoid processes, tubercle sellar; (b) pituitary adenomas; (c) craniopharyngiomas. Preoperative identification of various tumours that may interfere with elongated ICA and infraoptic A1 is important for successful removal of such tumours.

Arterial variants have unusual trajectories that may interfere with neurosurgical corridors. The tumours appear first in the neurosurgical field and deform or obscure normal anatomical elements such as the optic nerve, ICA and its branches.

Endoscopic transsphenoidal surgery for pituitary adenoma can also lead to vascular damage during dissection or removal of the tumour capsule.



### Pericalosal and transcalosal arteries arising from the anterior cerebral artery

The internal carotid artery bifurcates into the anterior cerebral artery (ACA) and middle cerebral artery (MCA) [45]. The ACA begins at the medial end of the trunk of the lateral cerebral fissure [18]. From its origin, the ACA passes posteriorly over the corpus callosum (CC), vascularizing most of the medial aspect of the cerebral hemisphere. It irrigates medial regions of the frontal and parietal cortex, CC and falx cerebri [42]. The ACAs are joined by the AComA which builds the anterior part of the nonagon of Willis.

The increasing use of the operating microscope for deep neurosurgical approaches has created a need for a better understanding of the microsurgical anatomy of the ACA [47]. I hypothesized that the topographic and morphologic possibilities of the distal ACA might be diverse and therefore set out to study the branching patterns of the ACA on computed tomography angiograms (CTA) [39].

A retrospective randomized group of 45 CTAs was studied. Of these, 32 were in male cases and 13 in female cases. Inclusion criteria were age of subjects (>18 years), adequate quality of CTAs, and absence of pathological processes distorting vascular anatomy in the CTA territory. Exclusion criteria were pathological processes distorting vascular anatomy and degraded or incomplete CTAs.

Eleven anatomical types of APCal have been defined and documented: '1': normal origin, above the knee of the corpus callosum (CC); '2': low origin, below the CC rostrum (either 2a, originating from the A1 ACA, or 2b, originating from the initial segment of the A2 ACA); '3': late origin, above the CC body; '4': Initial transcalosal tract, further continued as pericalosal; '5': duplicate (double) APCal; '6': azygos APCal, single initial trunk, further divided into two branches with pericalosal tract; '7': absent APCal, ACaIM type of ACA; '8': ACaIM continued as APCal; '9': APCal continued as ACaIM; '10': APCal type ACA, ACaIM absent. Other variants of APCal have been recorded as rare types: '11' [39].

Several variants of ACaIM were investigated: type "0": ACaIM absent; type "1": ACaIM with frontoparietal distribution; type "2": ACaIM with parietal distribution; type "3": low origin of ACaIM, either from A1 (subtype 3a) or from the initial part of A2 (subtype 3b). When ACaIM continued as APCal, ACaIM was recorded as type "4" [39]. In cases with type 2 ACaIM, common frontal trunks (TFs) originating from A2 were recorded, either with low origin (type 1 TF) or high origin (type 2 TF) [39].

The incidence of the types of APCal that we defined in the 90 parts that were investigated resulted, in descending order, as follows. APCal type 1 was found in 46/90 parts (51.11%), type 10 was found in 13/90 parts (14.44%), type 7 was found in 7/90 parts (7.78%), type 2b was found in 6/90 parts (6.67%), type 8 was found in 5/90 parts (5, 56%), types 3 and 4 (PCaIA transcalosal tract) were each found in 3/90 sides (3.33%), types 2a and 6, respectively, were found in 2/90 sides (2.22%), and types 5, 9 and 11 (triple APCal) were each found in 1/90 sides (1.11%). In the overall batch of 45 cases, we investigated 90 APCal and identified the incidence of types 1-11 defined for it. Type 1 prevailed (46/90 hemicaps). With lower prevalence were type 10 (13/90) and type 7 (7/90) (graph 1). APCal types 5, 9 and 11 were highlighted with the lowest prevalences of 1.11%.

