



2018 01 14 ABC WIN seminar@Val d'Iserre
Anatomy Biology Clinical Correlations

Embryology of the falco-tentorial dura mater

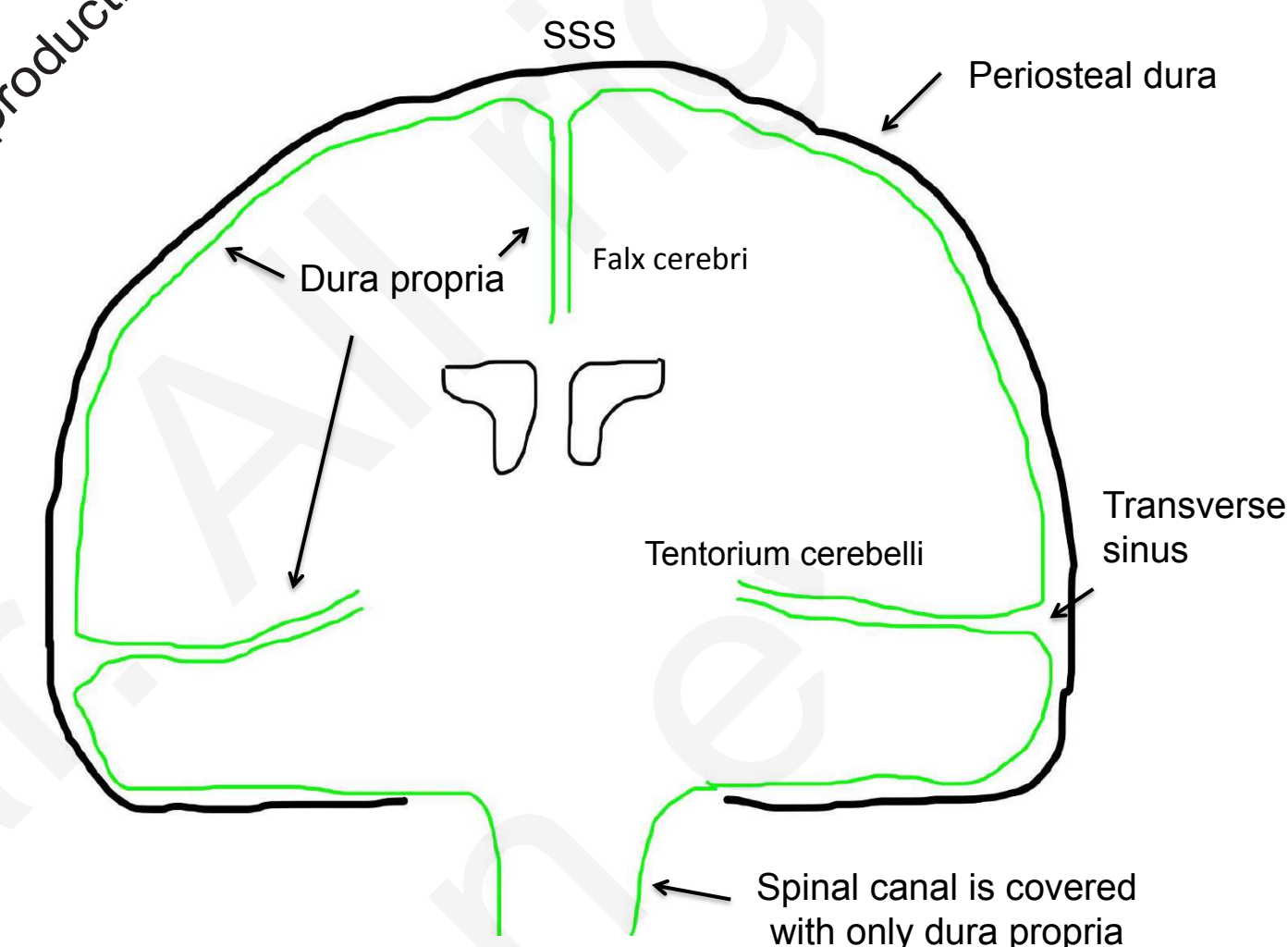


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Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



Menu

1. Embryology of the dura mater encephali
2. Neural crest cell and falco-tentorial dura mater
3. Clinical consideration of falco-tentorial dura mater

Keywords: dura mater encephali, falx cerebri, tentorium cerebelli, neural crest, dura propria

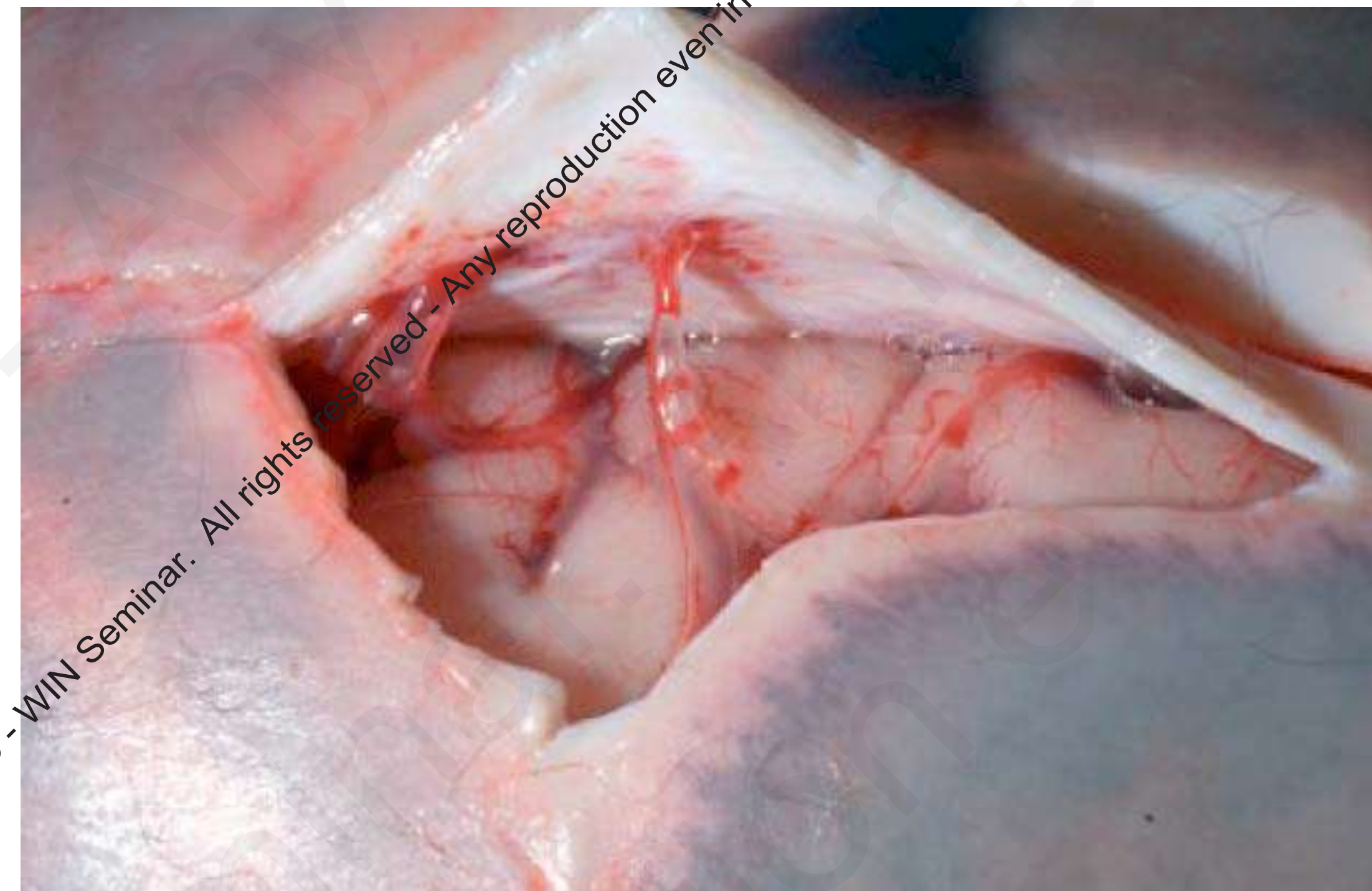
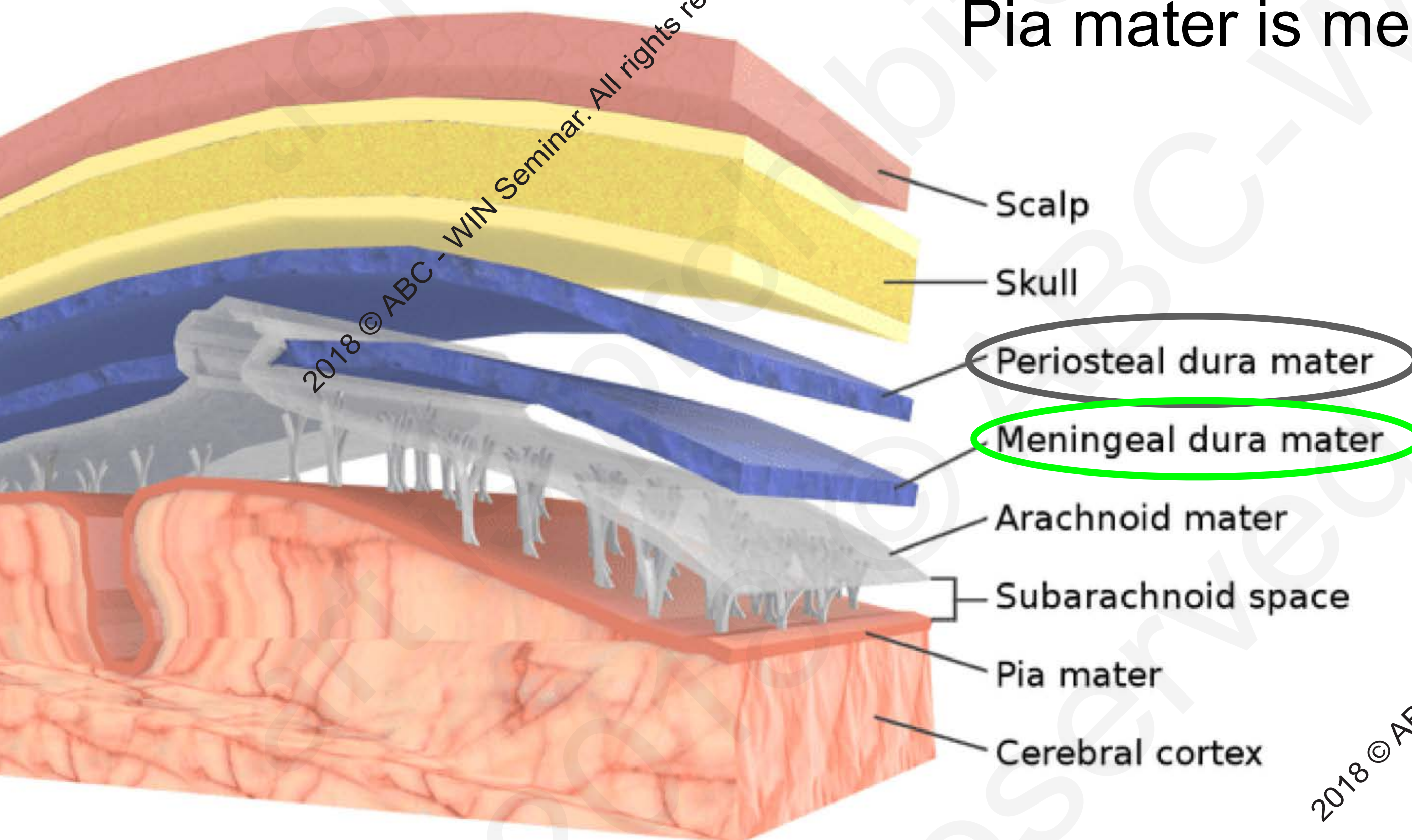


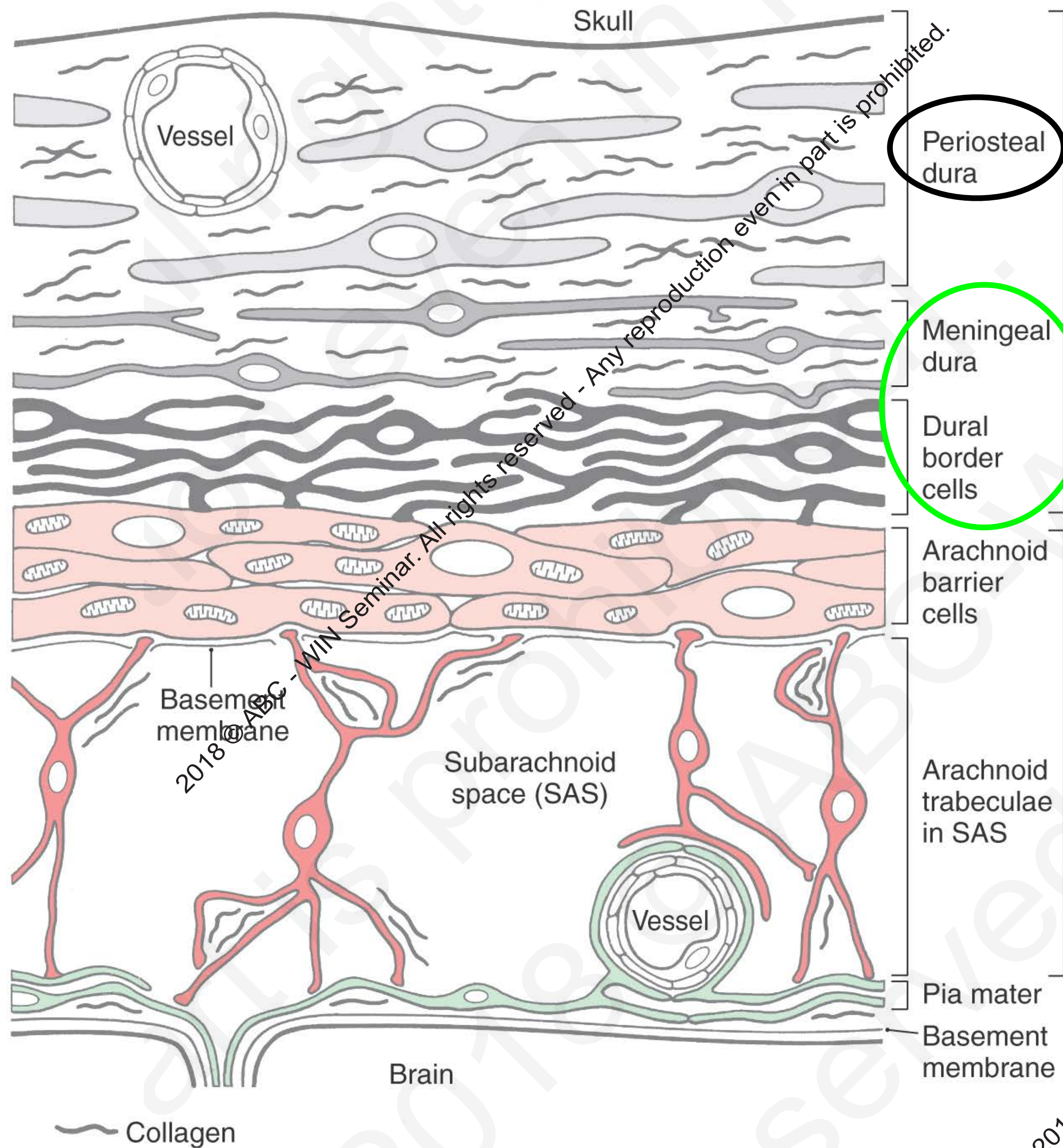
Dura mater (Latin, dura mater = hard, tough mother)

The outer tough connective tissue meningeal coat of the 3 layers that cover the central nervous system of 3 layers (overlays the arachnoid mater middle layer and pia mater inner layer).

All three layers form from the meninx primitiva, a meningeal mesenchyme that is **mesodermal and neural crest in origin**.

Pia mater is medieval Latin meaning "tender mother".

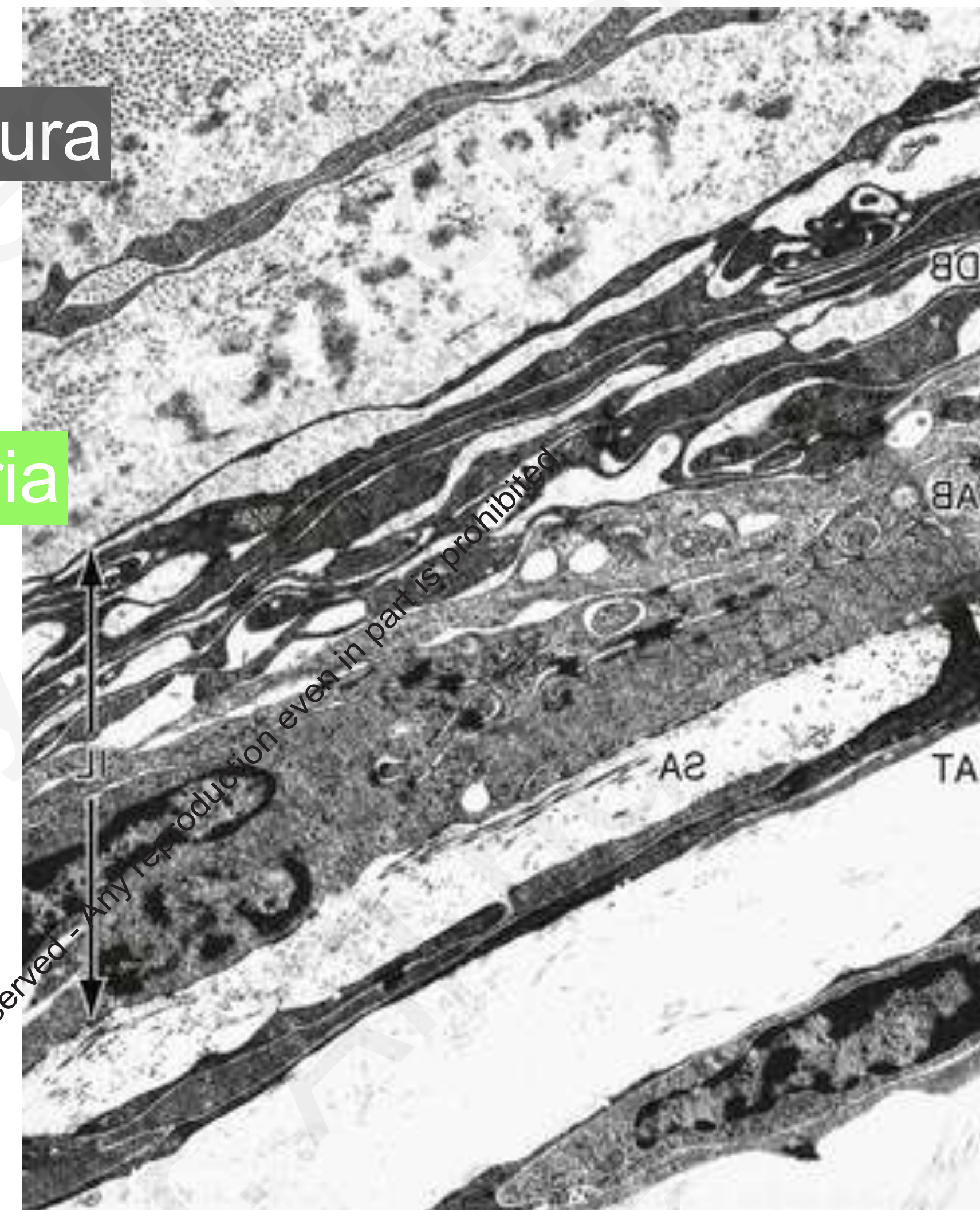


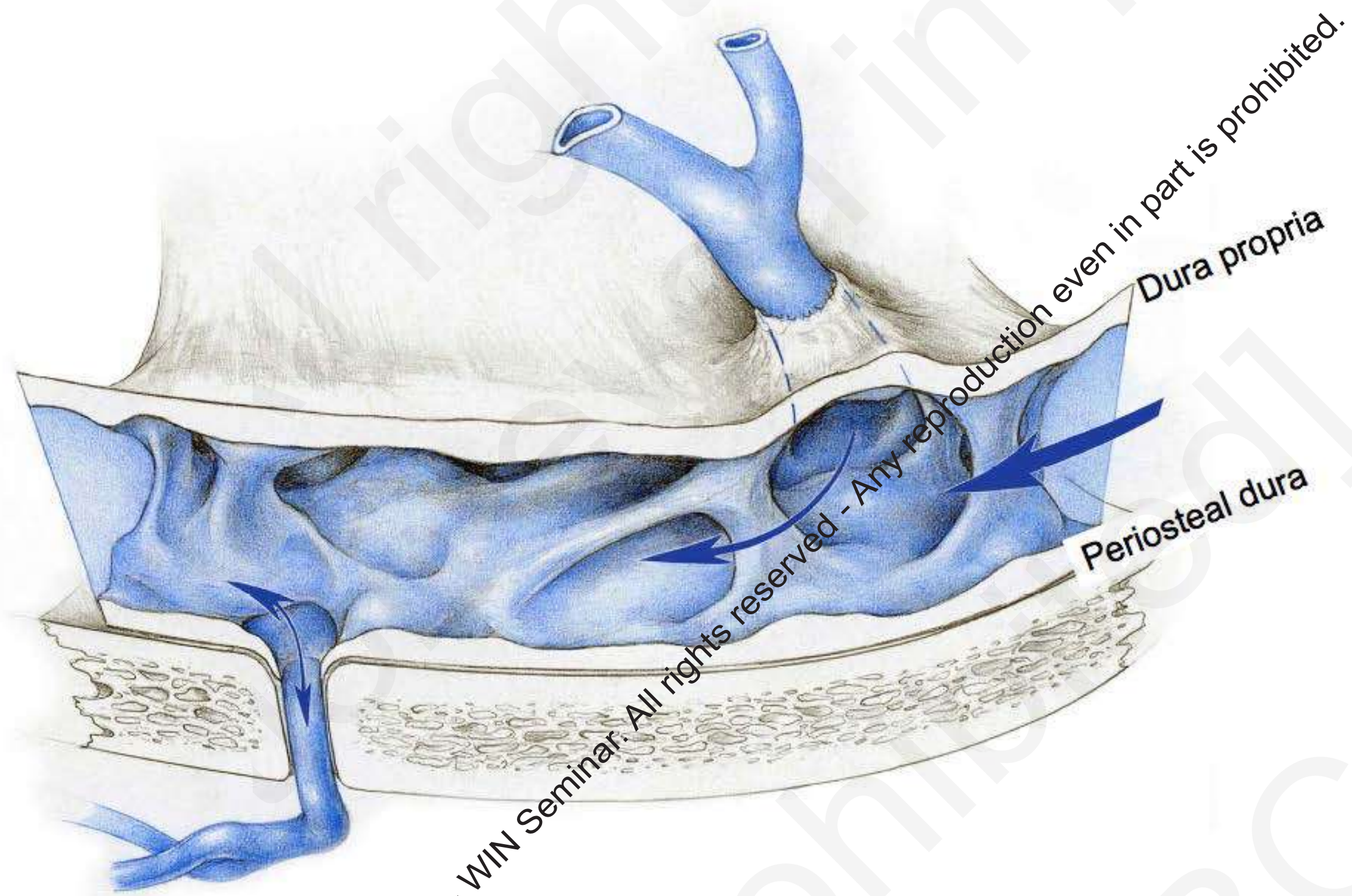


Periosteal dura

Dura mater

Dura propria

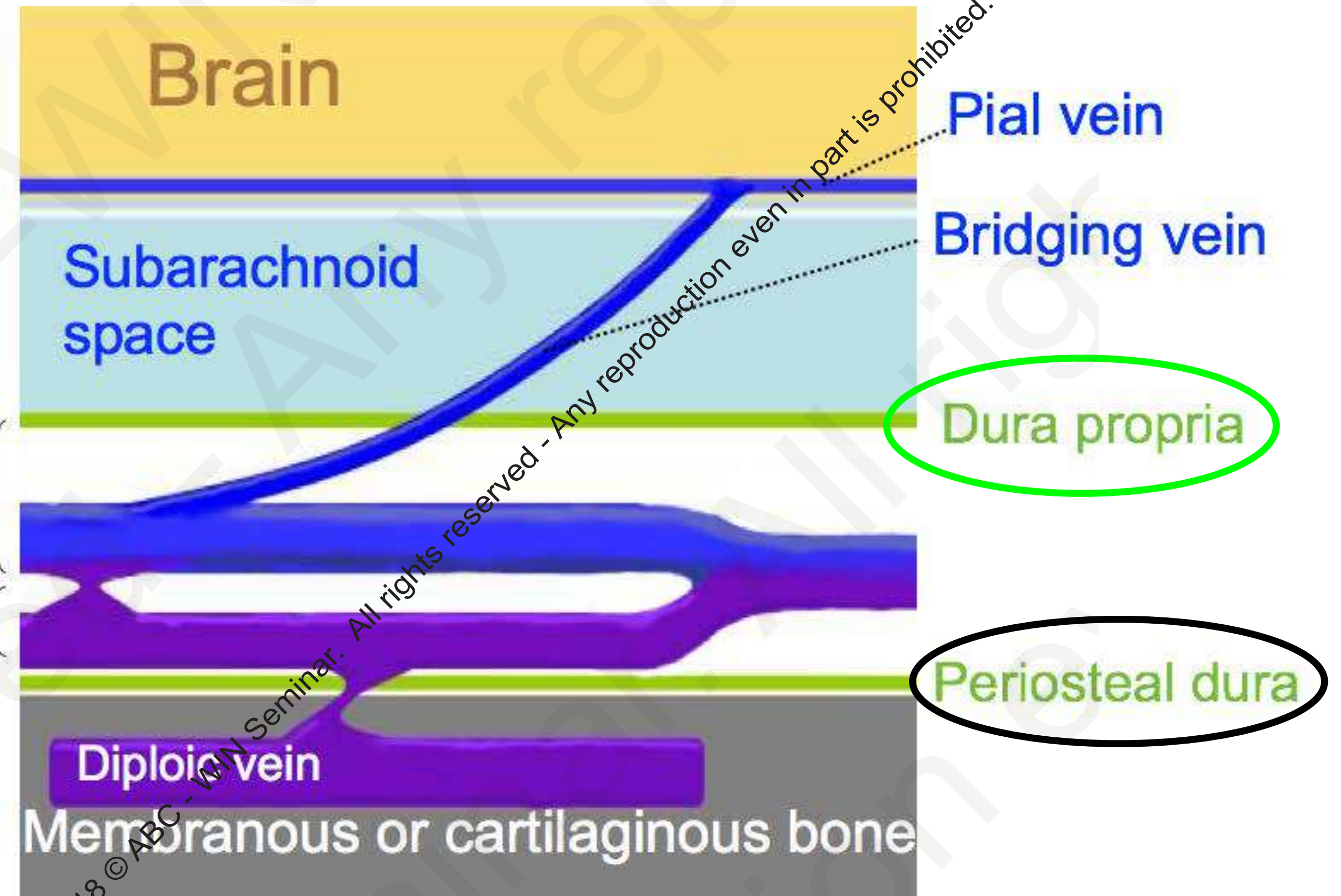


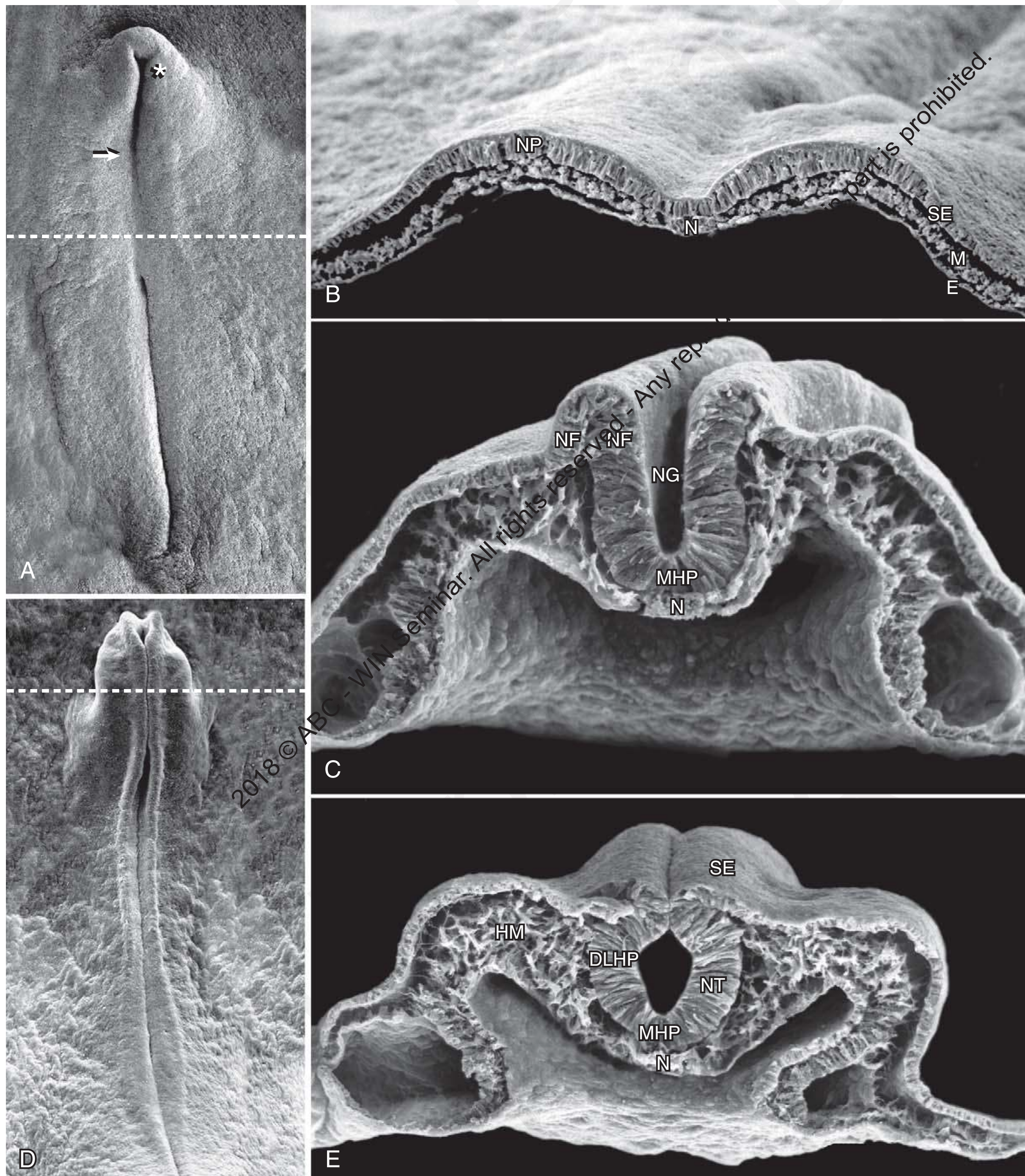


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Leptomeningeal
epidural V

Osseous
epidural V

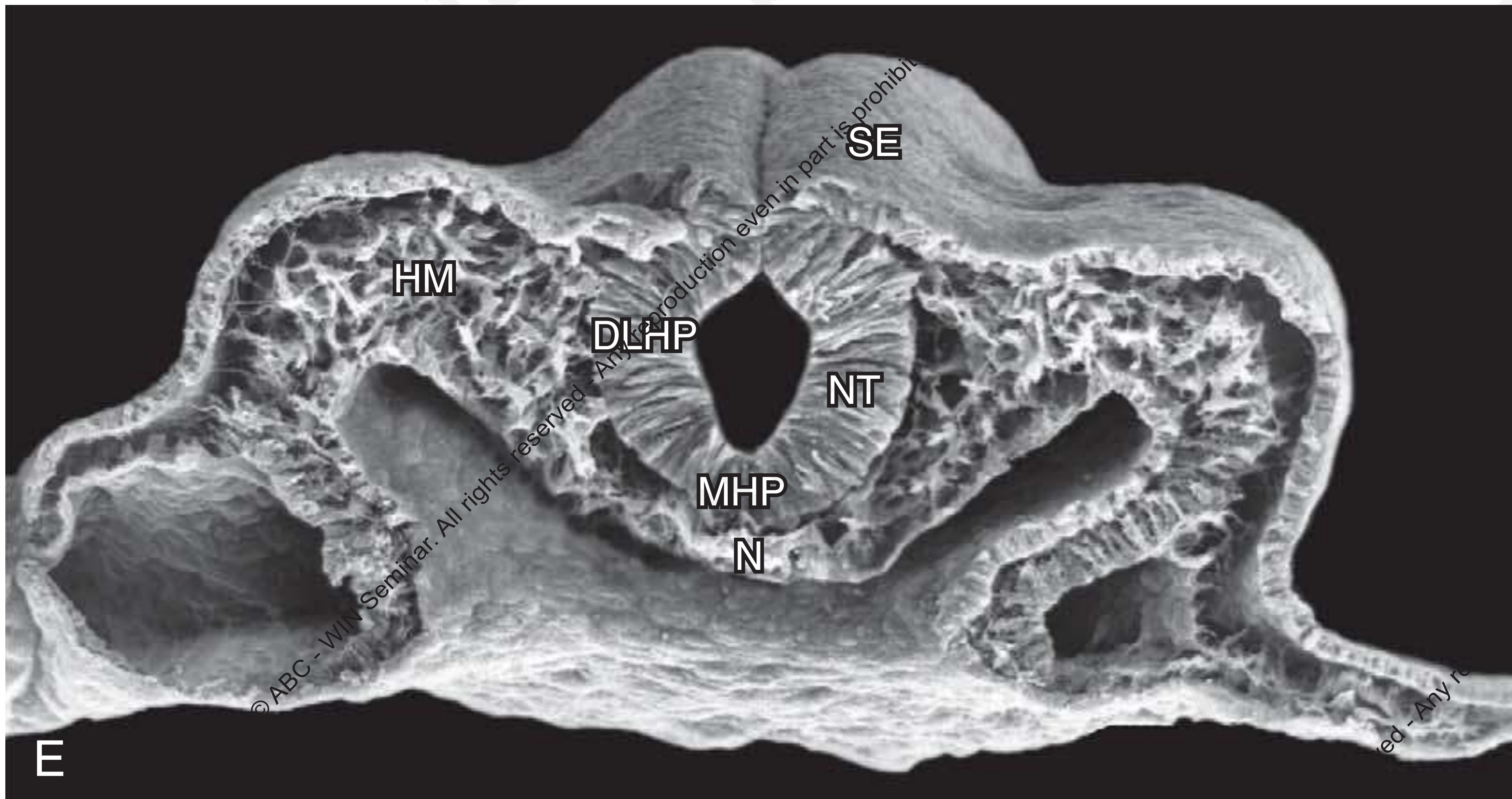




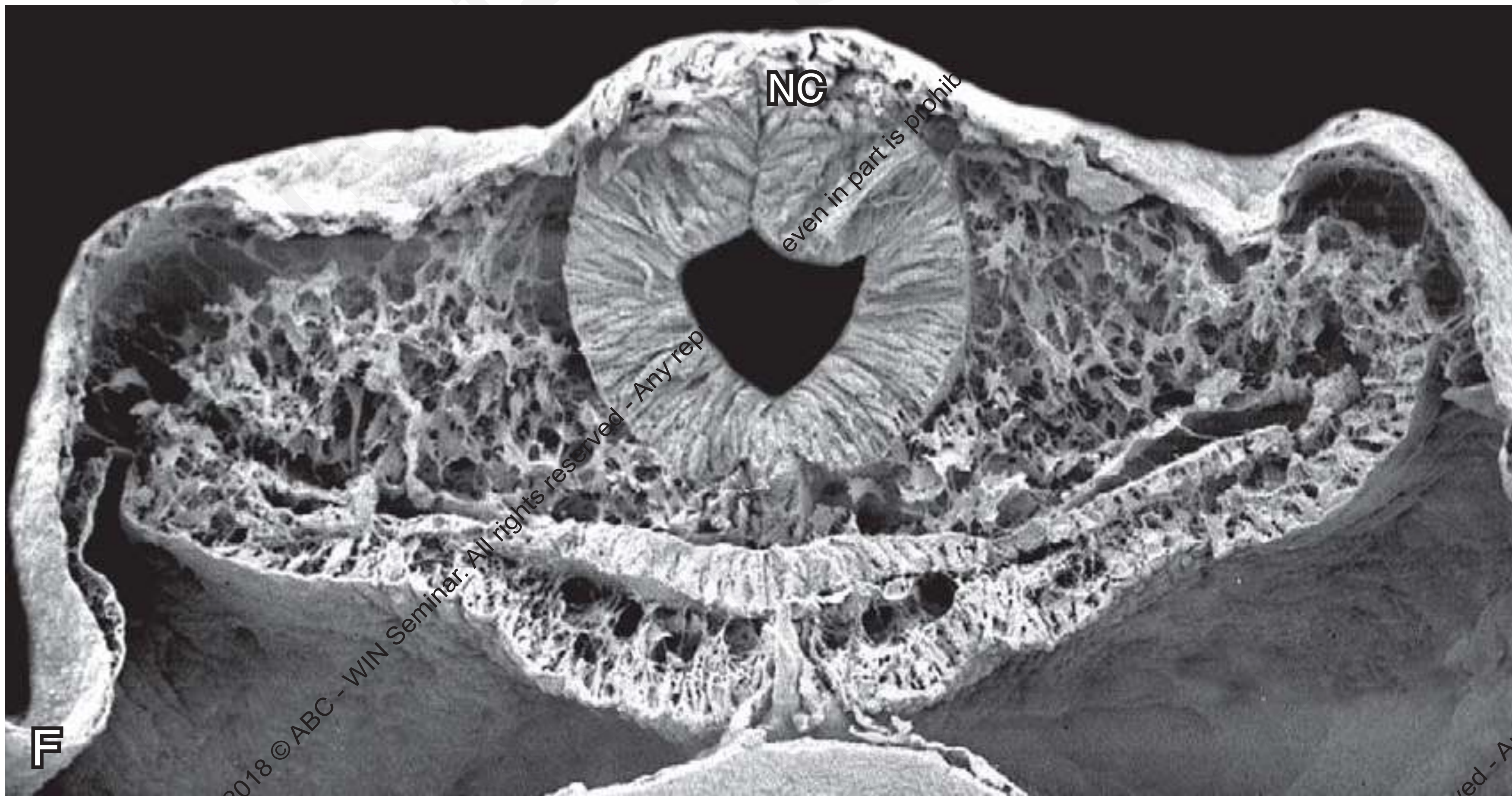
Neurulation: Establishing the Neural Tube, the Rudiment of the Central Nervous System

DEVELOPMENT

- developed from the cells of the neural crest & mesenchyme (mesoderm and neural crest) forming the primitive meninges
- differentiate into ectomeninx (outer more compact layer) & endomeninx (inner more reticulated layer)



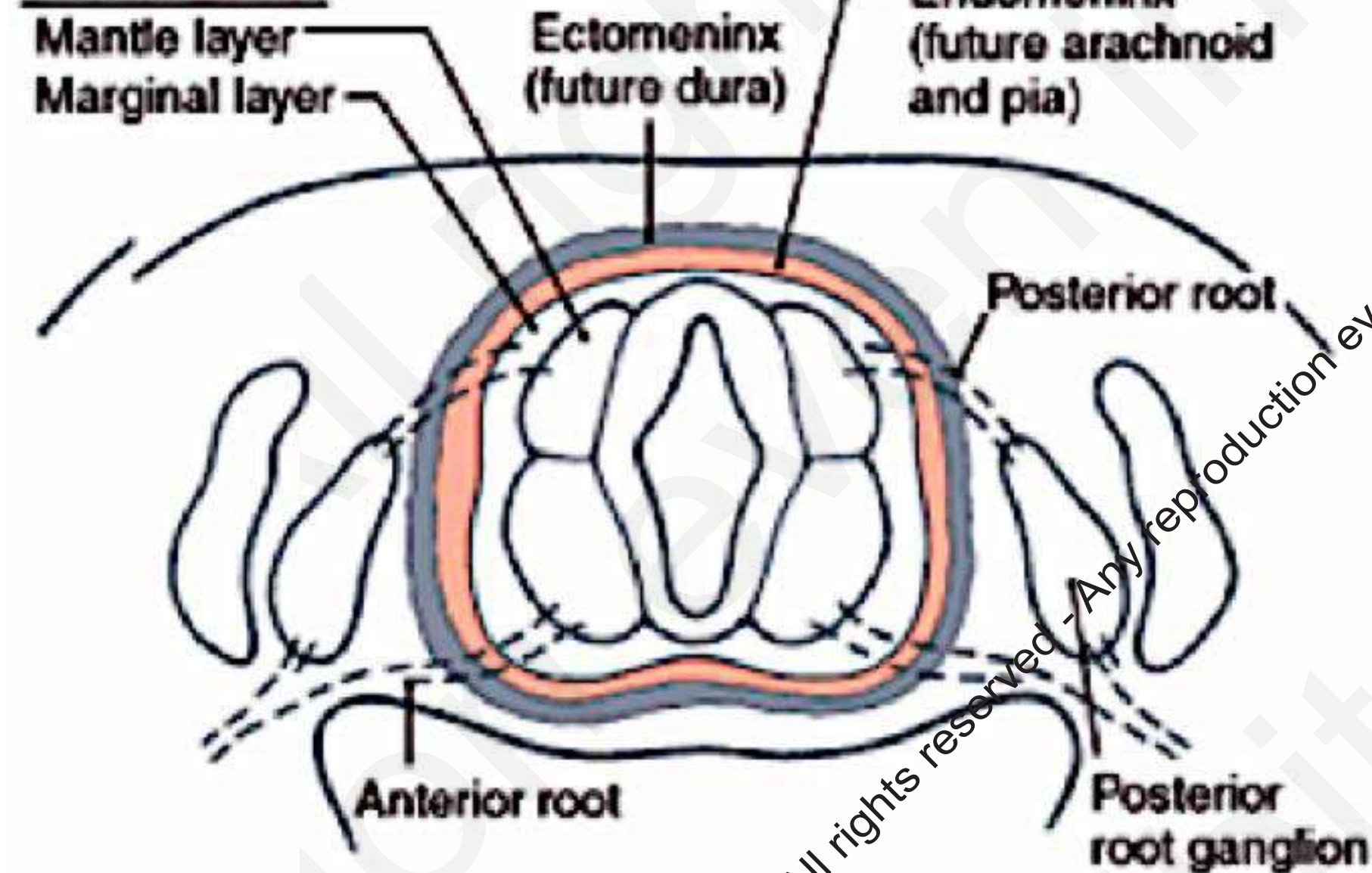
neural tube (NT). DLHP, dorsolateral hinge point; HM, head mesoderm; N, notochord; MHP, median hinge point; SE, surface ectoderm.



F, Transverse section showing a slightly later stage in neurulation than shown in E. Neural crest cells (NC) are beginning to form and emigrate from the fusing neural folds.

Larsen, W.J. Human Embryology 2009

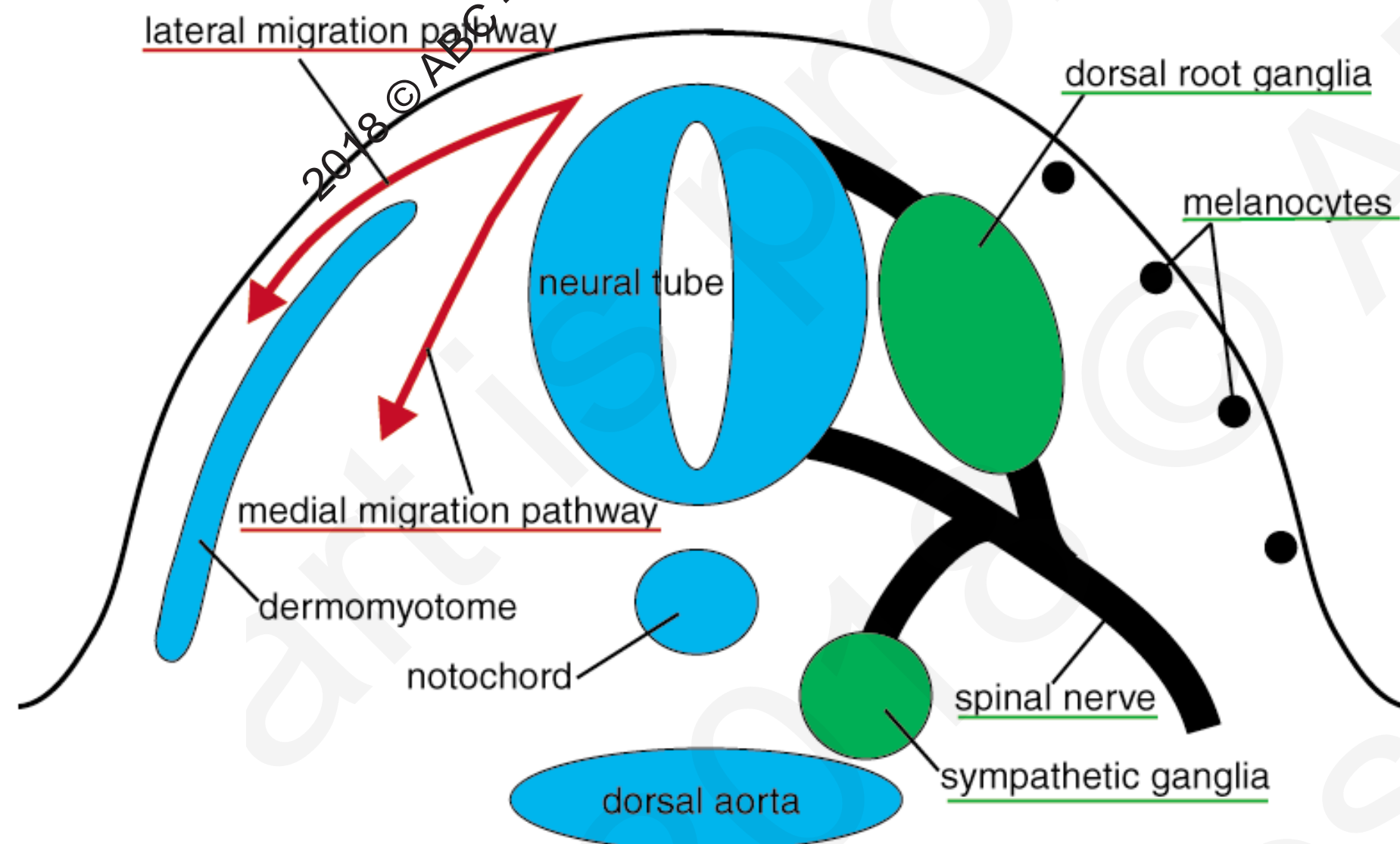
Neural tube



ectomeninx becomes more compact and with spaces (future sinuses)
dura mater (pachymeninx);

endomeninx becomes more reticulated with development of spaces (future SAS & cisterns) arachnoid & pia mater (leptomeninges)

neural crest migration pathways and crest-derived tissues



Period of organogenesis

Table 1. Stages of human embryonic developments

Weeks	Days	No. of somite	Carnegie stage	Selected external features
1	1-7	0	1	Fertilization
2	8-14	0	6	Primitive streak develops
3	15-21	0	7	Gastrulation commences and notochordal process forms
4	22-28	1-3	8	Primitive pit, neural plate, neural groove, neural folds form
		4-12	9	Somites begin to form
		13-20	10	Neural folds fuse, otic pits form
		21-29	11	Cranial neuropore closes. The first four somites are beginning to be incorporate into the occipital segmentation. Oropharyngeal membrane rupture, optic vesicles develop, optic pits begin to form
5	29-35	>30	12	Caudal neuropore closes. Pharyngeal arches 3 and 4 form
6	36-42	>30	13	Otic vesicles form. The meninx primitiva is first seen as the first signs of the cranial vault. Occipital sclerotomal mesenchyme concentrates around the notochord
			14	Cerebral hemispheres become visible
			15	Sensory and parasympathetic cranial nerve ganglia begin to form
			16	The skull has a membranous roof present during stage 16
7	43-49	>30	17	Cerebellum begins to form. Conversion of the ectomeninx mesenchyme into cartilage starts on 40-41 days. Pia mater is present around the brain
			18	Skeletal ossification begins
			20	The first indication of dura mater is found in the skull. Chondrification continues until stage 20
8	50-56	>30	21-23	By the end of 2nd month (57 days) the endomeninx covers significant portion of the brain and has develop into the arachnoid and the pia mater. Dural reflections begin to form

Timing of some events and stage can vary by up to 4-5 days during stages 10-23



Comparative anatomy of the meninges.

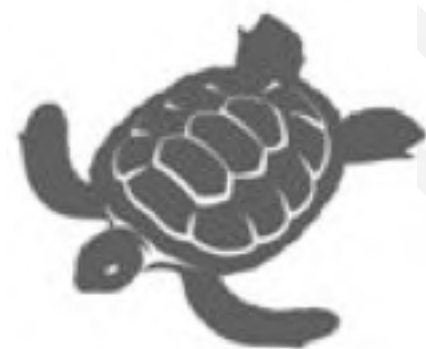
In fishes, only a single layer, the primitive meninx, is present.

Amphibians and reptiles have two meningeal layers, an outer dura mater (meaning "hard mother") and an inner thin layer, the secondary meninx.

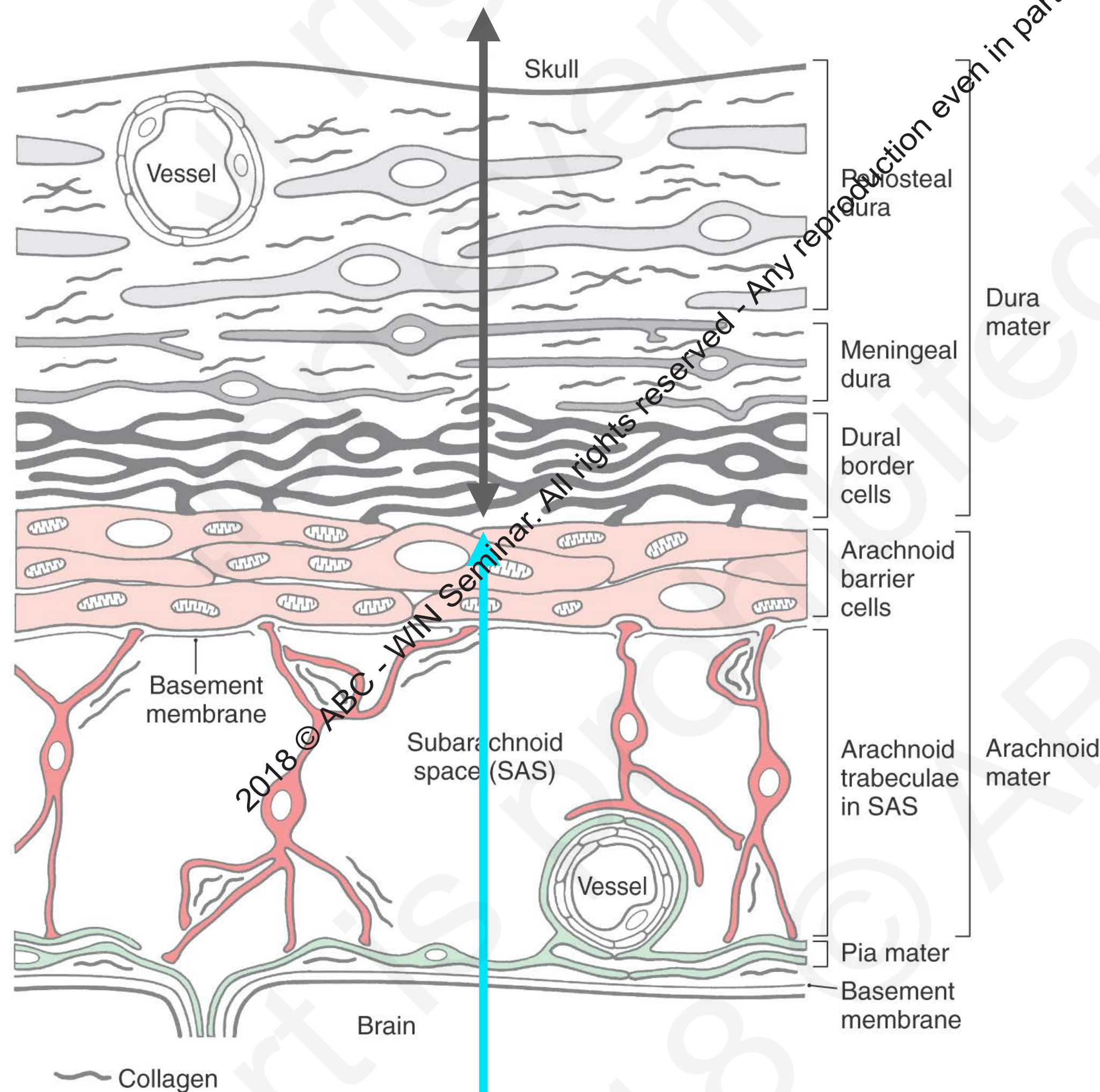
In reptiles, the dura mater is fairly well separated from the underlying arachnoid and pia mater.