Types of ACM were determined with the following incidences, in descending order: type 1 - 41/90 parts (45.56%), type 2 (fig.6E) - 20/90 parts (22.22%), type 0 (absent ACM) - 16/90 parts (17.78%), types 3b and 4, respectively, in 5/90 parts (5.56%), and type 3a in 3/90 parts (3.33%).

On each side of the median plane a number of combinations of the types defined for APCal and ACalM were documented. These combinations of individual ipsilateral arterial types were further classified as combinatorial A-P types.

In only 8/32 cases in men and in 4/13 cases in women, the combinations of APCal and ACalM types were bilaterally symmetrical. Therefore, in 33/45 cases (73.3%), 24 males and 9 females, bilateral asymmetry of combined APCal and ACalM anatomical patterns was documented.

In six cases, 5 males and 1 female, bihemispheric ACA were found. The dominant ACA was on the right side in three cases and on the left side in the other three cases. In two cases with right bihemispheric ACA, additional variants were found: (a) a CC median artery added to bilateral APCal (APCal type 11, triple APCal) and (b) a wide fenestration of the A2 segment.

In a male case with bilateral type A bilateral APCal/ACalM combinations, a peculiar arterial morphology was identified consisting of a left bihemispheric ACA connecting a hypoplastic right A1 segment. This left ACA fed both A2 segments which further had twisted tracts in the interhemispheric fissure. A large fenestration, consisting of postero-lateral and antero-medial arms, was found at the right A2 segment. From the antero-medial arm left the right ACalM. From the distally joined arms of this fenestration resulted a trunk further divided into the right cingulate artery and the right APCal.

Through this study [39] we identified rare anatomical variants in the territory of the ACA, such as the transcallosal course of the APCal, duplicated/doubled APCal, azygos APCal, triple APCal, ACalM continued as APCal or APCal continued as cingulate artery (sliding into the cingulate groove of the APCal), wide fenestration of the A2 and twisted (en.twisted) arteries of the anterior interhemispheric fissure.

ACalM is the second largest distal branch of the ACA, after APCal [4]. According to various authors, ACalM is absent in 15% to 40% of cerebral hemispheres 56, 136, 140. In this study [39] we found the absence of ACalM in 17.7% of cases. Furthermore, it is shown that, if present, ACalM has a certain topographic variability. ACalM anatomy has also been documented in fetuses [46]. The absence of ACalM was found in 36.06% of 452 fetal brains, and the site of origin of ACalM was also found to have possible proximo-distal variation [46]. The possible absence of ACalM has been argued for the use of the term APCal for the postcommunicating A2 segment of the ACA [9].

A subfalcine herniation can be complicated by compression of the ACA branches, particularly the APCal, leading to cerebral infarction. However, this may not be a frequent consequence because, as we demonstrate here, APCal is subject to different variations including its absence. Anatomical variability of APCal also implies possible symptoms of specific vascular compression [39].

Discrepancies in the anatomical definition of APCal result in variable definitions of an absent APCal. When the APCal is erroneously considered to be the postcommunicating A2 segment of the ACA, an absent APCal is an absent A2 segment, so the contralateral ACA becomes an azygos ACA or a bihemispheric ACA by this terminology. However, regardless of the anatomical distinction, if an endovascular approach is intended for an aneurysm of the distal APCal, the contralateral ACA should be used for endovascular access [39].

An azygos APCal, which has been classified as APCal type 6, has been found in previous studies in 3/112 brains (2.7%) [20] and in 1/38 brains (2.63%) [54]. In the present study it was identified in 2.2% of cases, confirming that it is a rare anatomical variant. Although it is rare,

it is important to identify it as a single arterial source of CC, especially when locating aneurysms, as its lesion could lead to isolated infarction of CC [21,56].

We found only one case (1.11%) with triple APCal (type 11) [39]. In this case a CC middle artery arose from the AComA. In a cohort of more than 900 patients, the median CC artery had an incidence of 3.0% [60]. To indicate the median CC artery, different terms have been used, such as "medial callosal artery", "third segment A2", "accessory CAA", "middle anterior cerebri artery" or triple/triple CAA [43,64].

The descriptions of the azygos and medial CC artery APCal, respectively, are similar [27]. However, when an azygos APCal leaves an A2 segment, the opposite A2 segment sends only ACalM, whereas the left and right APCal have a late origin above the CC [20]. When present, the medial artery of the CC arises from the AComA [1,43,46,64] and not from the A2 segment. This helps to differentiate anatomically with an azygos APCal arising from the ACA. This may not be exclusive as an azygos APCal has been found leaving the AComA, and not an A2 segment [54]. The CC medial artery represents a persistent fetal pattern 136, 140.

In this study a triple APCal was found [39]. This consisted of the left and right APCal and a medial CC artery. Such a rare anatomical variant should be identified before an endovascular approach to understand the correct pathway to a possible distal APCal aneurysm.

We highlighted two cases of APCal with transcallosal pathway, unilateral and bilateral, respectively [39]. No such particular variants have been previously reported. The only case in which APCal distorted CC anatomy was recently reported by Zytkowski et al. (2022), who found by dissection a particular bilateral variant of APCal: when these arteries reached above the body of the CC, they inferiorly angulated to result in a recess/fosette in the CC, reducing the thickness of the CC from 6.8 to 1.5 mm [69]. As Zytkowski concluded, arterial abnormalities can alter brain tissue [69].

Lower limb motor dysfunction could be caused by APCal stenosis [69]. Stenosis of the supracallosal segment of the APCal could also determine the callosal type of foreign hand syndrome (intermanual conflict, with the nondominant hand usually being affected) [56].

The distal portion of the ACA is difficult to approach surgically because of its location, deep in the interhemispheric fissure [47]. In no other location do the main trunks of two major cerebral arteries, the right ACA and the left ACA, approach so closely [47]. Due to the contralateral distribution of these two, lesion of the ACA on one side of the median plane can result in a contralateral cerebral infarction [47]. Distal ACA branches are exposed in surgical approaches to the sella turcica and optic chiasm, the sellate and chiasmatic regions, the third ventricle and lateral ventricle, the brain shell and parasagittal regions, and even in approaches to the medial parietal and occipital regions and the epiphysis [47]. The increasing use of the operating microscope for such deep approaches has created a need for a better understanding of the microsurgical anatomy of the ACA [47].

Aneurysms of the distal portion of the ACA, or APCal aneurysms, are rare (1-9% of intracranial aneurysms) [31,55]. Endovascular treatment of these aneurysms presents a number of challenges [55]. Various studies have reported high rates of arterial dissection, intraprocedural rupture and incomplete occlusion in such situations [55]. Coil embolization is emerging as a promising therapeutic option for distal ACA aneurysms [55]. Series of coiling cases for ruptured pericallosal aneurysms have reported low success rates and high technical difficulties [55]. A coiling success rate of only 25% has been reported [48,55].

PCalA aneurysms present several problems for direct surgical clipping, namely difficult exposure via an interhemispheric approach, especially in the situation of cerebral oedema after

subarachnoid haemorrhage, sacrifice of a bridging vein for adequate surgical exposure (thus increasing the risk of postoperative morbidity), difficult control of the mammary artery and unfavourable orientation of the aneurysm fundus [31]. Coil embolization has become equally effective as surgical clipping of PCaA aneurysms [31]; access is via the ACI pathway and therefore, accurate knowledge of ACA and PCaA morphology is extremely important for these embolizations [39]. Moreover, because of their distal location and small parent vessel diameter, PCaA aneurysms pose a technical challenge for endovascular therapy and, as with most bifurcation cerebral aneurysms, have a potentially high recurrence rate [31]. Endovascular treatment of distal ACA aneurysms can lead to good technical and clinical outcomes [63].