In mammals and birds, three meningeal layers are present.

The layer closest to the brain is a thin layer called the pia mater (meaning "tender mother"). The middle layer is a thin, avascular layer called the arachnoid due to its spider web-like appearance. The space between the pia mater and the arachnoid is the subarachnoid space.

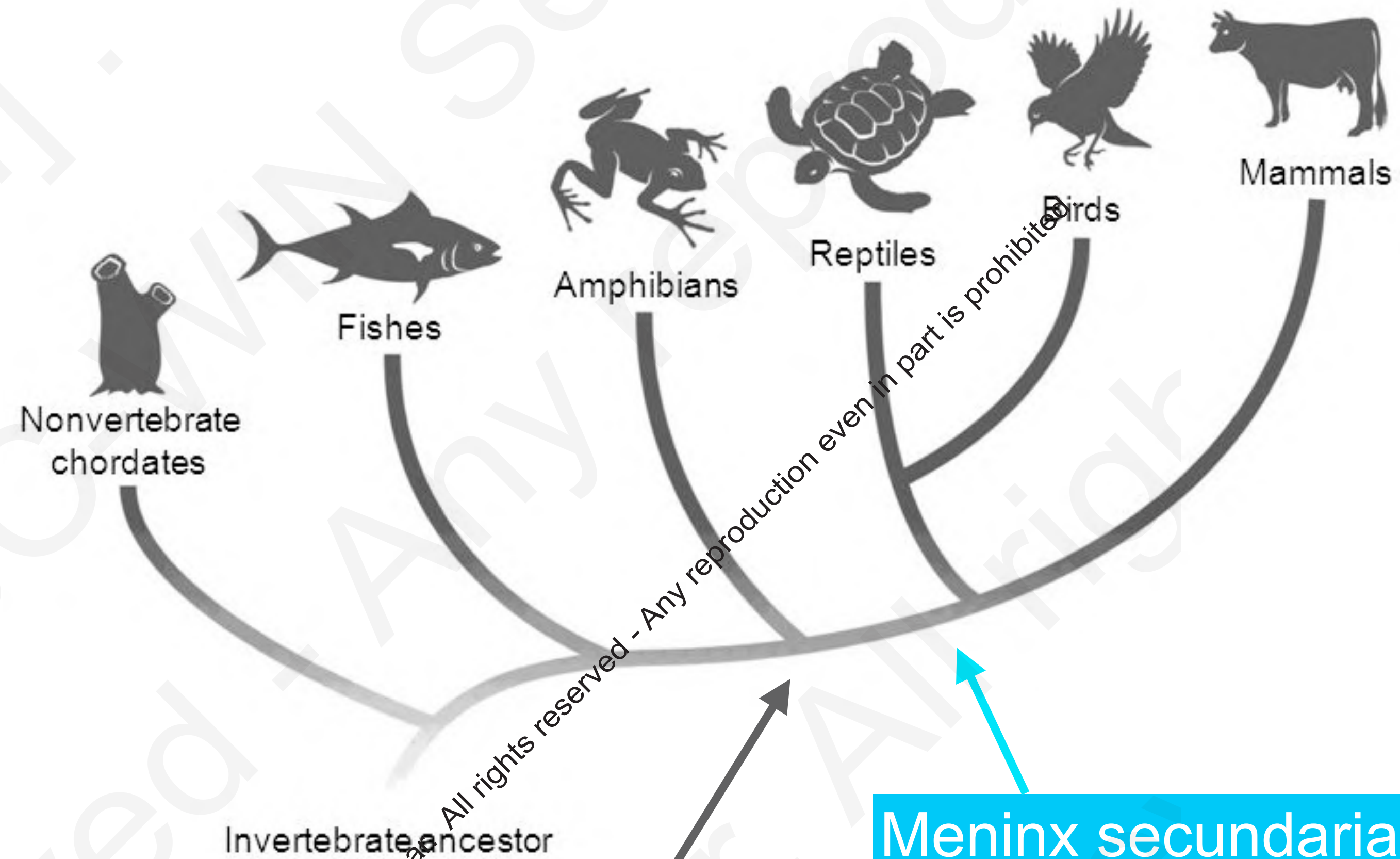


Meninx primitiva (Periosteal dura and meningeal dura)



Meninx secundaria arachnoid space and pia mater

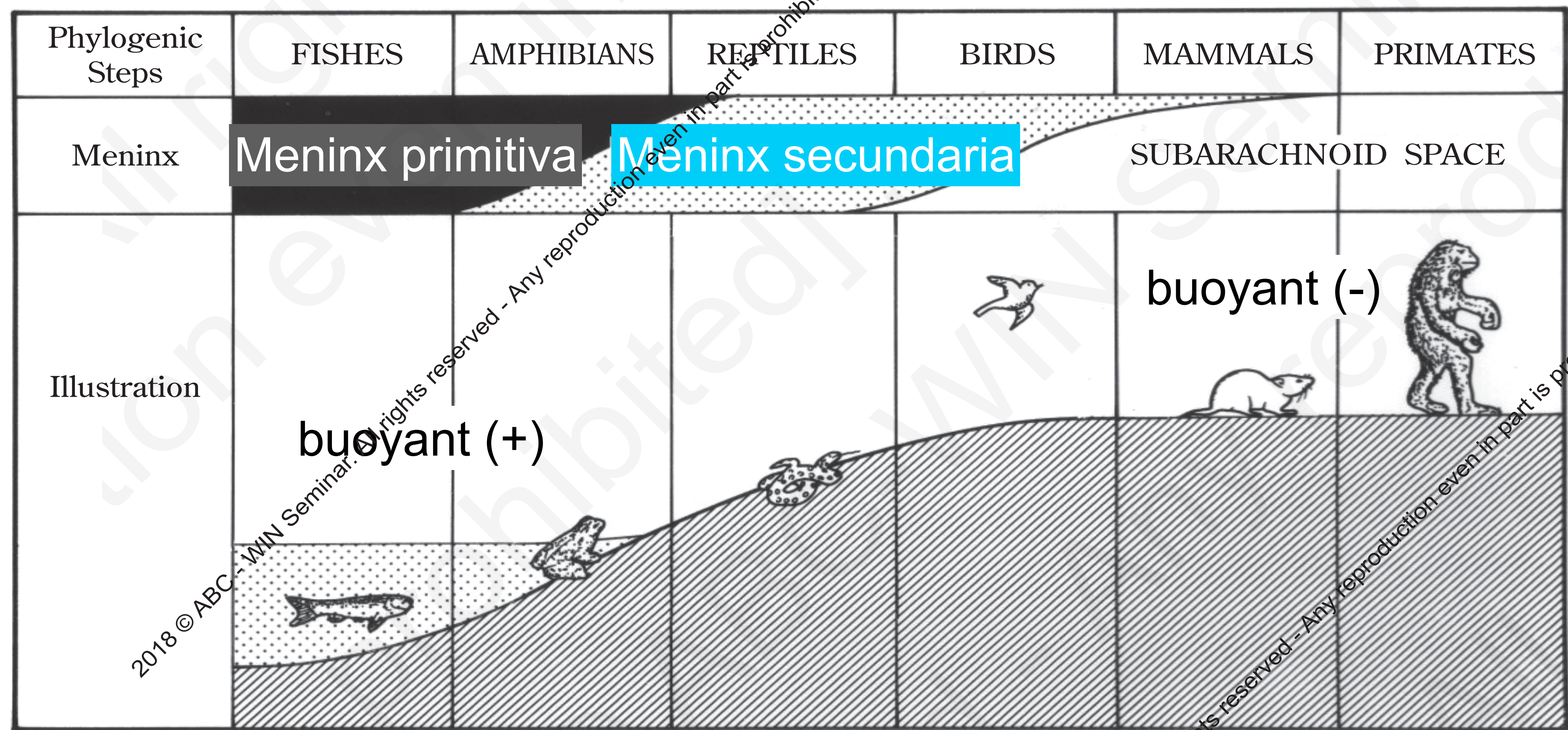
Comparative anatomy of the meninges

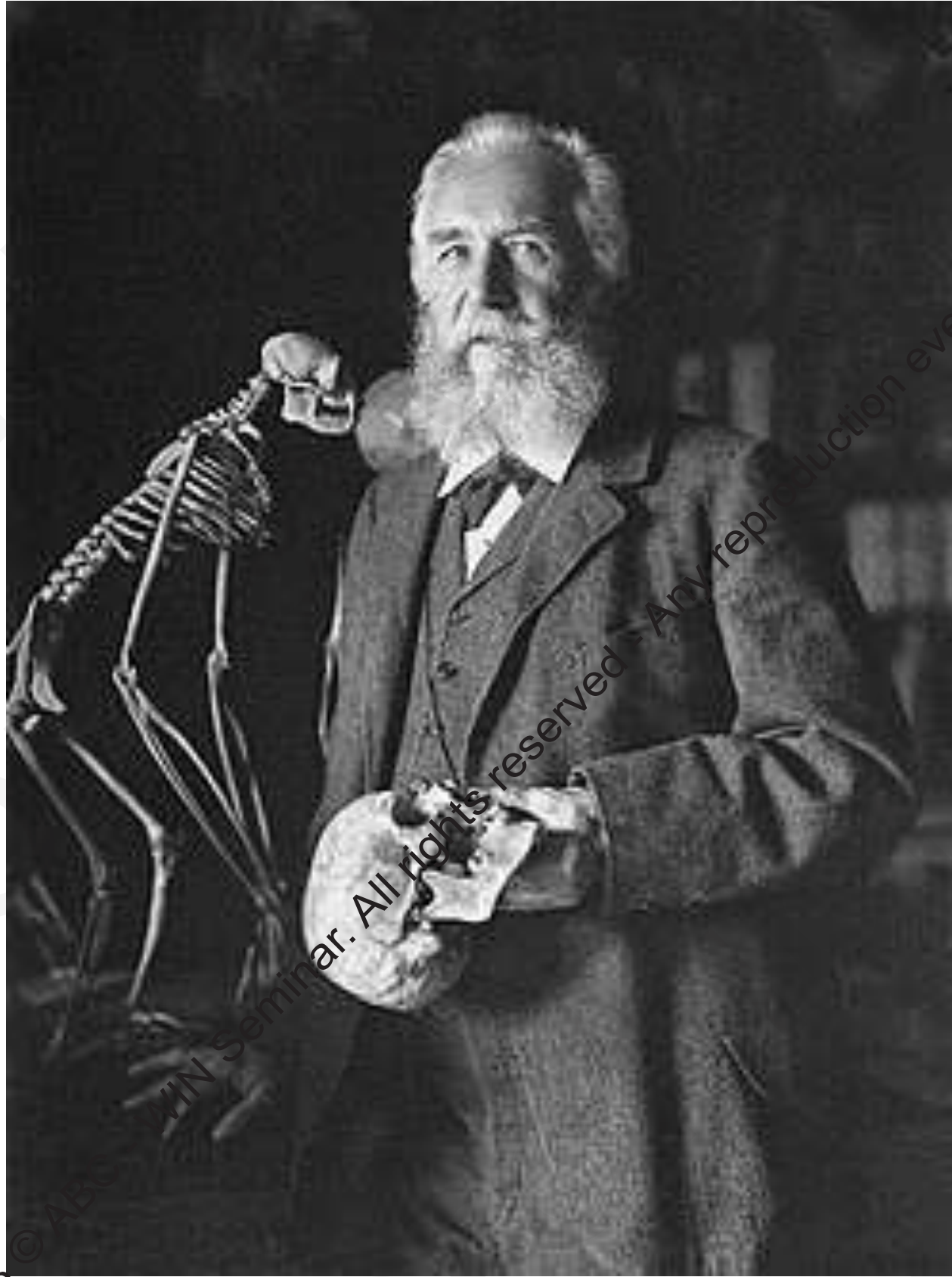


Meninx primitiva

Meninx secundaria

Phylogeny of meninx



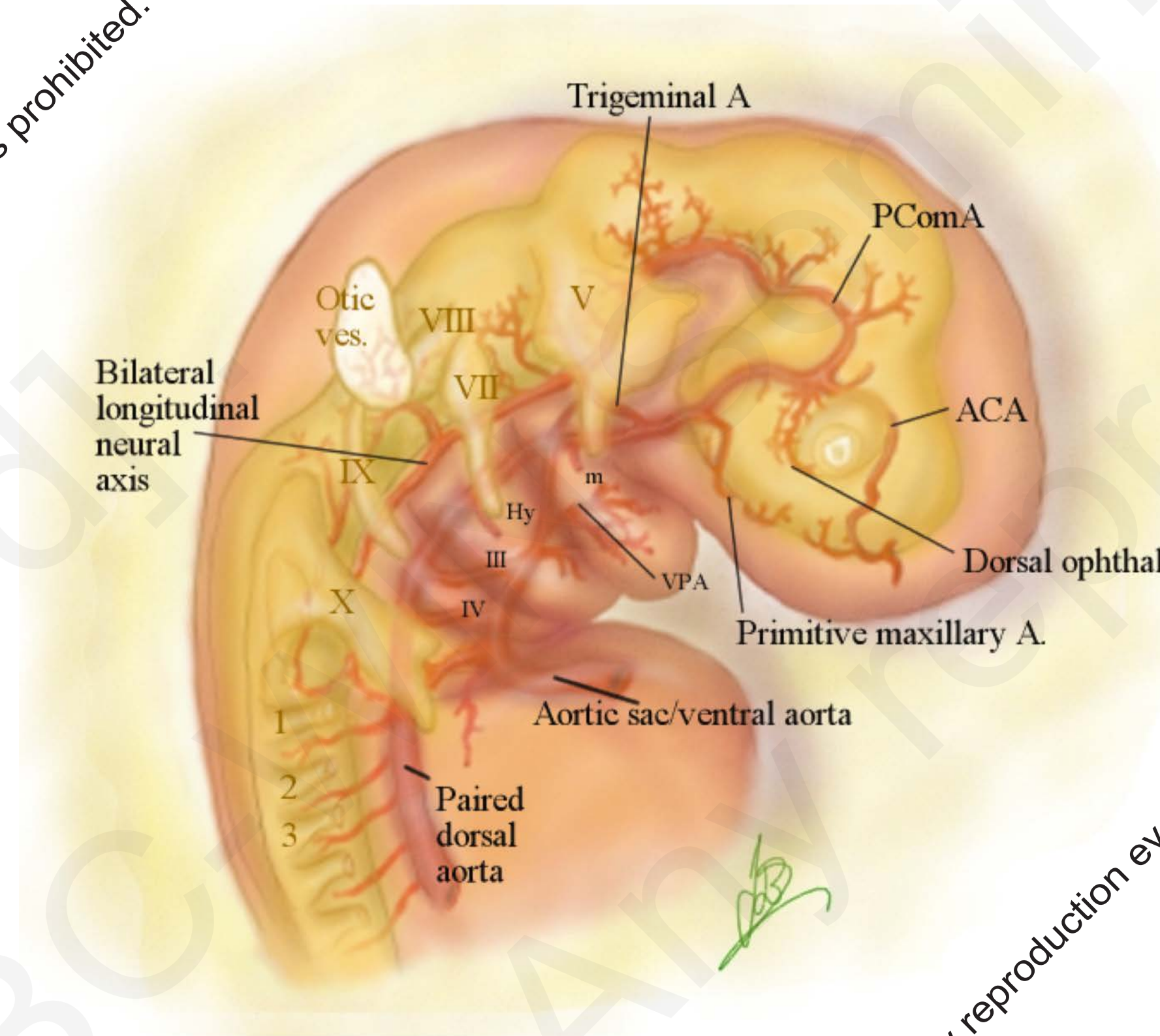


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Prof. Ernst Haeckel (1834 - 1919)

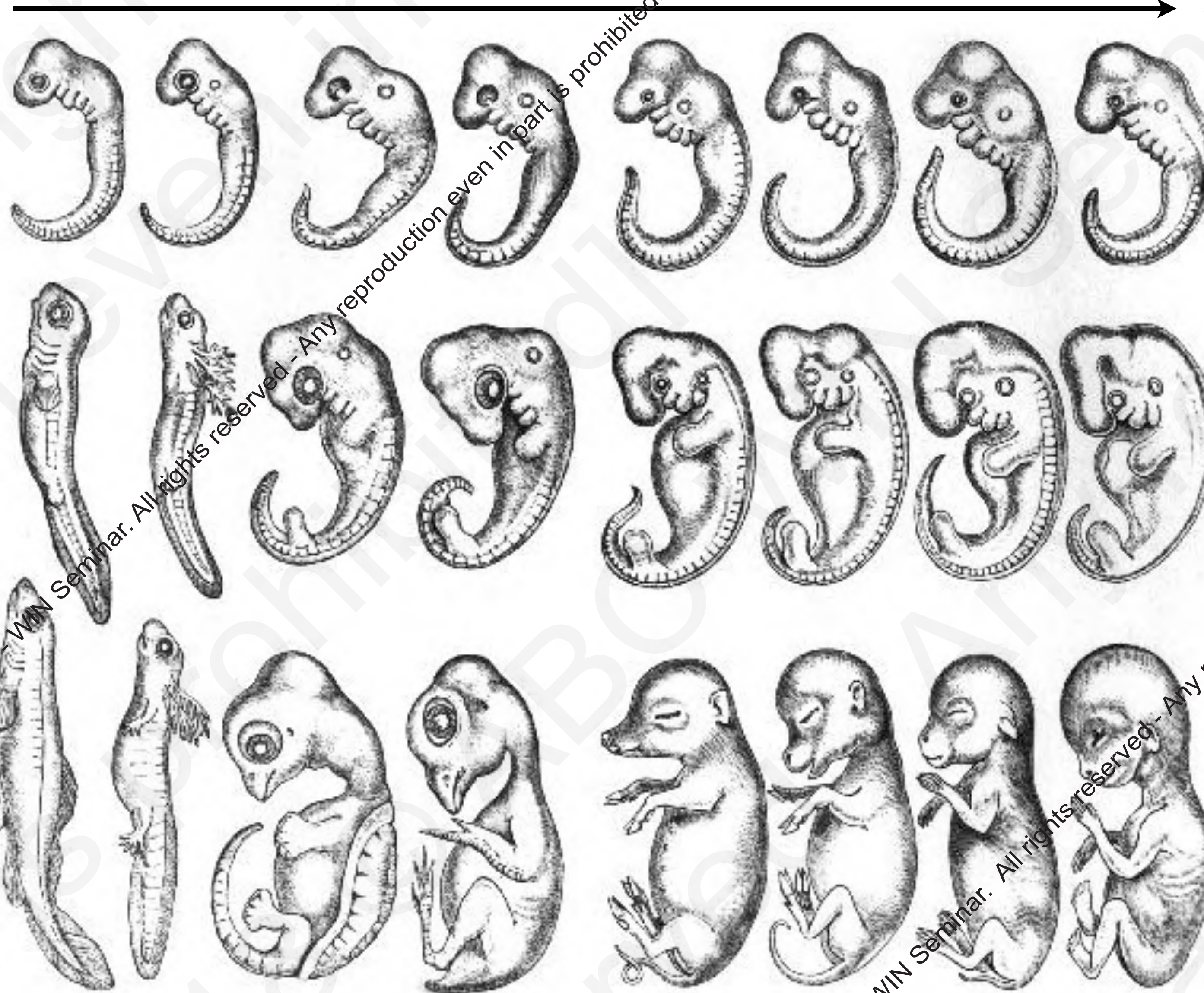
“Die Ontogenesis ist eine kurze und schnelle Rekapitulation der Phylogenesis”

“ Ontogeny recapitulates phylogeny ”



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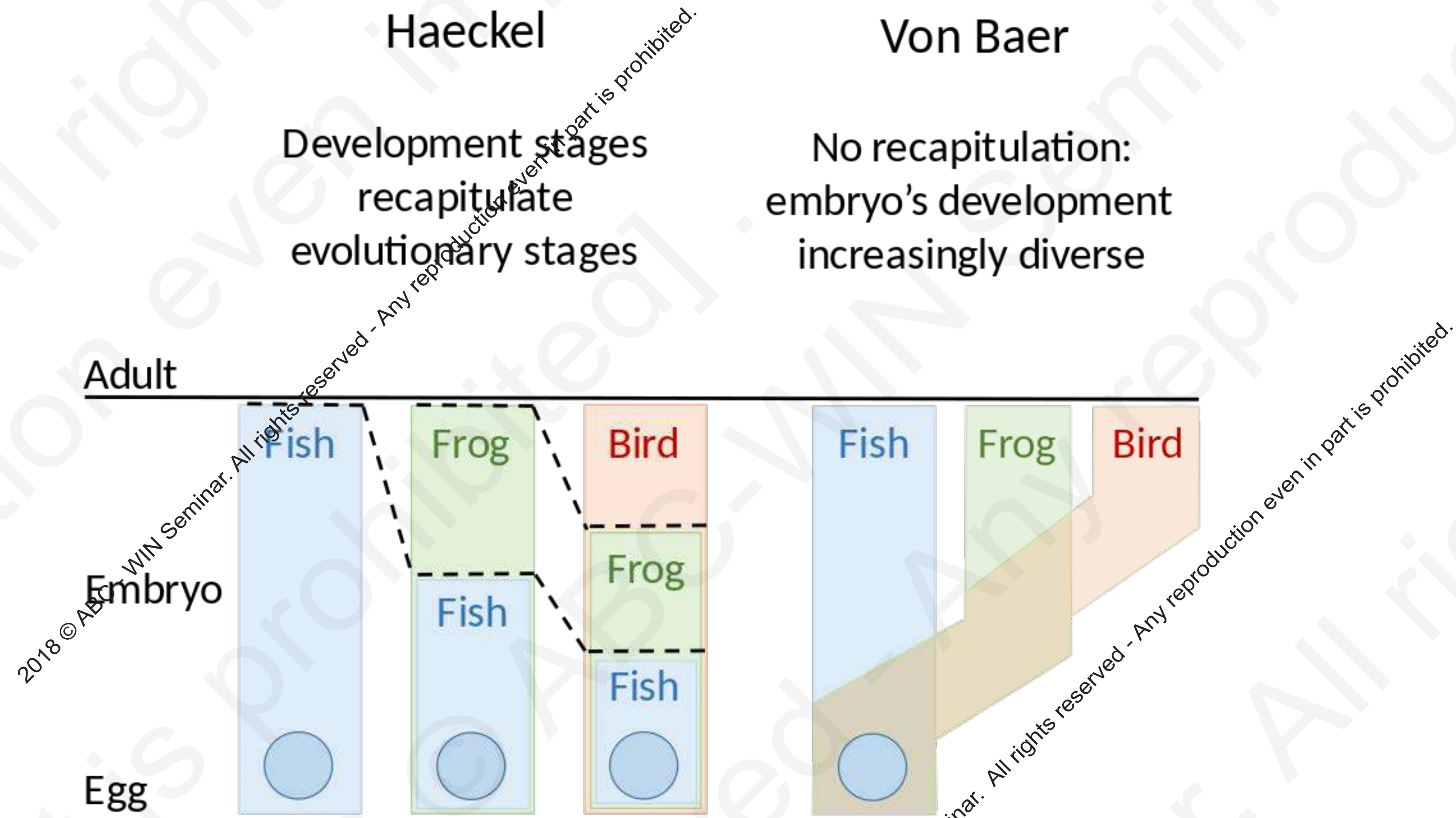
Phylogeny



Ontogeny

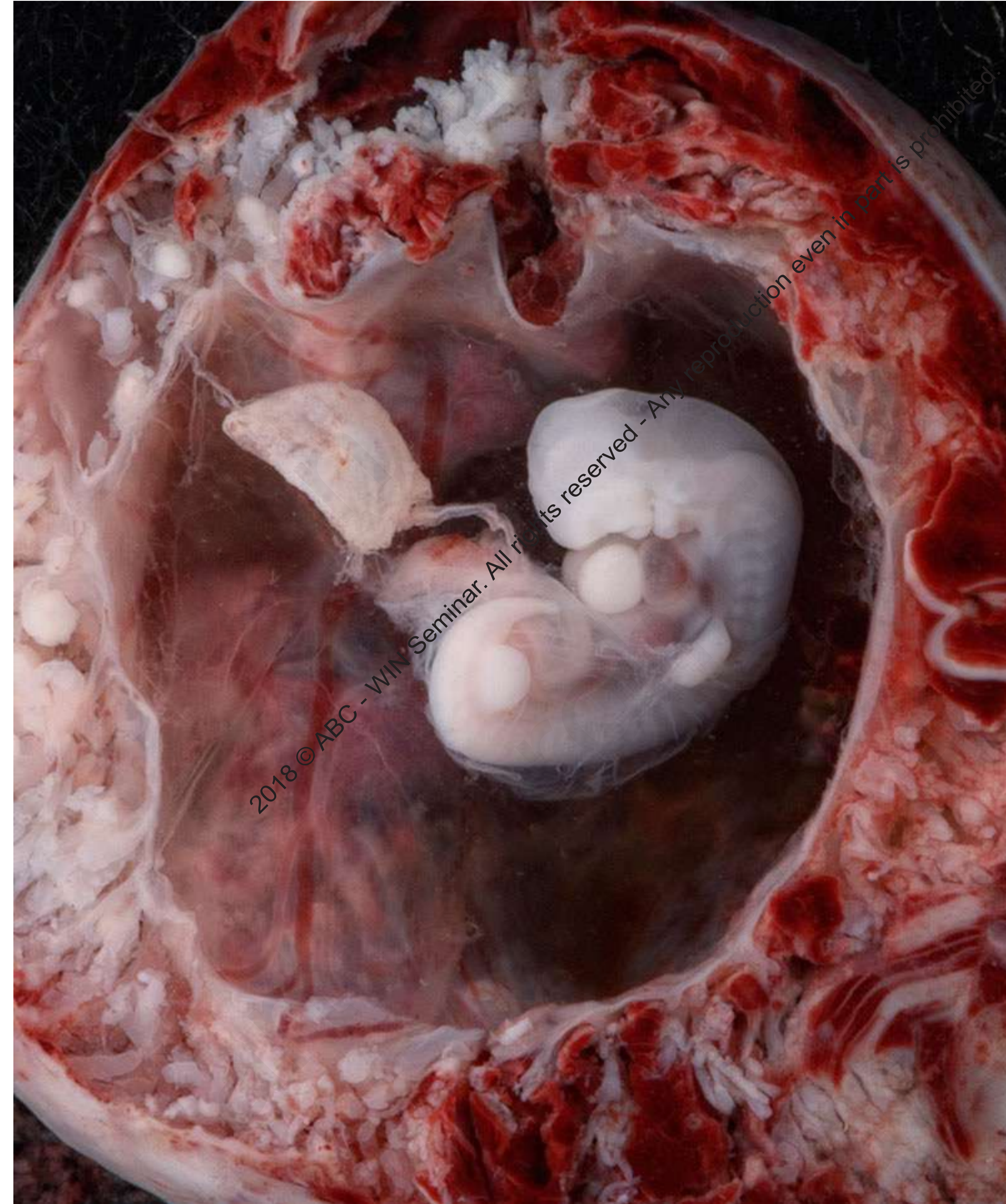
Fish Amphibian Reptile Bird

Mammalian



The Haeckelian form of recapitulation theory is considered defunct. However, embryos do undergo a period where their morphology is strongly shaped by their phylogenetic position, rather than selective pressures

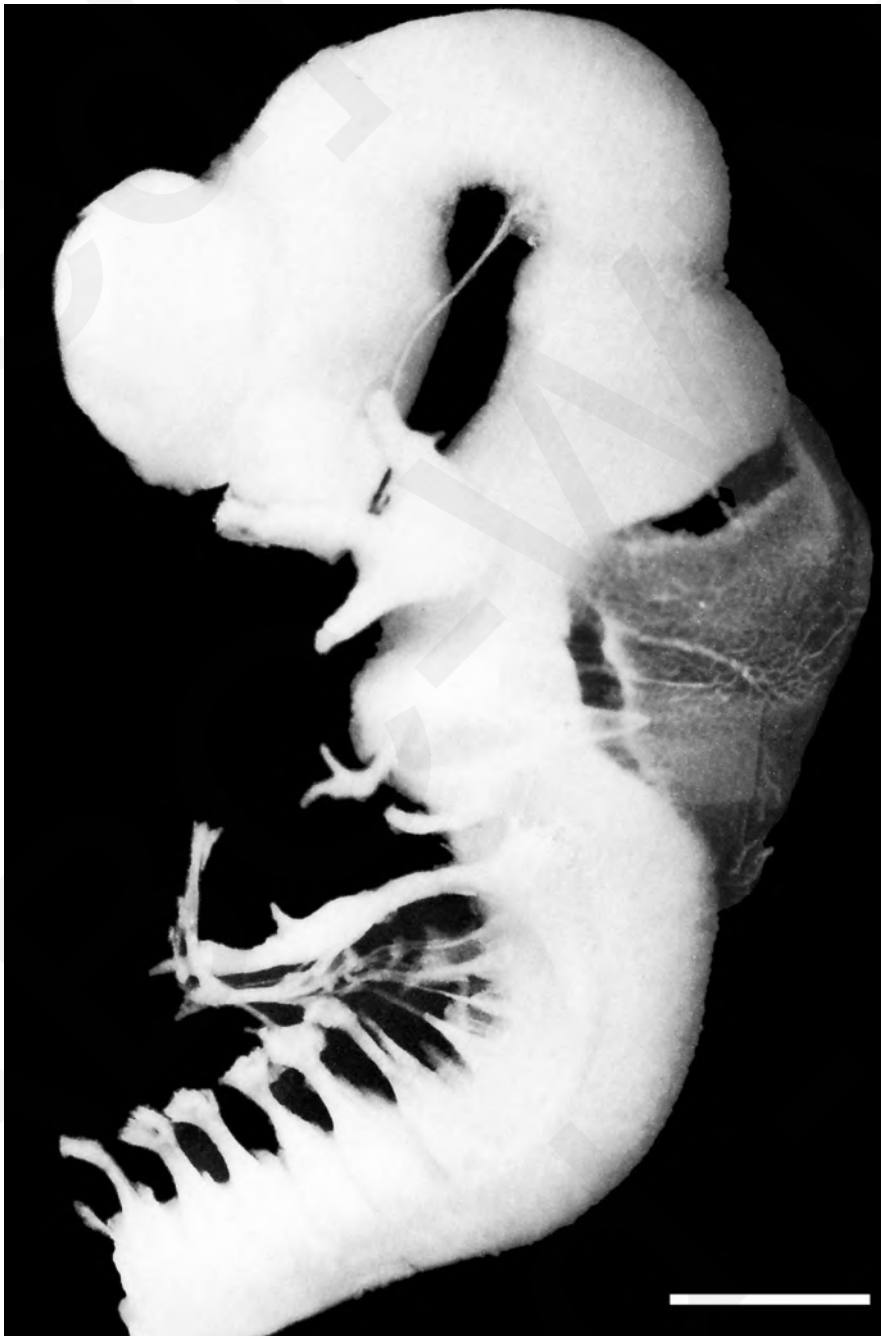
Carnegie stage 14 Week 5



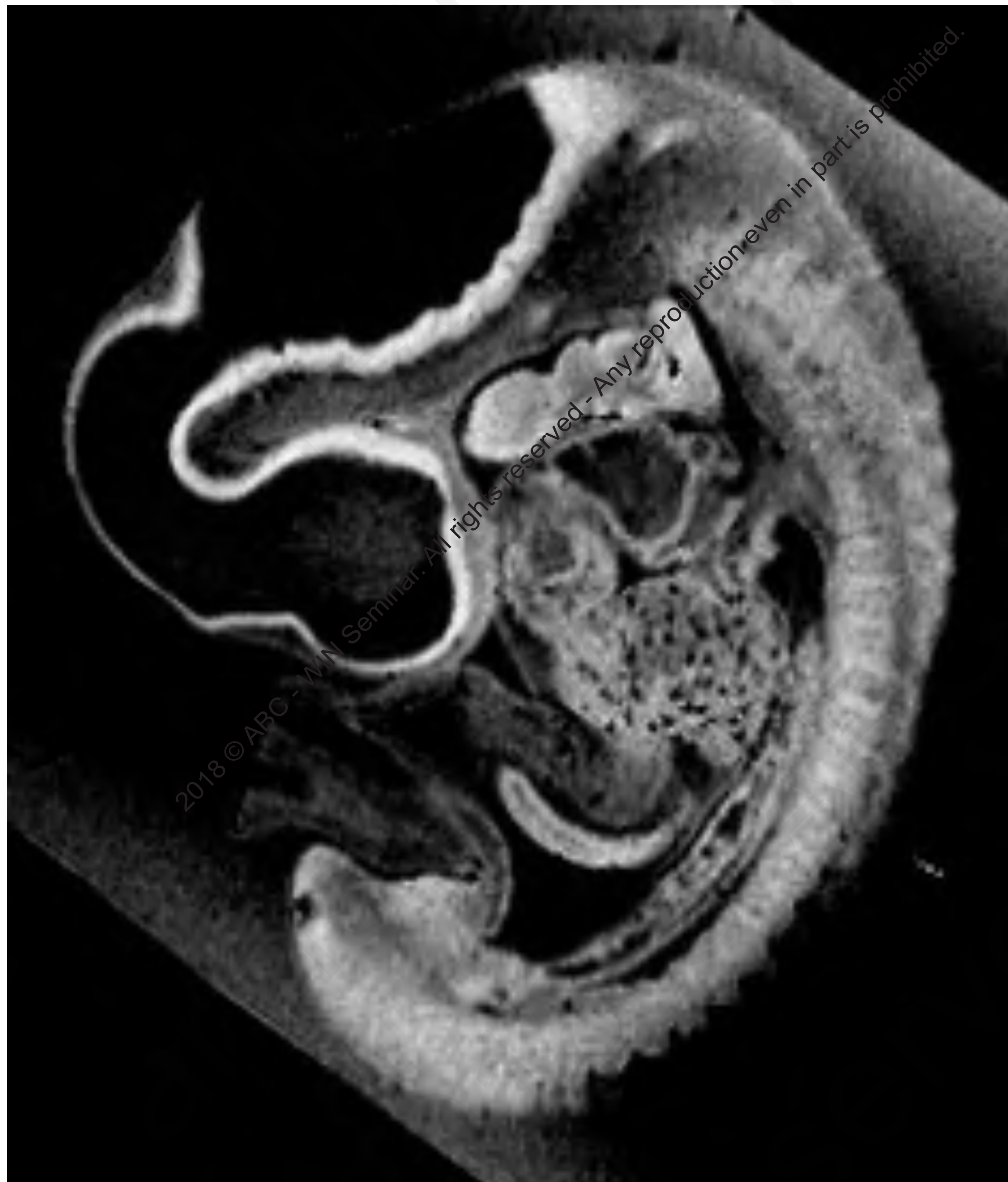
Placental blood vessels are visible extending lower left from umbilicus.



Week 4



Week 8



MRI sagittal scan @4 week embryo

Development of the vision and hearing sensory vesicles (optic and otic) and their relative positions (optic at the diencephalon; otic at the metencephalon).

The lamina terminalis at the end of the neural tube (site of cranial/anterior neuropore closure).

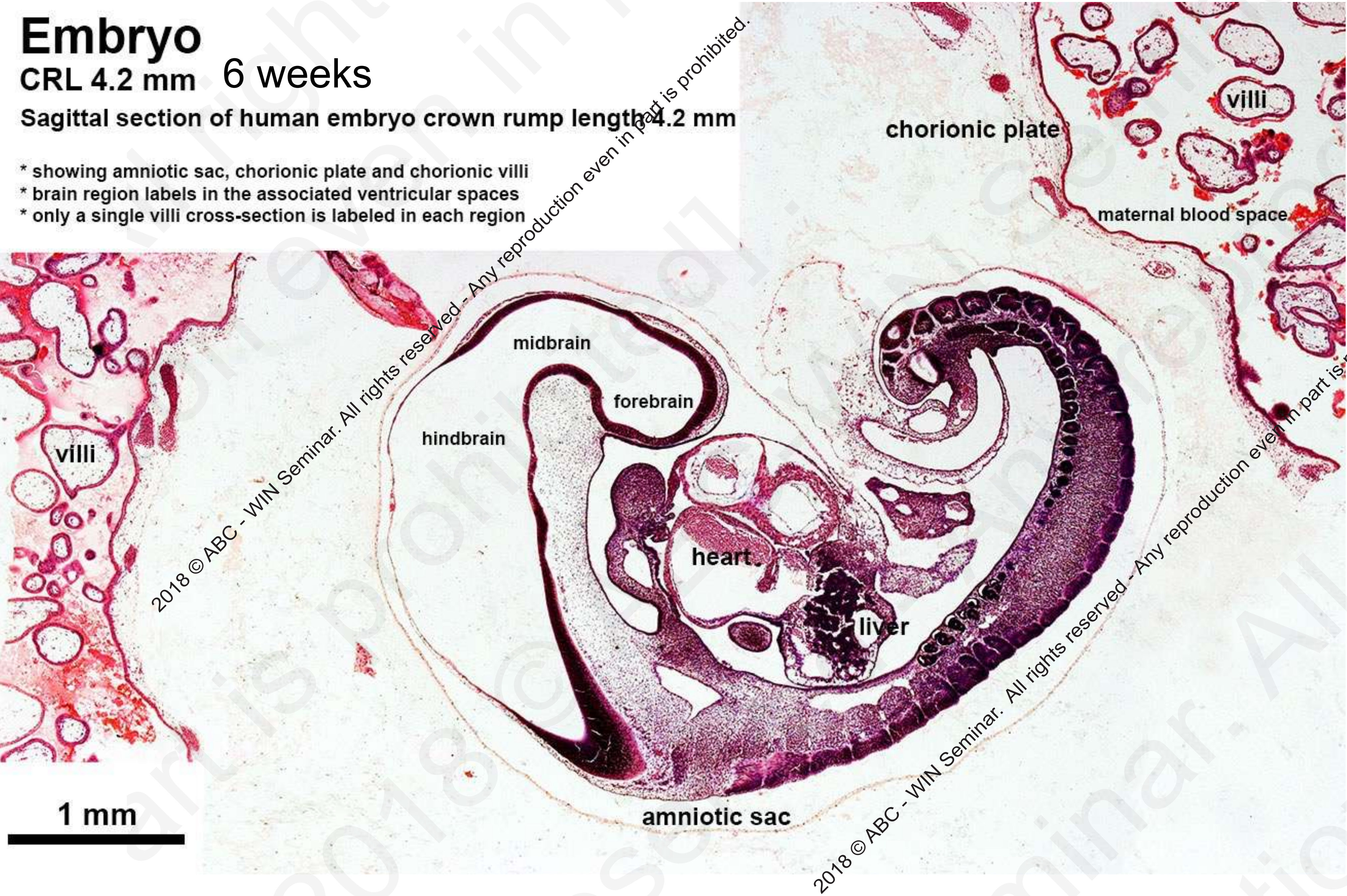
Meninx primitiva becomes visible, but meninx secundaria has not come yet.

Embryo

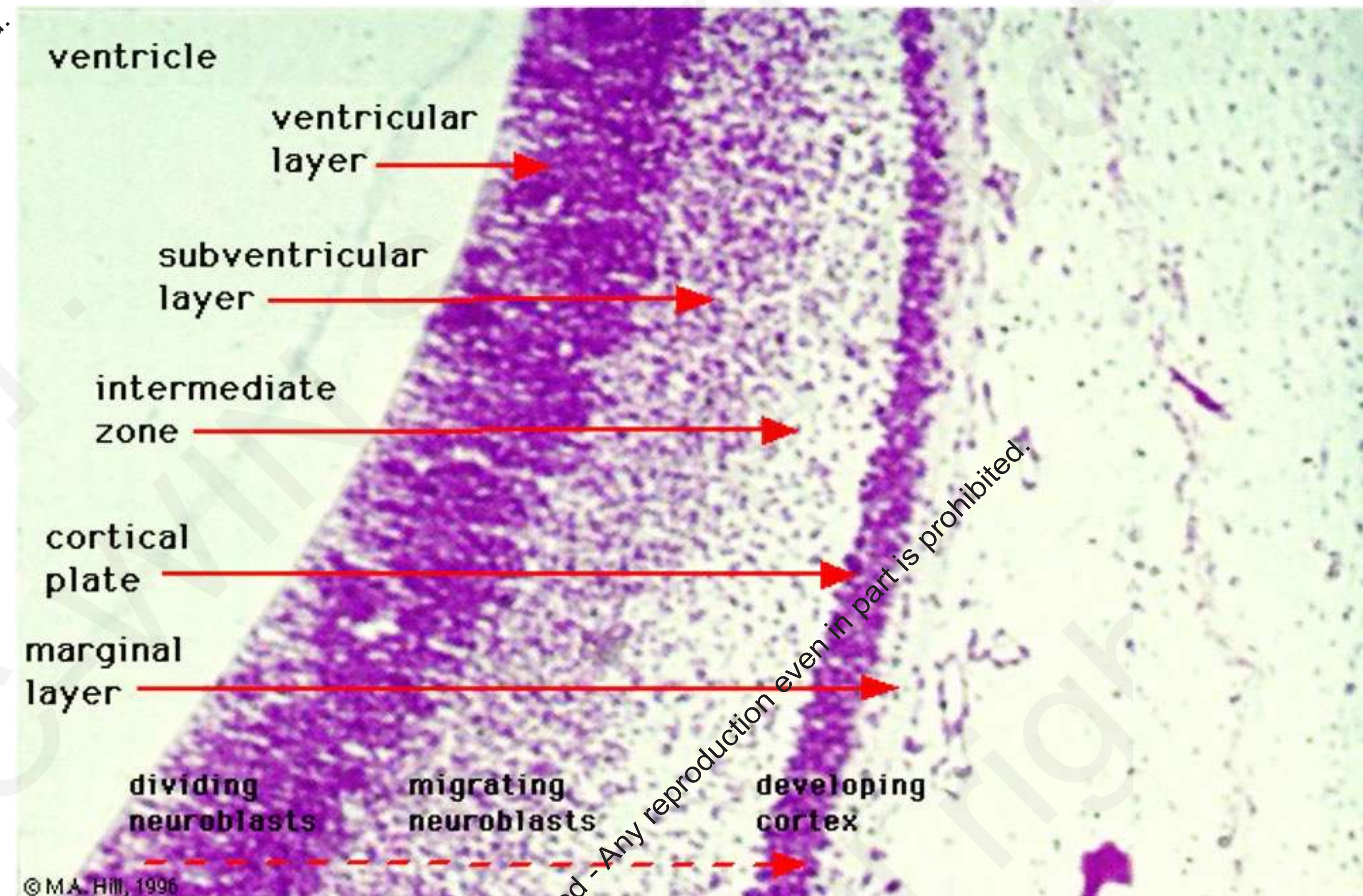
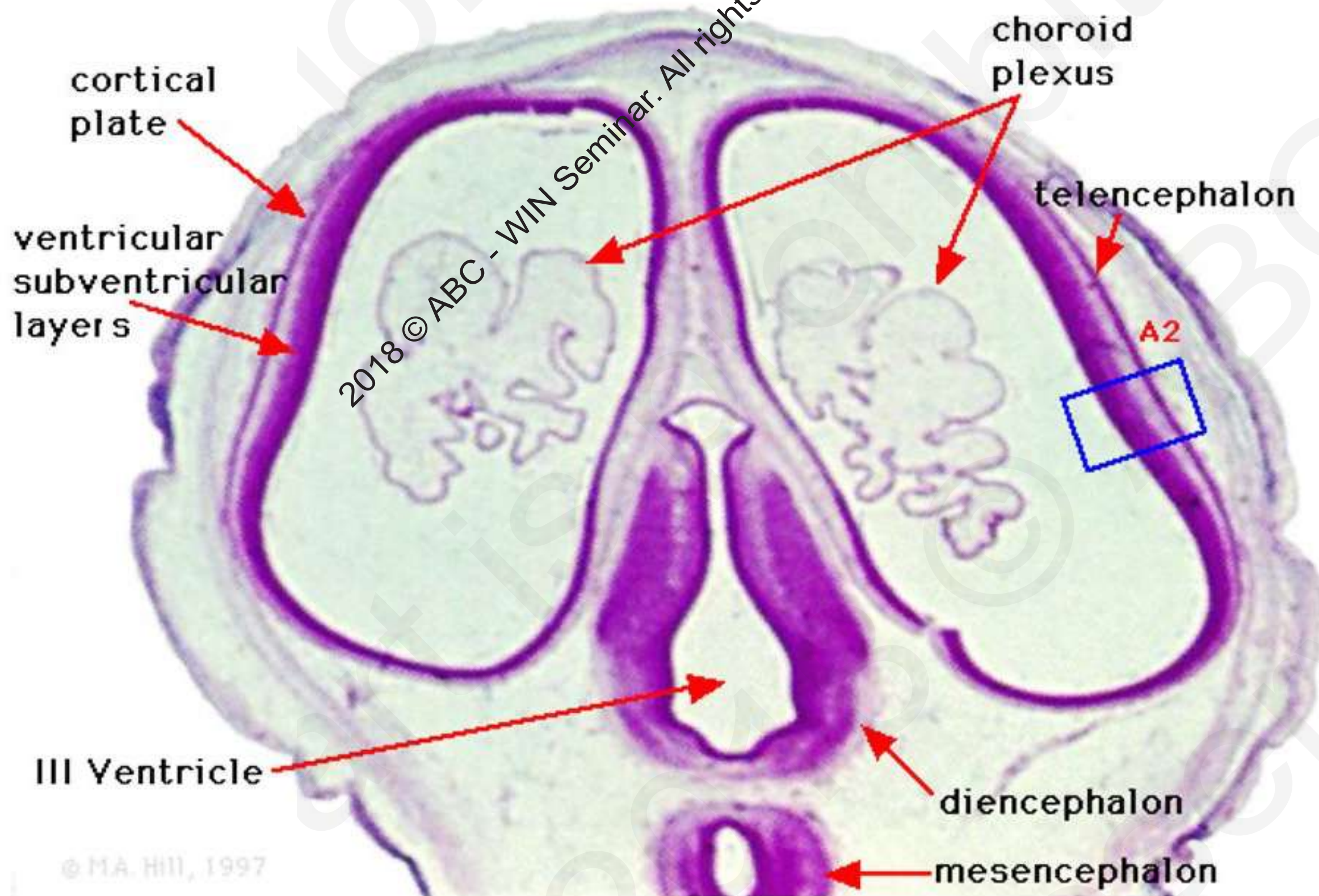
CRL 4.2 mm 6 weeks

Sagittal section of human embryo crown rump length 4.2 mm

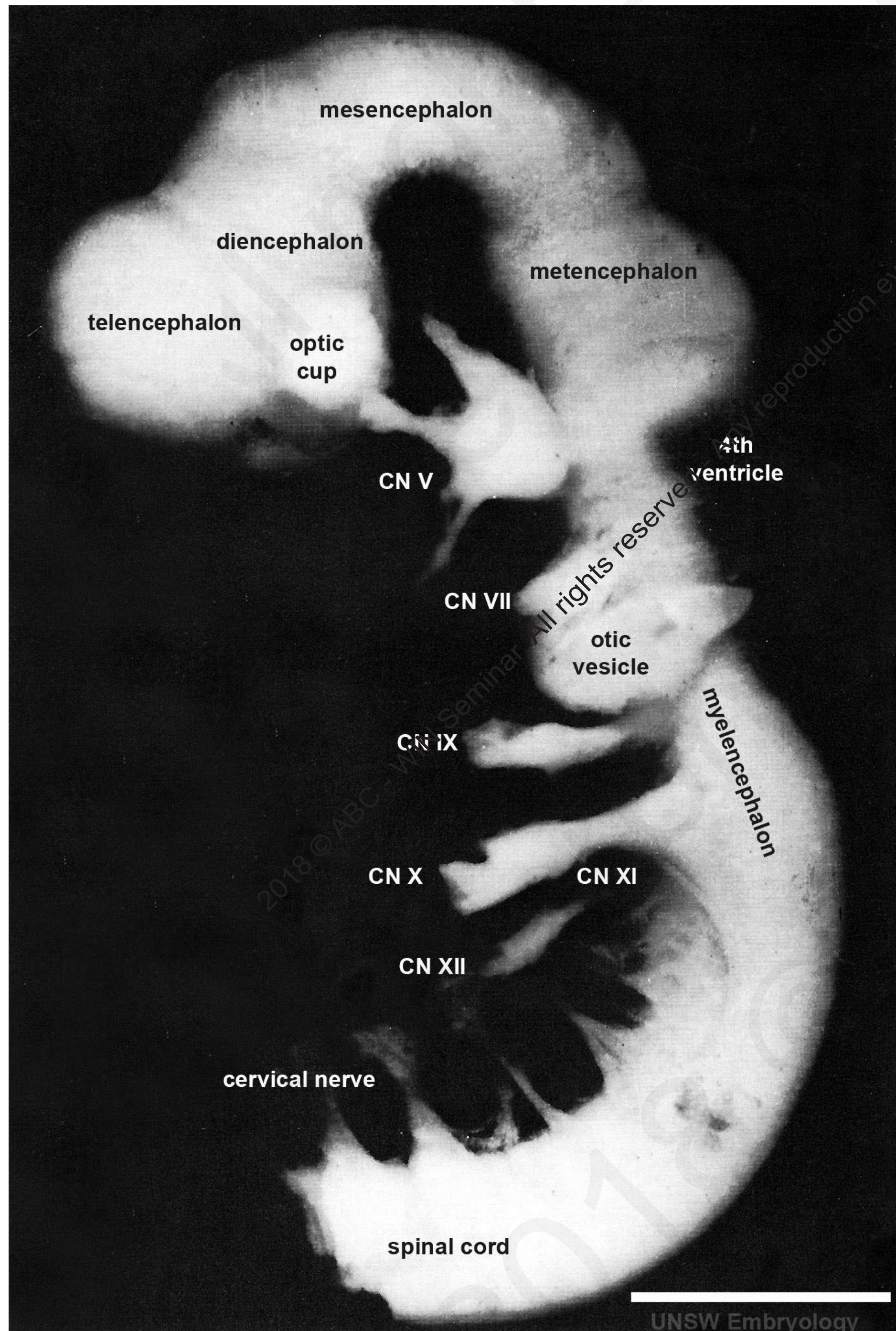
- * showing amniotic sac, chorionic plate and chorionic villi
- * brain region labels in the associated ventricular spaces
- * only a single villi cross-section is labeled in each region