### 3 Artera cerebrală posterioară de tip fetal

Willis' circle or polygon (cW) is one of the most famous anatomical structures indicated by the eponym [12]. Anatomical variation at the cW is a rule rather than an exception [45]. There are studies reporting that a classical cW may be present in 4.8-85.4% [26]. There appear to be no ethnic criteria for the distribution of anatomical variations of cW in the population [13]. Anatomical variations of cW may hinder the proper identification of clinical patterns of ischemic lesions and stroke etiology [49]. The standard type of cW is the nonagon type in which AComA joins the two ACAs, the A1 segments of the latter branch from the ACI; AComP branches from the ACI and ae joins the ACP, branch of the AB, completing the posterior part of the cW [58,65]. In the adult morphological type, the P2, postcommunicating segment of the ACP continues the precommunicating P1 segment.

The arteries of interest to neuro-ophthalmologists are the ophthalmic and central retinal arteries anteriorly and the ACP posteriorly [16]. Three types of cW configuration have been discussed in relation to the P1 segment of the ACP: (a) the adult configuration in which the P1 is thicker than the PComA, which is not hypoplastic; (b) the transitional configuration in which the ACP and P1 have the same diameter; and (c) the fetal or embryonic configuration in which the P1 diameter is smaller than the AComP diameter [61].

In the case of fetal types of ACP (FACP), the P2 segment is derived from ICA. The P1 segment can be either hypoplastic (partial FACP, p-FACP) or absent (complete FACP, f-FACP) (Fig. 1), as defined by van Raamt (2006) [62]. Patients with a partial FACP are likely to develop ischemic stroke [2].

Few studies focus exclusively on the anatomy of ACP [19]. In a recent study, FACP was found only unilateral in 5.6% of 231 cases [6]. van Raamt reviewed different studies and found that bilateral FACP occurs in up to 9% of cases [62].

I hypothesized that FACP occurs in different anatomical combinations, with variant sides of the cW, and aimed to document the incidence of these variants on a retrospective batch of computed tomographic angiograms (CTA) [11]. This is because CTA with three-dimensional rendering can adequately assess the many anatomical variants of cW [10].

A retrospective study was performed on 147 randomly selected computed tomography angiograms (CTAs) to assess the arteries in the cW composition. Inclusion criteria were age of subjects (over 18 years), adequate CTA quality, no pathological processes distorting the cW, and no history of cW surgery. Exclusion criteria were pathological processes distorting the arterial anatomy of the cW and degraded or incomplete CT scans. After applying these criteria, we retained 139 angiograms from 83 male and 56 female Caucasian subjects aged 58 to 74 years.

Out of the overall 139 cases, 13 cases with FACP (9.35%) were documented. Of these cases, there were 9 male cases (69.23%) and 4 female cases (30.77%). Seven cases, four male and three female, of the 13 cases with FACP had two variant sides of cW (53.84%). Five other cases, four male and one female, had three variant sides of cW (28.46%), and one male case had four variant sides of cW (7.69%).

Ten cases, six males and three females, out of the 13 cases with FACP, had this unilateral variant (76.92%). Three other male cases (23.07%) had bilateral FACP.

In the overall group, unilateral p-FACP was found in two male cases (2/139, 1.43%). Unilateral f-FACP was found in four male and four female cases (8/139, 5.75%). One male case showed bilateral p-FACP+f-FACP combination (1/139, 0.71%). Two male cases showed bilateral f-FACP+f-FACP combination (2/139, 1.43%), thus bilateral ICA vascularization of the PCA territory.

Different subvariants of FACP were found in different anatomical variants of the cW in terms of number of variant sides and overall morphology. Seven of the 13 cases with FACP had only posterior variants of the cW and 6/13 cases of FACP had arterial variants in both the anterior and posterior circulation.

I have found no single-sided cW variants leading to FACP in this study [11]. Such a unilateral cW variant with a flattened P1 segment was found by Coulier (2021) in 2.55% of cases [10]. However, Iqbal (2013) found unilateral variants of cW in 24% of cases [23]. FACP could only rarely be an isolated arterial variant of cW. Therefore, other variations of cW should be considered and documented when FACP is found.

#### 4 Modelele topografice ale venei lui Labbé (vena anastomotică inferioară)

Temporal lobe venous drainage is important in various neurosurgical procedures and combined skull base approaches [3]. The most important draining vein of the temporal lobe is the inferior anastomotic vein (Labbé's vein, VL) [3].