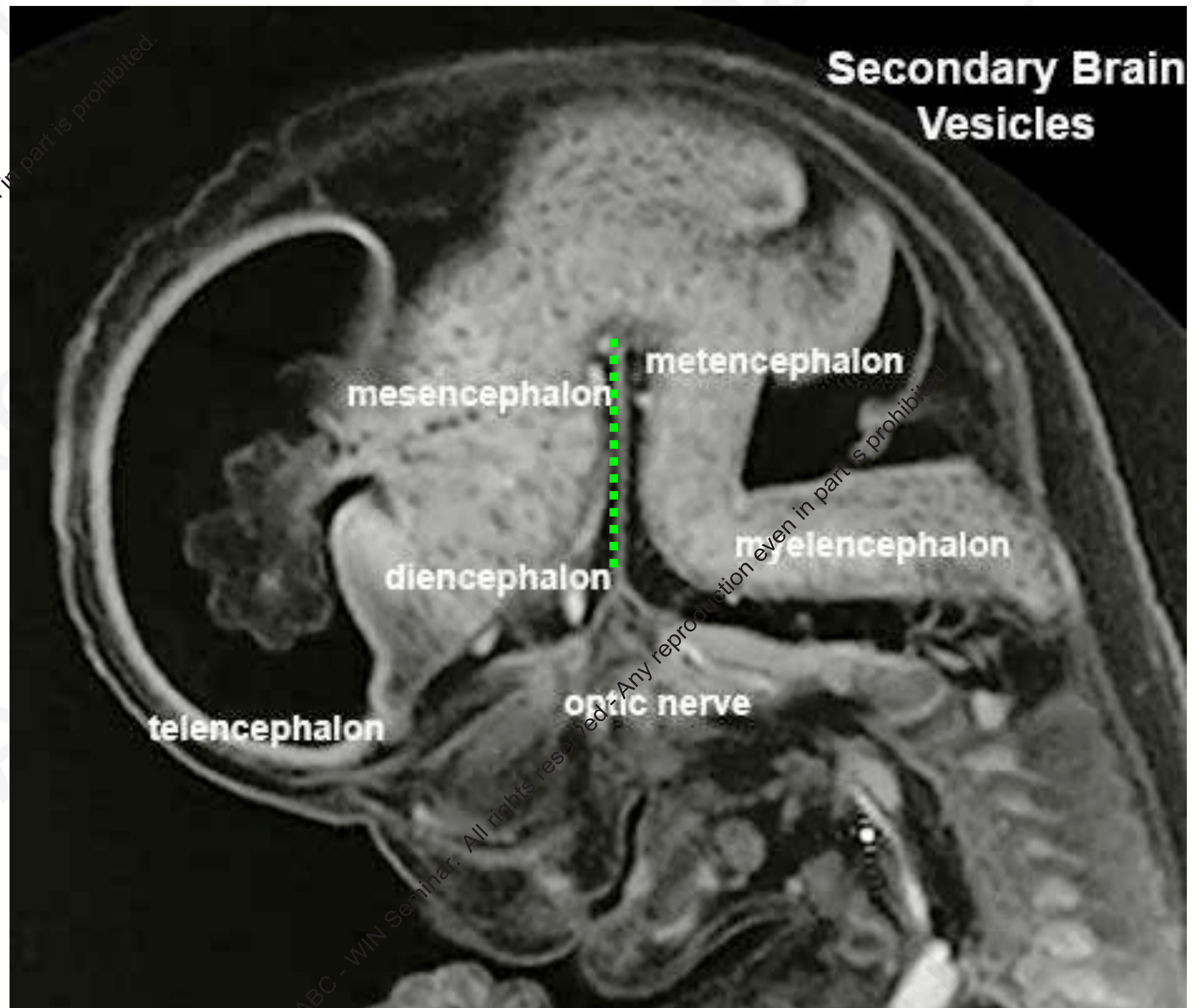
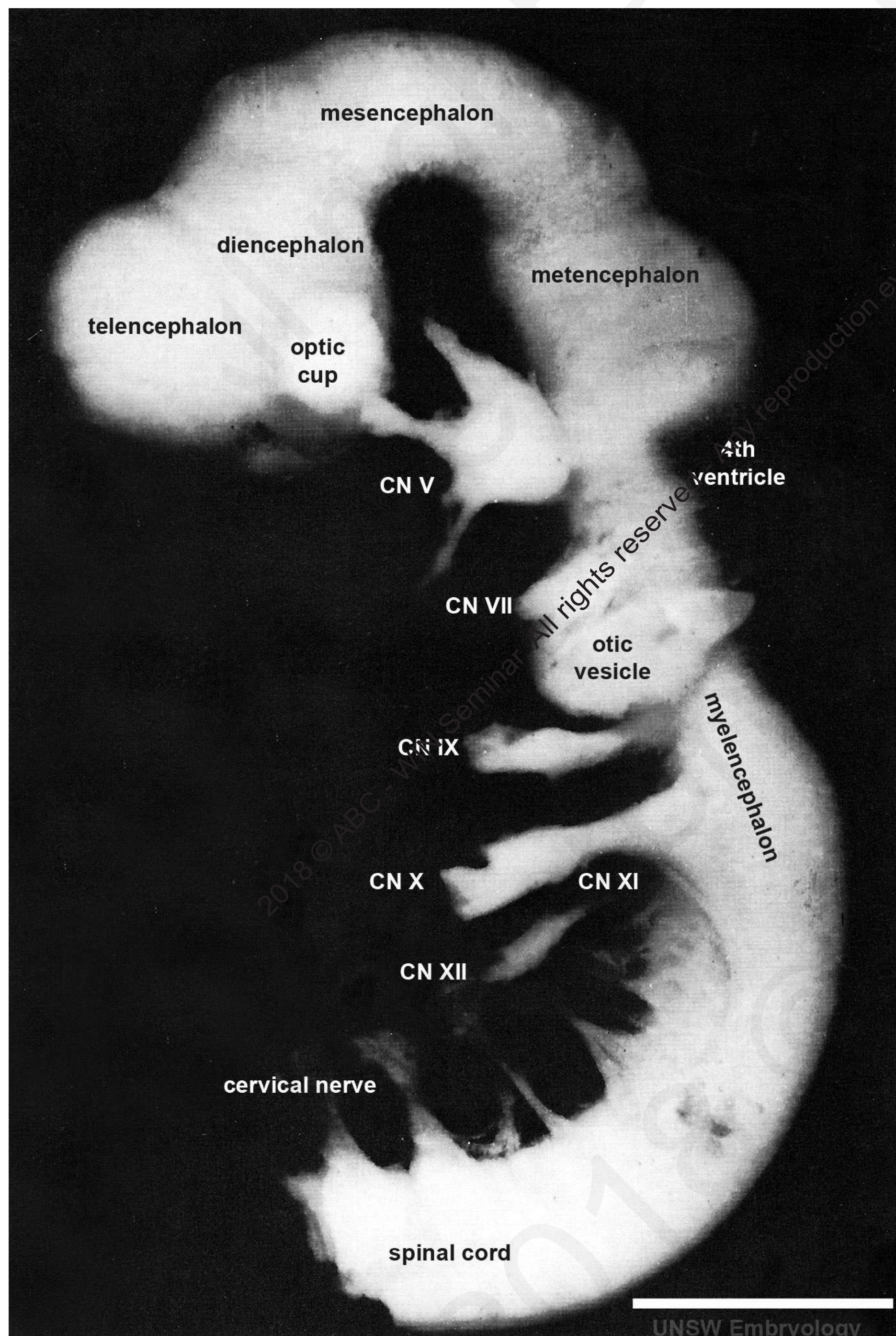
Human embryo is 27 mm (CRL) in size and approximately equal to day 54 - 56 of development (week 8)



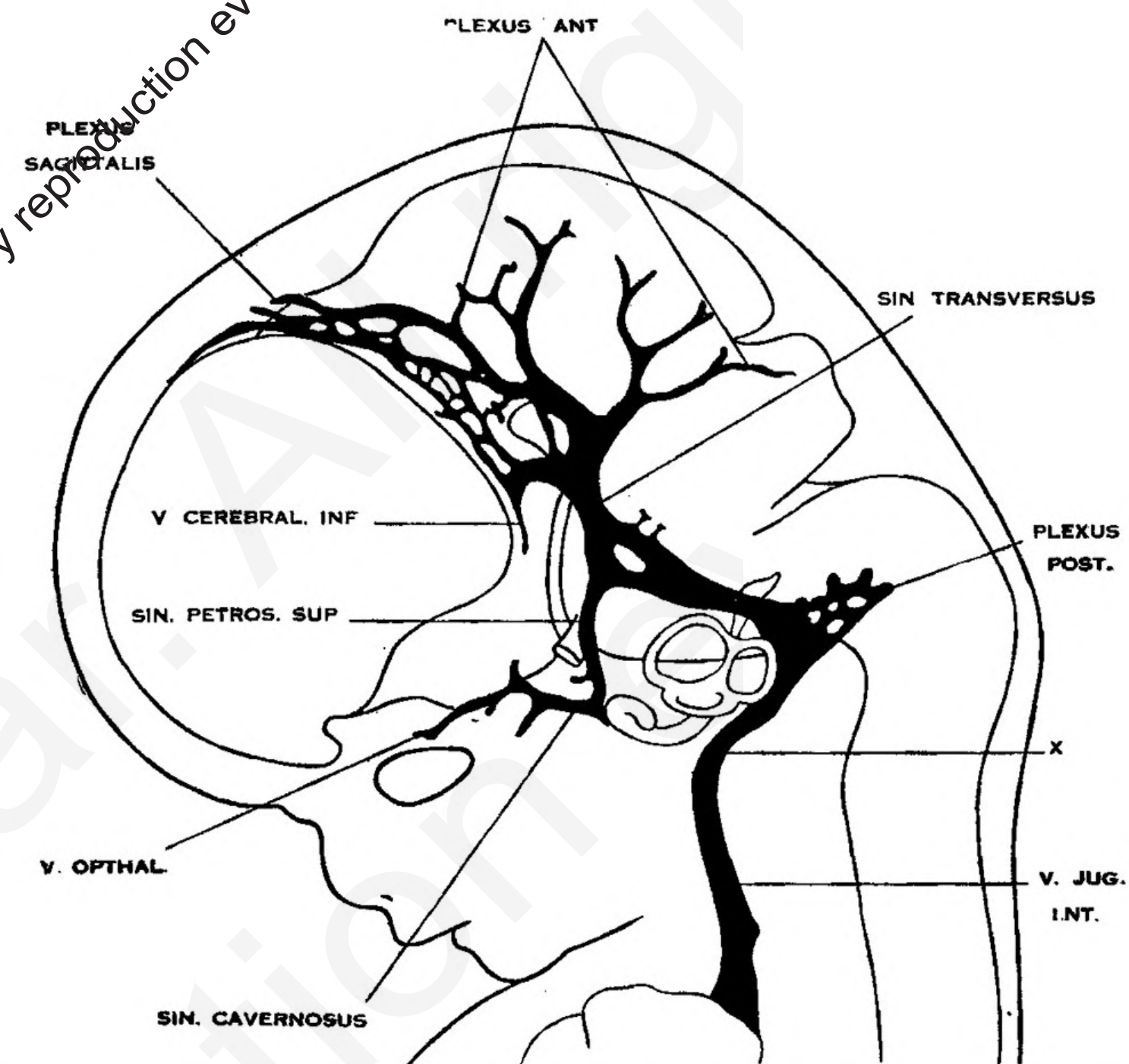
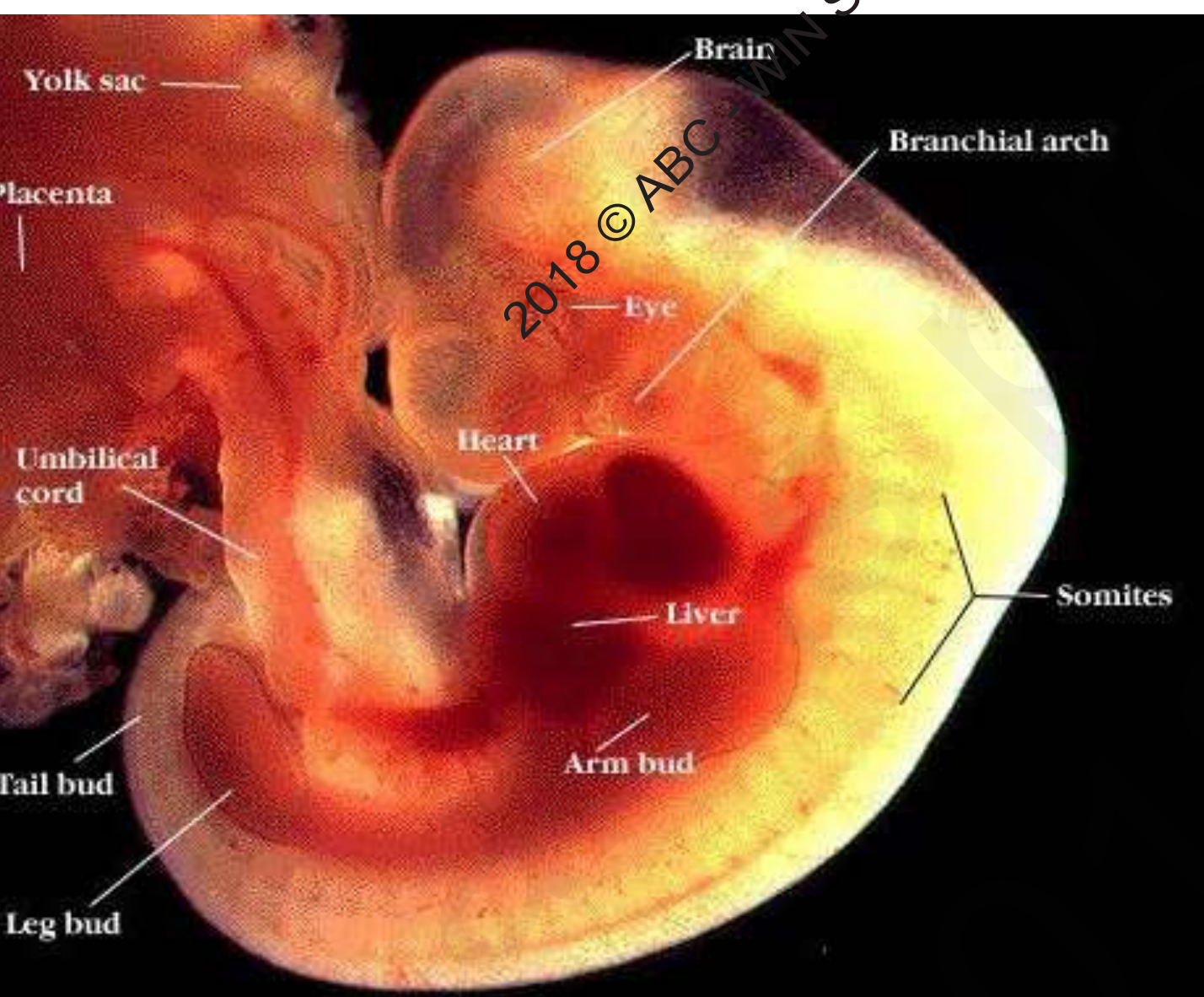
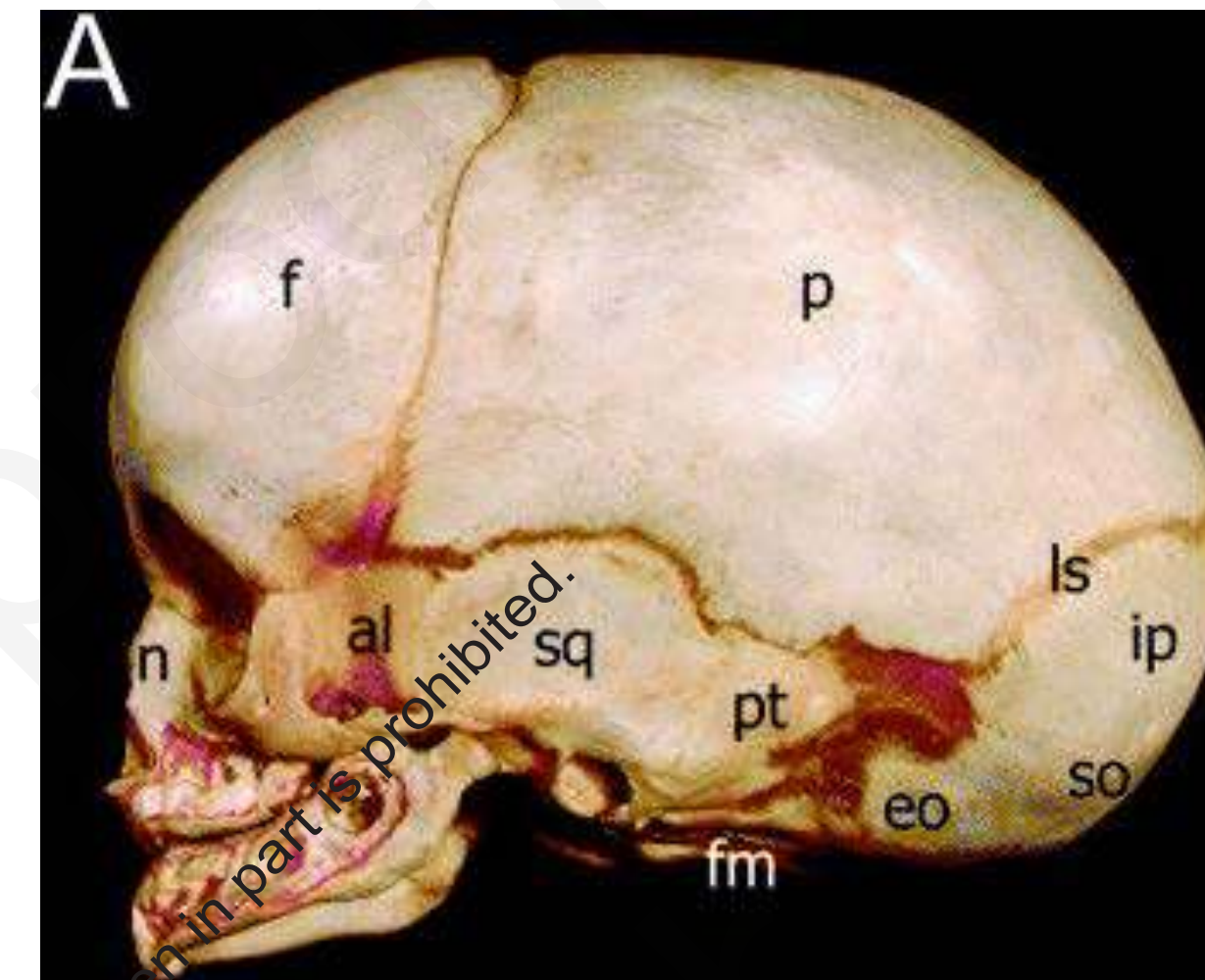
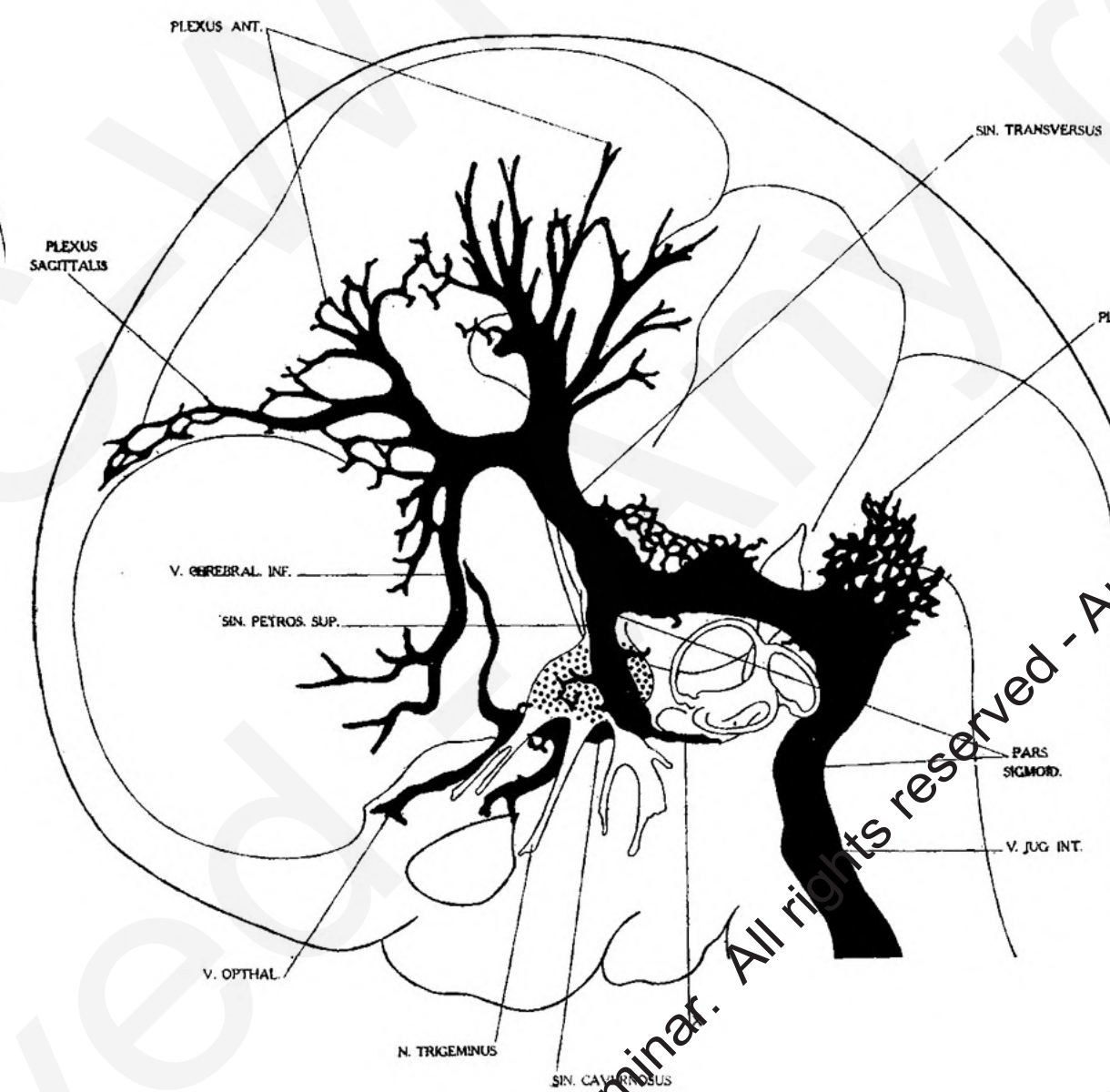
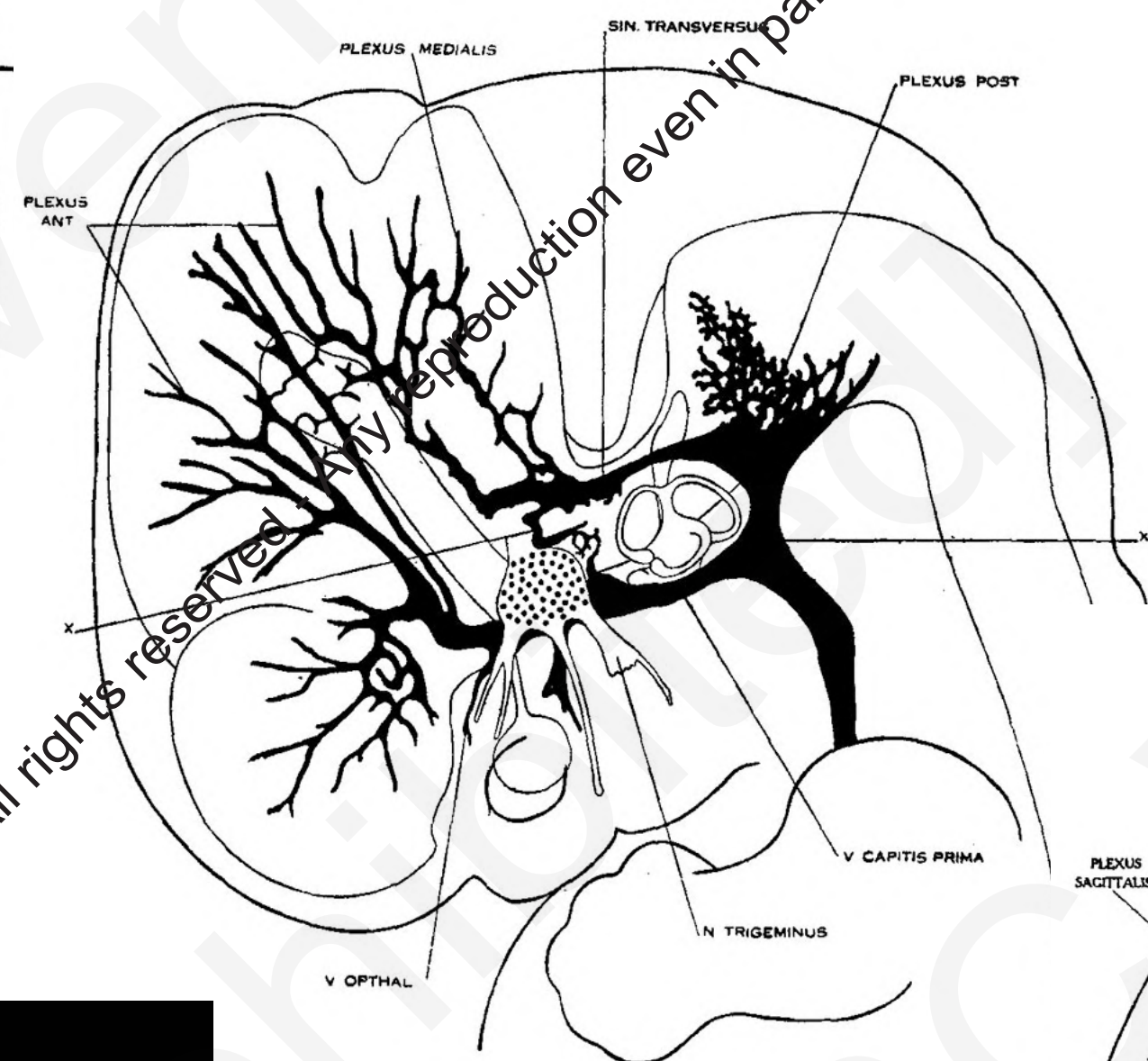
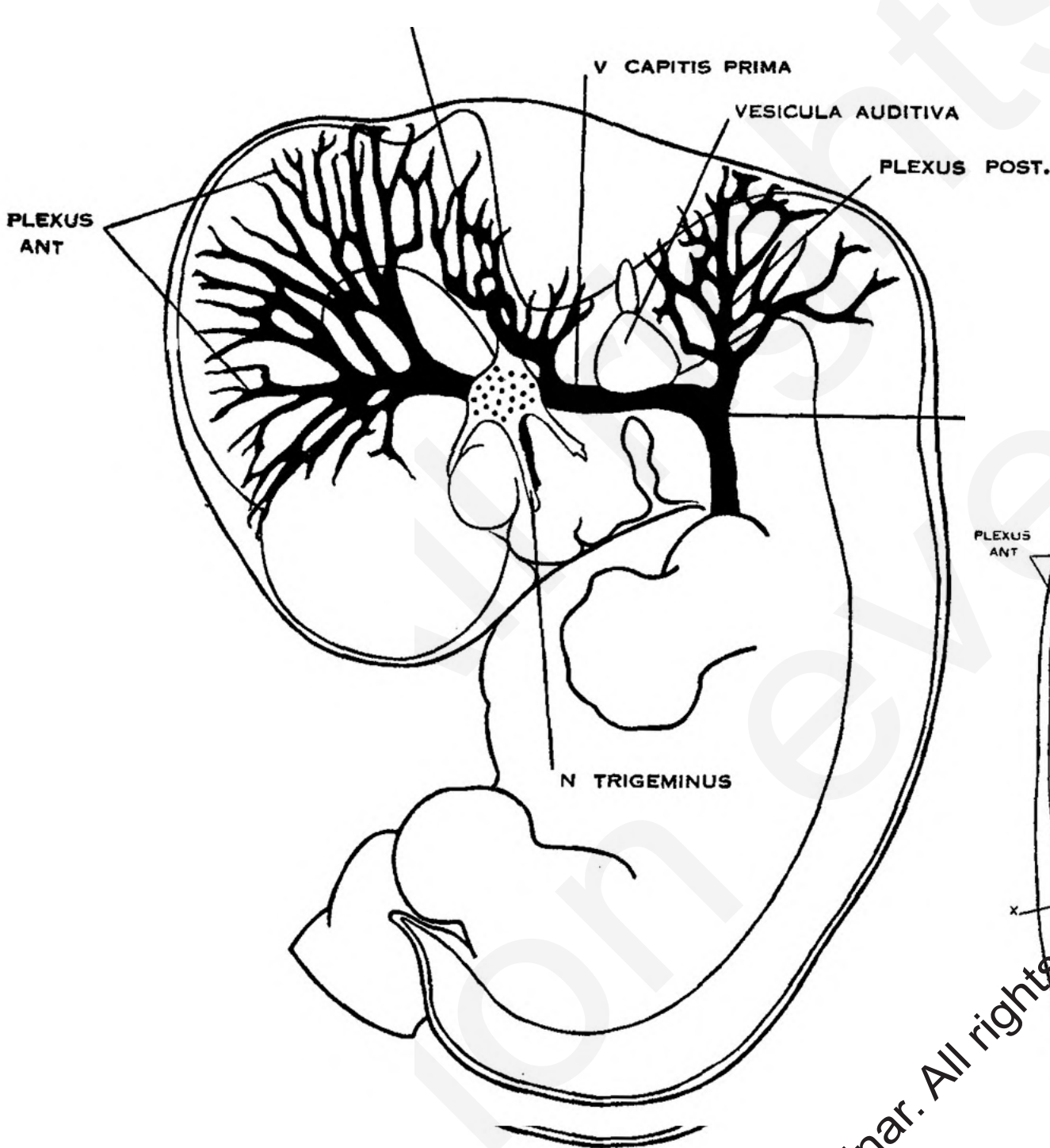
Matrix layer of telencephalon starts to develop, but no marked dura mater encephalii is not yet emerged.



Week 8

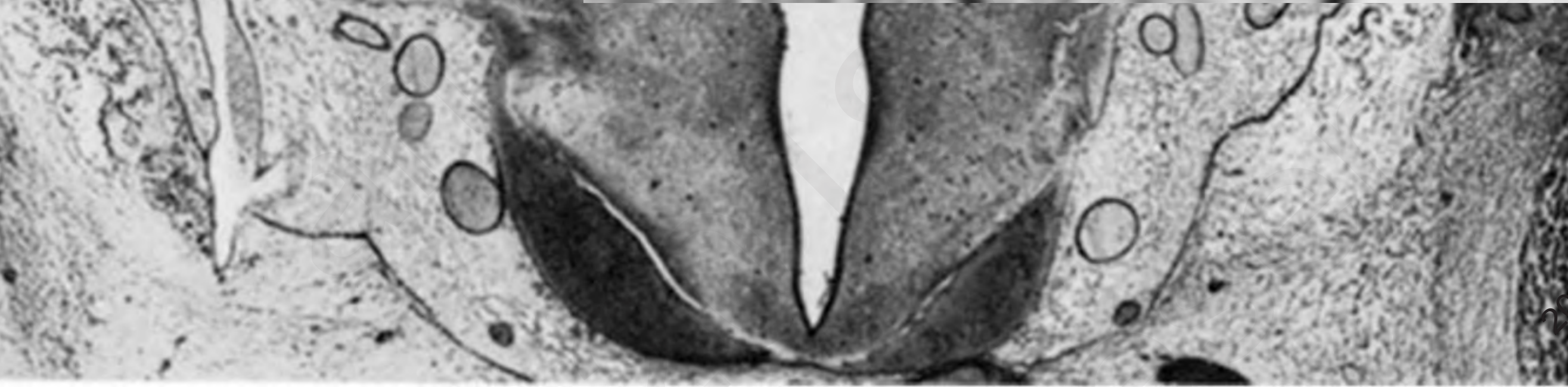
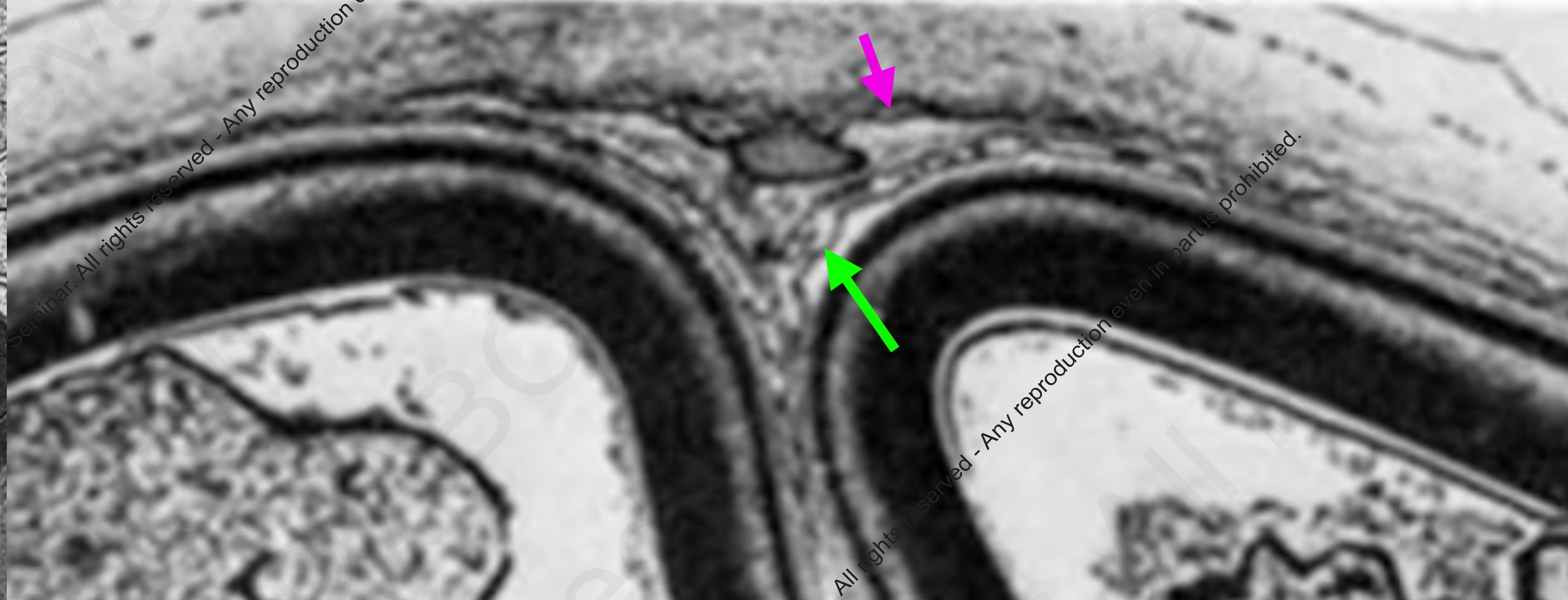
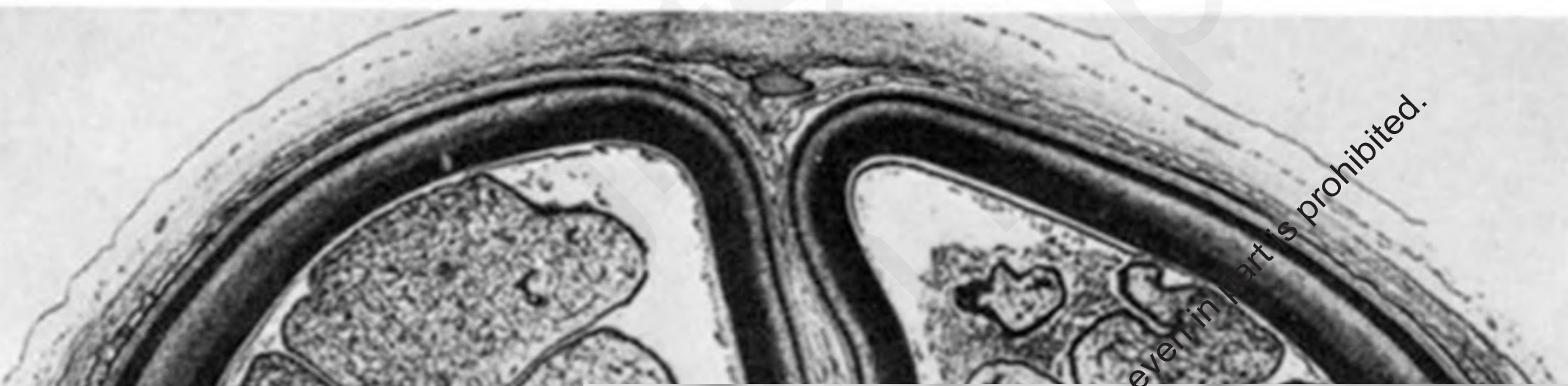


Week 8: Future's tentorium cerebelli is formed.

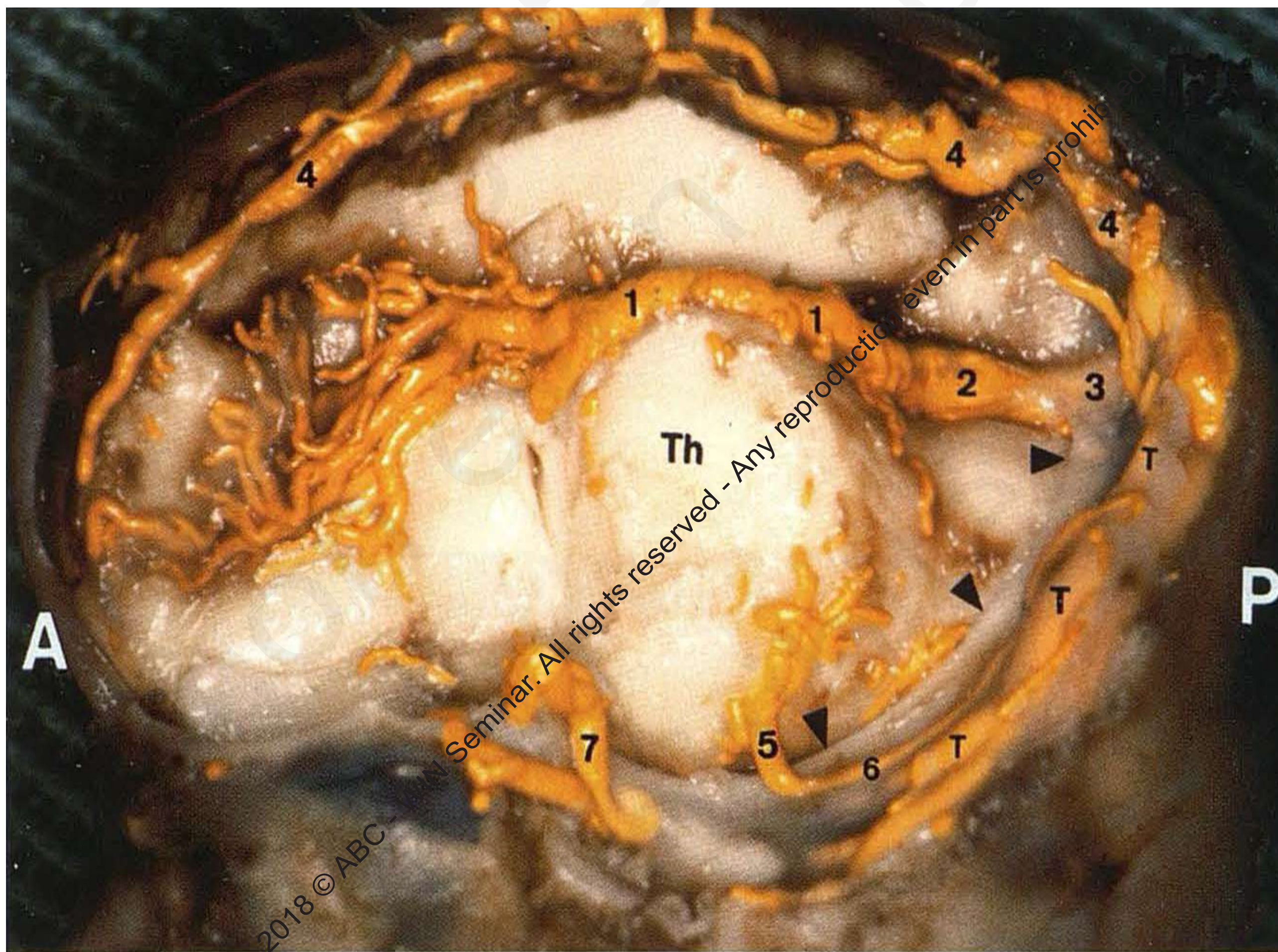


Dural mater is formed around 12 weeks

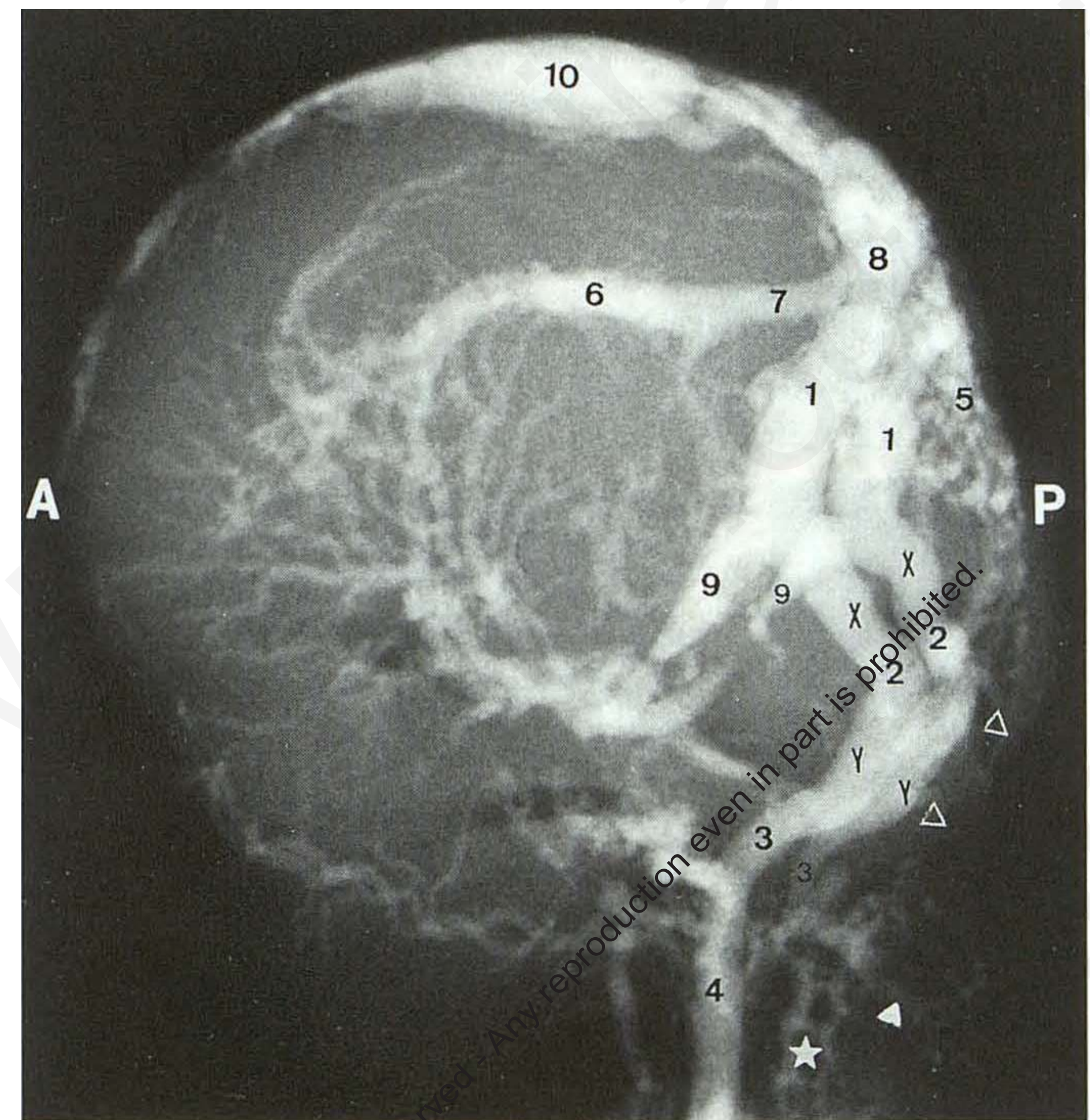
Week12



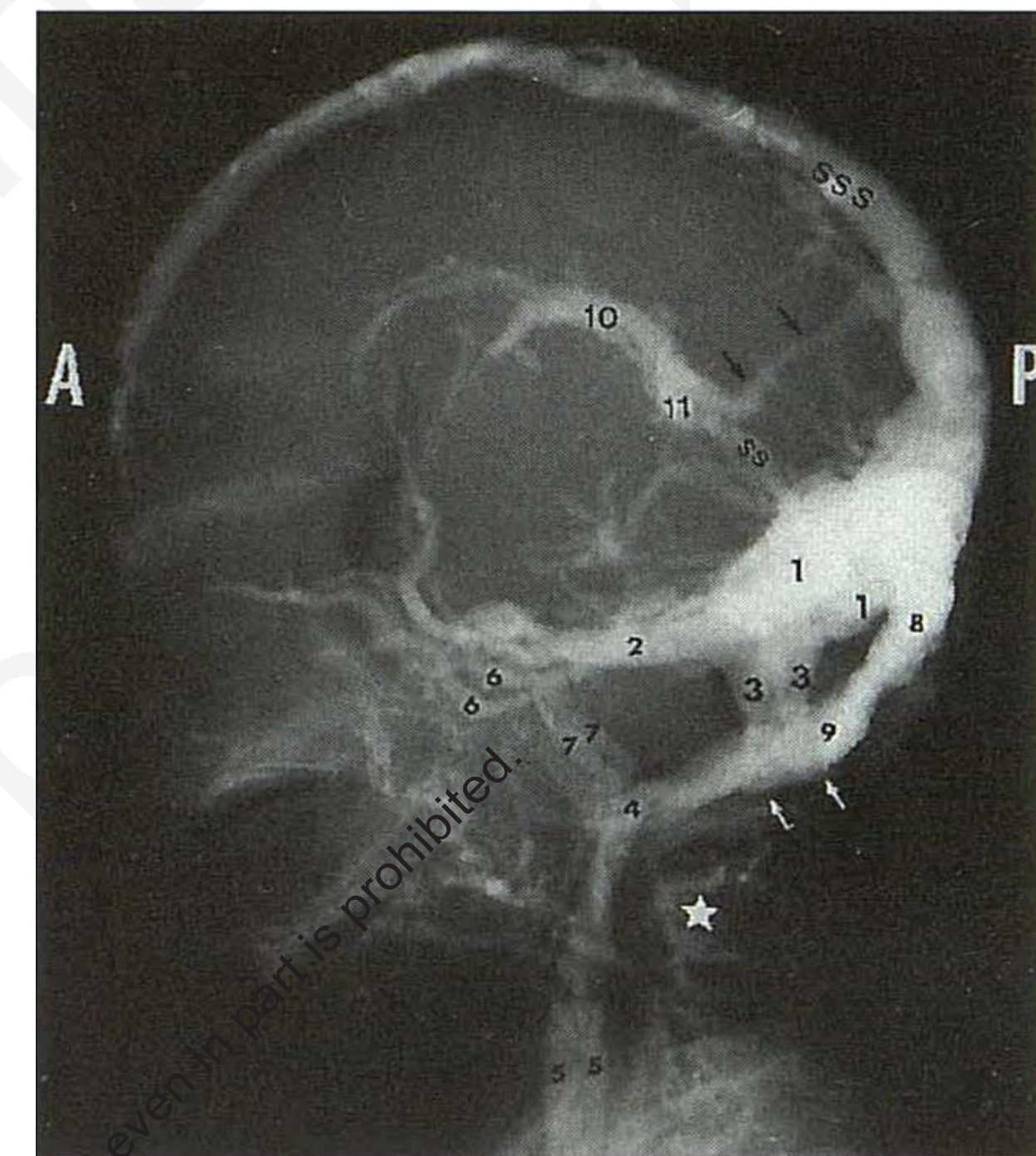
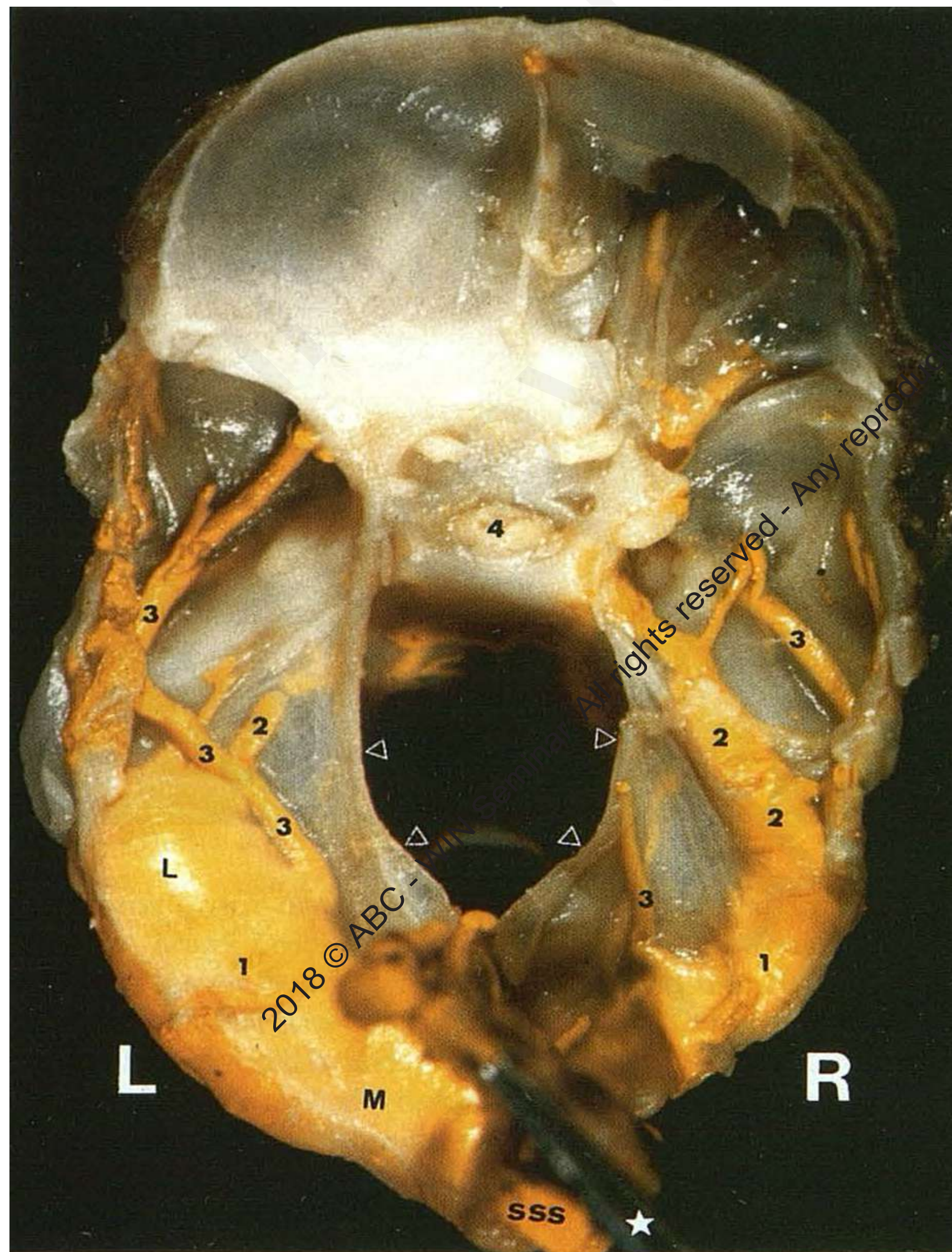
Meningeal dura (dura propria)
developed earlier than osteal dura.



A 12-week-old fetus (65-mm crown-rump length).

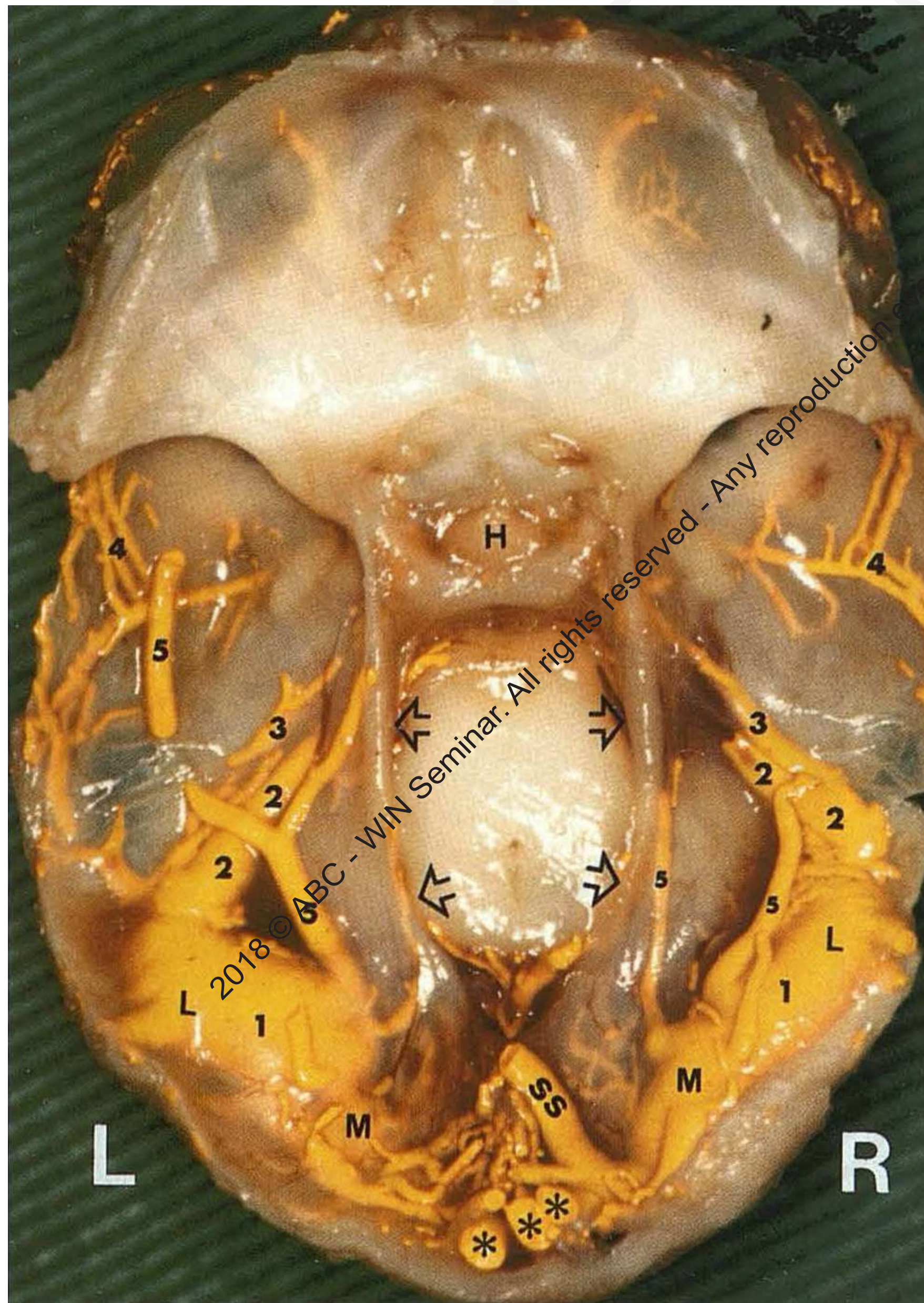


1. Transverse sinus
2. Sigmoid sinus
7. Vein of Galen
8. Straight sinus
6. Internal cerebral v.
9. Superior petrosal sinus
10. SSS



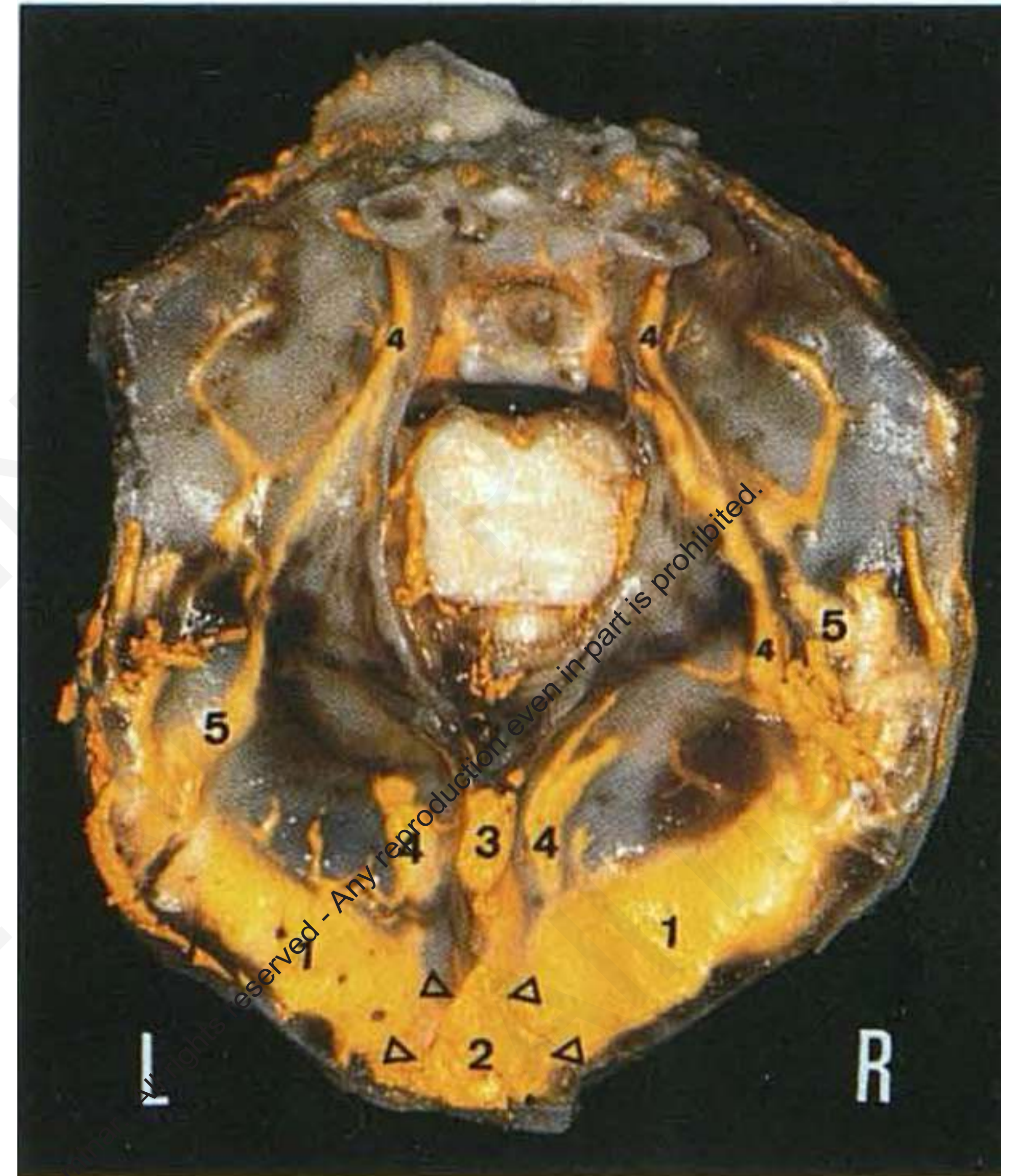
1. Transverse sinus
2. Superior petrosal sinus
3. Tentorial sinus

A 16-week-old fetus (115-mm crown-rump length)



A 17-week-old fetus (130-mm crown-rump length)

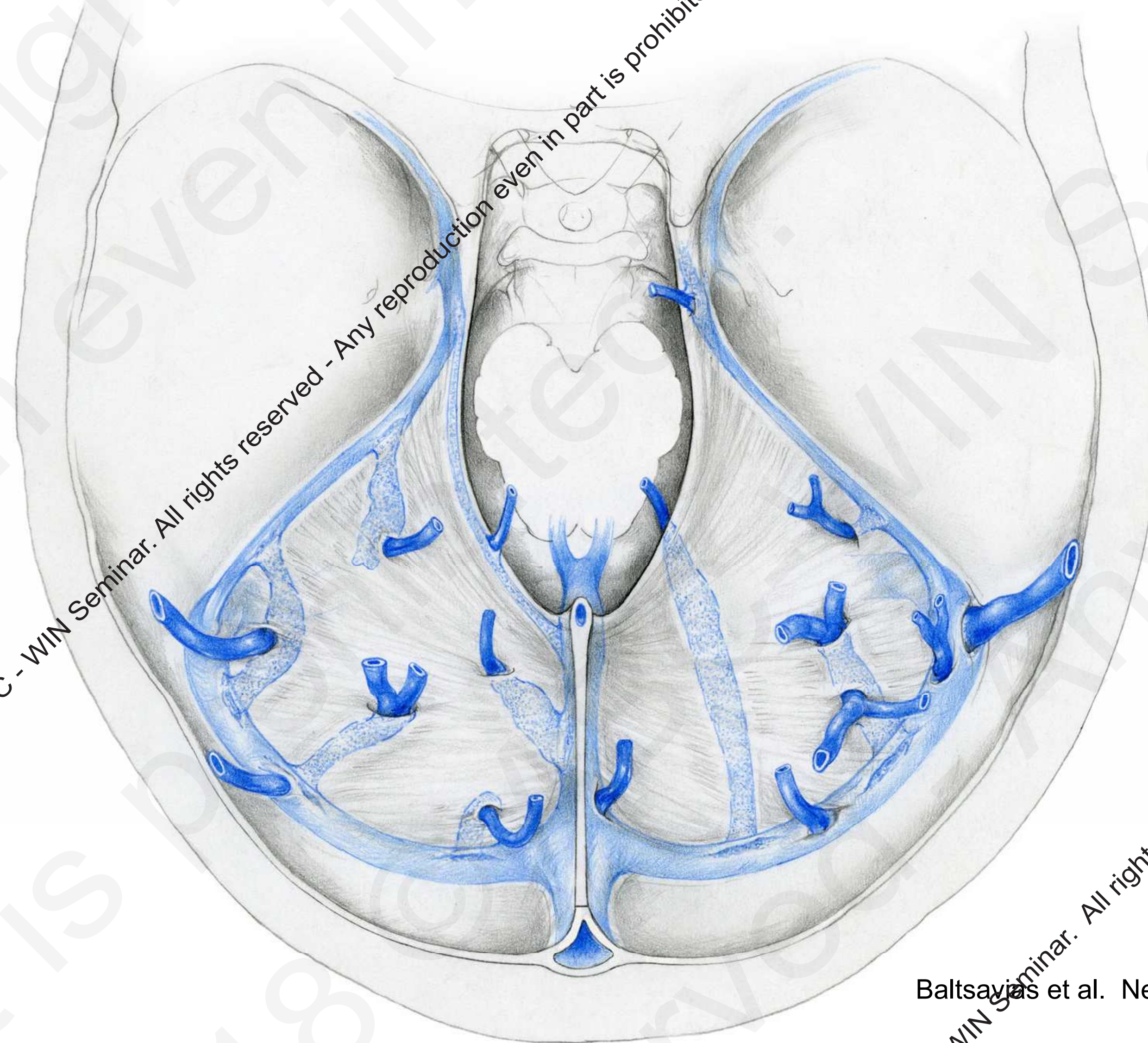
- 2. SPS
- 5. Tentorial sinus



7-month-old (25-week) fetus (225-mm crown-rump length). 4. Tentorial sinus, 5.SPS

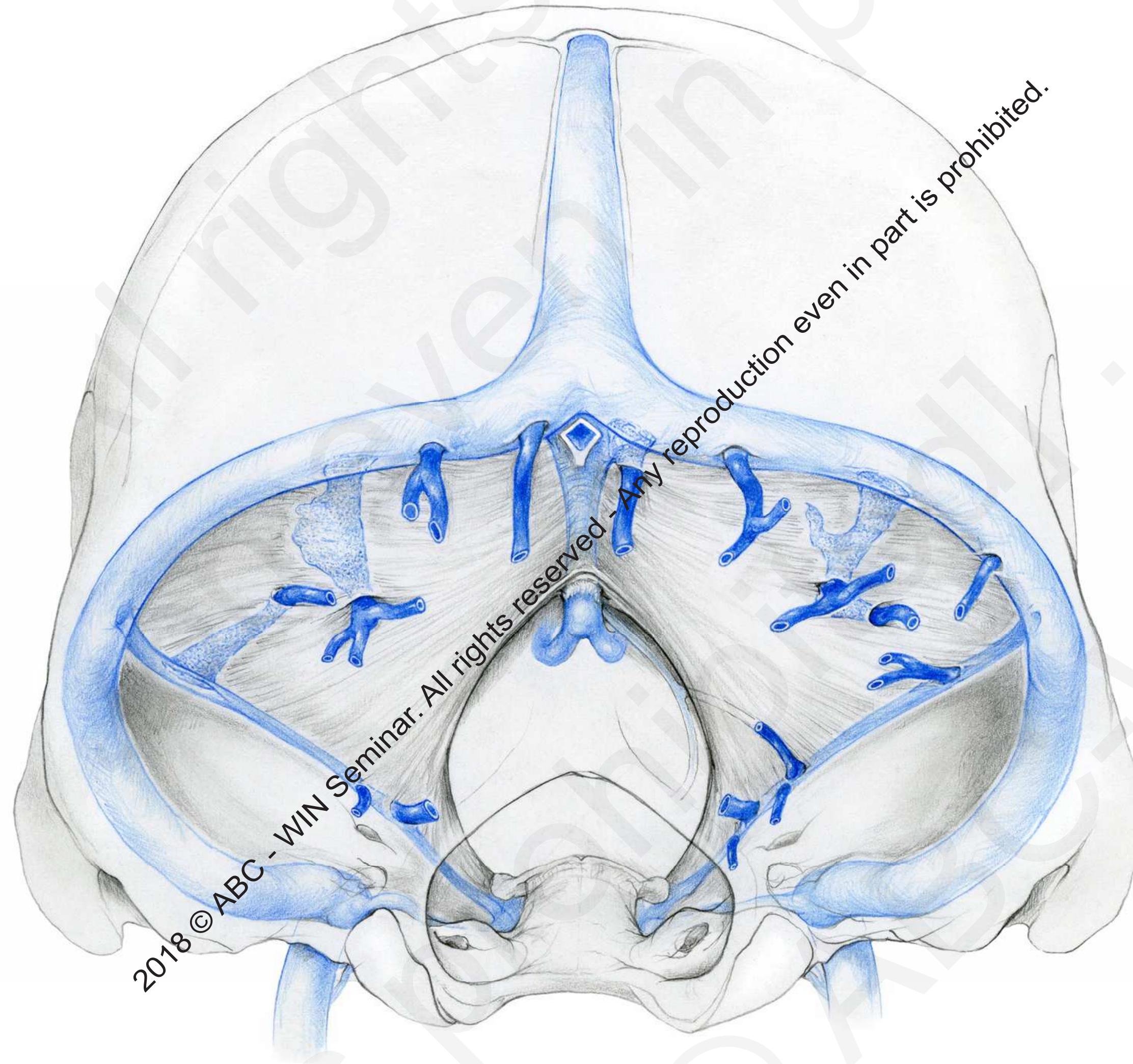
Okudera et al. AJNR 1994

Sinuses and bridging veins structure on the surface of tentorium cerebellum



Baltsavias et al. Neurosurgical Review 2014

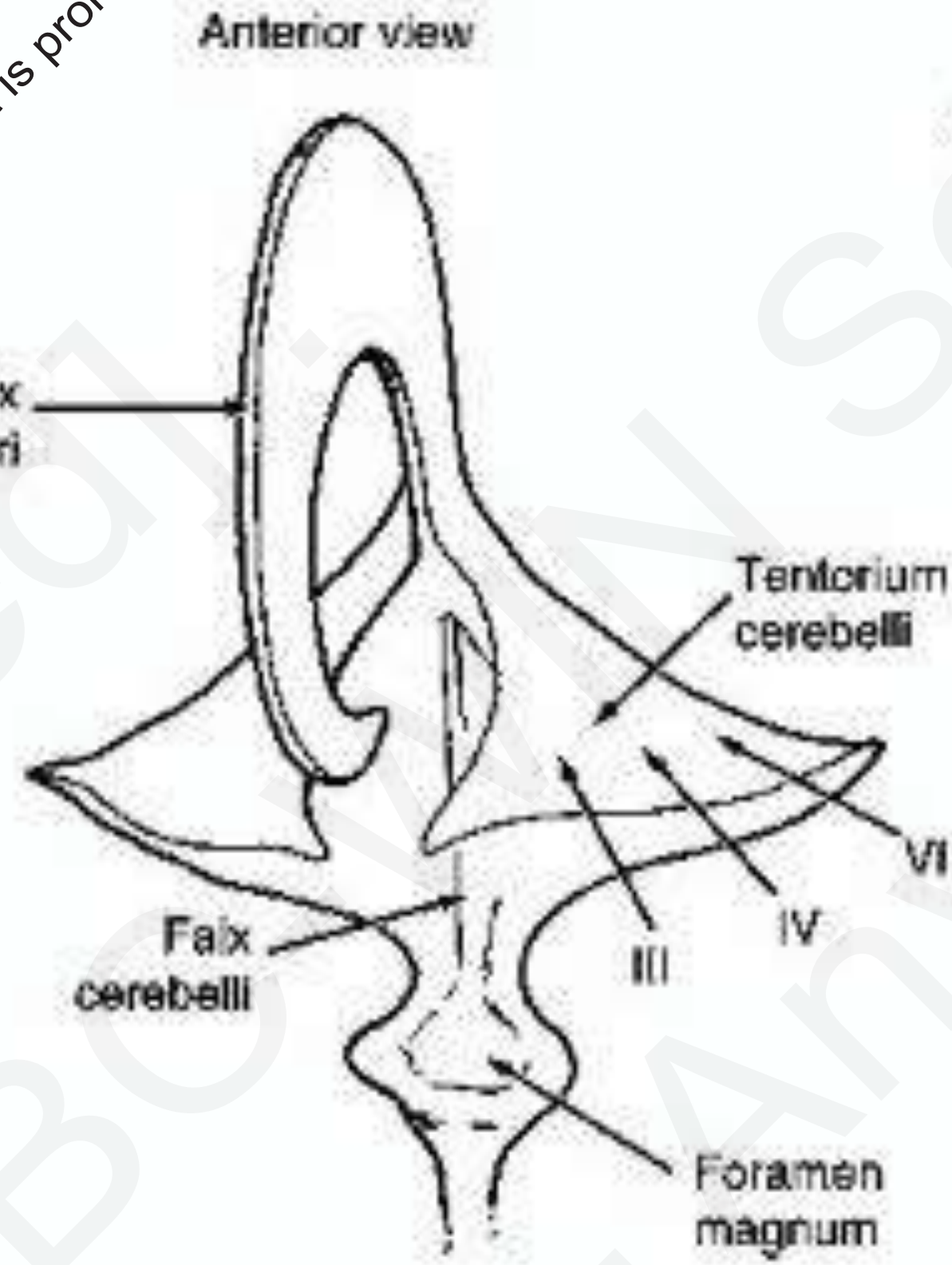
Schematic illustration, focusing on the superior tentorial BVs and showing some of the many possible venous anatomic configurations, not necessarily coexisting in one individual.



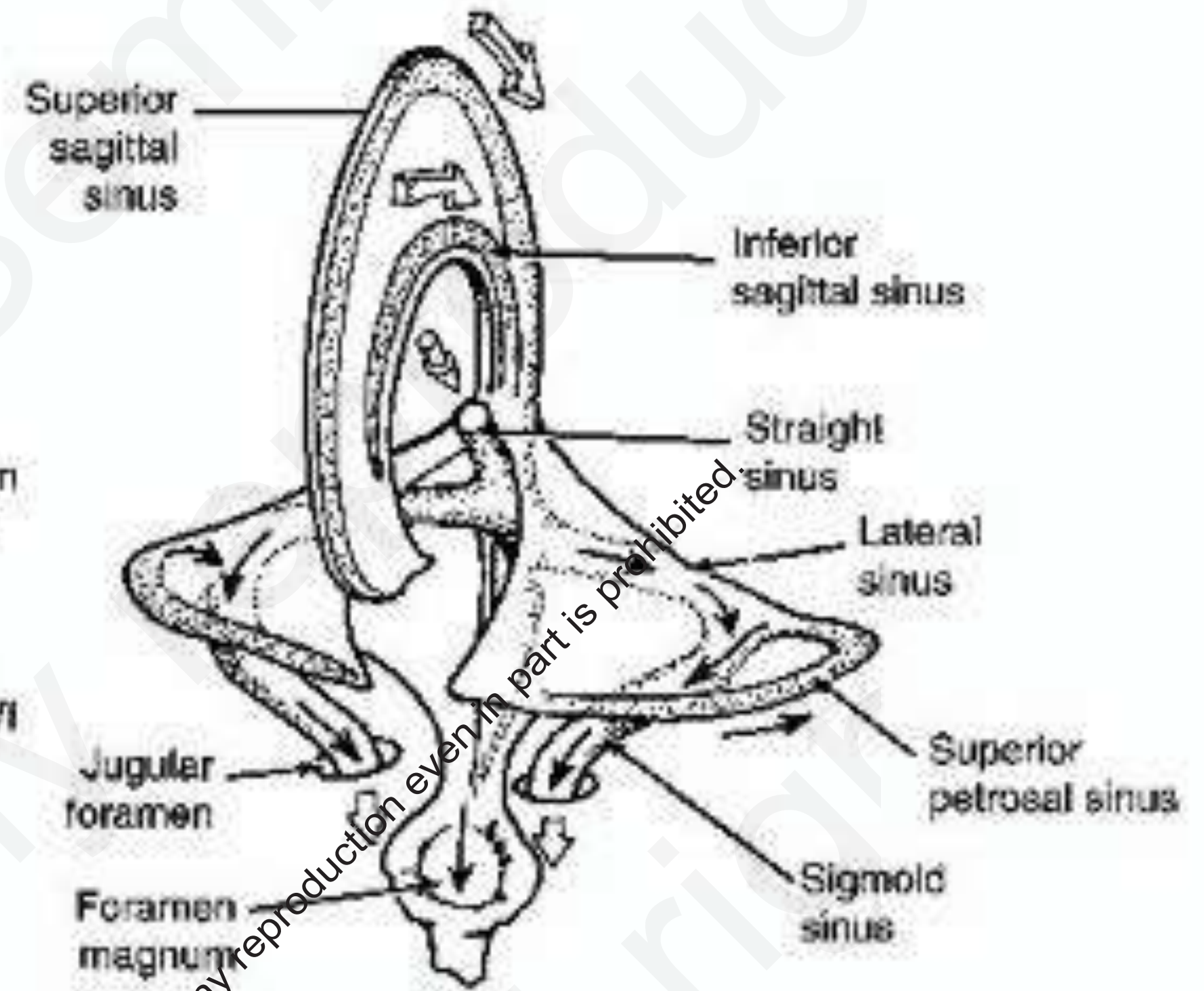
The inferior tentorial BVs, including the petrosal BVs as seen from a caudal view. It shows some of the many possible venous anatomic configurations, not necessarily coexisting in one individual.



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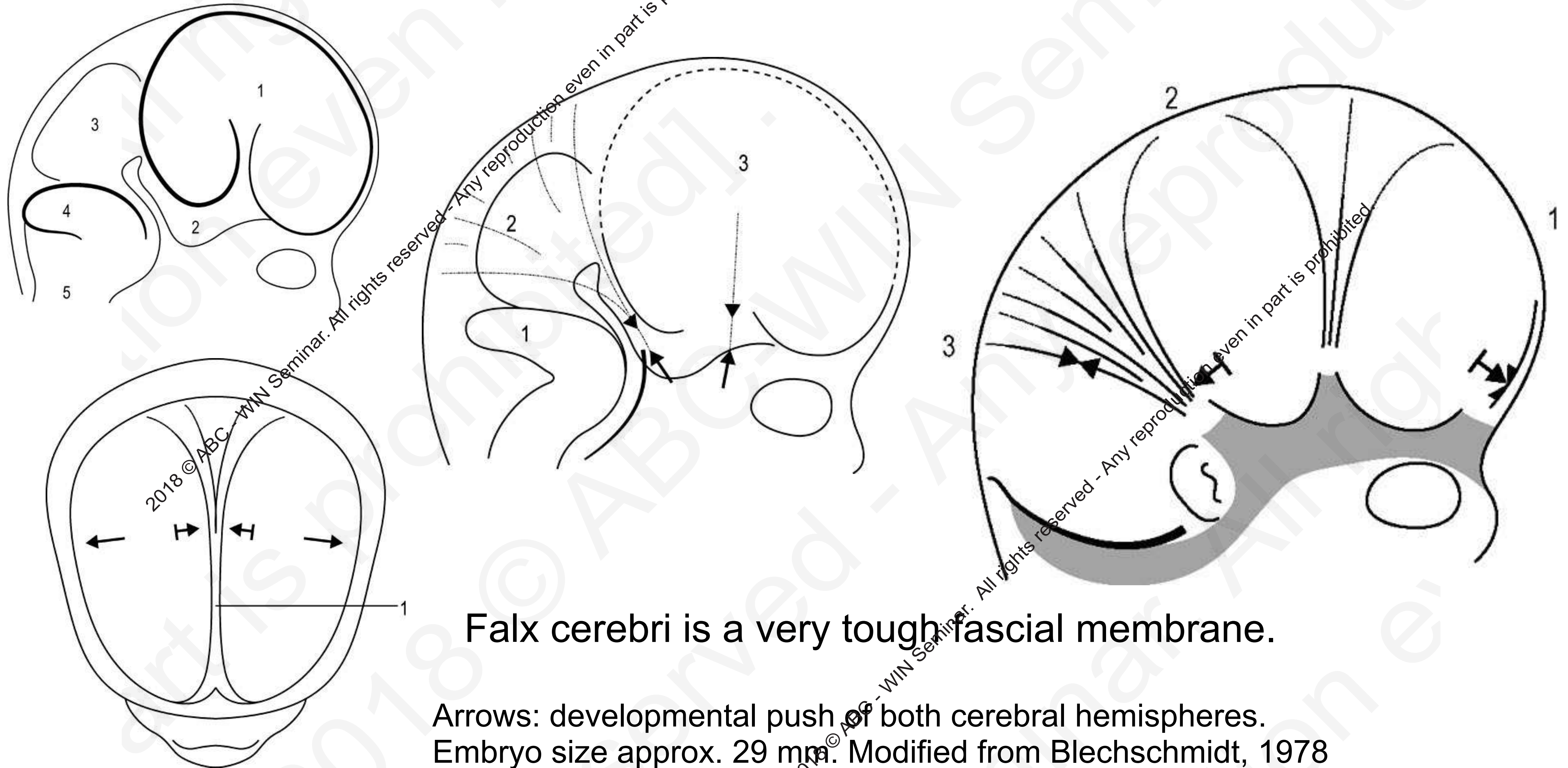


(Arrows indicate direction of venous drainage.)



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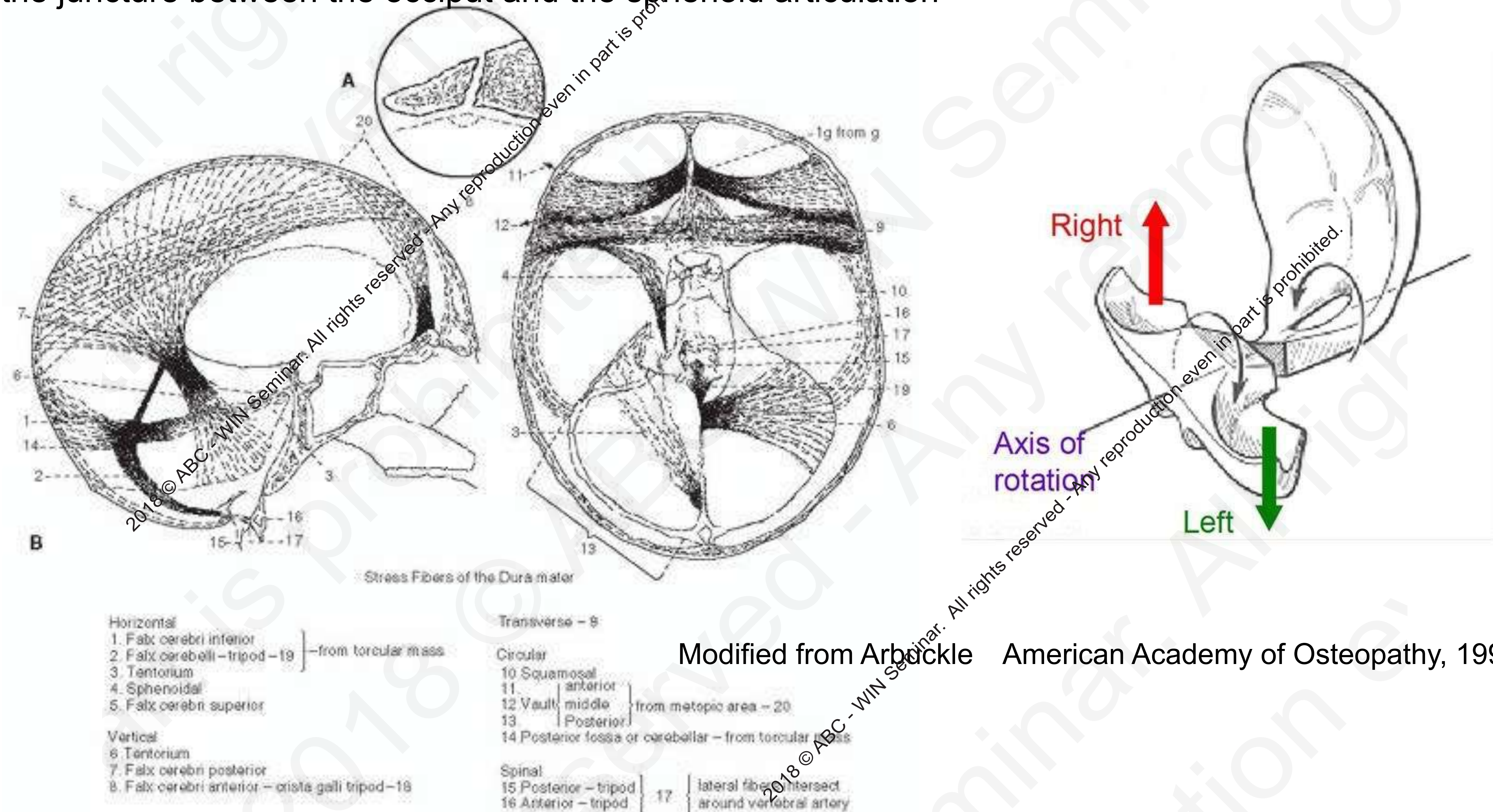
Falco-tentorial junction is a pivotal point for the development of telencephalon.



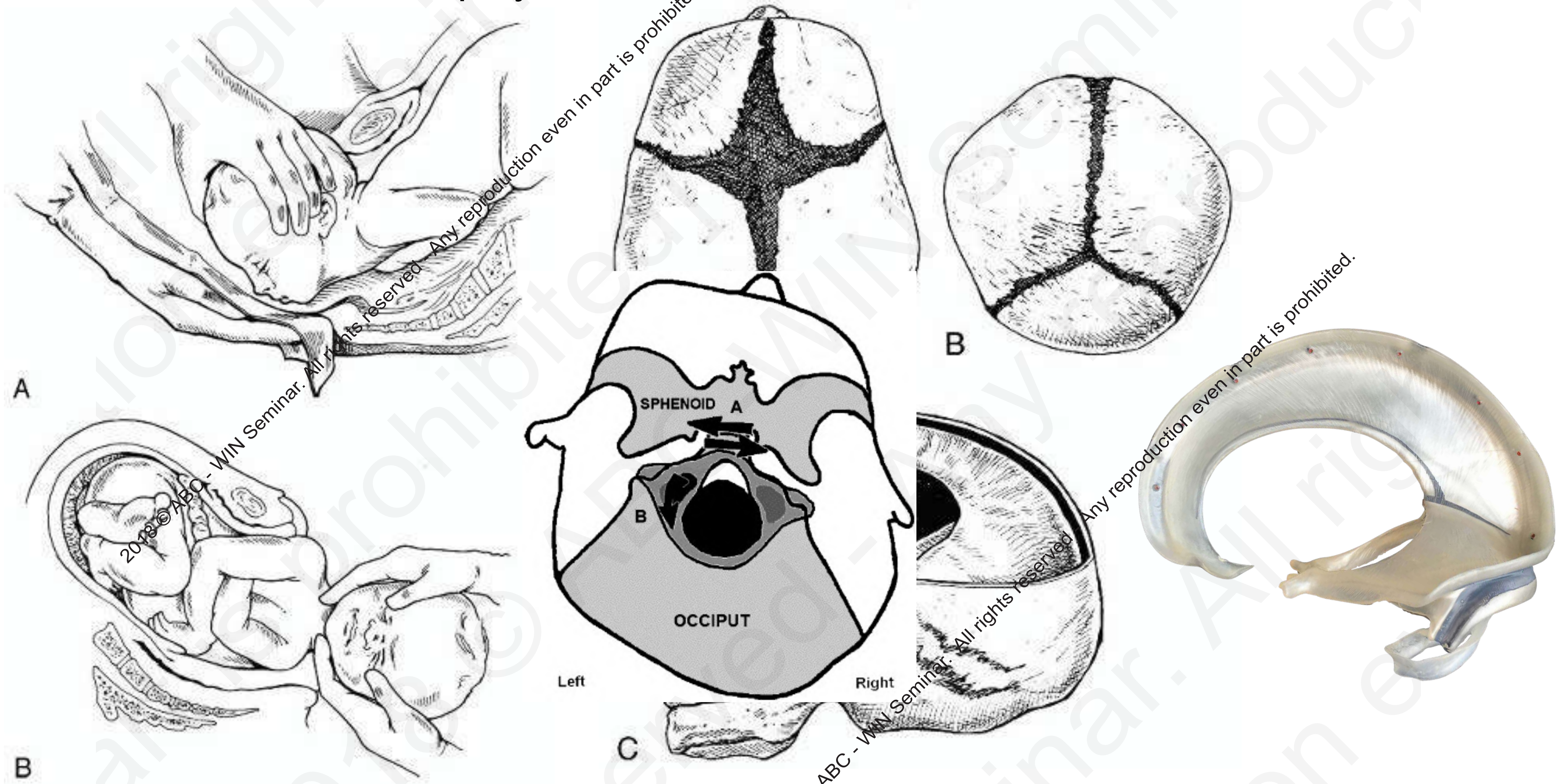
Falx cerebri is a very tough fascial membrane.

Arrows: developmental push of both cerebral hemispheres.
Embryo size approx. 29 mm. Modified from Blechschmidt, 1978

Sphenobasilar Articulation: The most important of the cranial articulations, the SB synchondrosis is formed at the juncture between the occiput and the sphenoid articulation



Falco-tentorial membrane plays a role of biomechanics as the reinforce of skull bones.

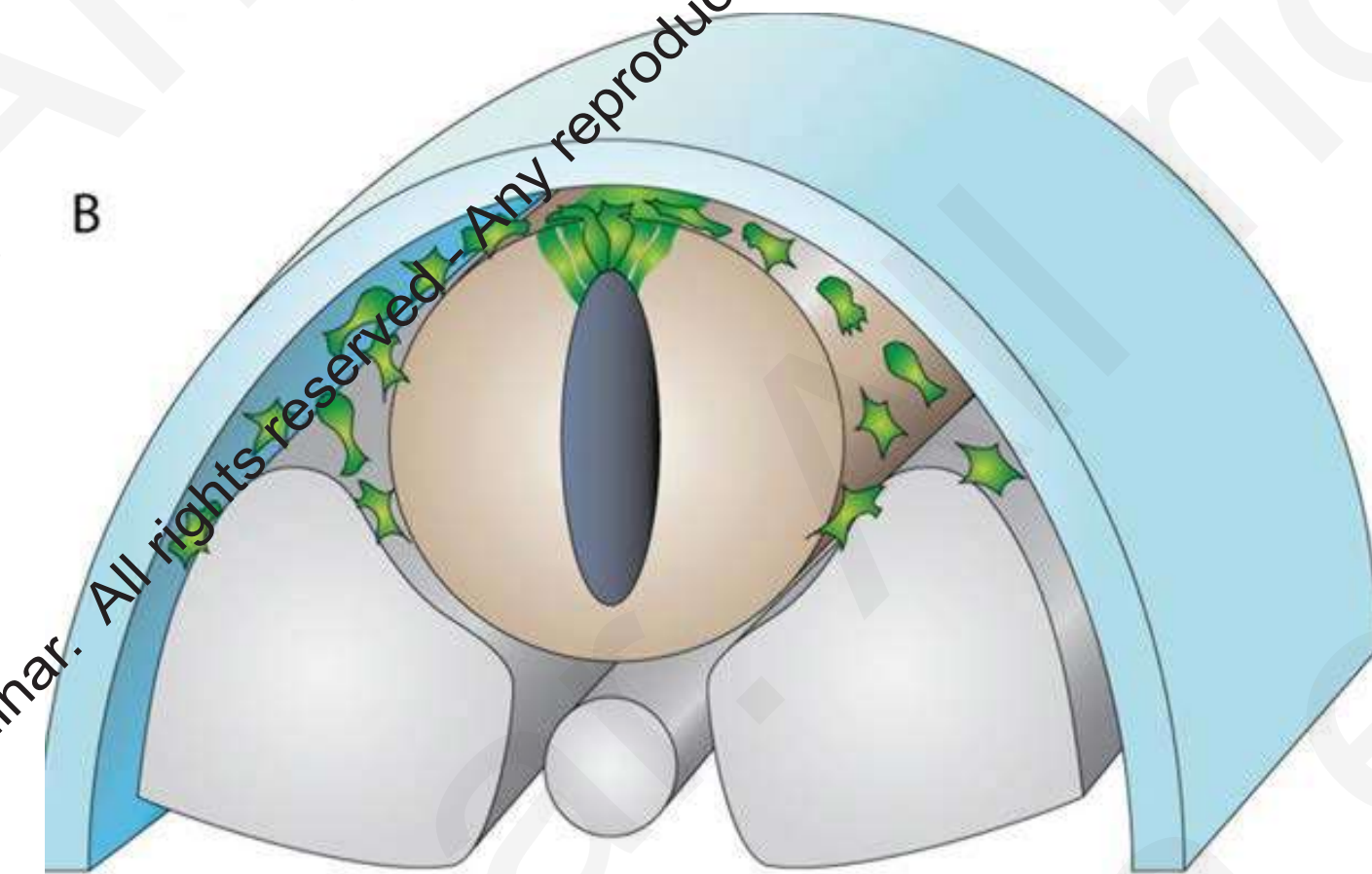


Menu

1. Embryology of the dura mater encephali

2. Neural crest cell and falco-tentorial dura mater

3. Clinical consideration of falco-tentorial dura mater



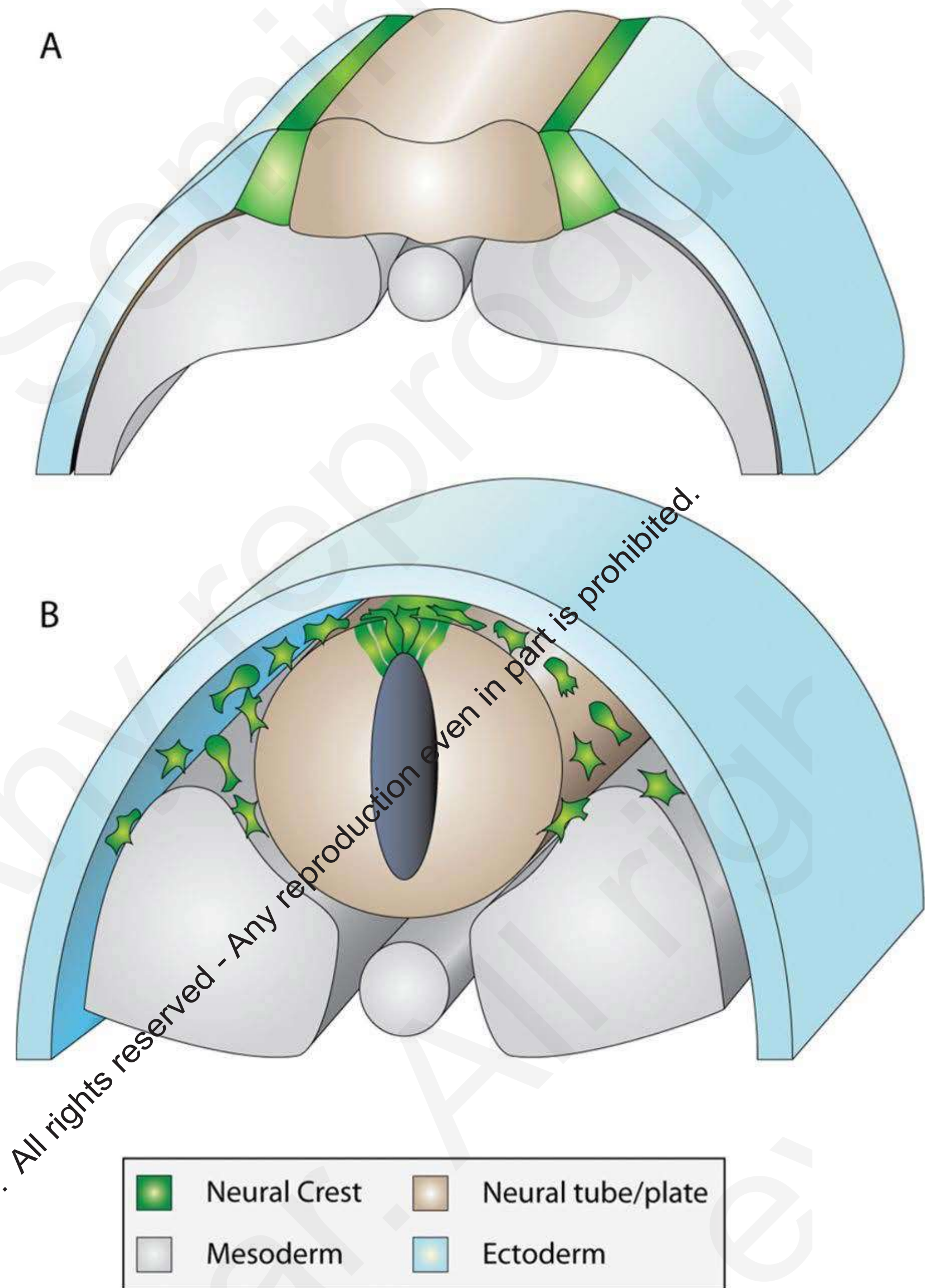
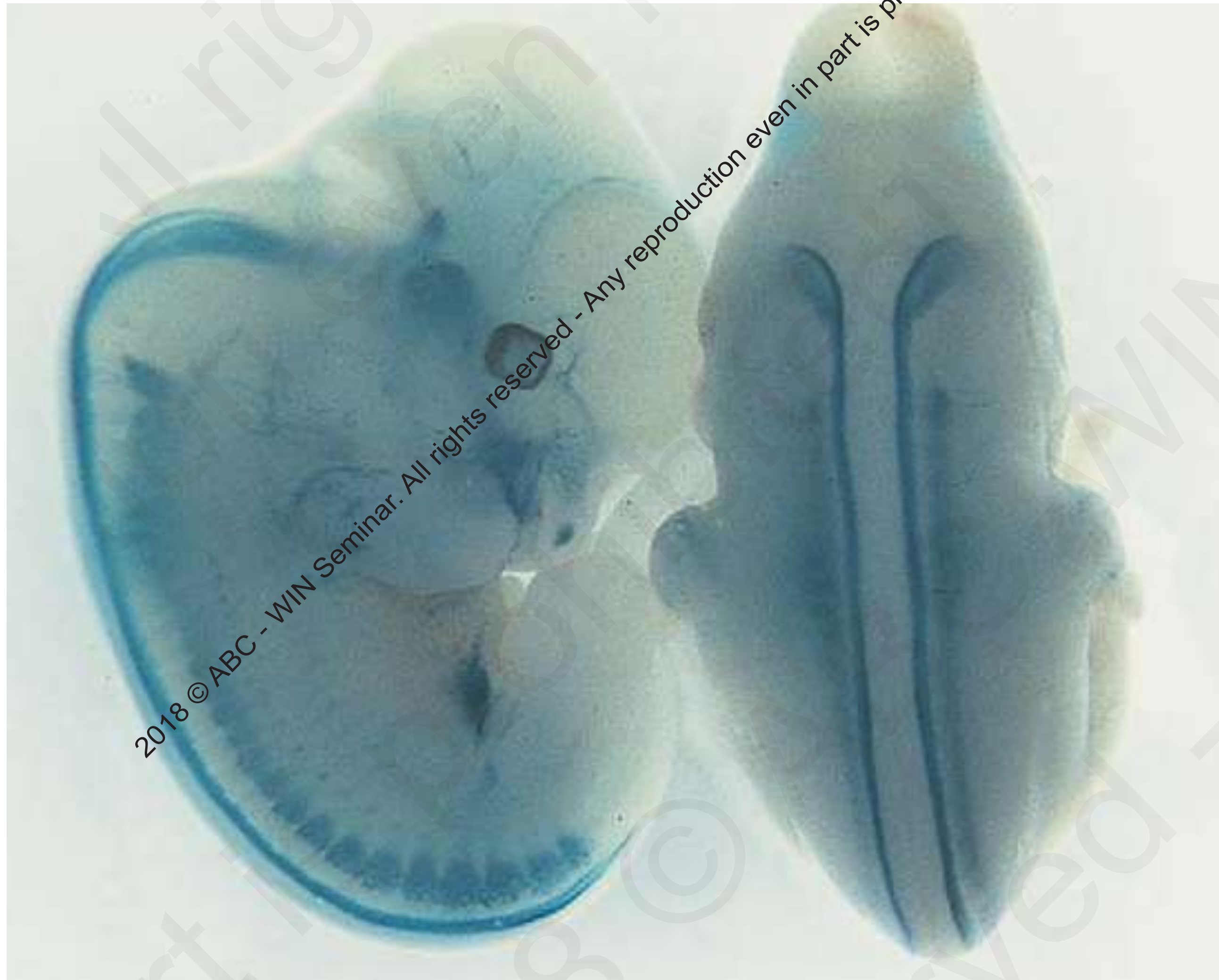
What is the Neural Crest (NC) ?

The neural crest (NC) is a transient, embryologic structure that was first found by a famous anatomist Wilhelm His in 1868 .

NC is called the fourth germ layer and is characteristic to the vertebrates phylogenetically.

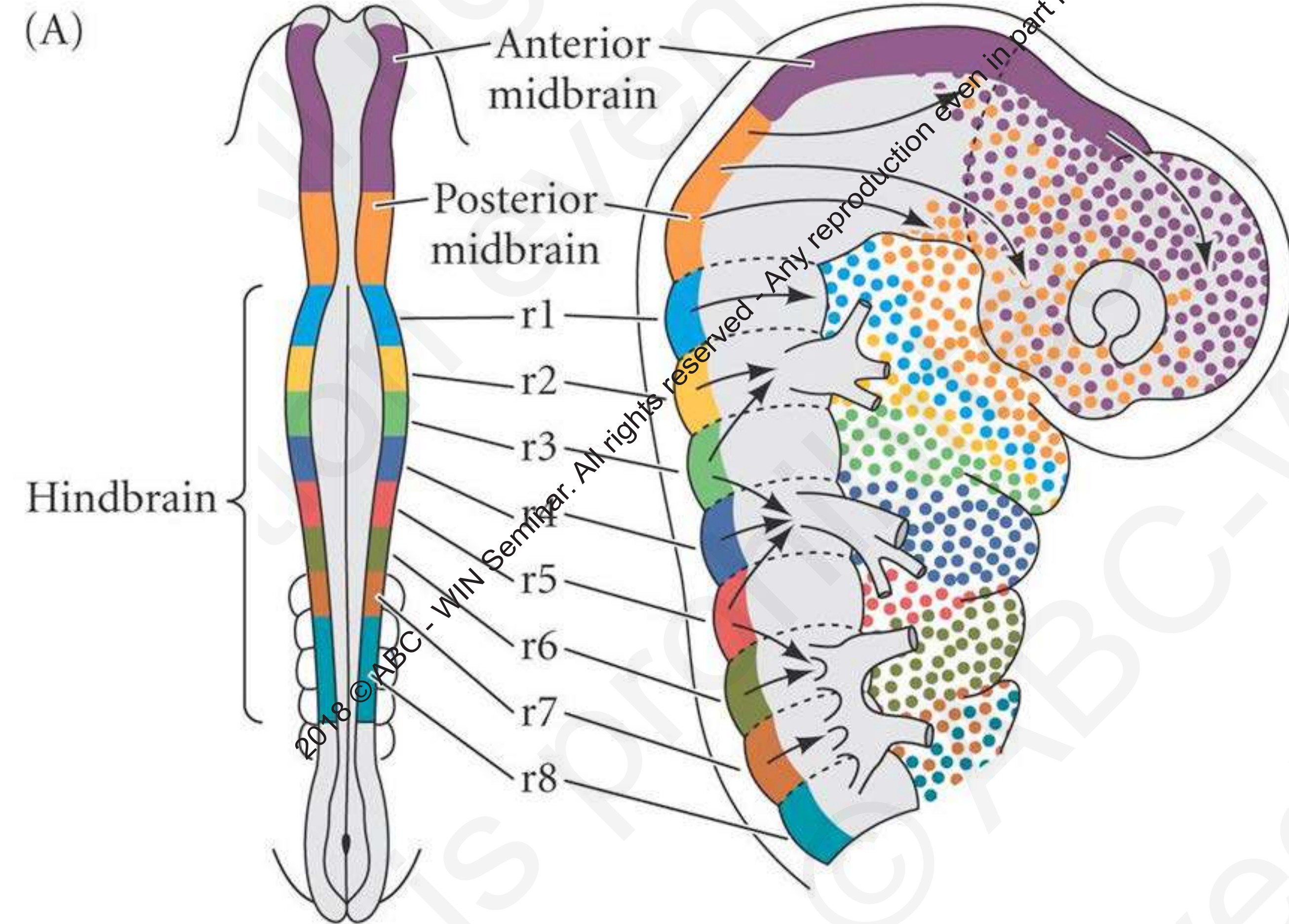
Neural crest cells (NCCs) are pluripotent and give rise to a variety of derivatives after migration in early embryogenesis, such as neurons, glia, cartilage, connective tissue, pigment cells, and adrenal cells.

What is the Neural Crest (NC) ?