Little attention has been paid to superficial anastomotic veins in studies, although severe postoperative complications may be caused by iatrogenic venous lesions [52]. The importance of LV topography is related to skull base approaches and medial tentorial lesions resulting in posterior temporal approaches [52].

Based on the hypothesis of as yet unidentified anatomical possibilities of the LV, we aimed in this research to document in a retrospective angioCT batch the superficial venous topographic patterns at the lateral and inferior faces of the cerebral temporal lobe [38].

I have studied a retrospective randomized batch of 50 angioCT scans [38]. Of these, 32 were in male cases and 18 in female cases. The research was conducted in accordance with the principles of the World Medical Association Code of Ethics (Declaration of Helsinki).

We defined [38] four topographic types of VL: type 0 - absent VL; type 1 - anterior, temporal type, with the VL having a trajectory applied only to components of the temporal bone (squamoso-pietro-mastoid type); type 2 - intermediate, temporoparietal type, with the VL having a trajectory corresponding to the temporal squama (optional), the mastoid angle of the parietal and the mastoid portion of the temporal (squamoso-parieto-mastoid type); type 3 - posterior type, parieto-occipital, with the LV having a trajectory corresponding to the temporal

squama (optional), the mastoid angle of the parietal and the occipital squama (squamoso-parieto-occipital type).

We recorded situations with multiple, duplicate, triplicate or quadruplicate VLs. We recorded cases with dominance of sylvian drainage on the LV pathway.

We also recorded the mode of LV drainage into the TS: (type A) via a tentorial sinus, (type B) directly, or (type C) via a dural lacuna.

There were no statistically significant gender differences in the study group.

Type 0, VL absent, was identified as follows. In 3/50 cases (6%), two male and one female, VL was absent bilaterally. Type 0 was identified unilaterally on the right in 5 specimens, 4 male and one female. Unilateral type 0 was evident on the left side in 5 different cases, 2 male and 3 female.

Type 1, temporal, VL was not identified bilaterally in any case in the specific documented group. It was found unilateral in 6/50 cases (12%), with equal left-right prevalence (3 cases on each side); right in 2 male and 1 female cases, left in 2 female and 1 male case.

Type 2, intermediate or temporoparietal, was present bilaterally in 23/50 cases (46%), and unilaterally in 18/50 cases (36%). Unilateral presence was in 14/50 cases on the right and 4/50 cases on the left.

Type 3, posterior or parietooccipital, was present bilaterally in 4/50 cases (8%), one male and three female. This type was present unilaterally in 16/50 cases (32%), on the right side in 4 cases, two male and two female, and on the left side in 12 cases, 10 male and 2 female.

In one male case we identified topographic type 2 of the left-sided LV. Interestingly, it did not drain into the ST but traced across it continuing with branches into dural and tentorial veins.

In 12/50 cases (24%) we identified duplicate VLs, 7 male and 5 female. Of these, one male case had complete bilateral LV duplication (2%); its morphology had bilateral symmetry, consisting of a combination of types 1+3 - anterior LV, type 1 temporal, draining into a wide tentorial sinus but continuing to terminate in the sinus confluence; posterior LV, type 3 posterior or parietooccipital, draining convergently with the anterior only into the tentorial sinus on that side. We identified unilateral duplications in 11 cases, 2 on the right side and 9 on the left side. Right duplicated VL was present only in male cases. Left duplicated VL was identified in 4 male and 5 female cases. Unilateral duplications were complete, with distinct terminal drainage, or incomplete, with terminal drainage through the common trunk. One female case had a complete type 2+3 dedubulation of the left LV, but the anterior type 2 component also had a partial dedubulation.

In one male case we identified right-sided LV quadruplicity. The four veins descending laterally and then inferiorly from the cerebral temporal lobe formed a palisade from antero-inferior to posterosuperior, corresponding in this sequence to LV types 1-2-2-3 defined in this study. The first two connected distally to a tentorial sinus through which they drained into the ST. The latter two drained through dural lacunae also into the ST.