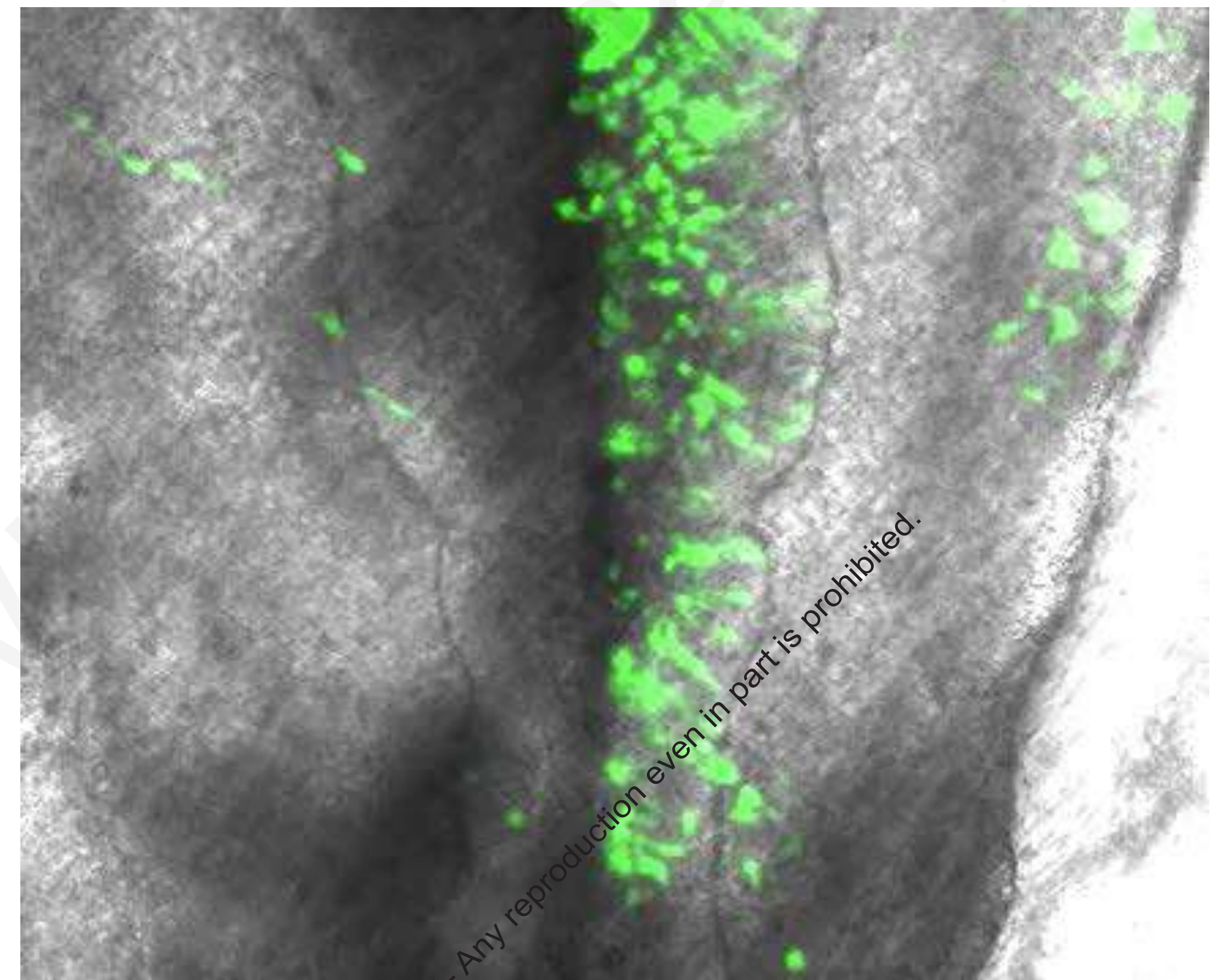
The blue stain is localized in small neurons of the neural crest cell–derived dorsal root ganglia and in the axons of these cells that penetrate the spinal cord in a region overlying the dorsal gray columns of the spinal cord (parasagittal stripes).

What is the Neural Crest (NC) ?



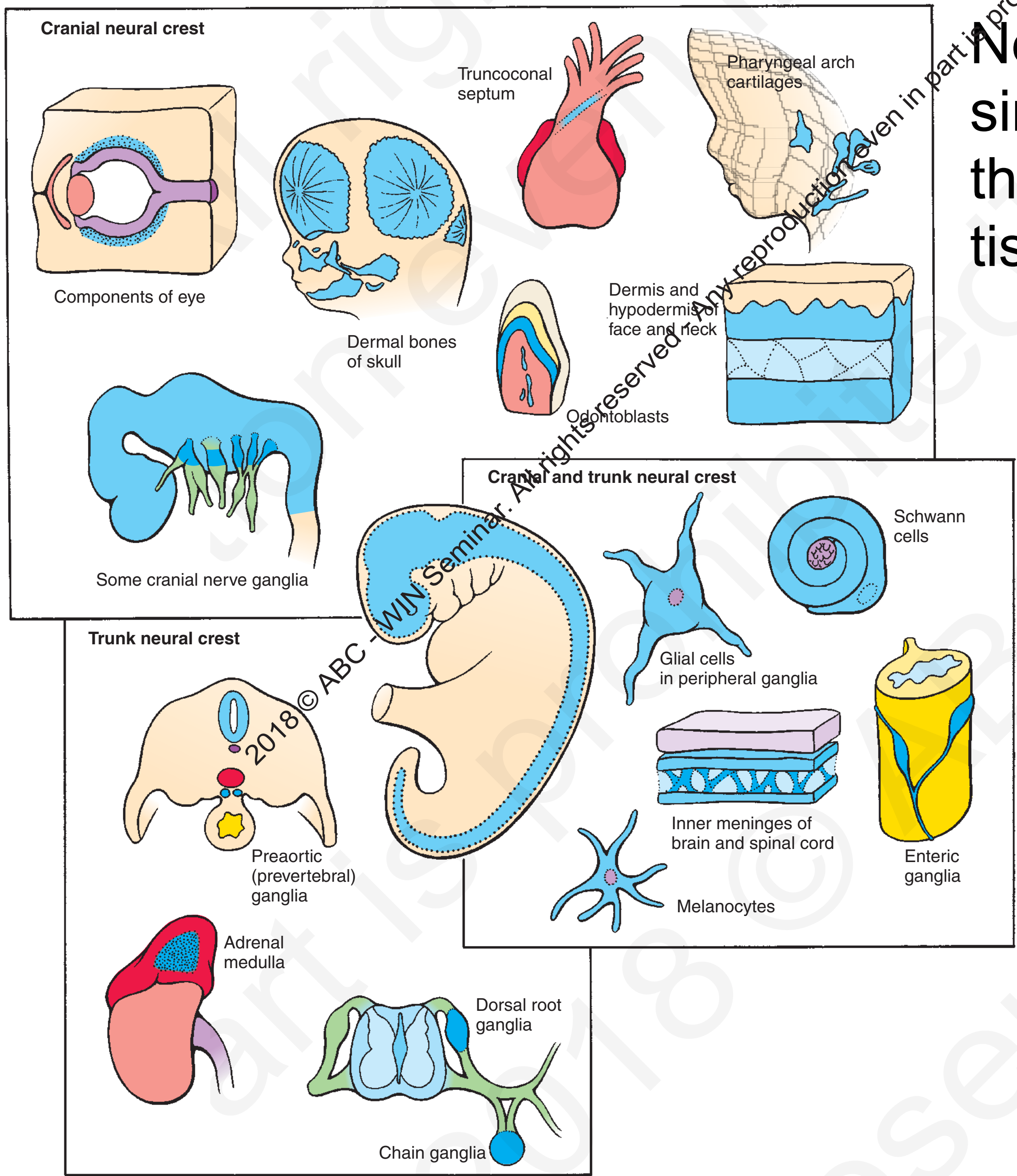
DEVELOPMENTAL BIOLOGY, Eighth Edition, Figure 13.9 (Part 1) © 2006 Sinauer Associates, Inc.

These cells undergo an **epithelial-to-mesenchymal transformation** as they detach from the neural tube.

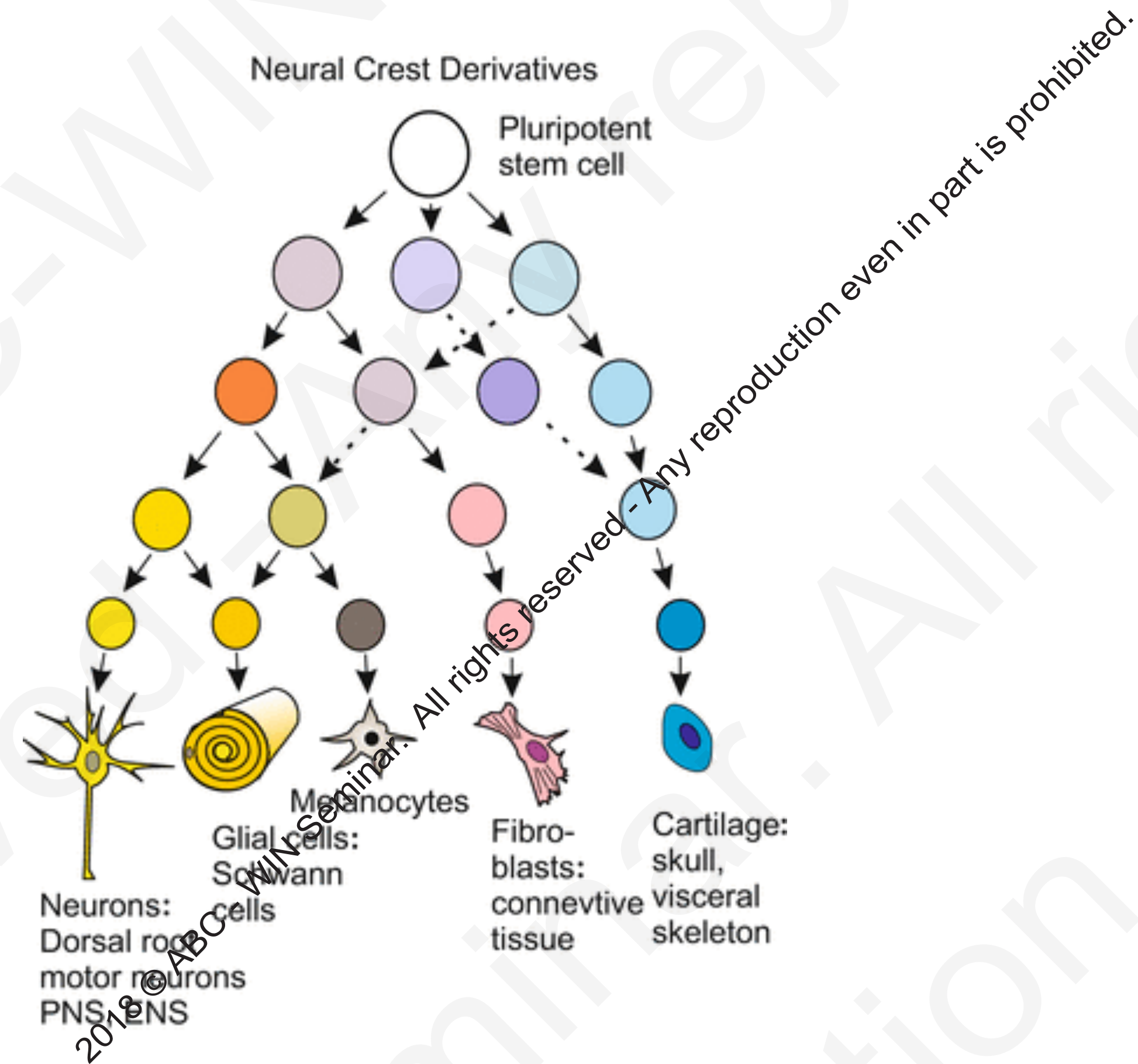


Neural crest cells are a temporary group of cells unique to vertebrates that arise from the embryonic ectoderm cell layer, and in turn give rise to a diverse cell lineage—including melanocytes, craniofacial cartilage and bone, smooth muscle, peripheral and enteric neurons and glia.

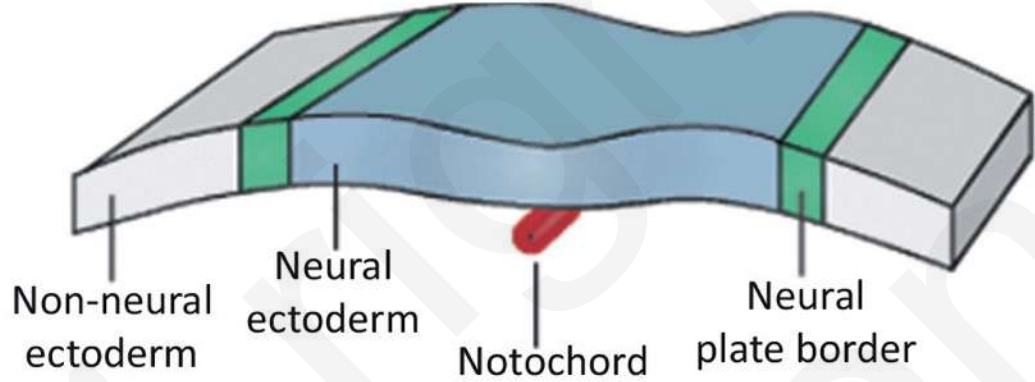
Multipotency and migratory capabilities of neural crest



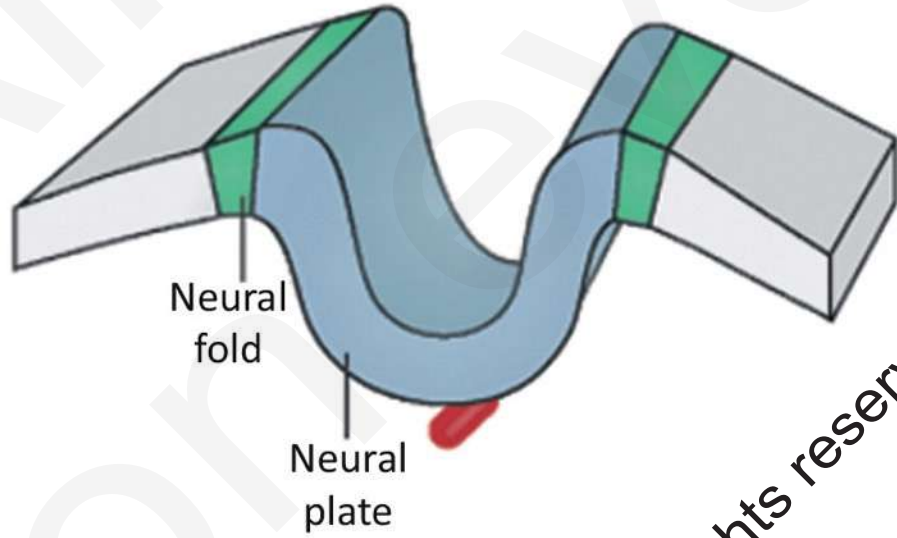
Neural crest is called "The fourth germ layer" since the number of cell types that arise from the NC is truly astonishing as is the number of tissues and organs.



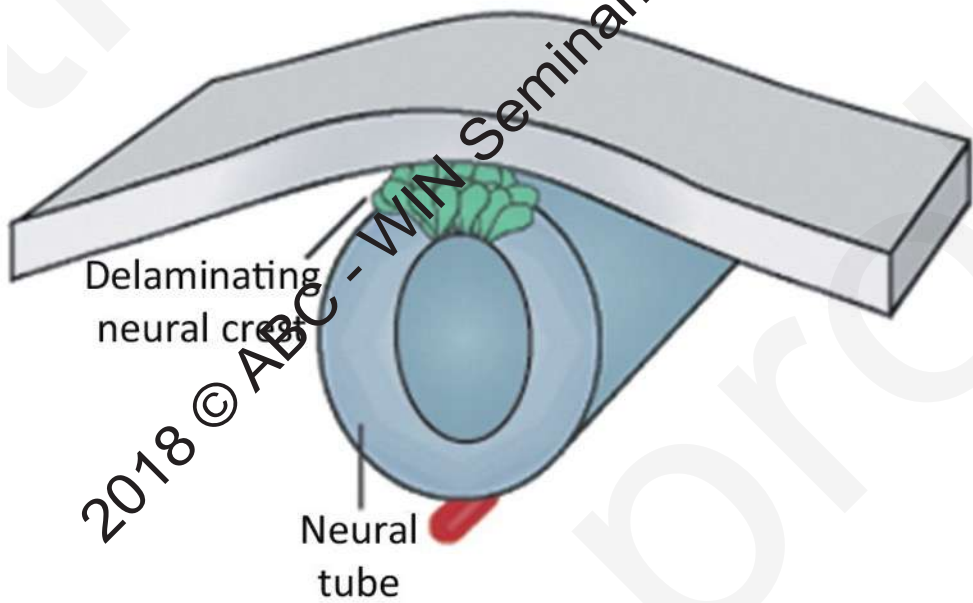
(A) Neural plate border specification



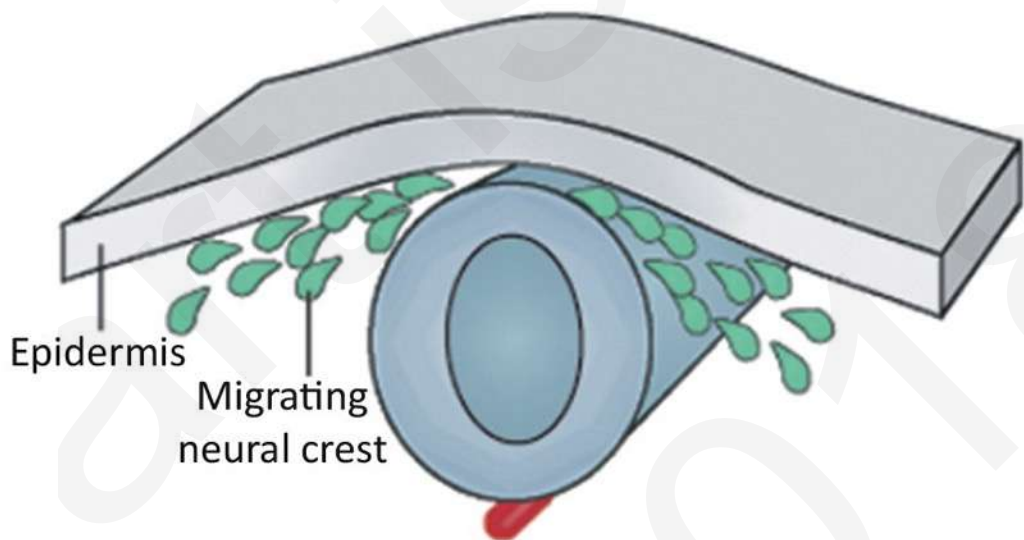
Neural crest specification



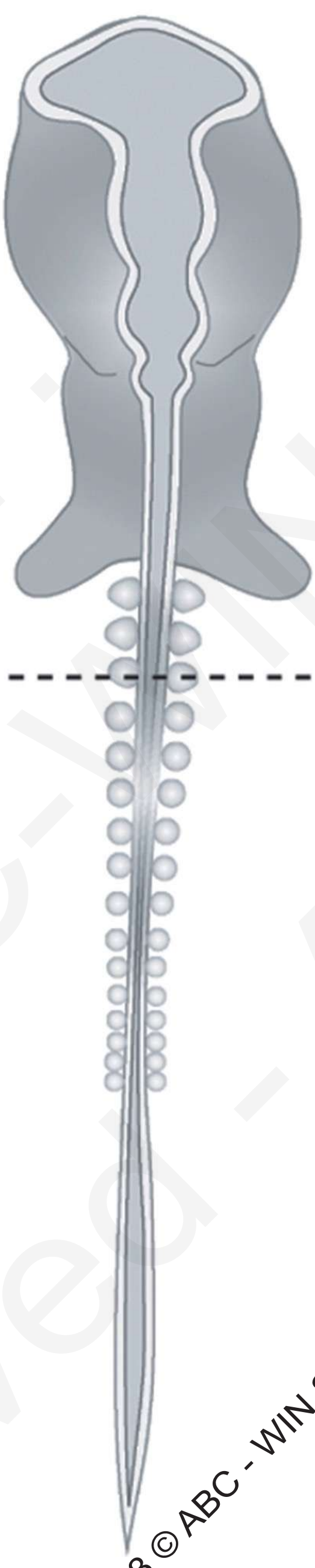
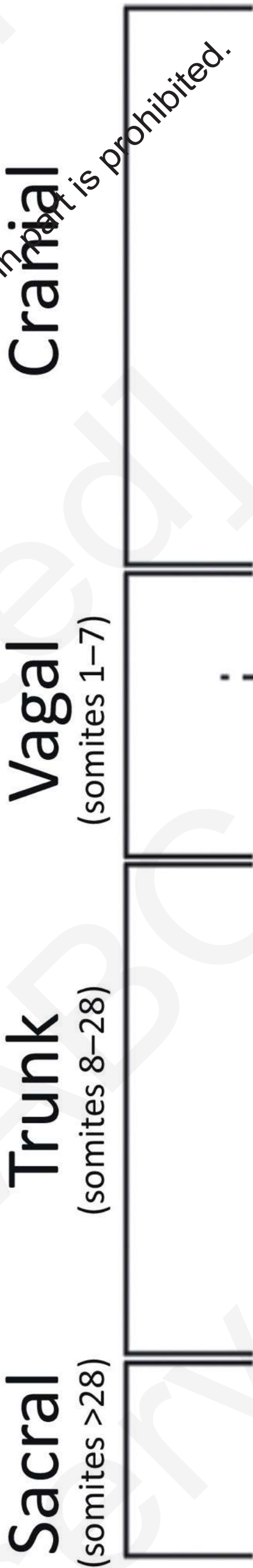
Neural crest EMT/delamination



Neural crest migration



(B)



Cranial neural crest

- Chondrocytes
- Osteocytes
- Cranial sensory ganglia
- Odontoblasts
- Melanocytes
- Ciliary ganglia

Vagal neural crest

- Aorticopulmonary septum
- Enteric ganglia
- Sympathetic ganglia
- Parasympathetic ganglia
- Melanocytes
- Cardiac ganglia

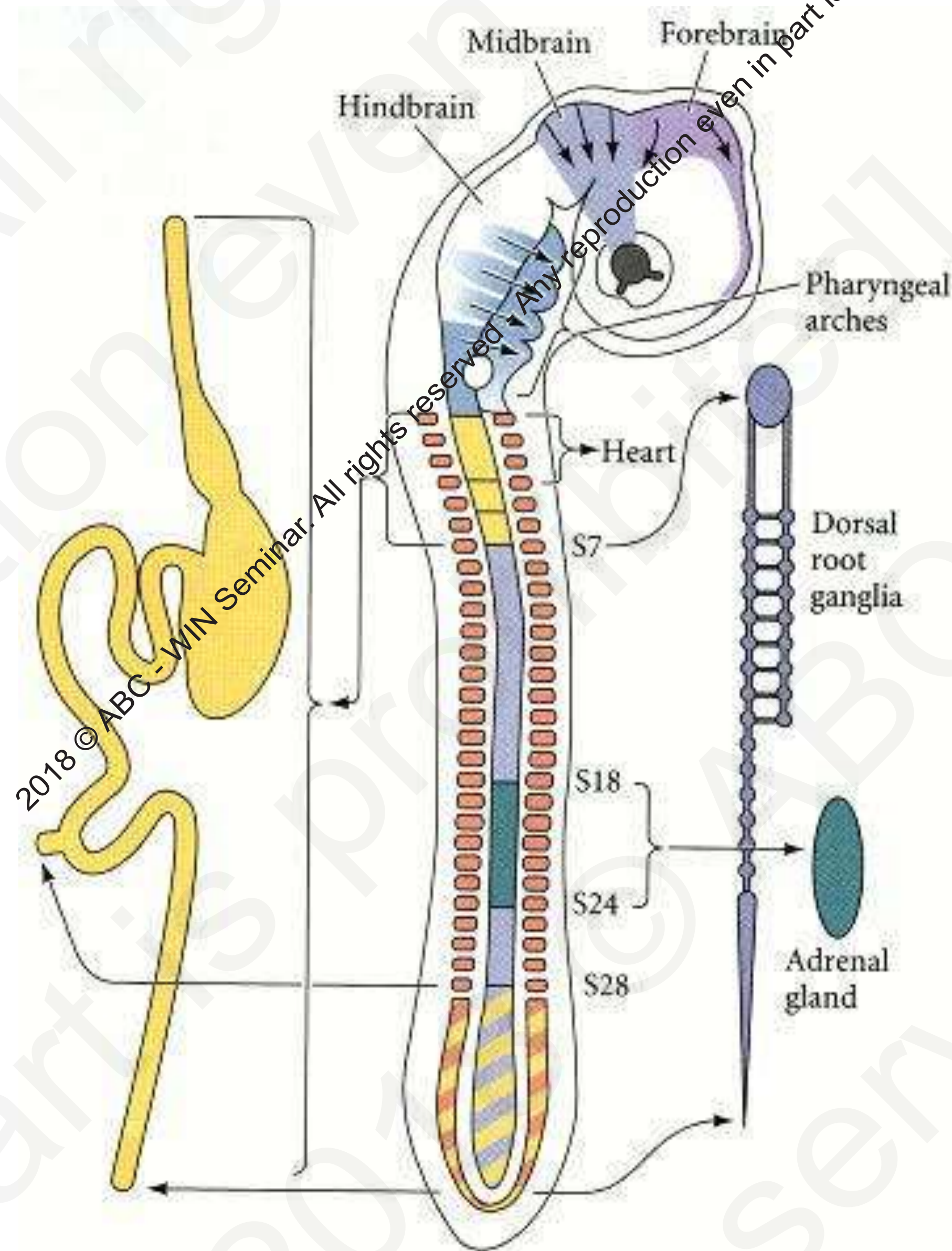
Trunk neural crest

- Adrenal chromaffin cells
- Dorsal root ganglia
- Sympathetic ganglia
- Schwann cells
- Melanocytes

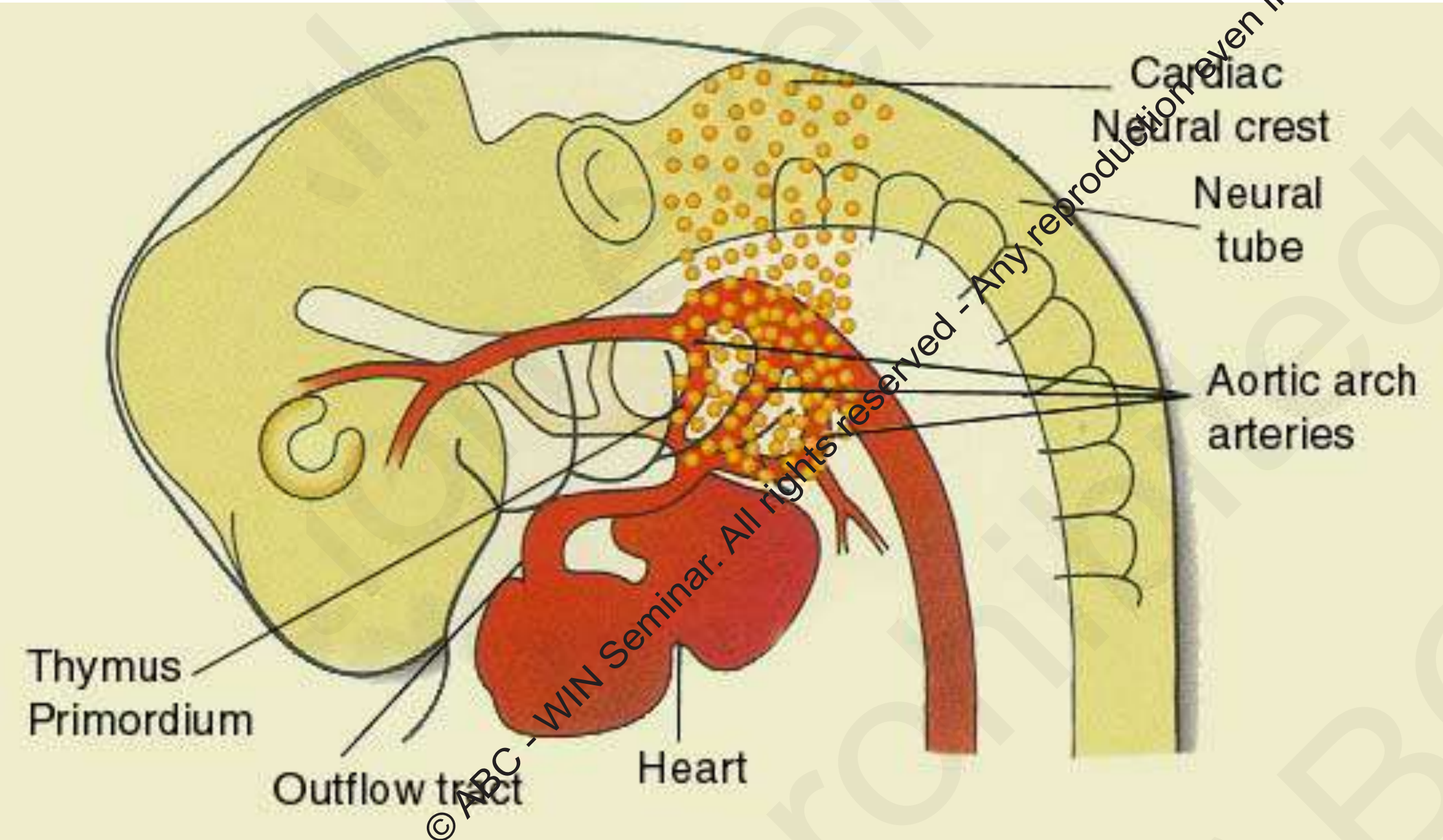
Sacral neural crest

- Enteric ganglia
- Sympathetic ganglia

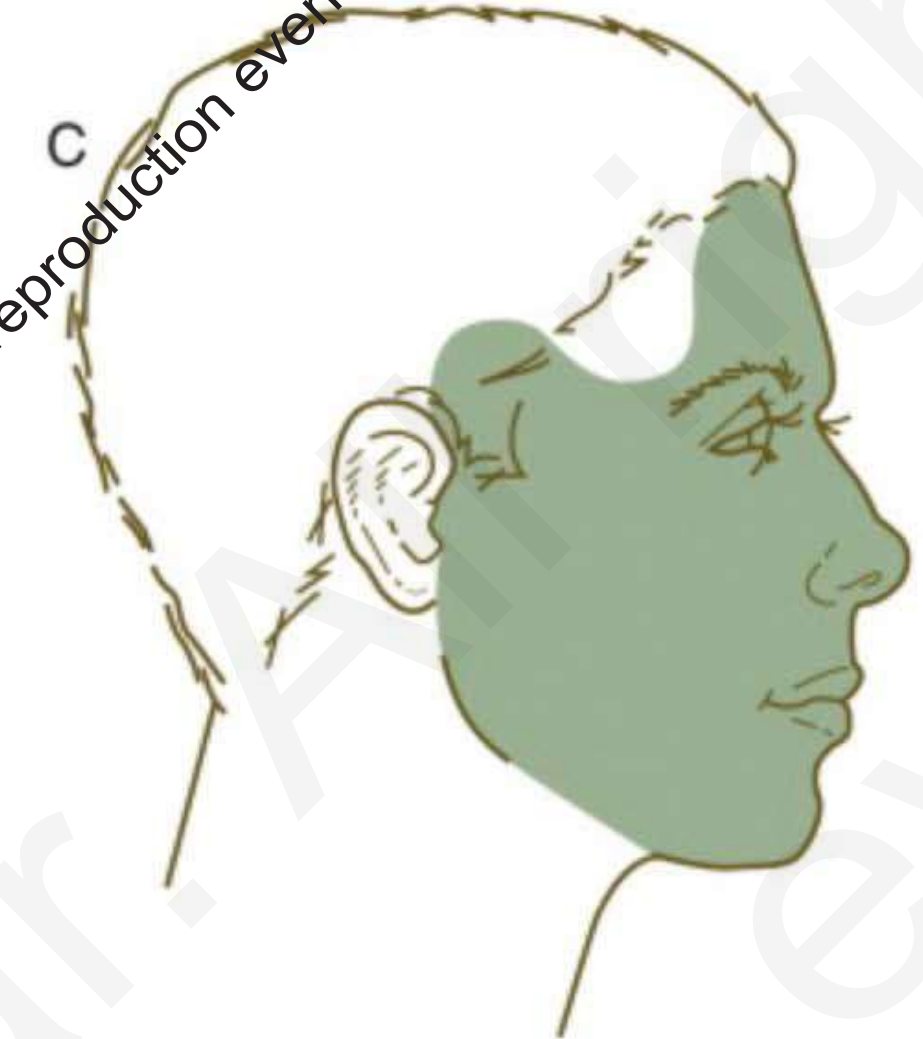
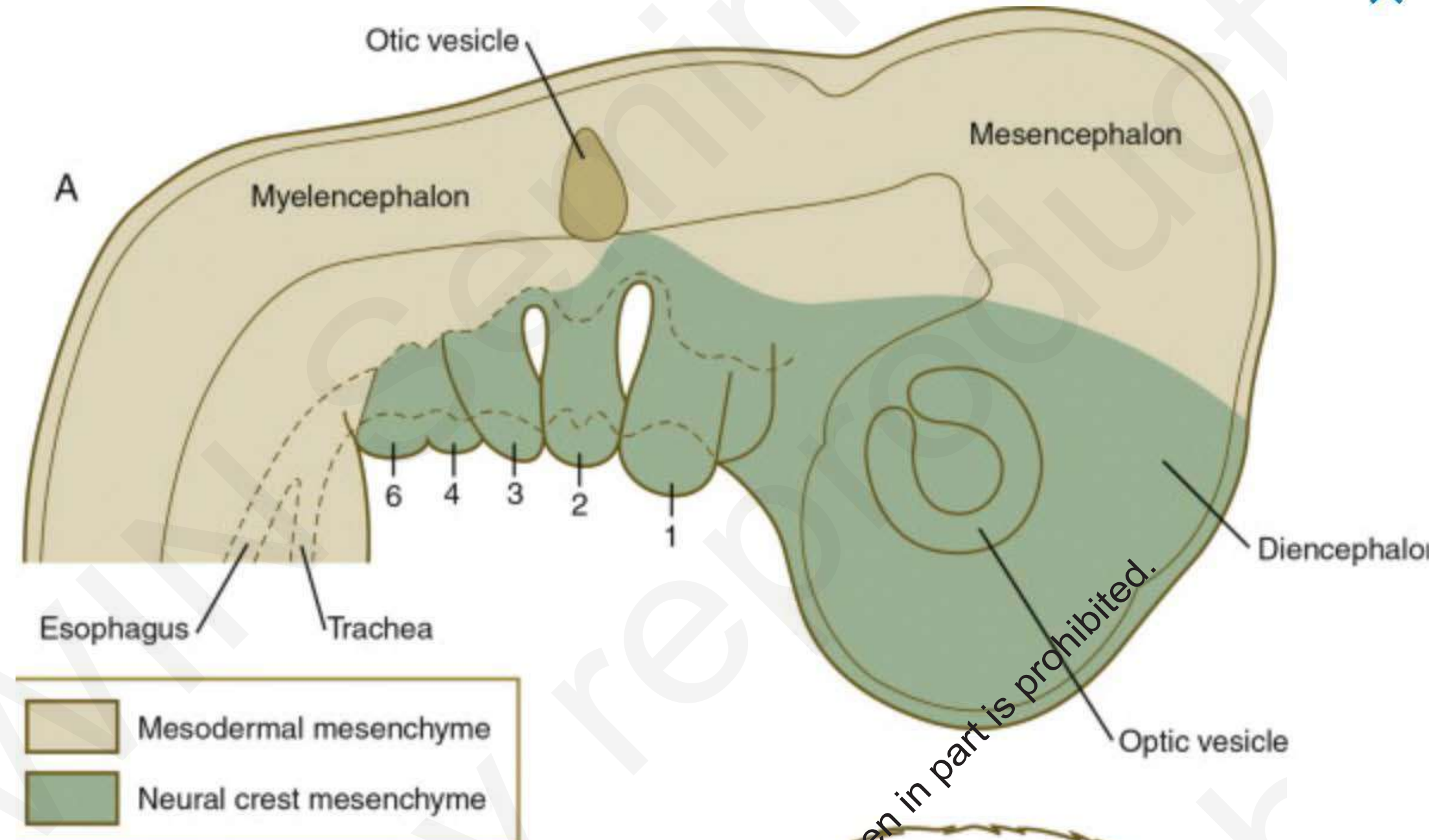
What is the Neural Crest (NC) ?



1. The cranial (cephalic) neural crest from Rhombomere
 2. The cardiac neural crest cells arise from the neural crest by somites 1–3;
 3. The trunk neural crest
 4. The vagal and sacral neural crest, whose cells generate the parasympathetic (enteric) ganglia of the gut
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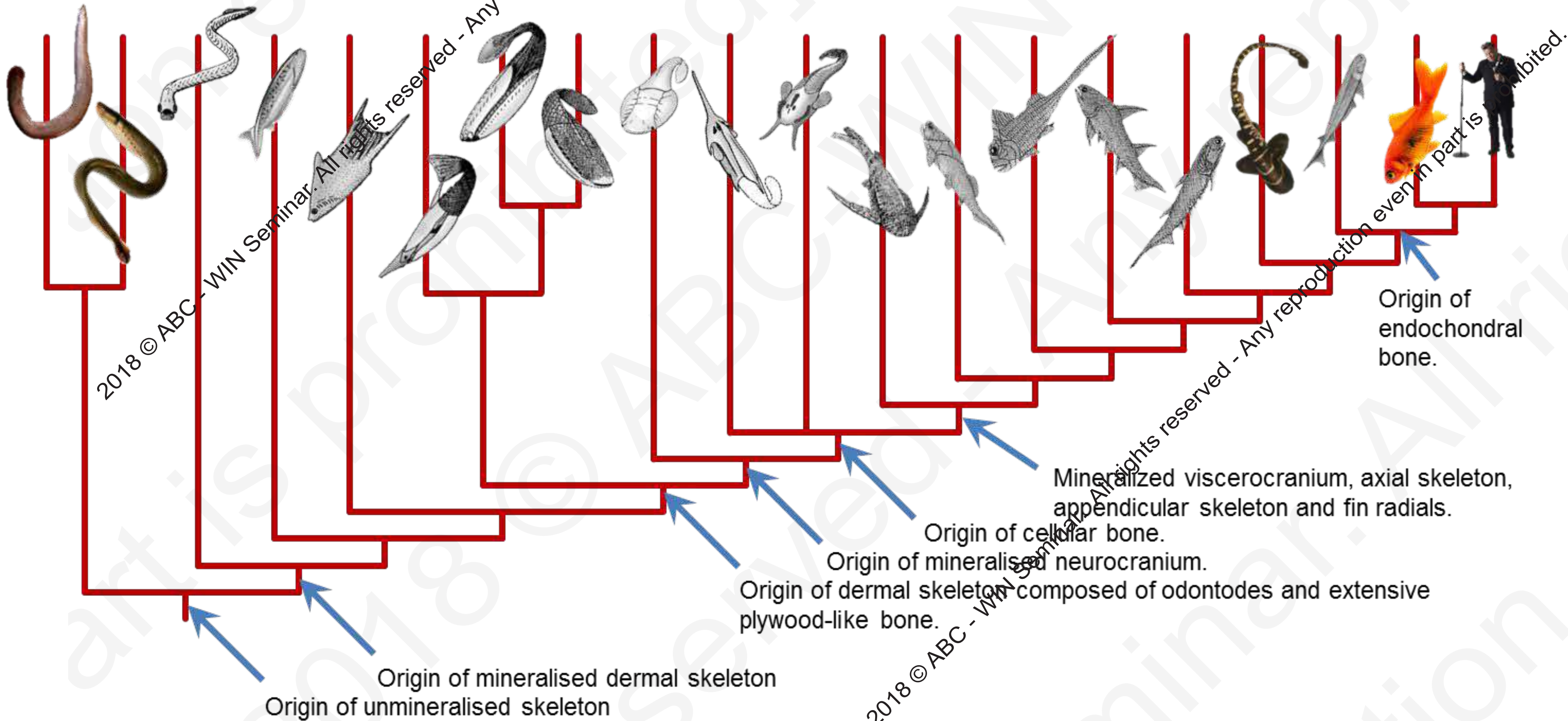
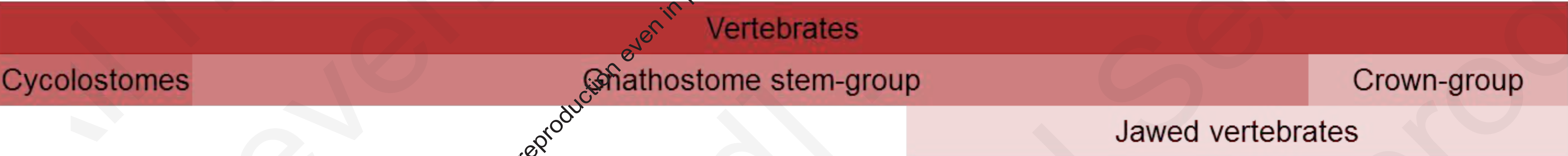


Cardiac Neural Crest

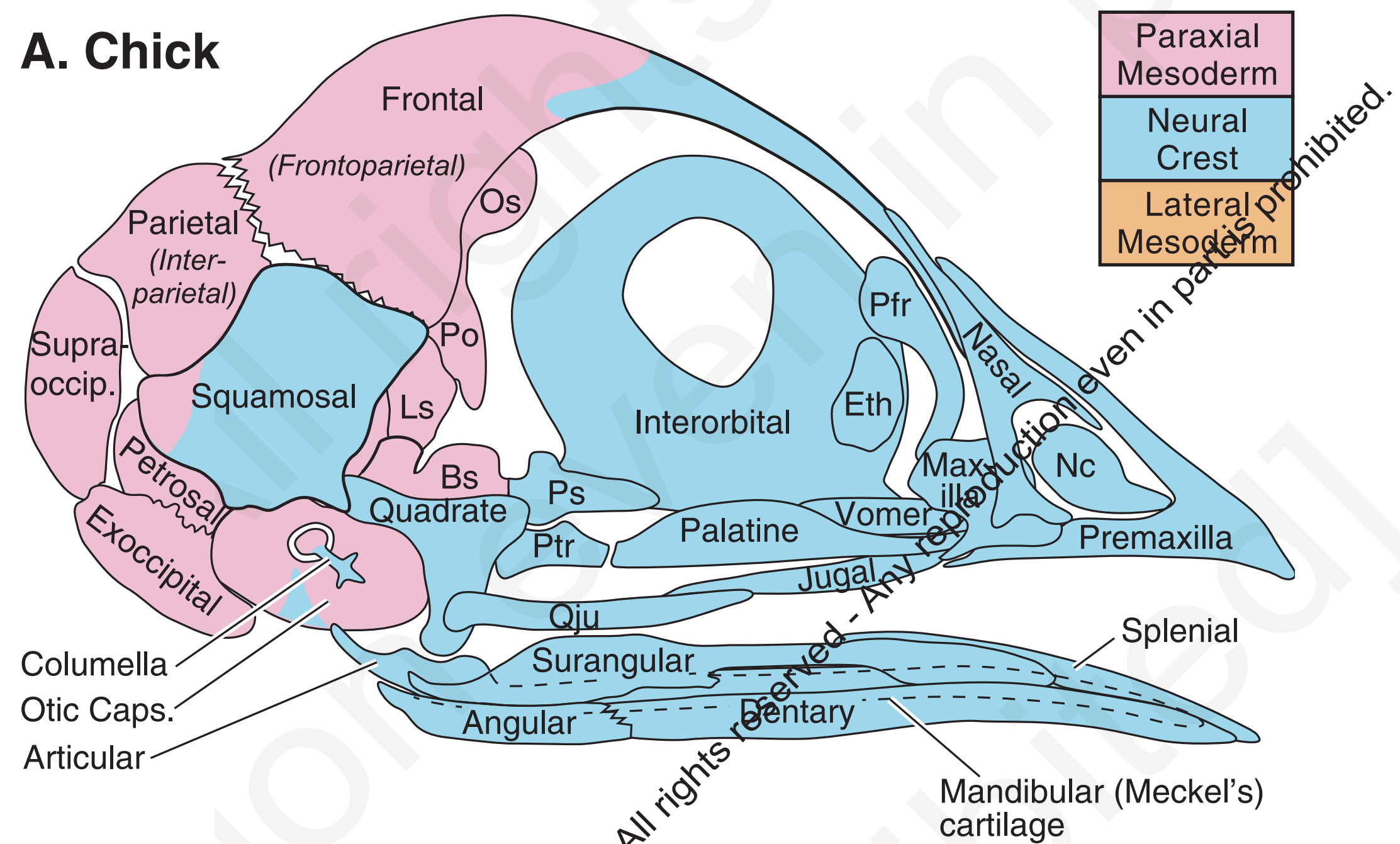


Cranial Neural Crest

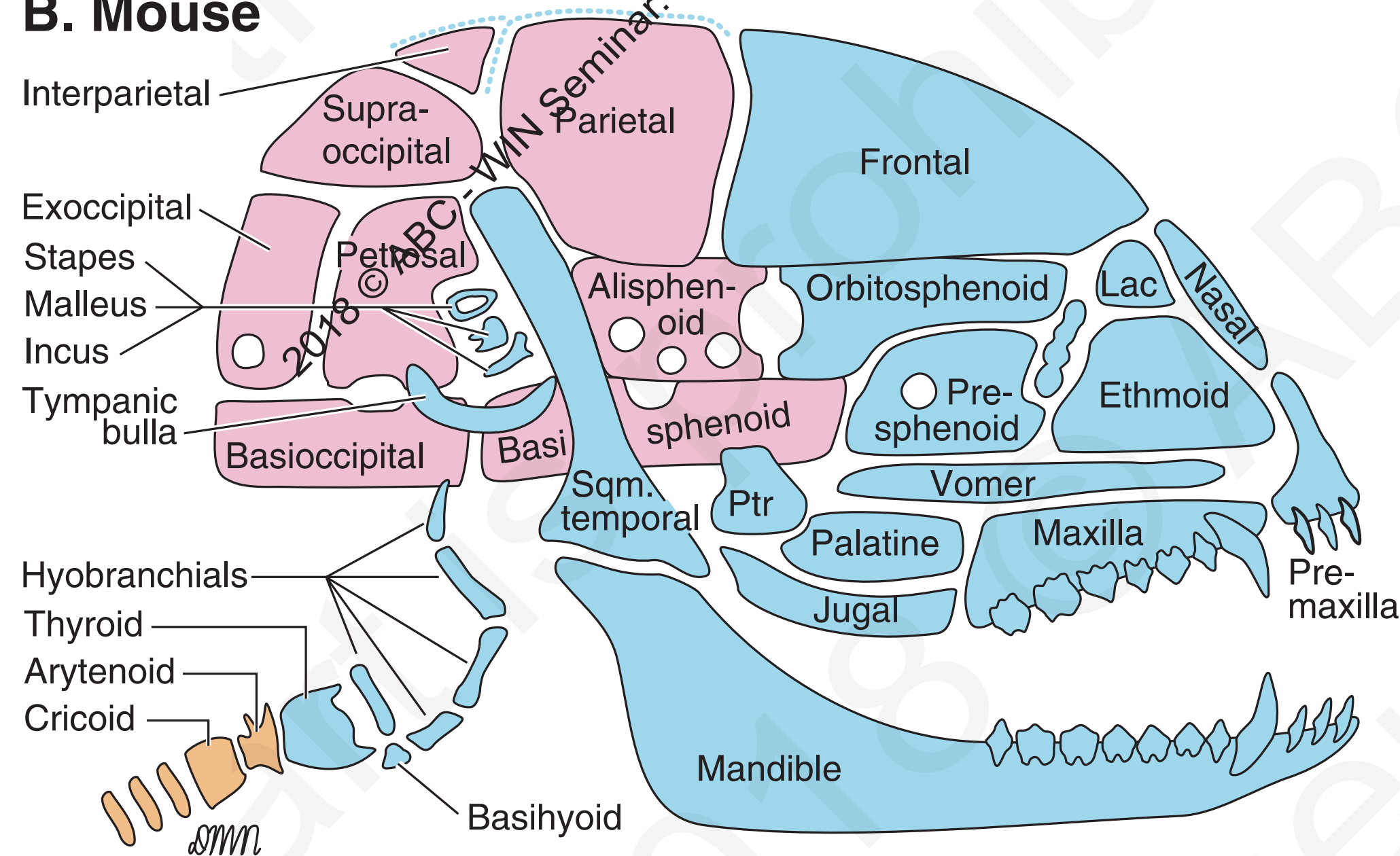
Vertebrates are characterized based on the endoderm, mesoderm, ectoderm and neural crest. Especially **head and neck consist from neural crest** that is so called the fourth germ layer. Pharyngeal system is also formed with neural crest.