I have found dominant VL in 40/50 cases (80%). There was bilateral dominance in 28 cases (56%), 19 male and 9 female. There were 4 male cases with unilateral VL dominance, 1 on the right side and 3 on the left side. There were 8 female cases with unilateral LV dominance, 3 right-sided and 5 left-sided.

Considering cases with duplicated and quadruplicated VL, as well as the 16 sides with absent VL (type 0), we recorded the drainage modality for 100 VL. Drainage was (i) type A in ST for 49 LVs, 25 right, 24 left; (ii) type B in ST for 29 LVs, 13 right and 16 left; (iii) type C in ST for 21 LVs, 11 right and 10 left; (iv) in one case, the left LV did not drain into ST but diptomized distally into a dural occipital vein and a tentorial vein.

During combined craniotomies of the middle and posterior cranial fossae ("pietrous" approaches), the LV, which connects the basal face of the temporal lobe to the ST, is compromised [35]. Occlusion of the LV, which may be the only venous drainage pathway to a large brain territory of the temporal and parietal lobes, can lead to devastating neurological damage [35]. For this reason, the presence of multiple LVs, albeit with contiguous cerebral territories, may represent an anatomical safety feature.

It has been suggested that digital subtraction angiography or CT venography performed preoperatively could be useful to design the neurosurgical approach [15]. When approaching the cerebellum, the least chance of injury to the LV is via the median approach [15]. On the other hand, when imaging examination reveals that the LV is too close to the sinus confluence or that the dural veins are too long, the surgical approach pathway should be redesigned [15].

An LV draining through a tentorial sinus is more susceptible to injury during cerebellar cortex sectioning than an LV with a different drainage pattern. Therefore, studies showing exclusively a direct drainage of the LV into the ST, although rigorously performed, could mislead neurosurgeons. On the other hand, multiple LVs may have different drainage patterns, so that if a posterior one is avoided, an anterior one could be affected when accessing the transtentorial corridors.

## 5 PhD thesis conclusions and original contributions

### Thesis Conclusions

1. Careful anatomical dissection, careful observation of vascular morphology in angioCT scans, coupled with documentation of the literature can provide details of rare anatomical variants that have been reported long ago and have not been supported by the respective original evidence or at least anatomical drawings.
2. Minor fenestrations of the vertebrobasilar system may not produce clinical effects but large, giant fenestrations bring an additional vascular element into a narrow surgical field and must be carefully documented preoperatively to avoid hemorrhagic incidents.
3. Large fenestrations of the A2 segment of the anterior cerebral artery should be considered when multiple and occasionally twisted arterial trunks are identified intraoperatively in the anterior interhemispheric fissure.
4. The study of the infraoptic course of the A1 segment of the anterior cerebral artery demonstrates that such a course may occur in cases with elongated internal carotid arteries (internal carotid dolichodes). Such anterior cerebral arteries with late, posterior, infraoptic tracts could also present with a supracarotid tract, above the internal carotid artery, which modifies the usual neurosurgical landmarks. Preoperative anatomical documentation is thus preferable on a case-by-case basis.
5. Infraoptic A1 segment of the anterior cerebral artery, or an anterior carotid-cerebral anastomosis, could cause visual changes and should be investigated on CT angiogram as a potential etiology of these visual changes.
6. Morphological and numerical variations of the sides of the Willis polygon are unpredictable and must be documented preoperatively to avoid intraoperative lesions.
7. Arterial morphology of the distal branches of the anterior cerebral artery, as presented in anatomy textbooks, could be found in only half of the cases. The heterogeneous actual anatomical possibilities, as well as the combinations of individual variants of the pericalosal

and calosomarginal arteries, indicate the fact of the diversity of the respective anatomical possibilities. The combinations of anterior cerebral artery branch types are rather asymmetrical bilaterally.

8. During craniotomies for pyloric approaches the vein of Labbé represents an anatomical element of surgical risk. Its interruption may be followed by neurological damage if the vein is the only temporoparietal venous drainage route. Therefore, anatomical variants with multiple Labbé veins serving neighbouring cerebral territories represent anatomical safety conformations.
9. Multiple Labbé veins may have different drainage patterns, so that if a posterior one is avoided, an anterior one could be injured if transtentorial neurosurgical corridors are accessed.
10. Rare vascular structures represent surgical risk elements. Pterional approaches to the middle fossa may intersect the ophthalmopseal sinus of Hyrtl.
11. Variational changes in cerebral vascular topography require redesign of neurosurgical approach corridors.

### Original Contributions

1. I demonstrated the possibility of infraoptic or infrachiasmatic tracts of the anterior cerebral artery arising from an elongated internal carotid artery (infraoptic A1 segments of the anterior cerebral artery arising from the internal carotid artery with distal bifurcation and not proximal as previously known). This possibility has not been previously documented. Three anatomical types of the precommunicating segment of the anterior cerebral artery resulted: type 1 - supraoptic A1 segment tract or absent A1 segment; type 2 - infraoptic A1 segment tract; type 3 - infrachiasmatic A1 segment tract.
2. I demonstrated multiple anatomical patterns of the perichalosal artery. Such a classification has not been performed before.
3. I have provided the first evidence of the possibility of pericalosal artery path through the corpus callosum.
4. I have identified high and wide fenestration of the A2 segment of the anterior cerebral artery. This anatomical variant has not been previously reported.
5. In this study I obtained original evidence of rare anatomical variants, partial deduplication of the posterior communicating artery and fenestration of the precommunicating segment of the posterior cerebral artery.
6. Hyrtl's sinus - the anatomical variant documented in the paper represents the first dissection evidence of this sinus, a combination of it with a lateral type of superior stony sinus; we could not document any anatomical relationship of the association of this type of stony sinus with Hyrtl's ophthalmopseal sinus.
7. I made a new anatomical classification of Labbé's vein into four topographic types: type 0 - absent vein; type 1 - anterior, temporal type, with the Labbé vein having tracts applied only to components of the temporal bone (squamoso-pietro-mastoid type); type 2 - intermediate, temporoparietal type, with the Labbé vein having tracts at the level of the temporal squama, the mastoid angle of the parietal and the mastoid portion of the temporal (squamoso-parieto-mastoid type); type 3 - posterior type, parieto-occipital, with Labbé's vein tracing the temporal squama (optional), the mastoid angle of the parietal and the occipital squama (squamosal-parieto-occipital type).
8. I obtained rare anatomical evidence of anterior communicating artery deduplication and bilateral absence of transverse sinuses.



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## List of published scientific papers

Total: 7 publications in WOS indexed journals (SCIE, Core Collection), as follows:

### First Autor

1. **Minca DI**, Rusu MC. The Ophthalmopetrosal Sinus of Hyrtl: The Evidence of A Rare Variant. *Journal of Craniofacial Surgery* 2021; **32**(7): 2551-2.
2. **Minca DI**, Rusu MC, Radoi PM, Hostiuc S, Toader C. Transcallosal and Pericallosal Courses of the Anterior Cerebral Artery. *Medicina (Kaunas)* 2022; **58**(10).
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4. **Minca DI**, Rusu MC, Radoi PM, Vrapciu AD, Hostiuc S, Toader C. The Infraoptic or Infrachiasmatic Course of the Anterior Cerebral Artery Emerging an Elongated Internal Carotid Artery. *Tomography* 2022; **8**(5): 2243-55.

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### Co-author

6. Radoi PM, **Minca DI**, Rusu MC, Toader C. Bilateral absence of the transverse sinuses with fenestrated superior sagittal sinus draining through enlarged occipital and marginal sinuses. *Folia Morphol (Warsz)* 2021; 10.5603/FM.a2021.0070.
7. Radoi PM, Rusu MC, **Minca DI**, Toader C. Huge Fenestration of the Vertebral Artery and Fenestrated Basilar Artery. *J Craniofac Surg* 2022; **33**(2): 693-5.