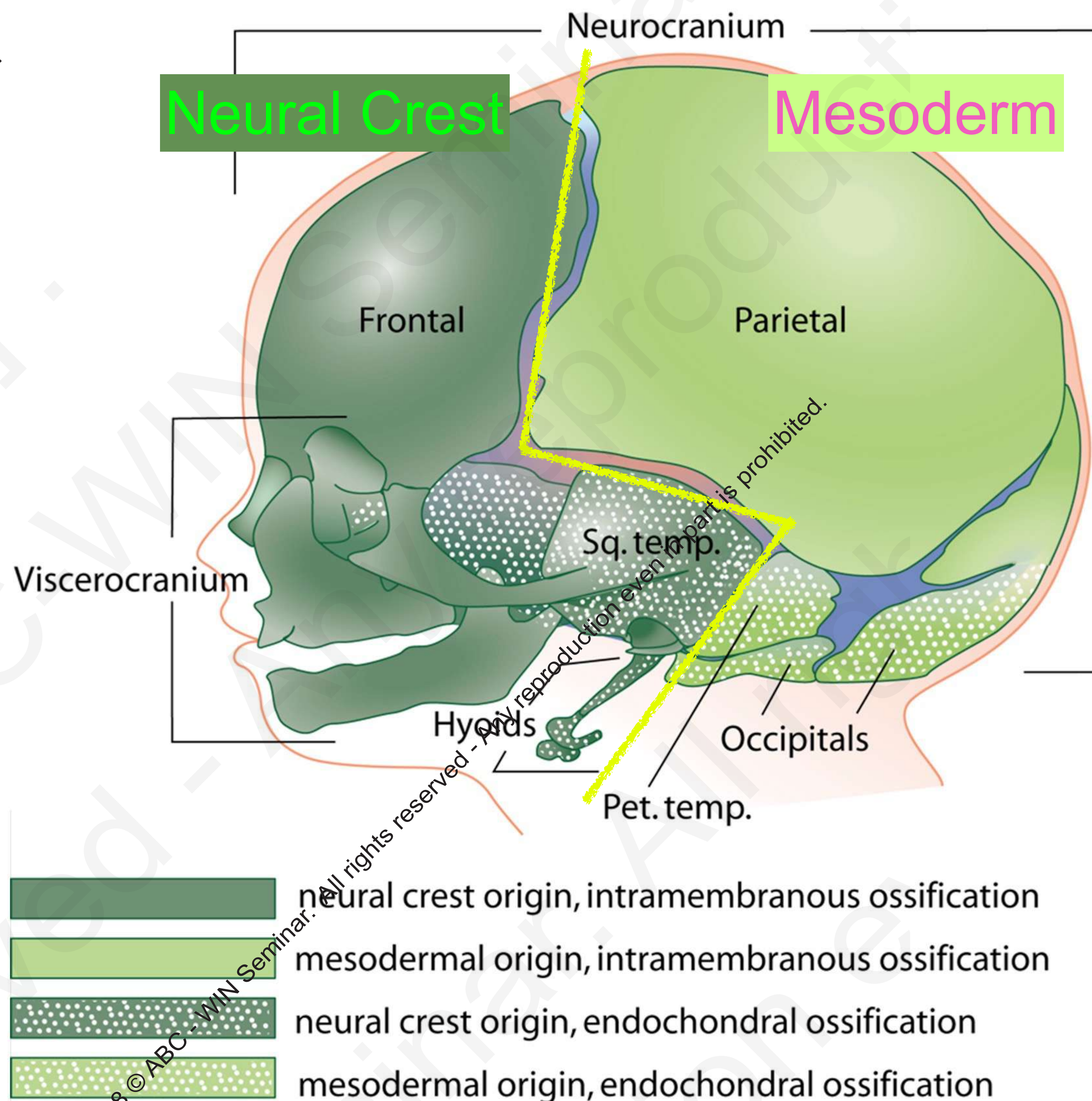
A. Chick

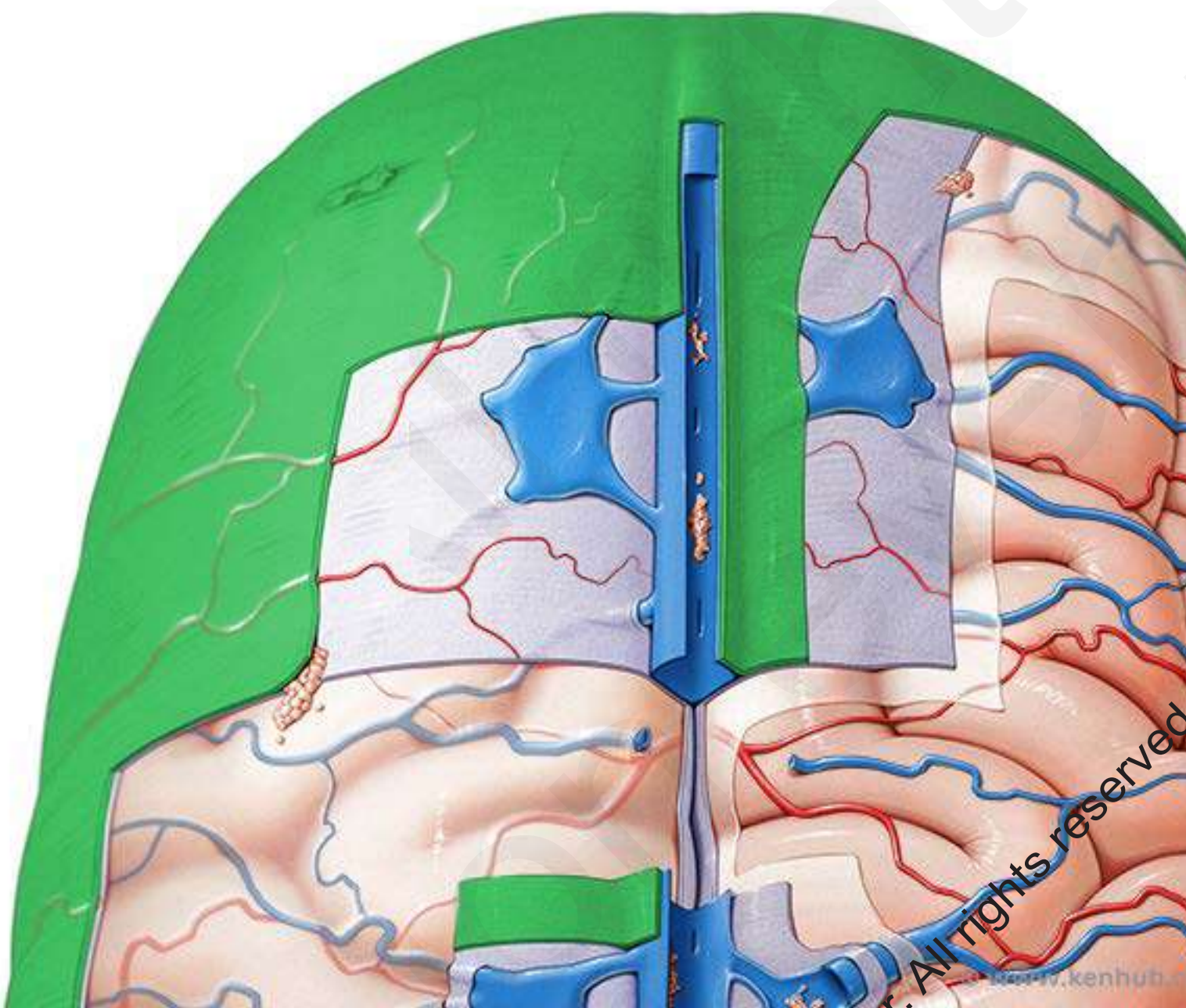


B. Mouse

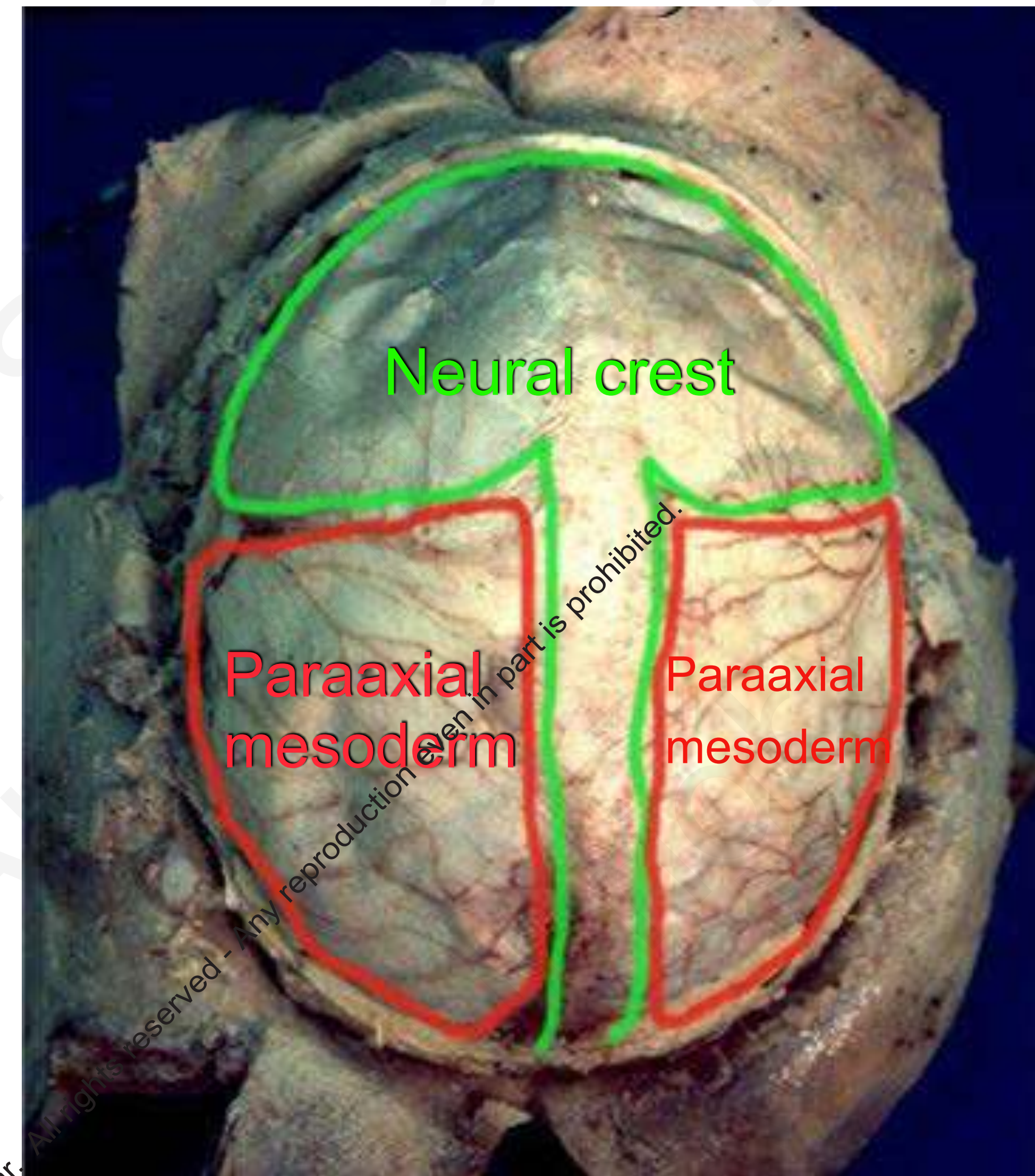
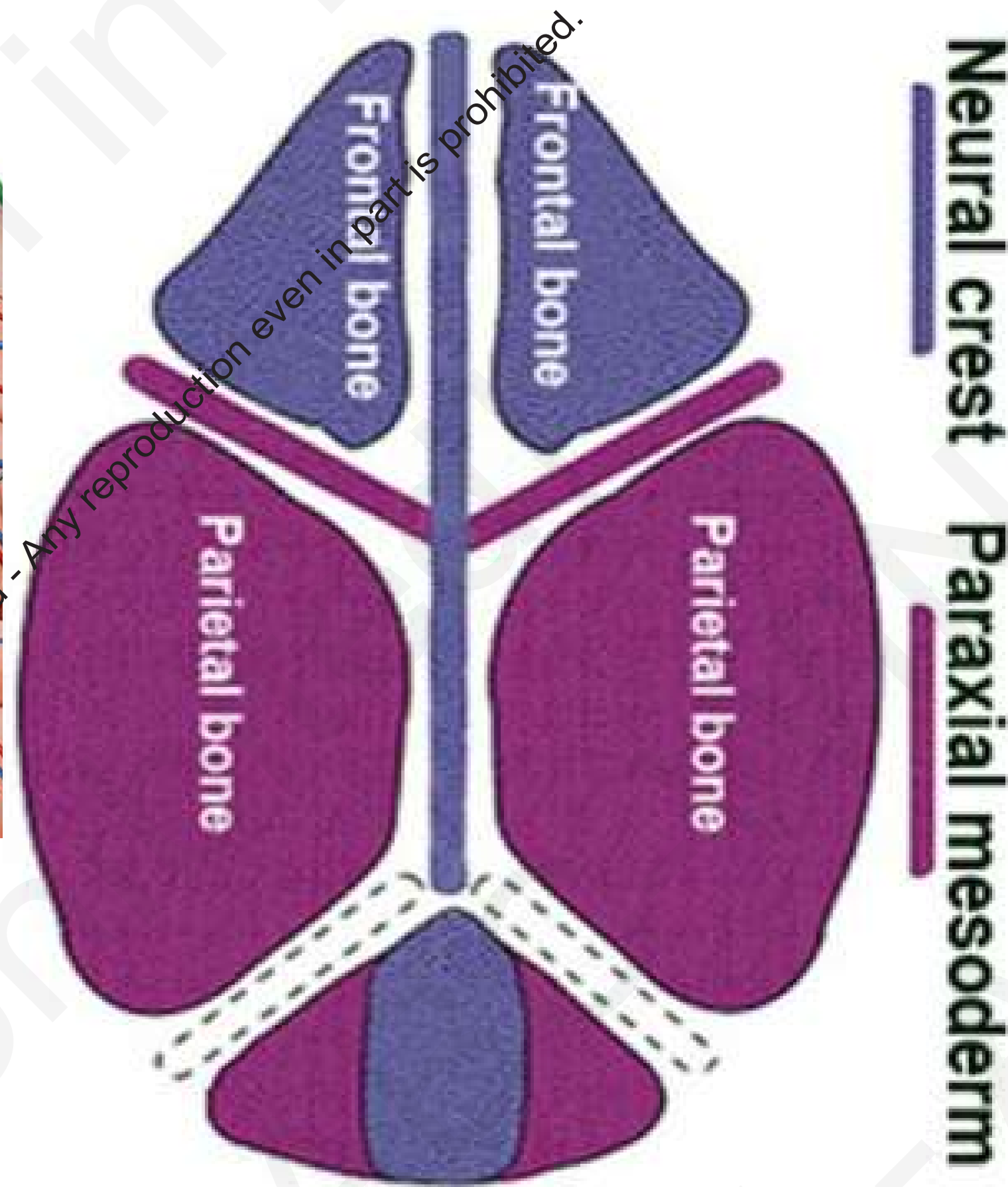


Noden et. al. J. Anat. (2005) 207, pp575–601



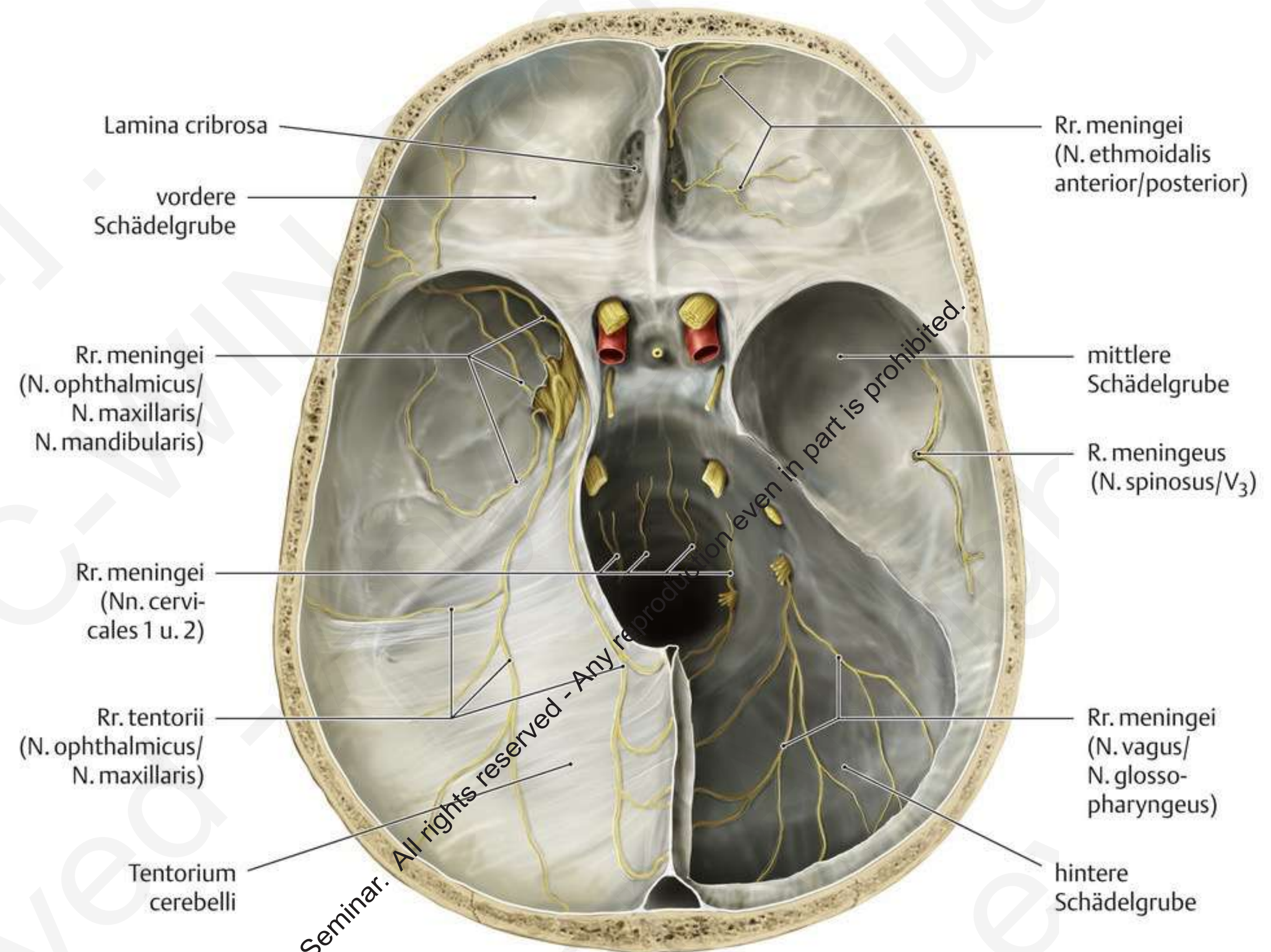
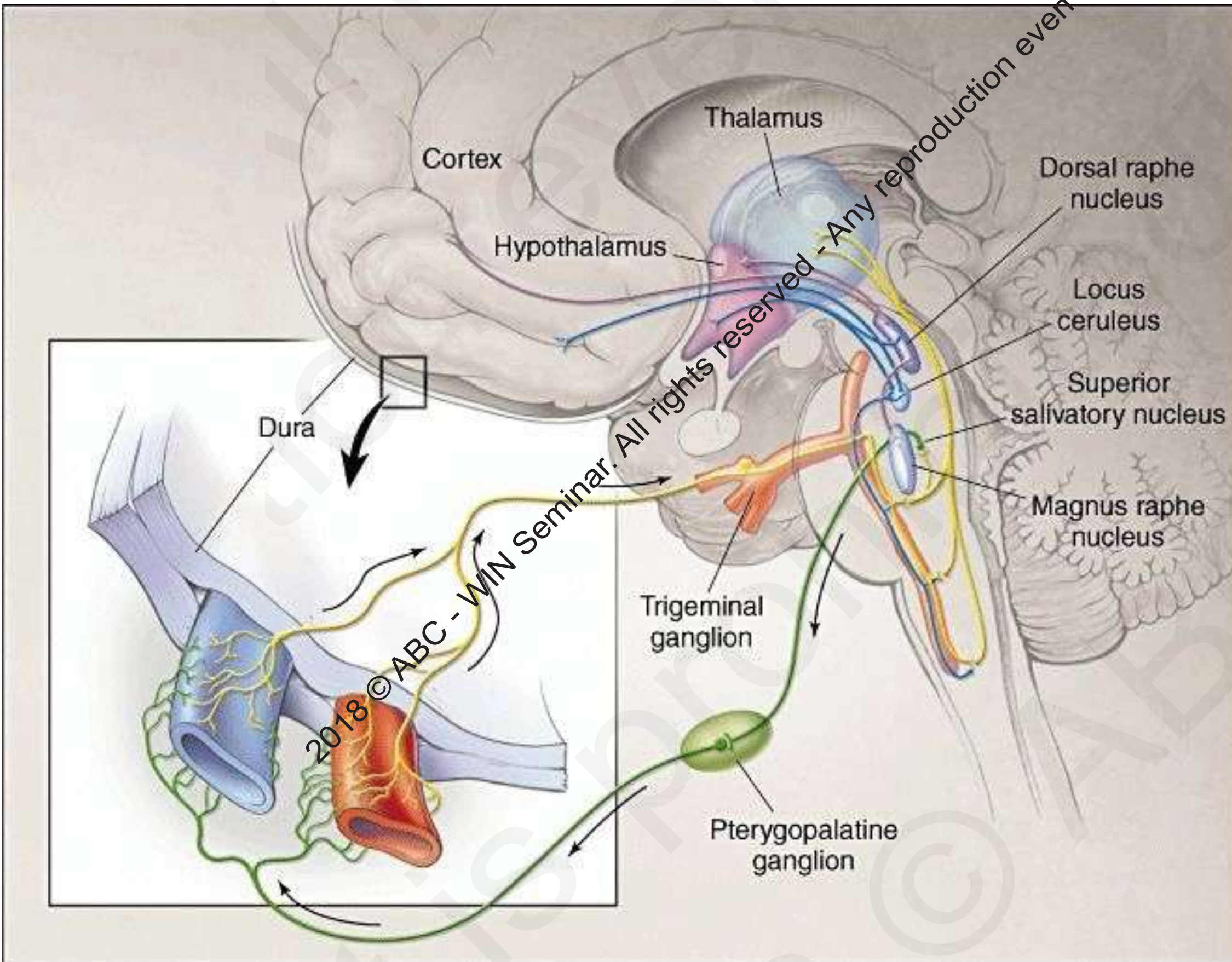


Dural membrane has two major Germ layers. One is Neural crest and the other is mesoderm.

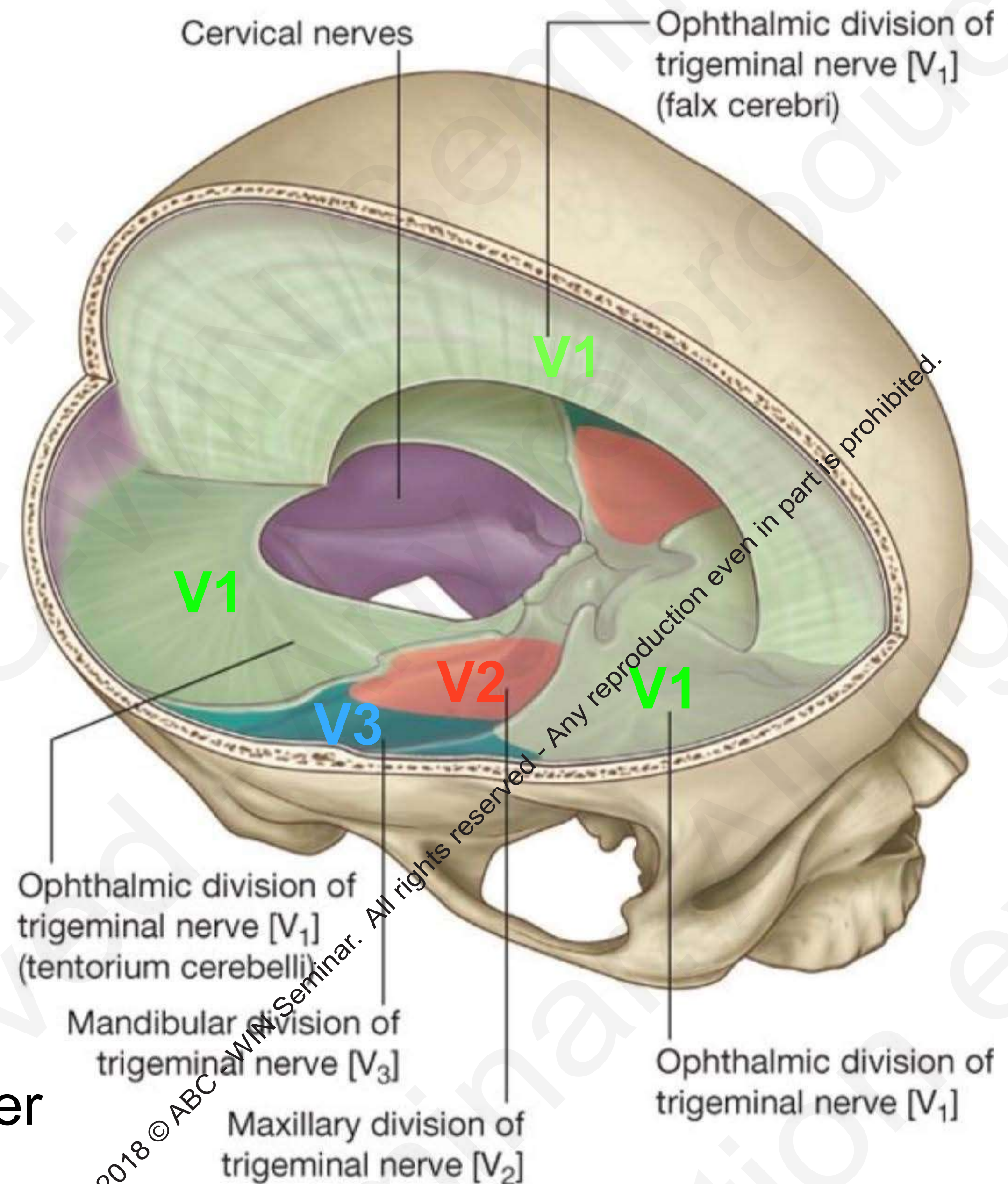
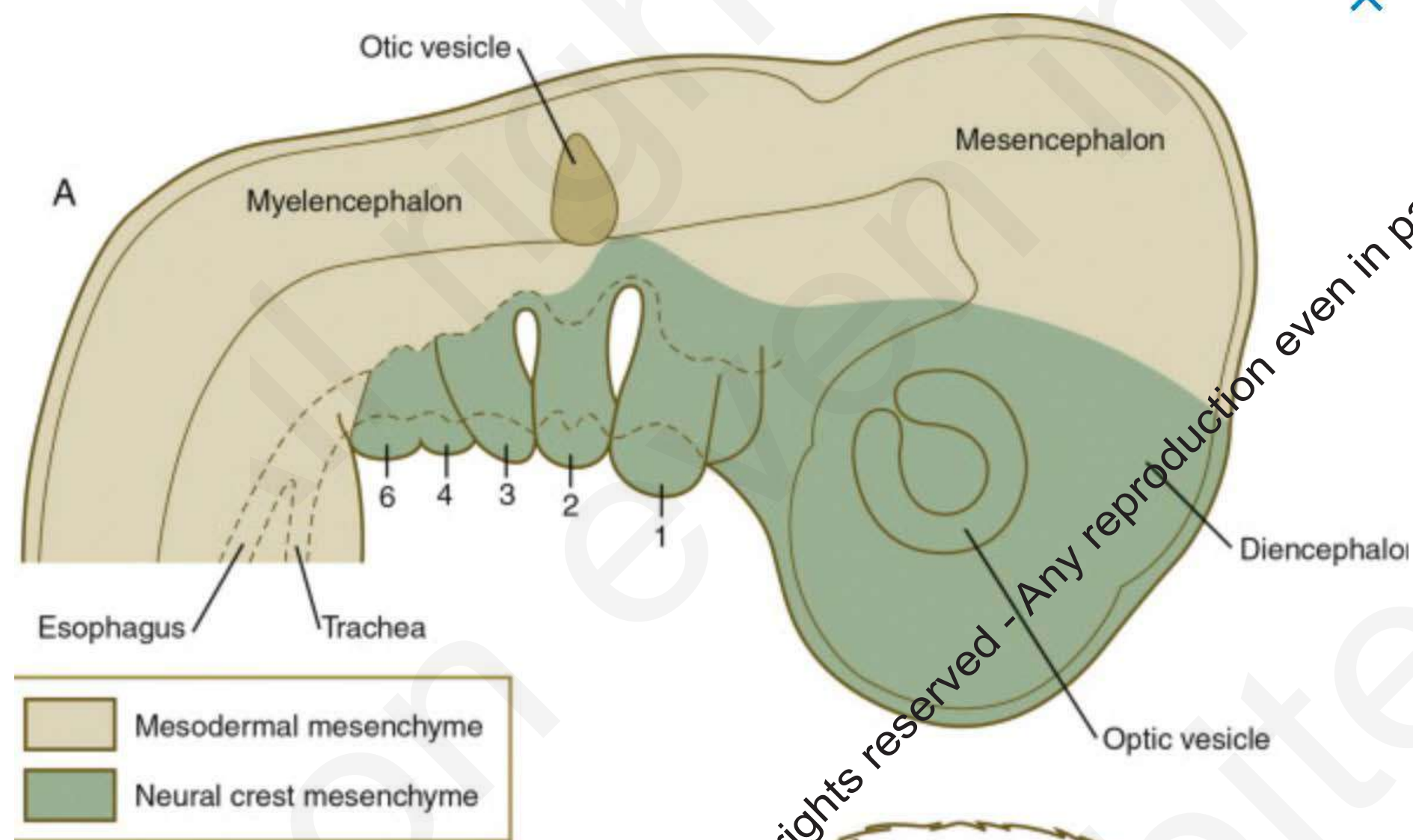


The sagittal suture is formed from neural crest cells and separates the two mesodermally derived parietal bones. The coronal suture is derived from mesoderm

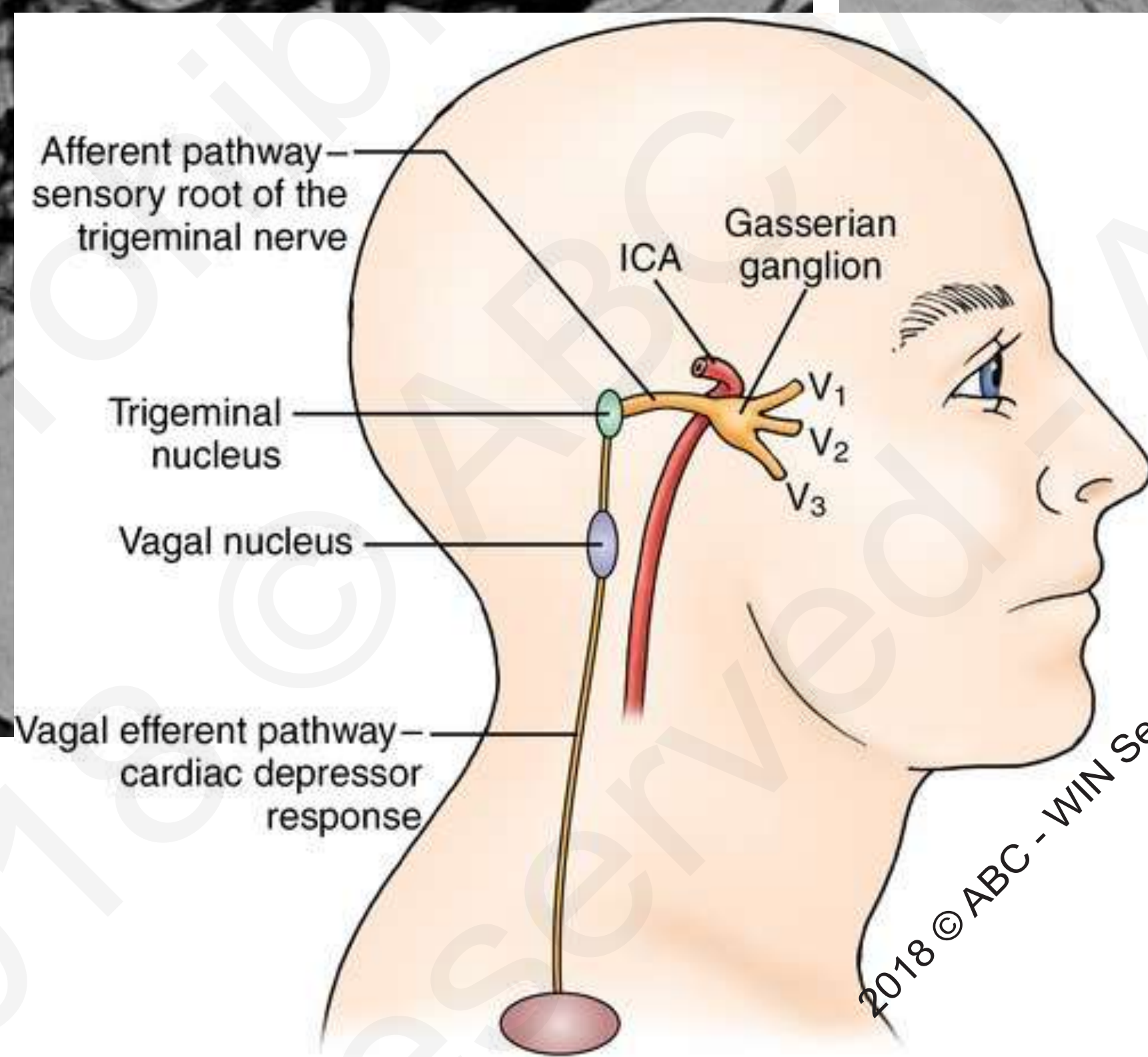
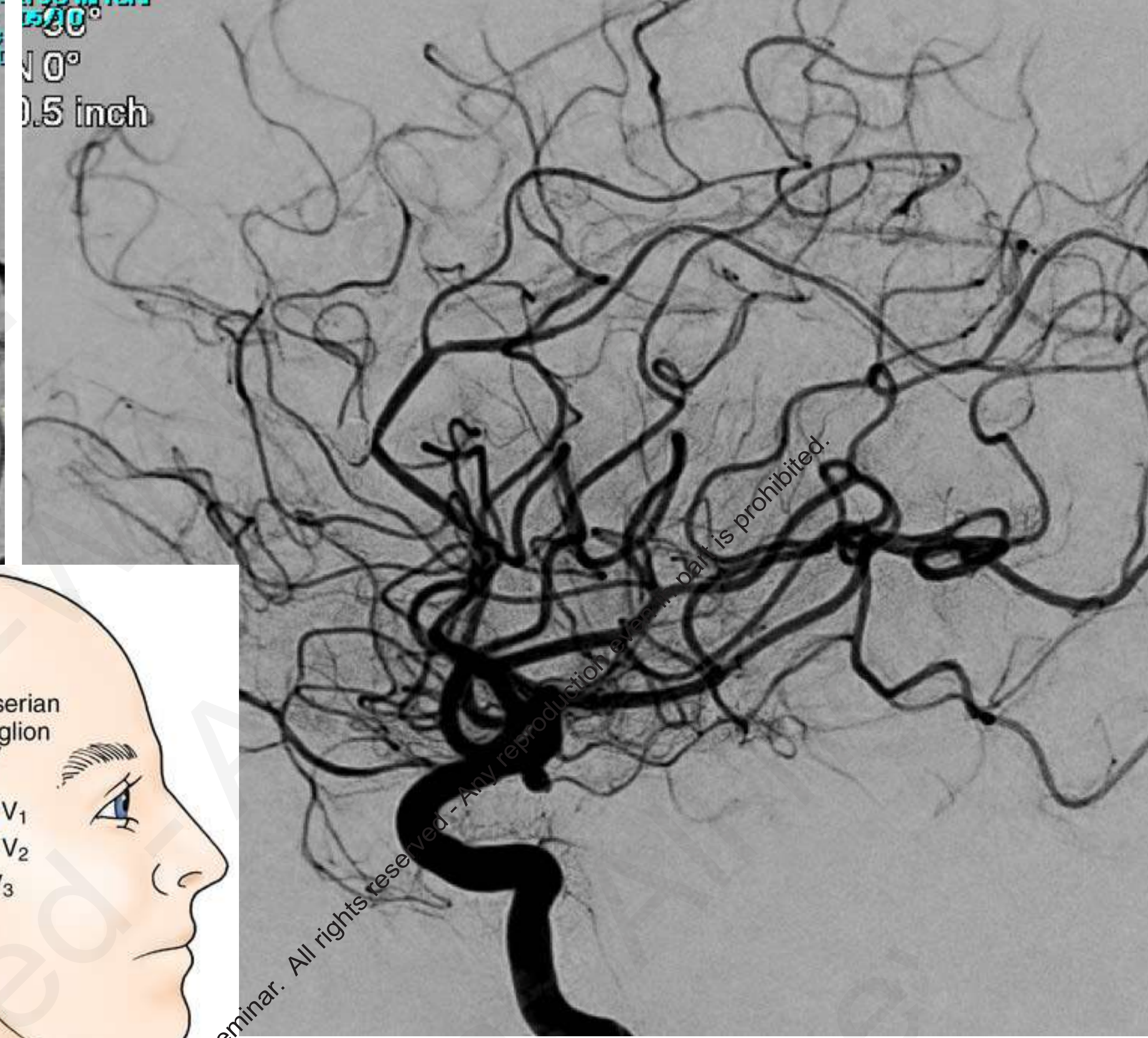
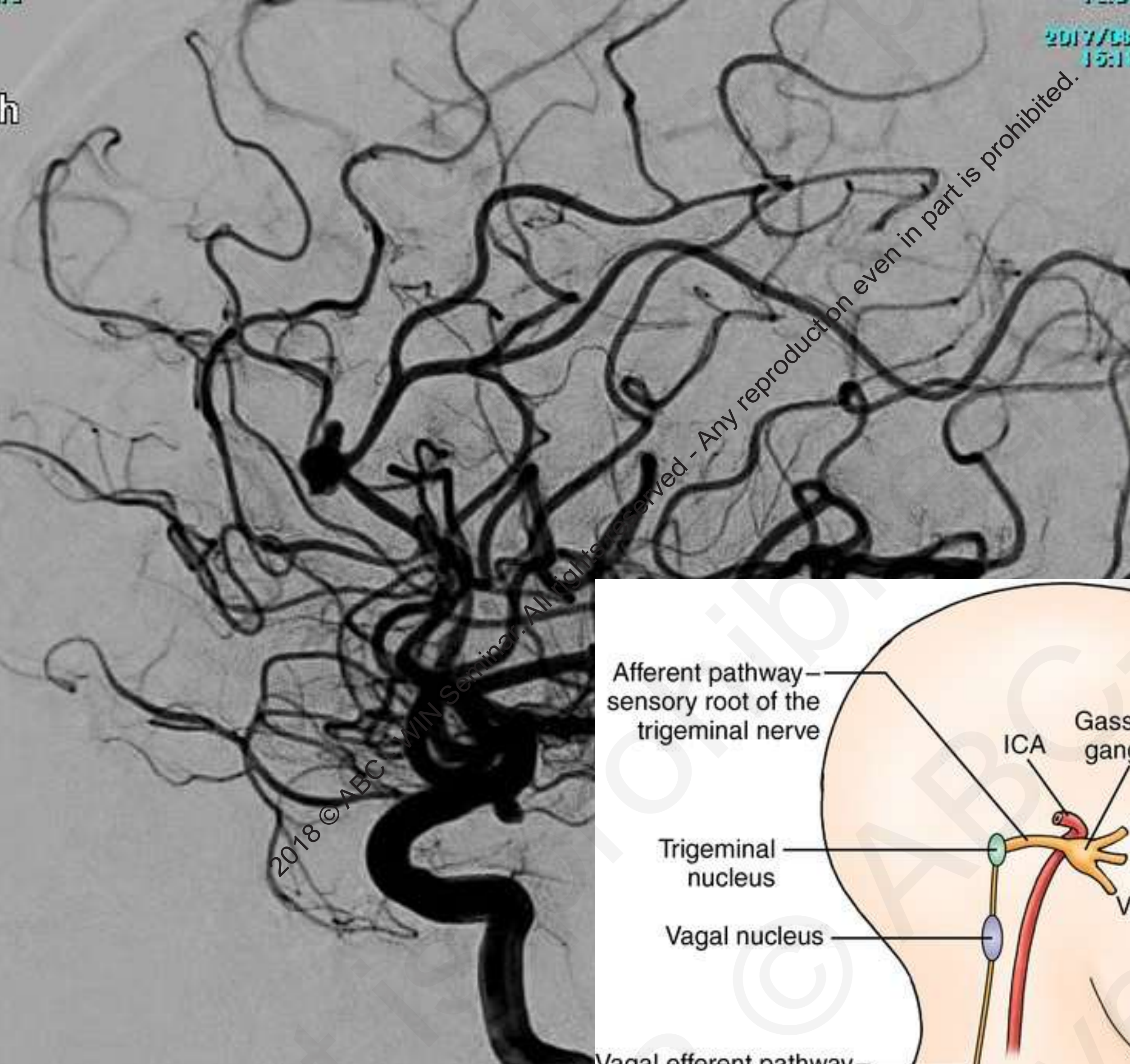
Innervation of falco-tentorial dura mater



Dural innervation



The innervation of falco-tentorial dura mater is trigeminal nerve V1.



V1 was stimulated with devices and it caused trigeminal cardiac reflux.

Menu

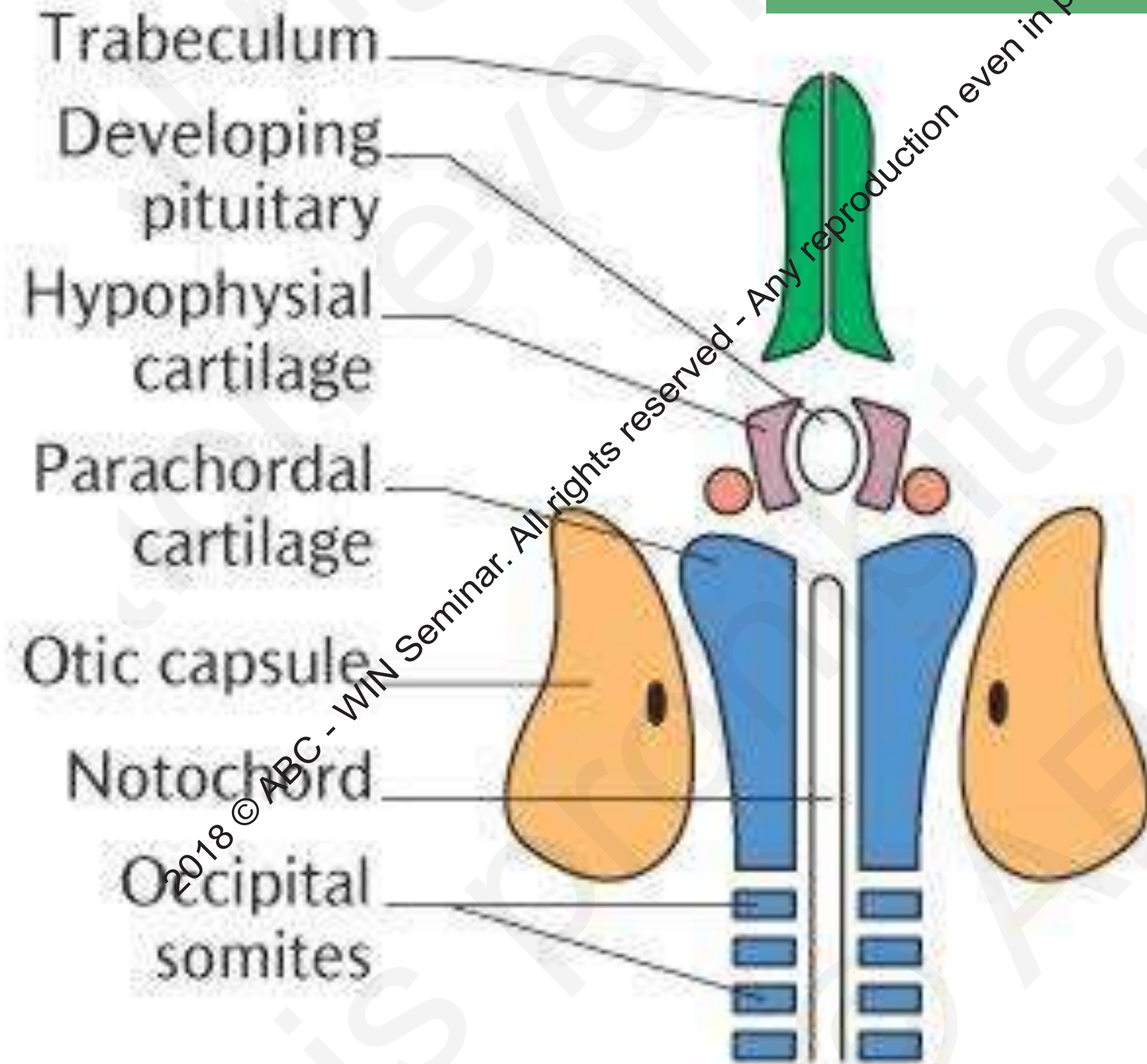
1. Embryology of the dura mater encephali

2. Neural crest cell and falco-tentorial dura mater

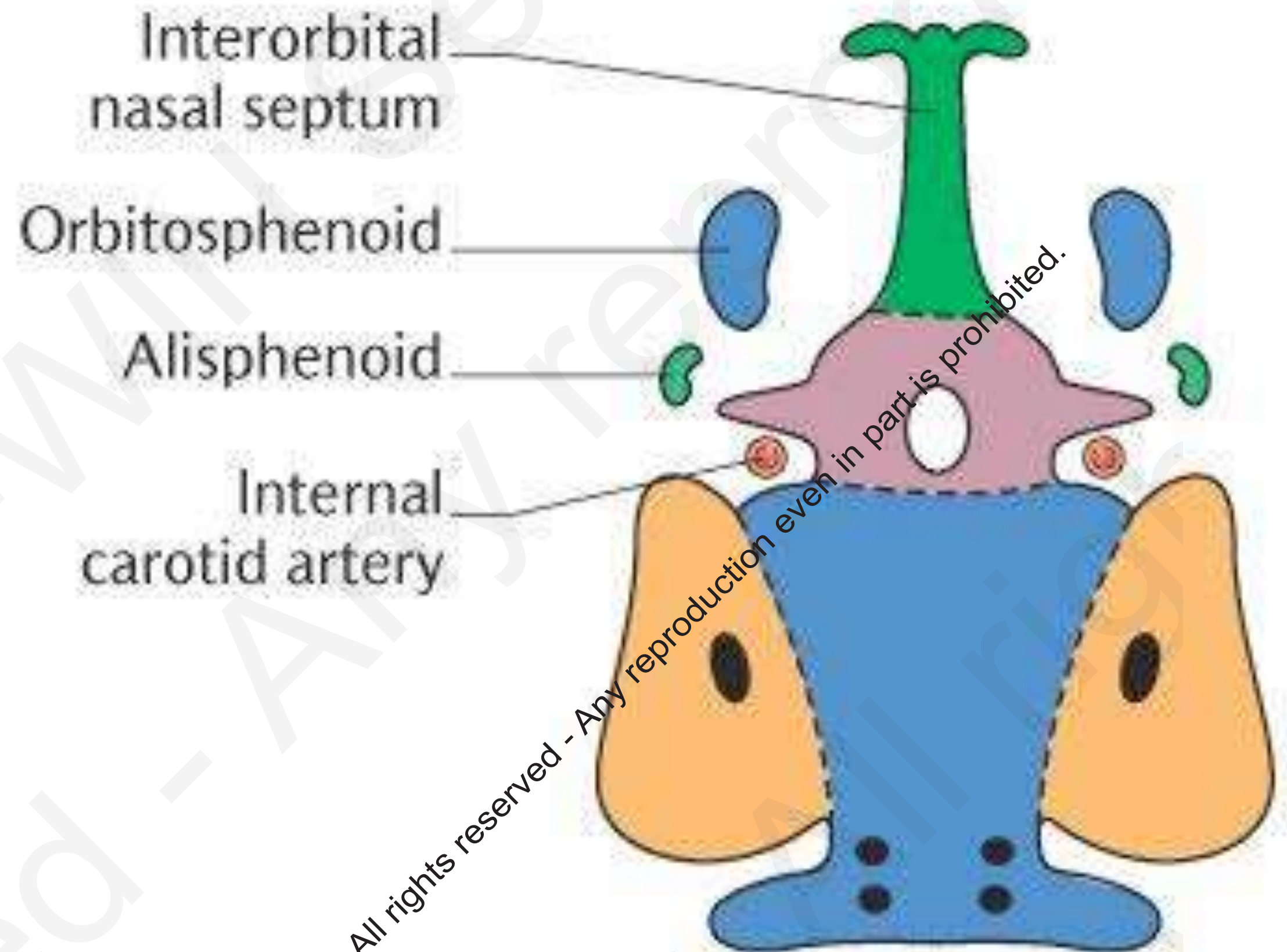
3. Clinical consideration of falco-tentorial dura mater

A

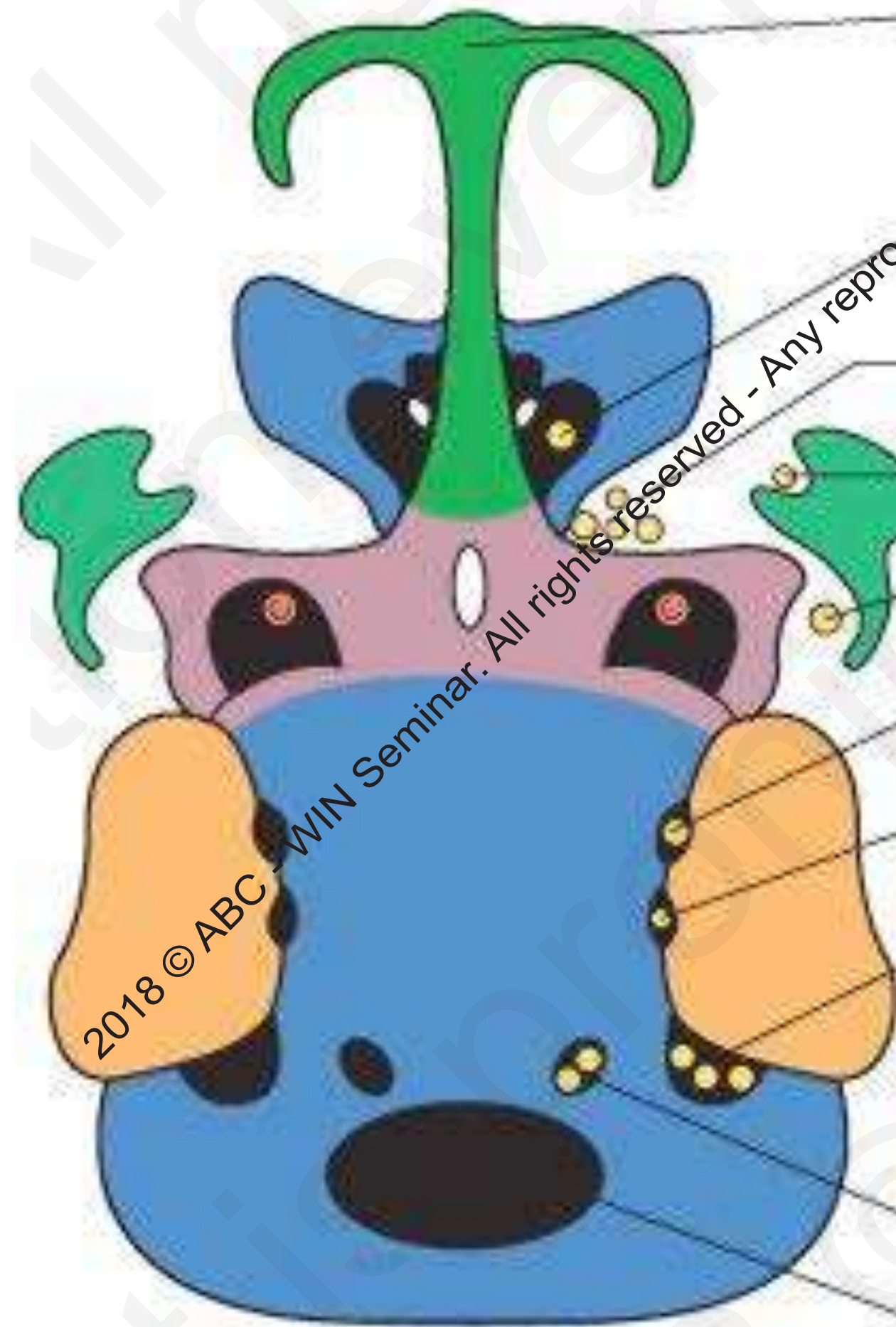
neural crest cells



neural crest cells



C



Nasal capsule

II

III IV V1 VI

V2

V3

VII

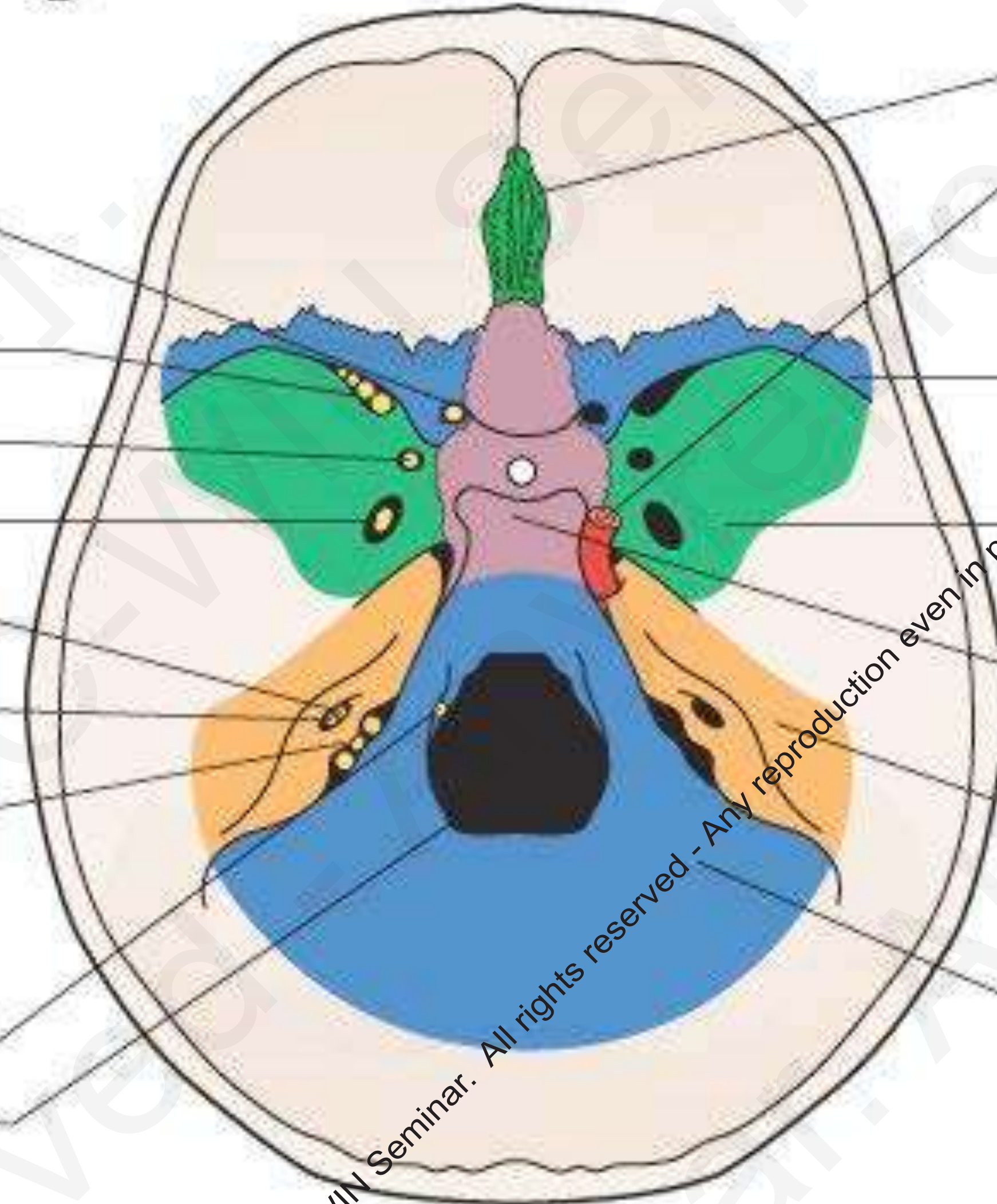
VIII

IX X XI

XII

Foramen magnum

D



Ethmoid

Internal carotid artery

Lesser wing

Greater wing

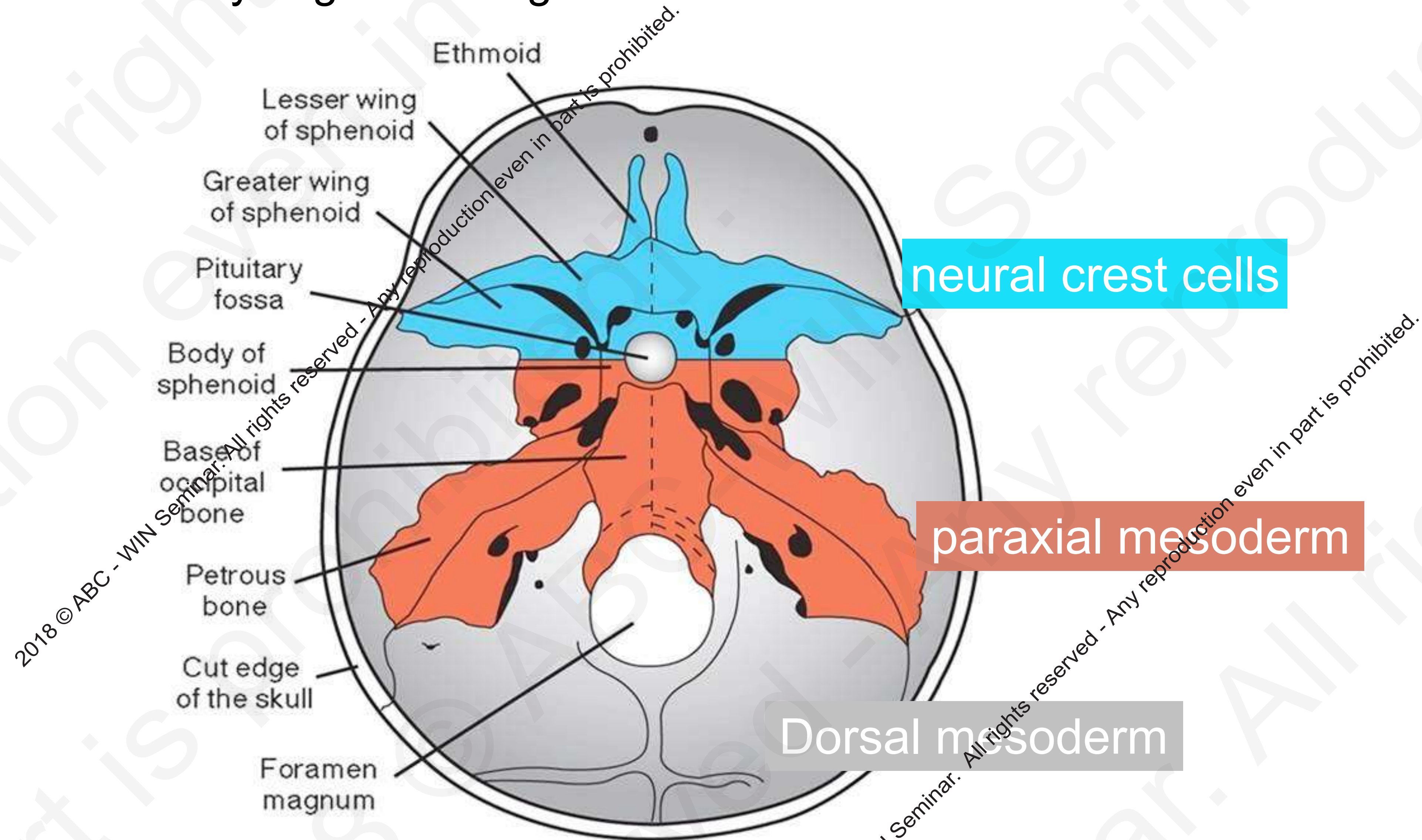
Body

Petrous temporal

Occipital

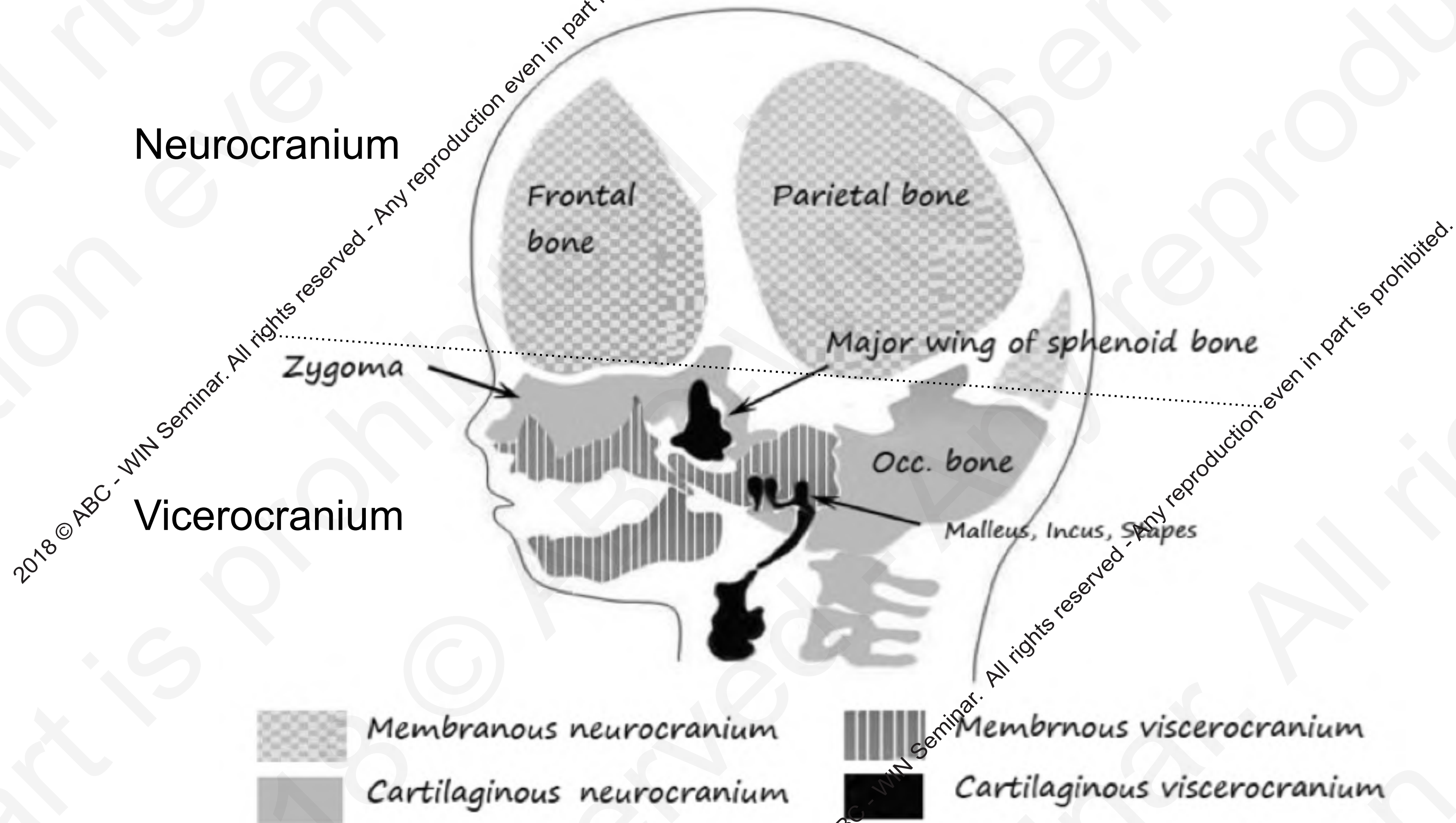
Sphenoid

Embryological back ground of skull and dural membrane



(Copyright © 2010 Wolters Kluwer); Base of the skull in adult showing the various embryonic components that participate in its formation. Part derived from neural crest cells (blue) and paraxial mesoderm (red) (2010)

Embryology of ossification in relation with Membranous bone and Endochondral (cartilaginous) bone



SKULL of the NEWBORN

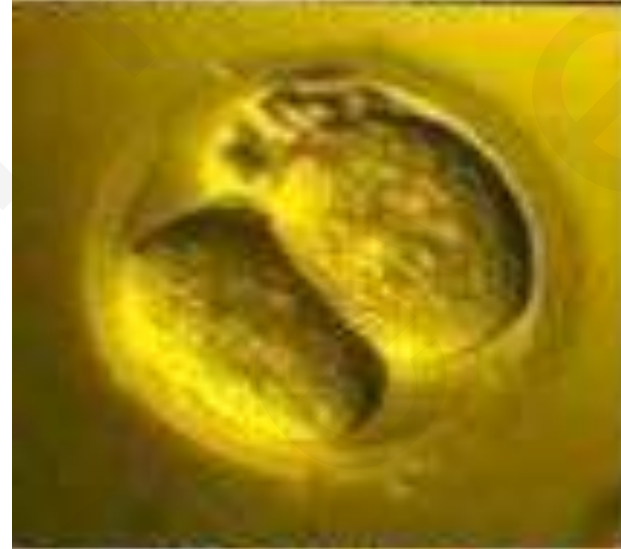
Flat bones are connected through seams of connective tissue

SUTURES.

Sagittal suture- neural crest cells

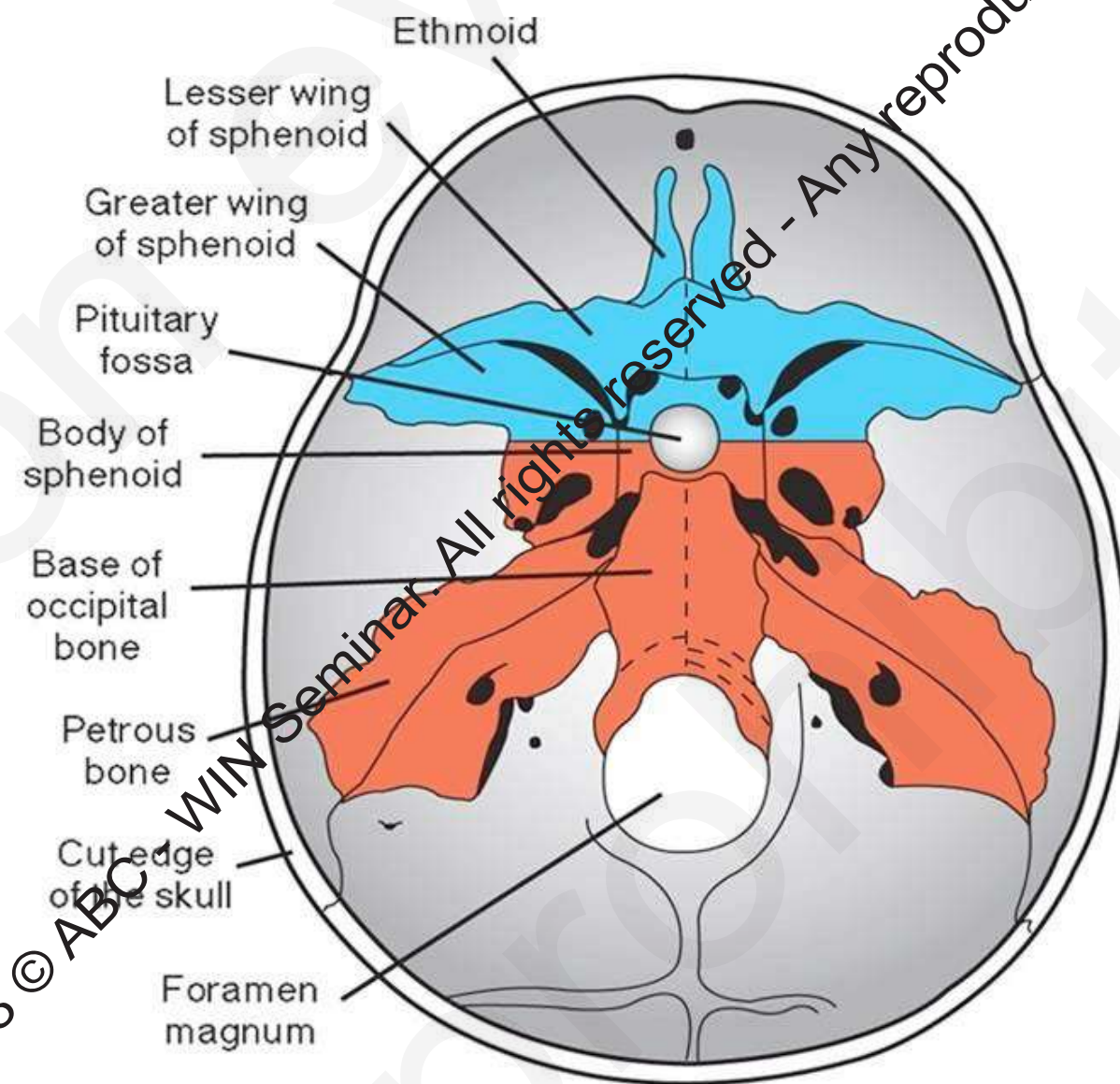
Coronal suture- paraxial mesoderm

FONTANELLES-more than two bones meet, sutures are widened.



Introduction of embryological concept of domains

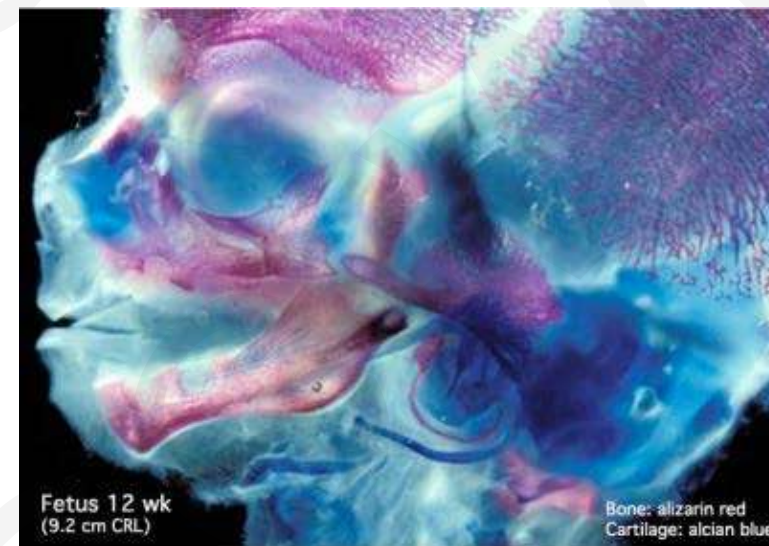
Neural crest cells



Paraxial mesoderm

Dorsal mesoderm

Endochondral bone



Membraneous bone

Neural crest

Paraxial mesoderm

dorsal mesoderm

Cephalic neural crest as the risk factor of dural AVFs

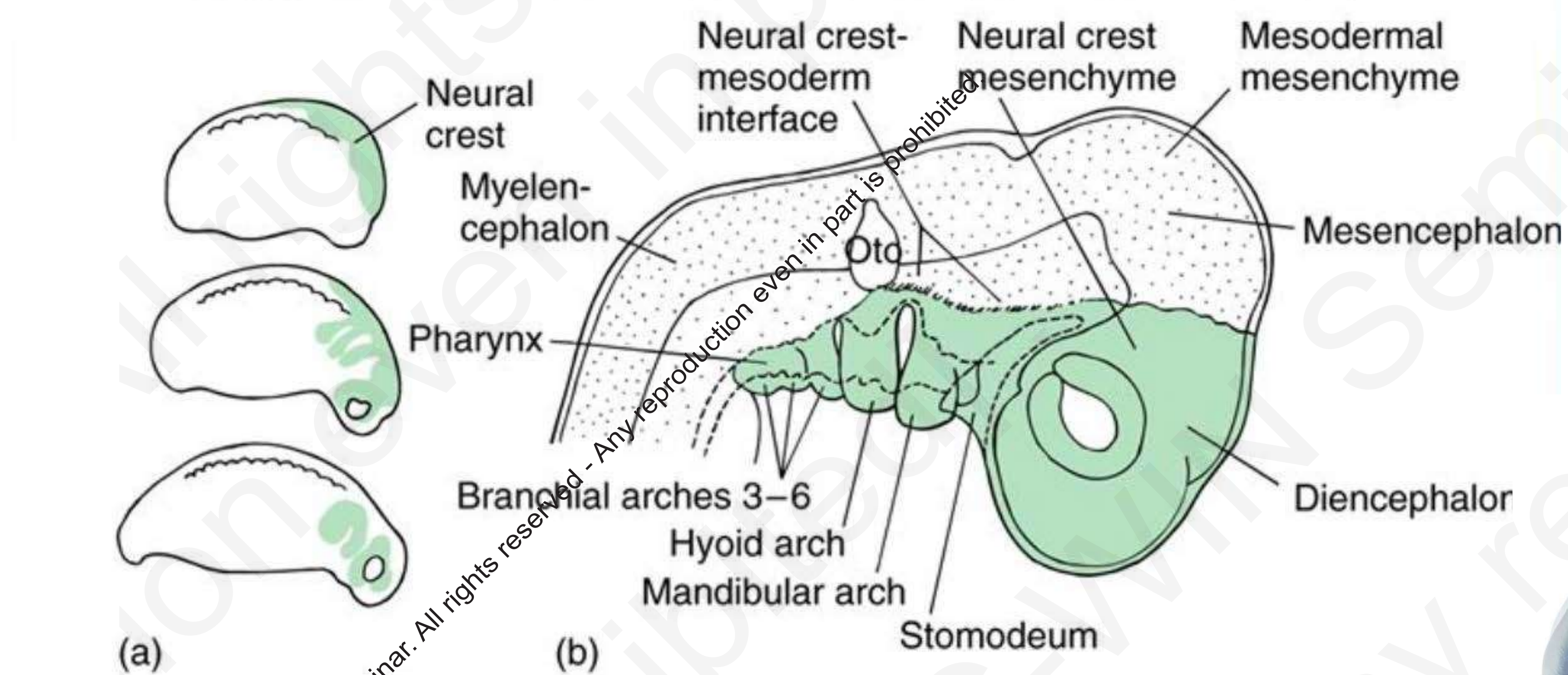
Purpose:

This study retrospectively analyzed the correlation between the distribution of DAVFs and the dural membrane derived from neural crest cells (NCC).

Material and Methods:

Sixty-six consecutive of DAVFs (32 men and 34 women, mean 68.4 years) were analyzed. Superselective digital subtraction angiography and high-resolution cone beam CT were performed in order to identify the shunt point.

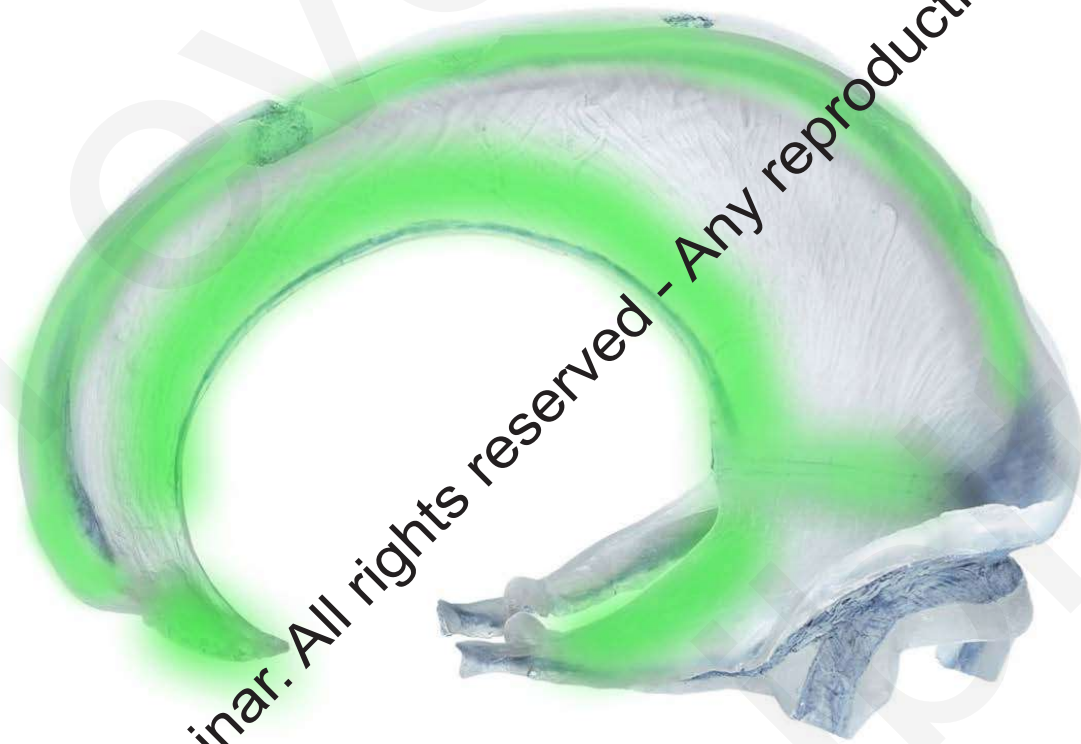
The topographical area derived from NCC was reviewed and identified from the literatures.



Neural crest contributions to the skull

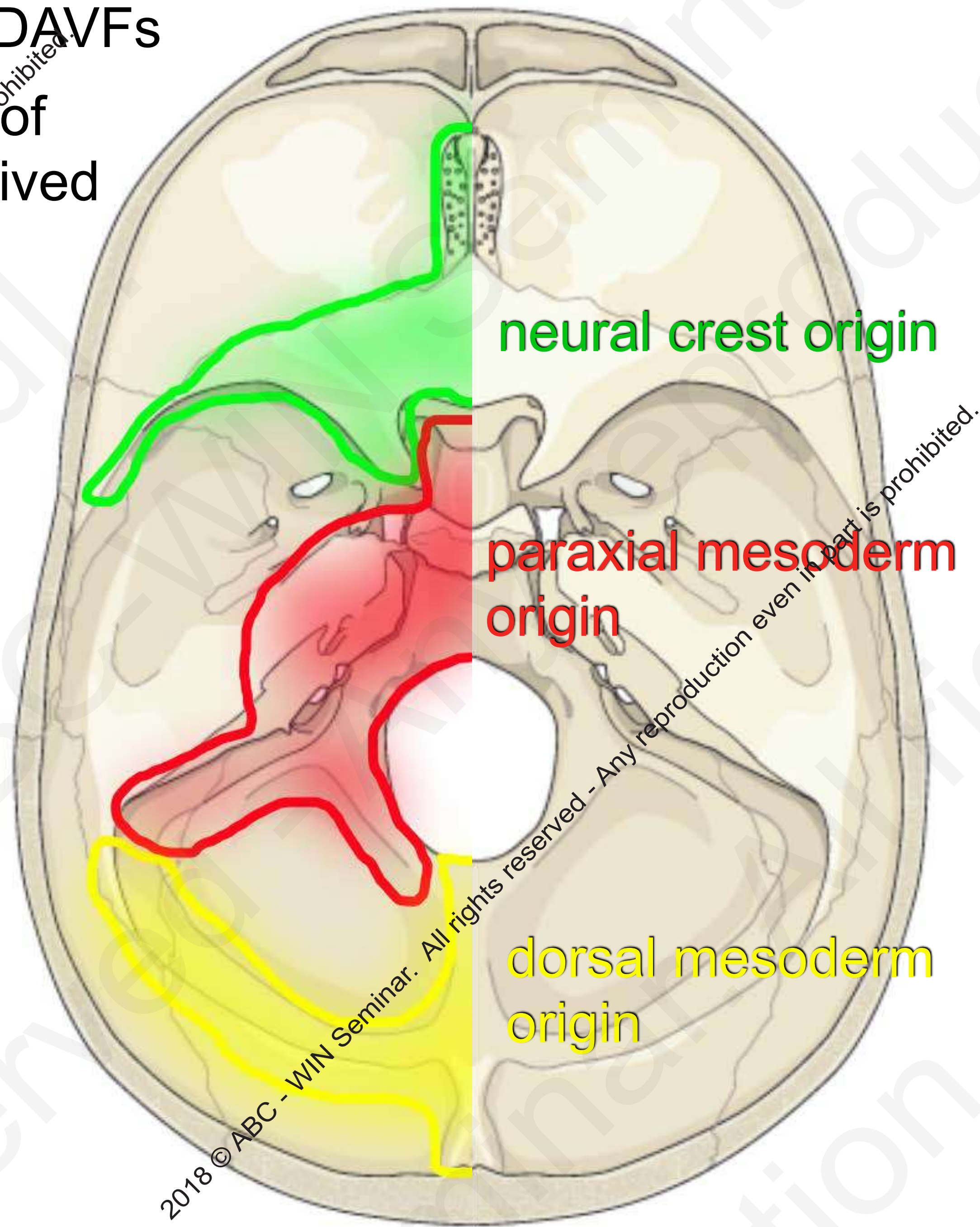
Proposed classification of DAVFs

- FT group: Falx and Tent of the cerebellum group derived from neural crest cells



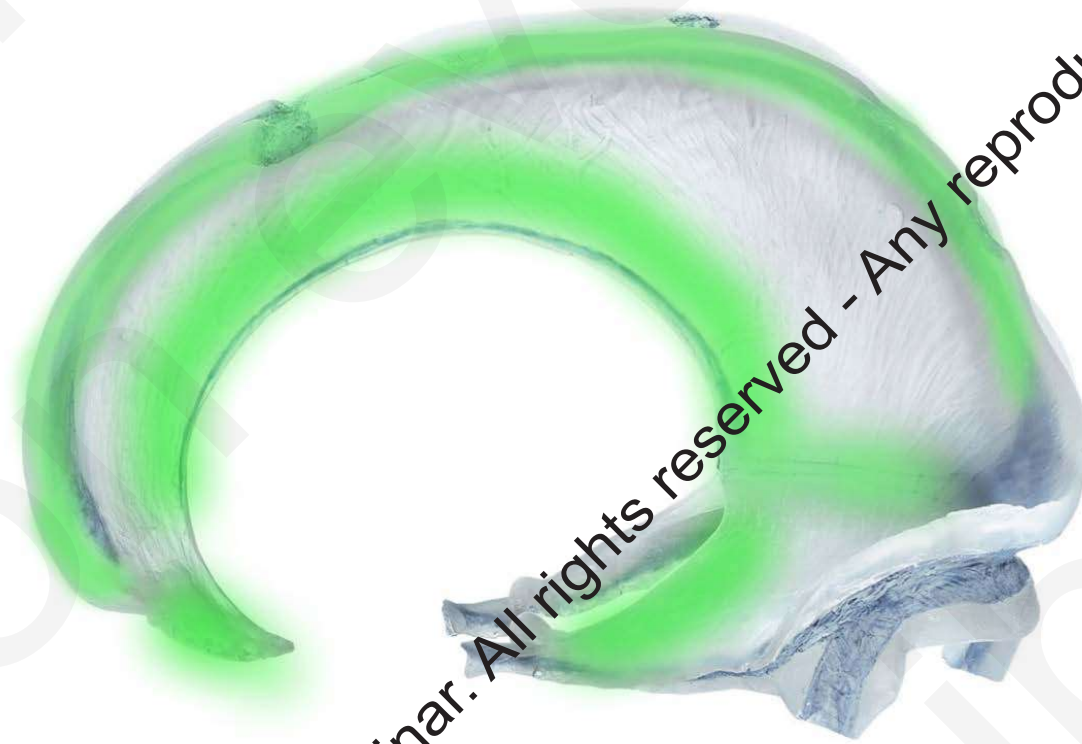
- VE group: Ventral group on the surface of Endochondral bone

- DM group: Dorsal group on the surface of Membranous bone



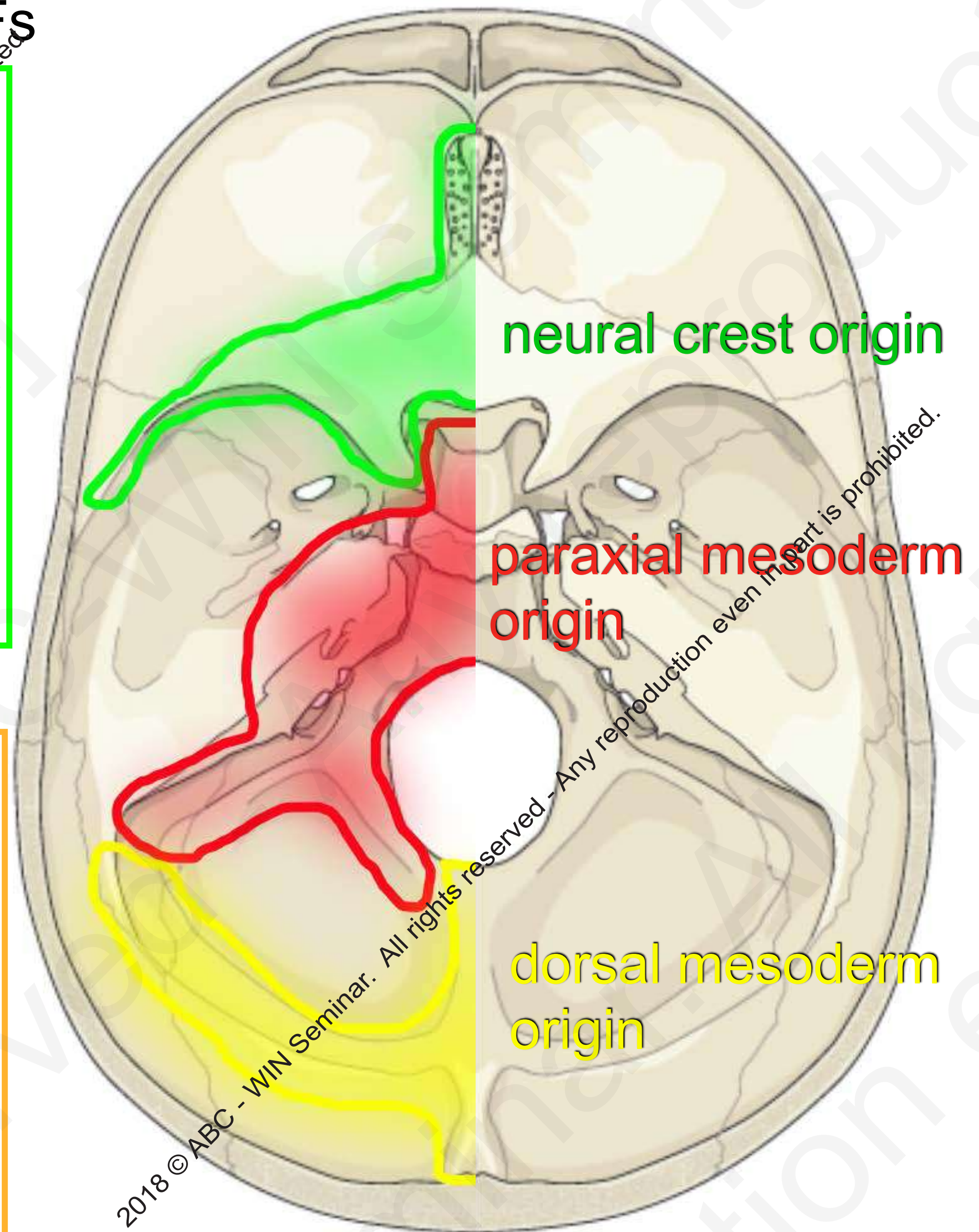
Proposed classification of DAVFs

- FT group: Falx and Tent of the cerebellum group derived from neural crest cells



- VE group: Ventral group on the surface of Endochondral bone

- DM group: Dorsal group on the surface of Membranous bone



Three different domains of dural membrane

Dura propria alone
(inter dural space between two layers of dura propria)

YES

NO

FT group

Periosteal dura and Dura propria
on the surface of endochondral bone

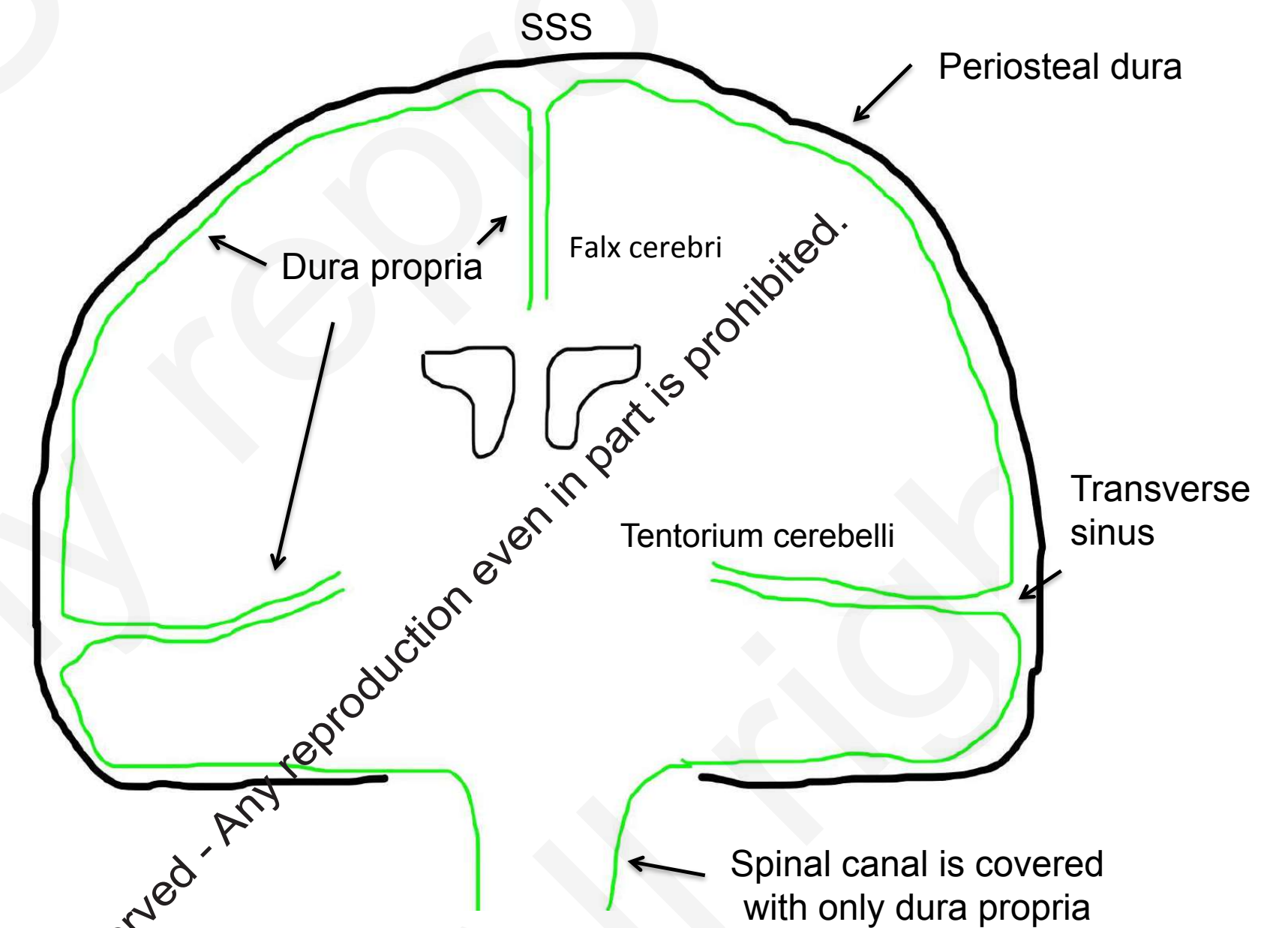
YES

NO

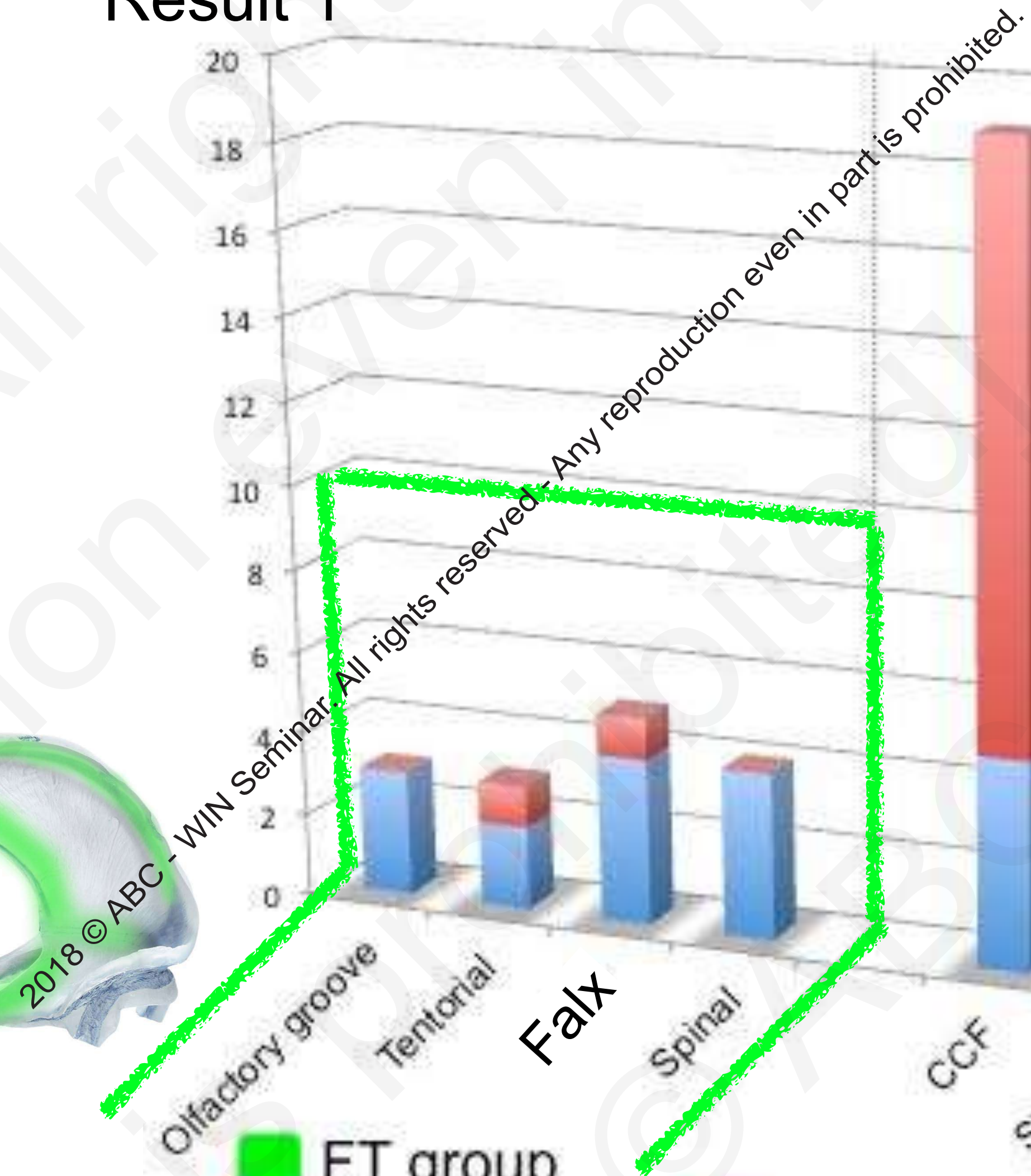
VE group

Located on the surface of
membranous bone

DM group



Result 1

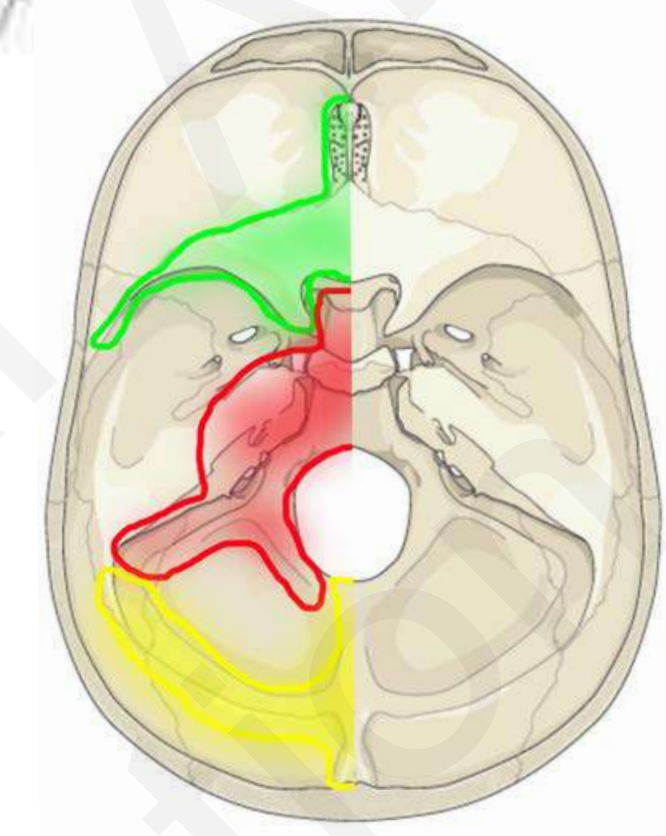


Neural crest derived
(Neurocristopathy)

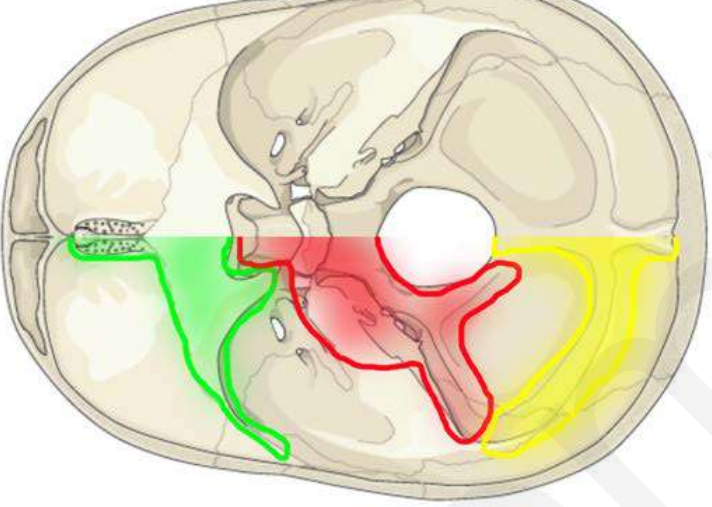
FT group

VE group

DM group



Result 2

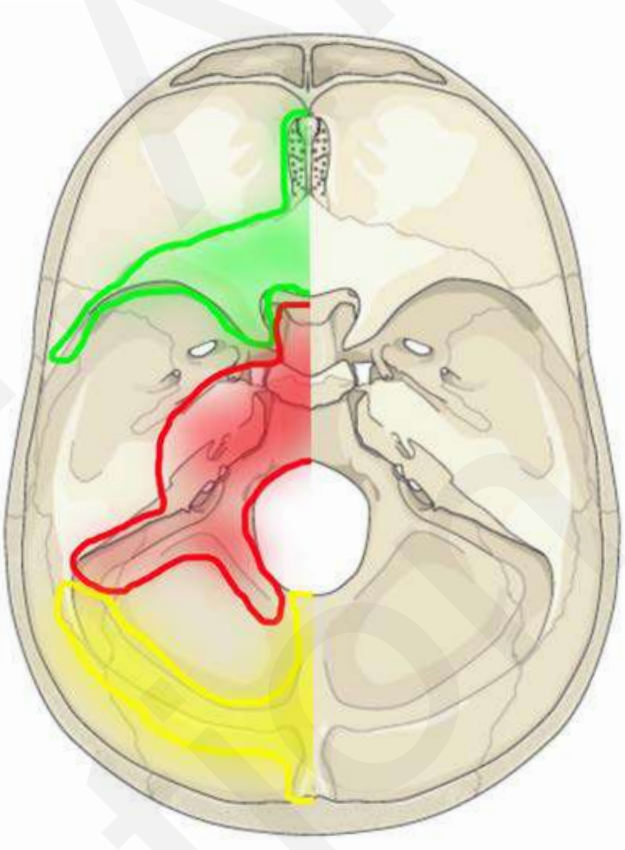
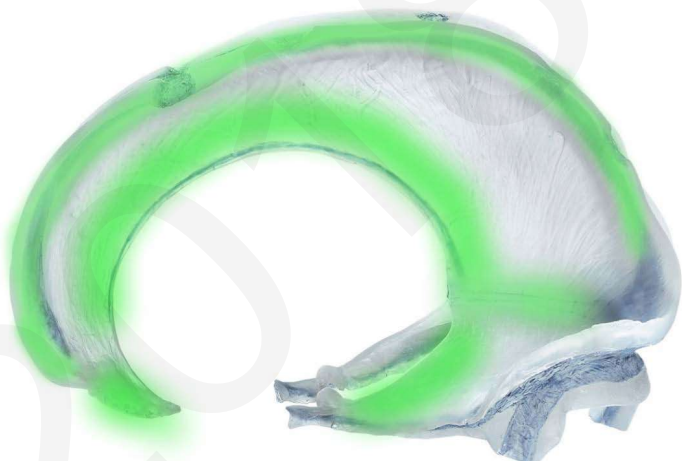
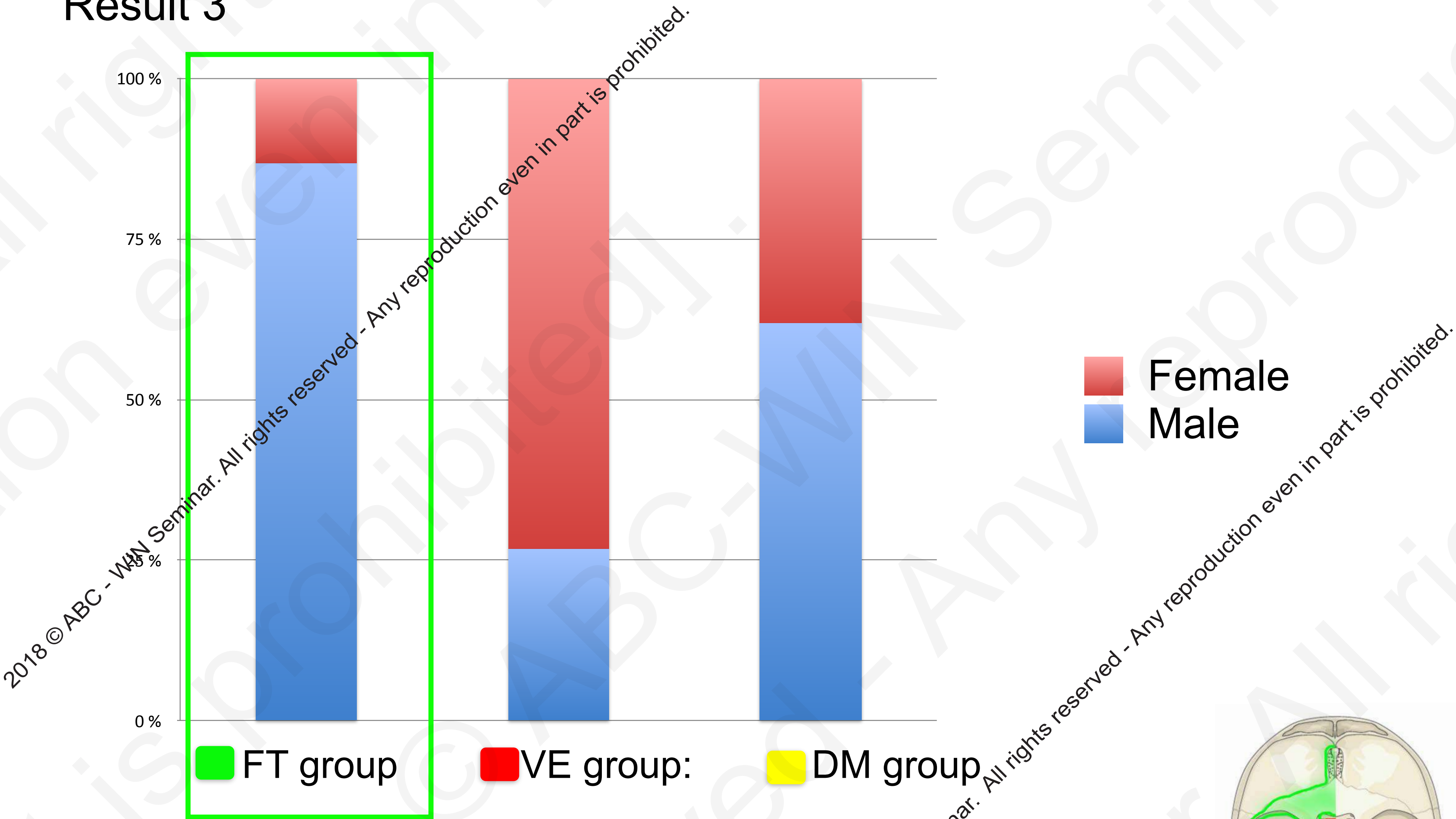


	FT : Falx and tent of the cerebellum derived from neural crest cells	VE : Ventral group derived from endochondral bone	DM: Dorsal group derived from membranous bone
N (male/female)	15 (87% / 13%)	30 (27% / 73%)	21 (62% / 38%)
Mean age (year)	65.1	78.4	59.8
Cortical venous reflux	93%	37 %	52%
Major symptoms	headache, neurological deficit associated with venous infraction, hemorrhage, paraplegia (central myelopathy)	diplopia, chemosis, bruit	headache, tinnitus
Mode of embolization	TAE 93%, TAE+TVE 7%	TVE 60%, TAE 7% TAE+TVE 33%	TVE 52%,TAE 19% TAE+TVE 29%

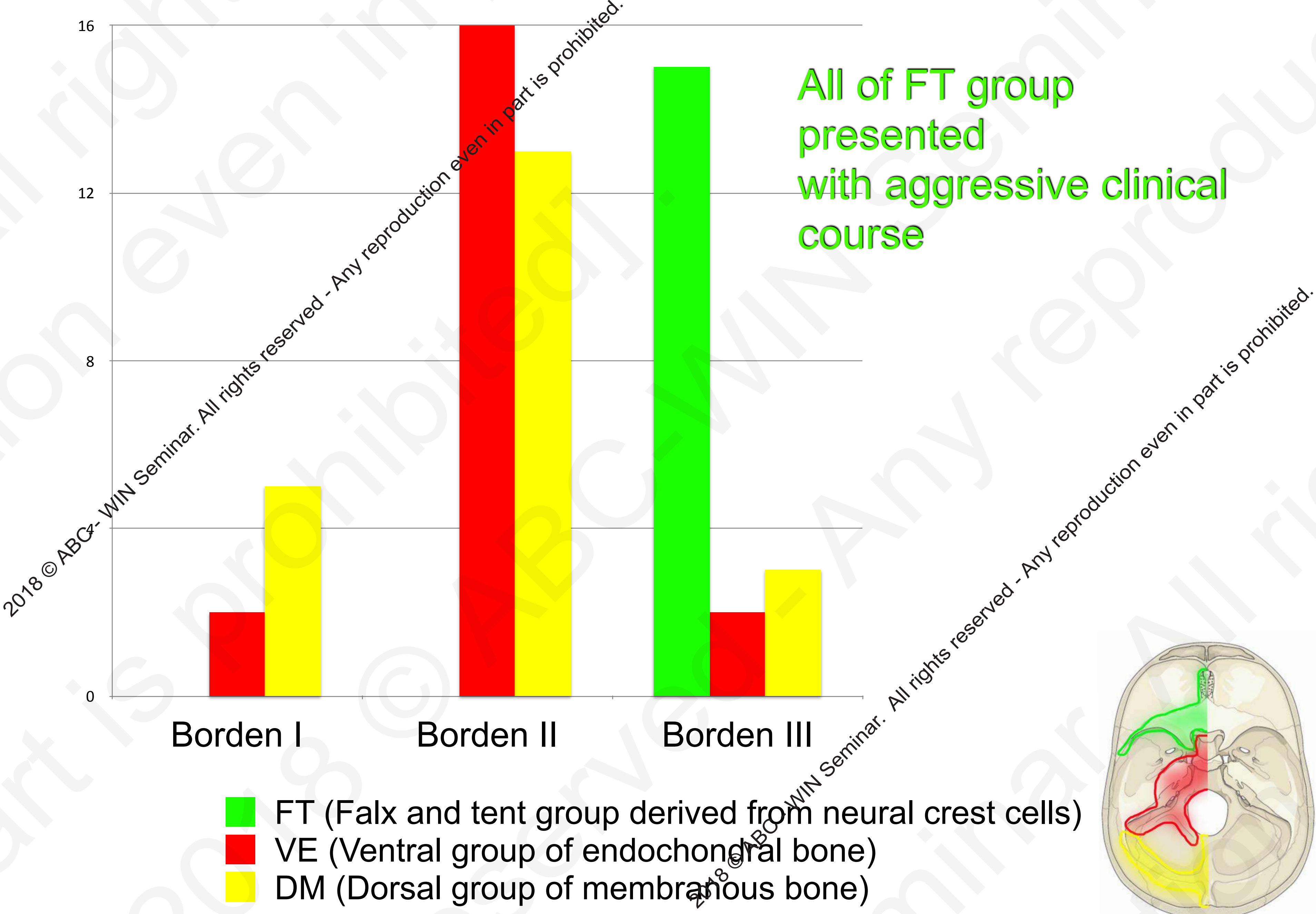
Result 3

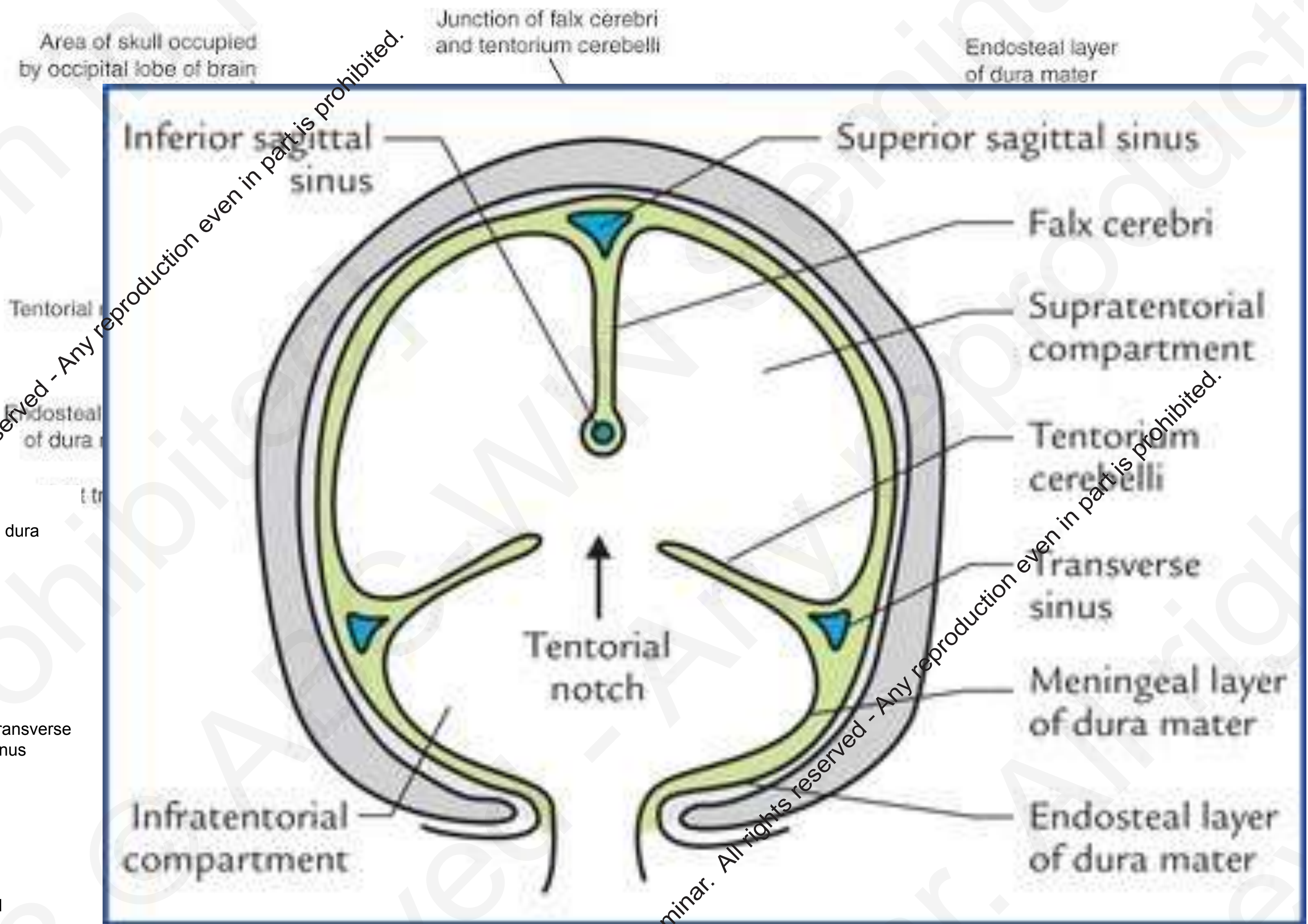
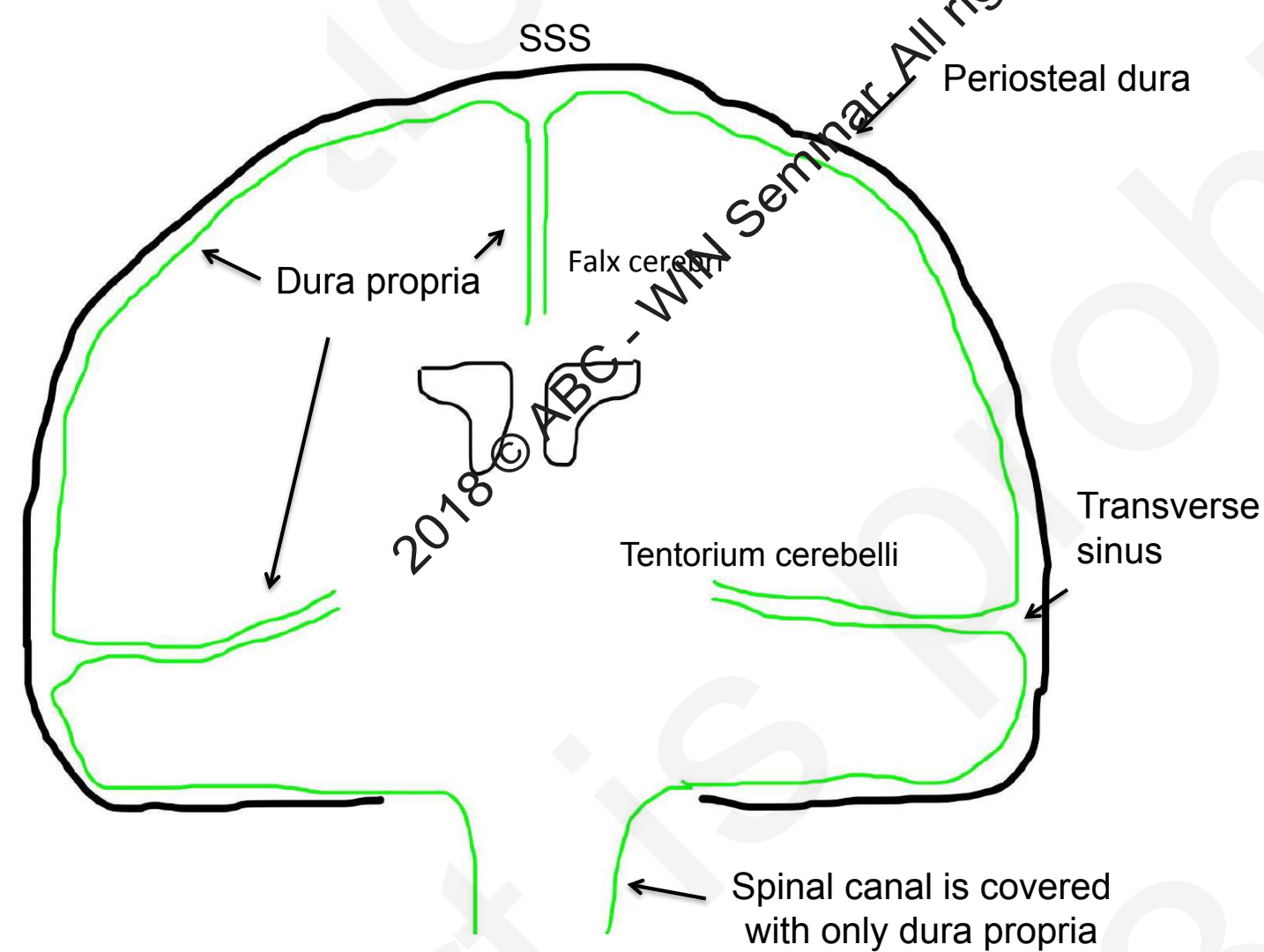
	FT : Falx and tent of the cerebellum derived from neural crest cells	Non FT: Independent from Neural crest cells
N (male/female)	15 (87% / 13%)	51 (45% /55%)
Mean age (year)	65.1	68,3
Cortical venous reflux	93%	42 %
Major symptoms	headache, neurological deficit associated with venous infraction, hemorrhage, paraplegia (central myelopathy)	diplopia, chemosis, bruit headache, tinnitus
Mode of embolization	TAE 93%, TAE+TVE 7%	TVE 60%, TAE 7% TAE+TVE 33%

Result 3

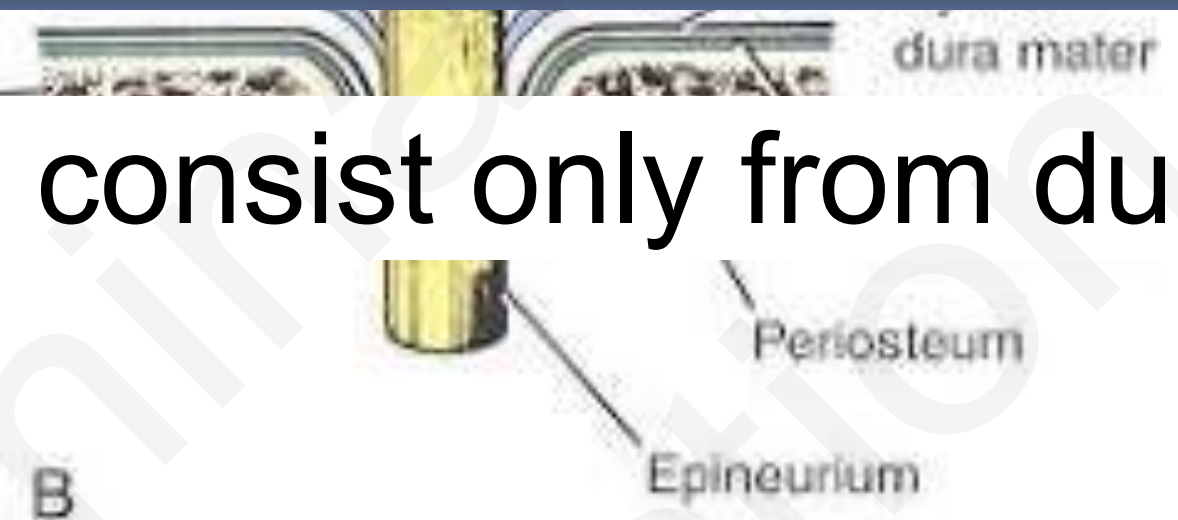


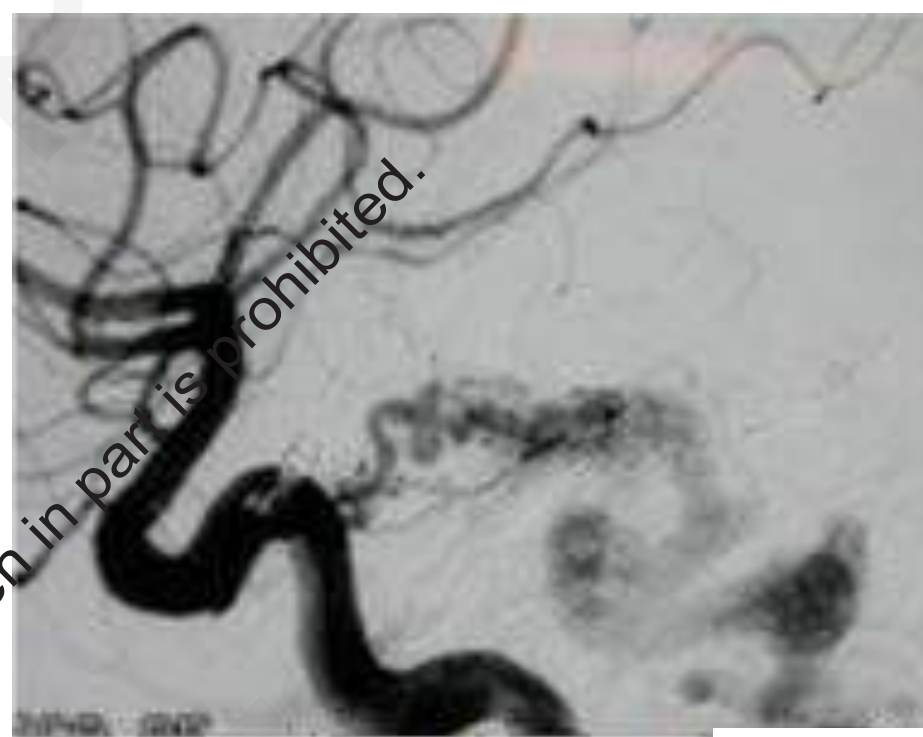
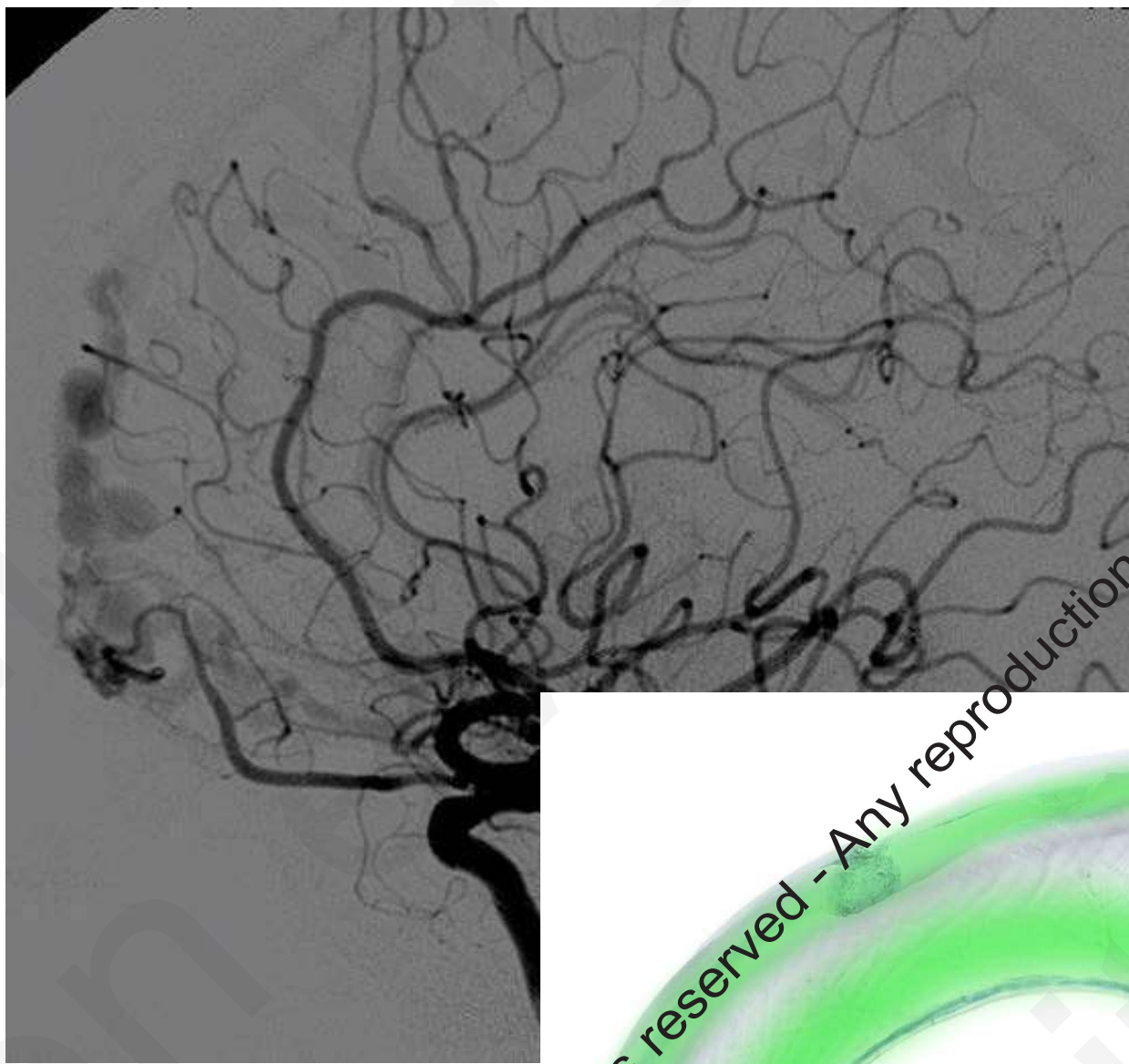
Result 4



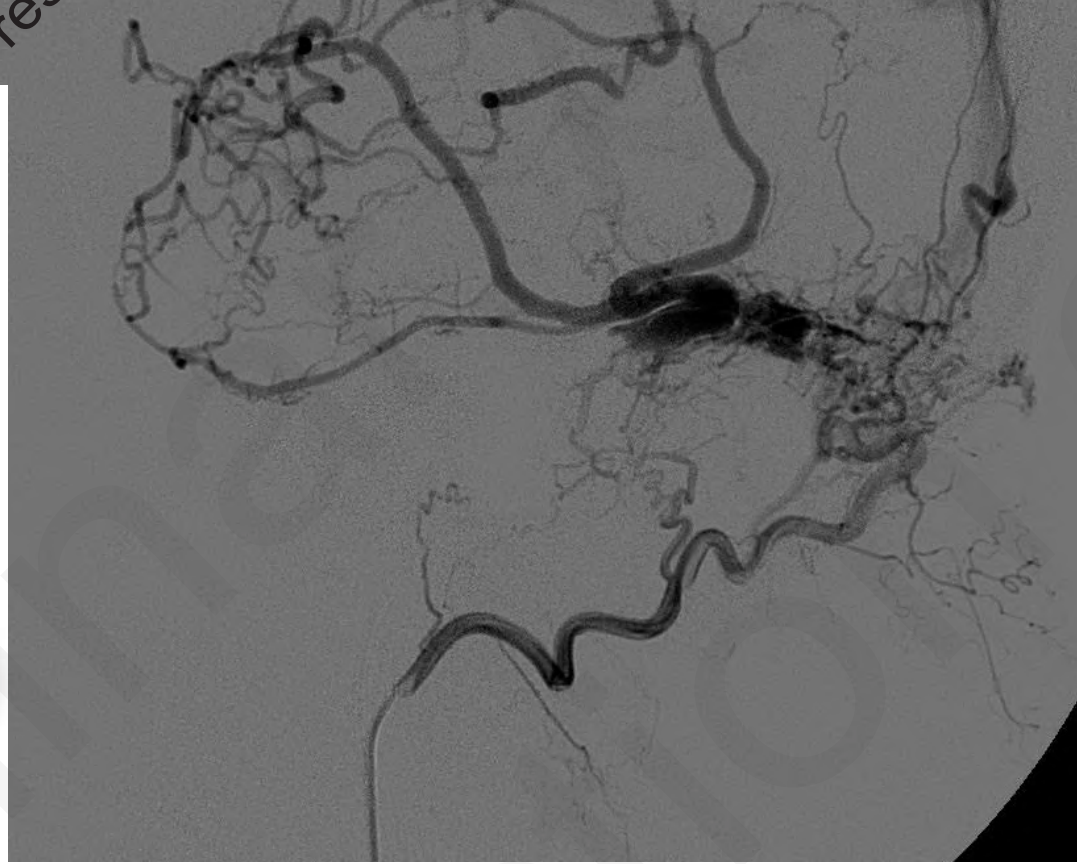
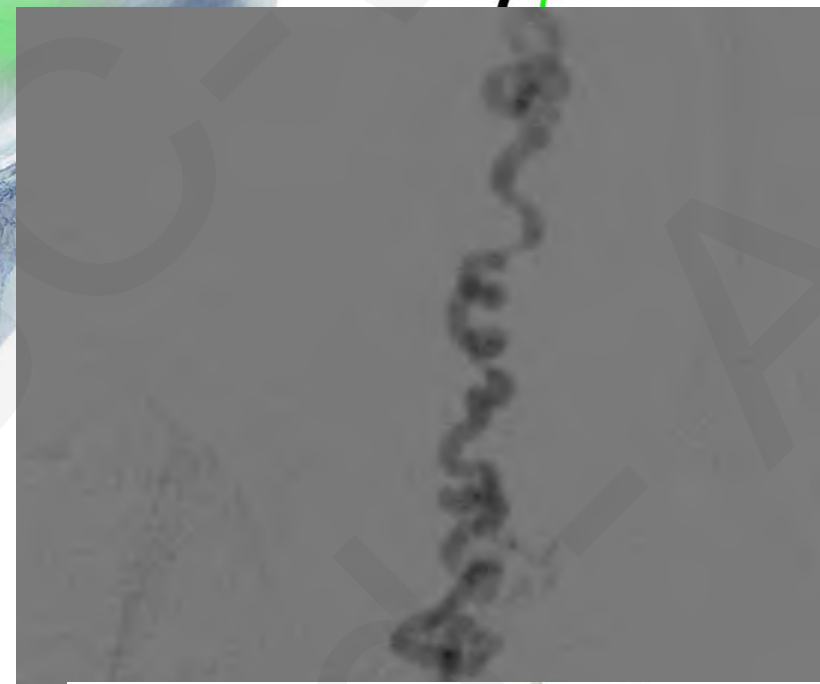
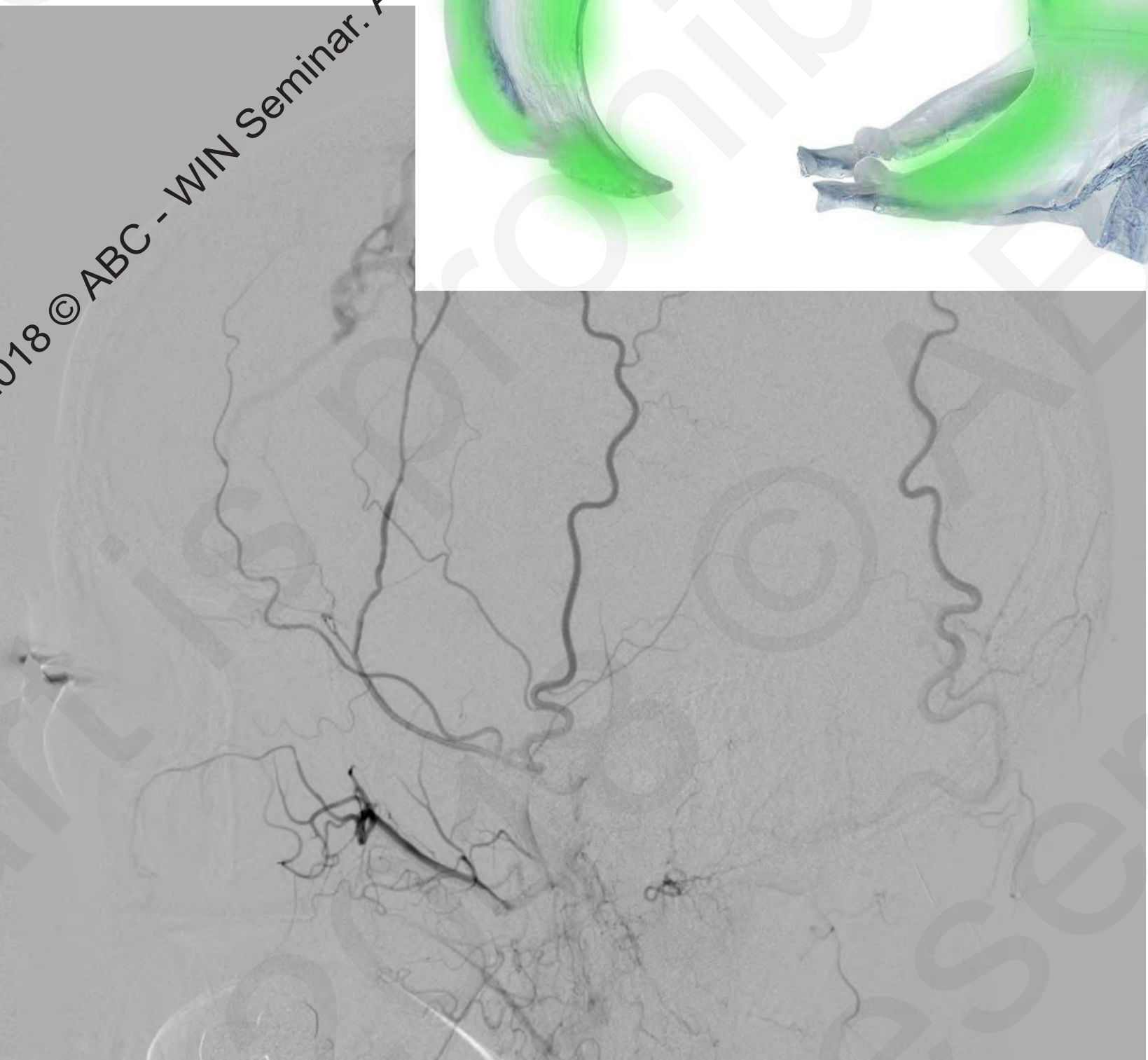
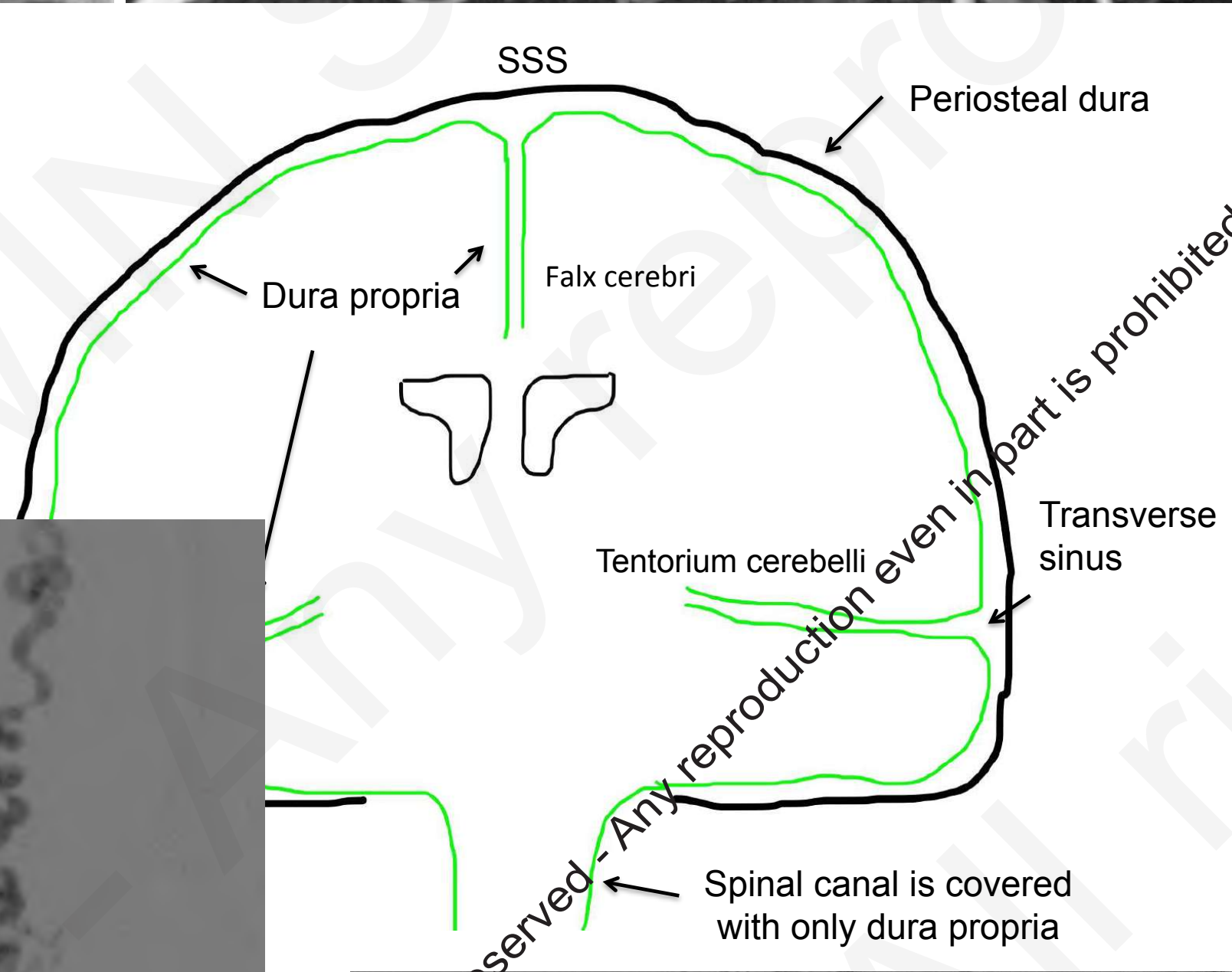


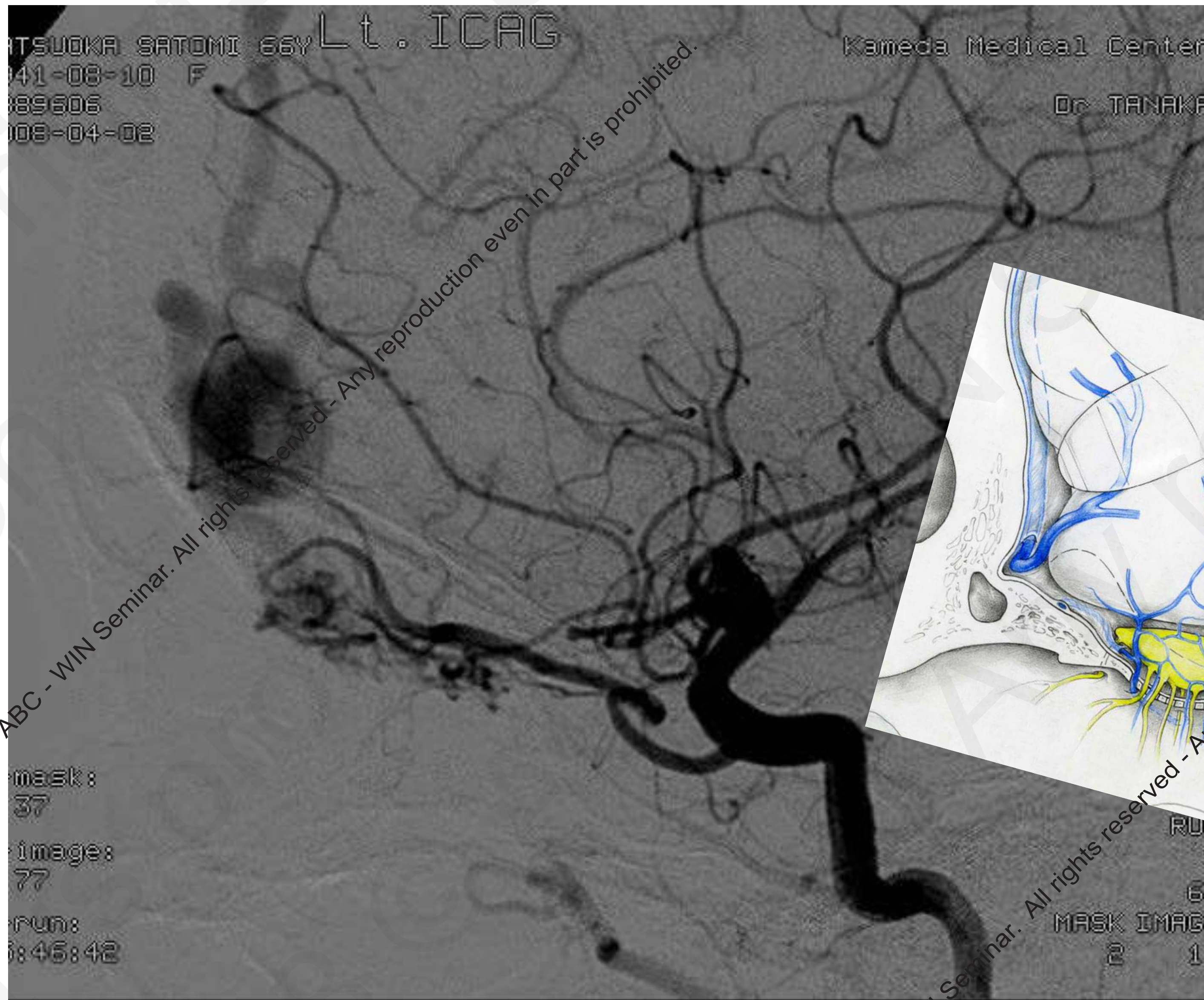
Falx, tentorium, olfactory groove and spinal canal consist only from dura propria.



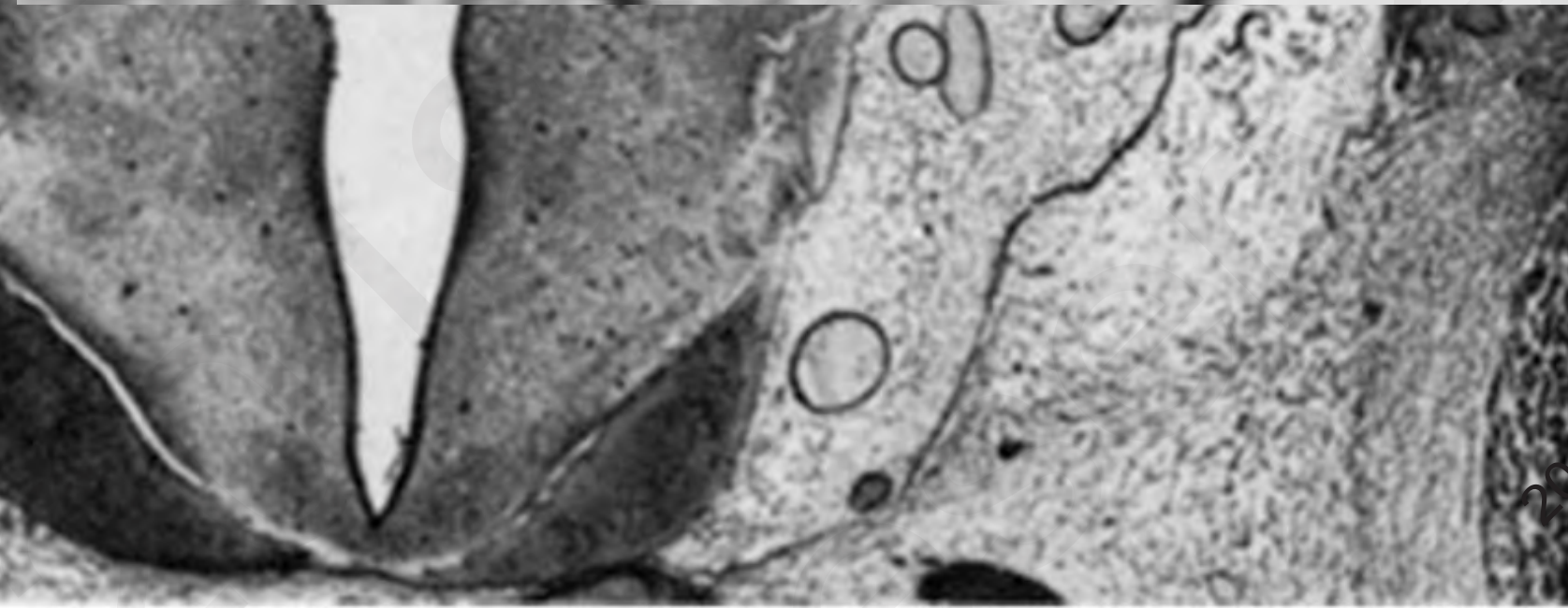
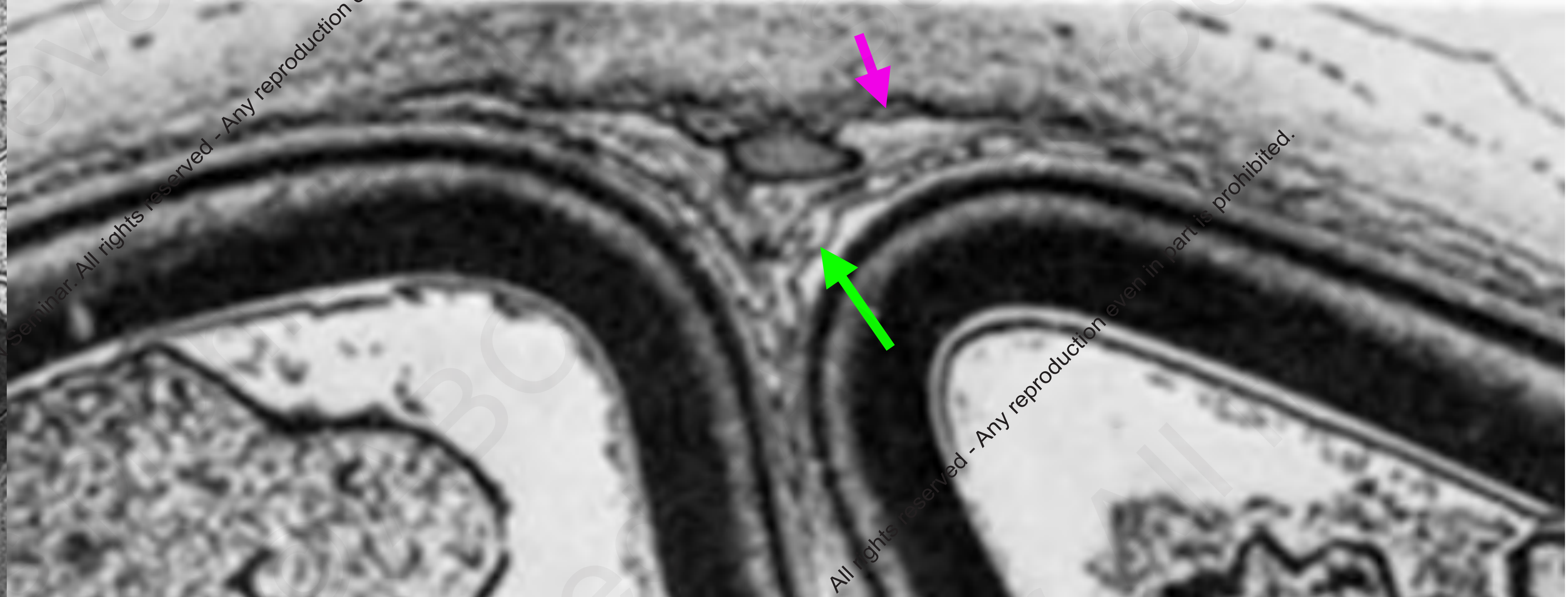
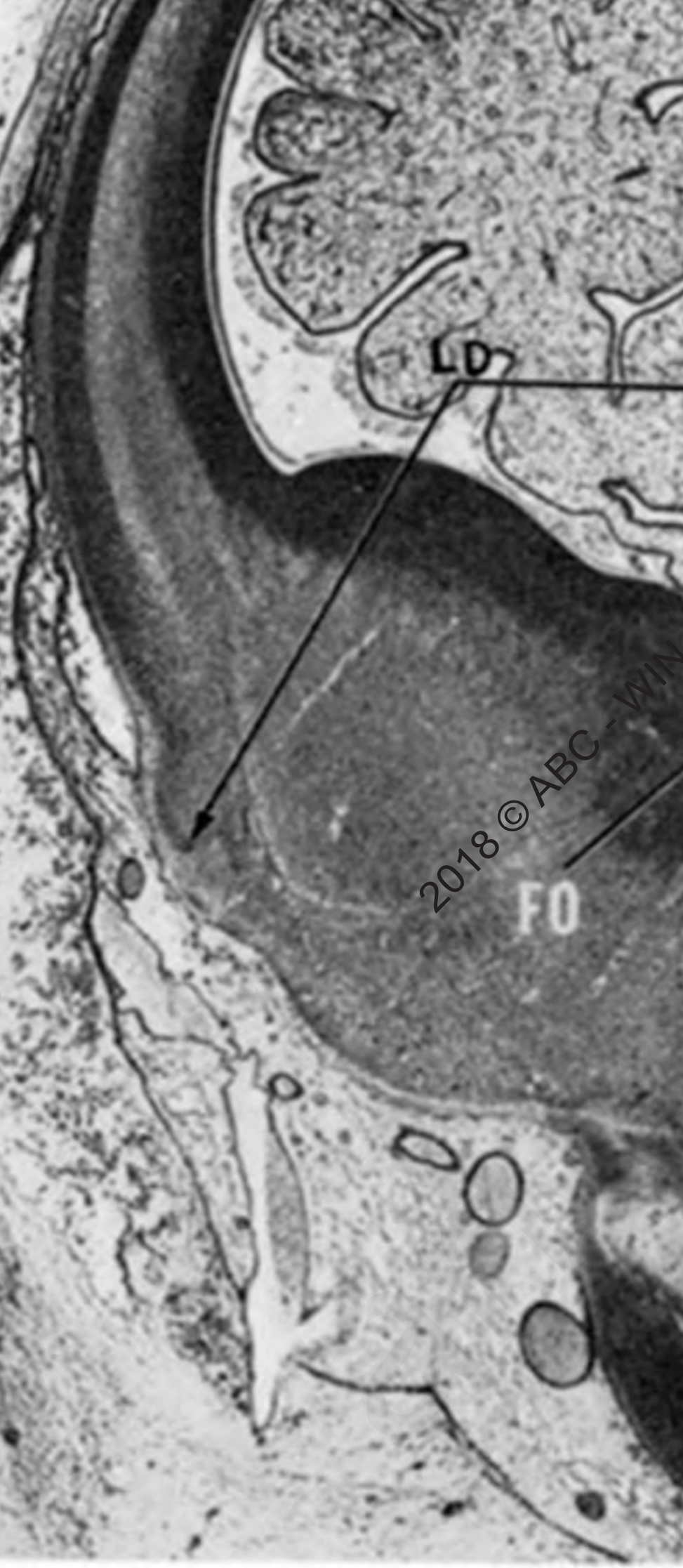
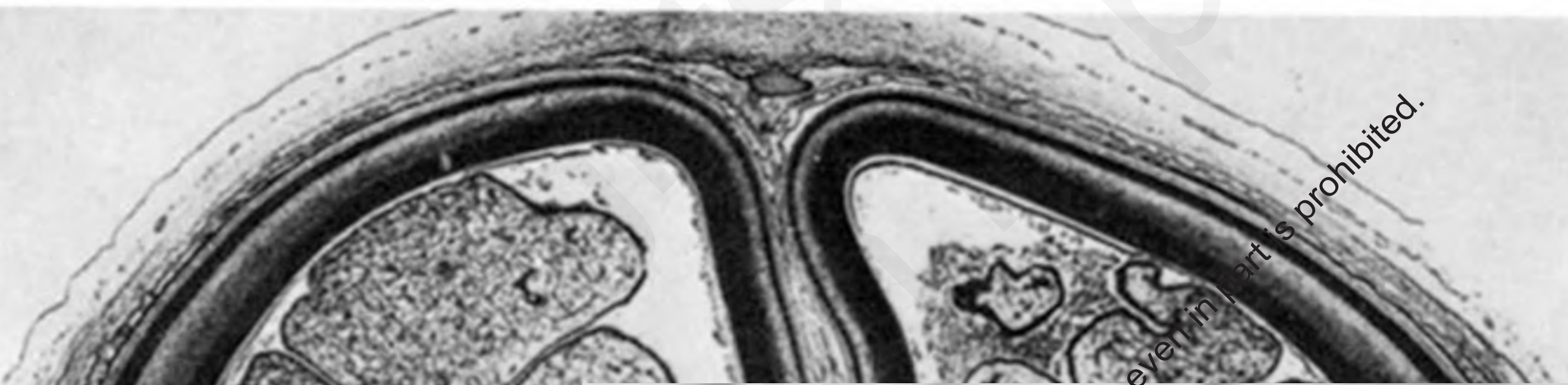


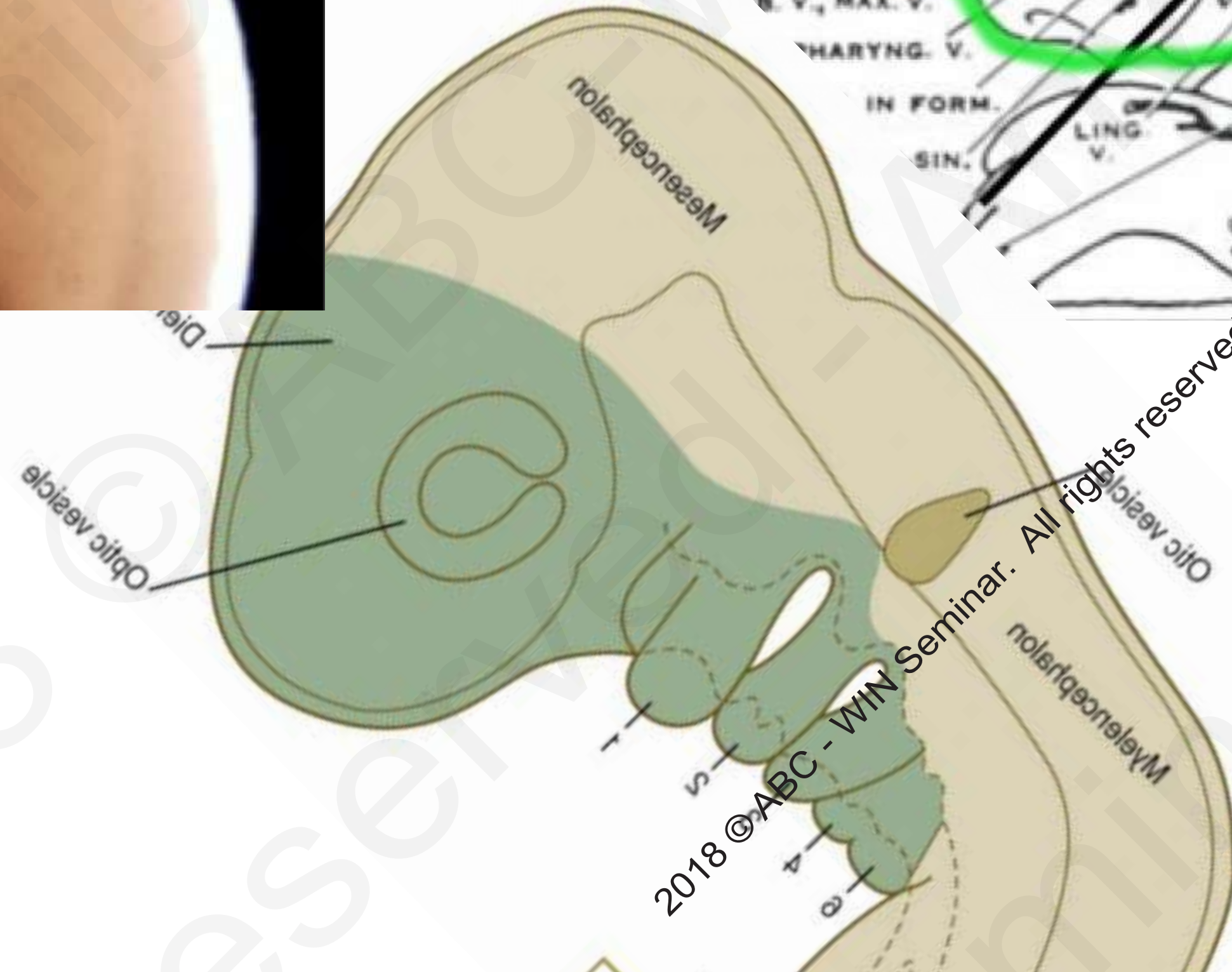
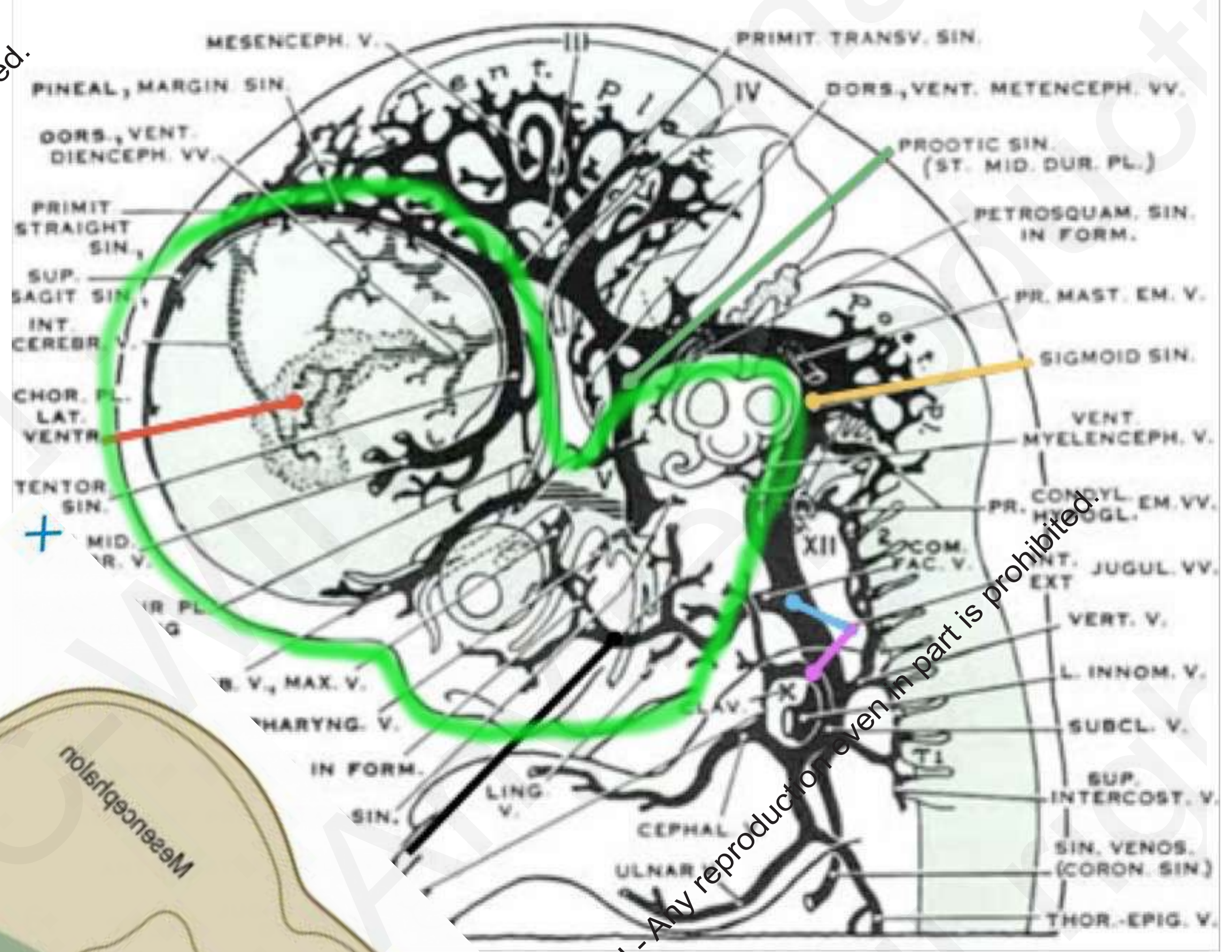
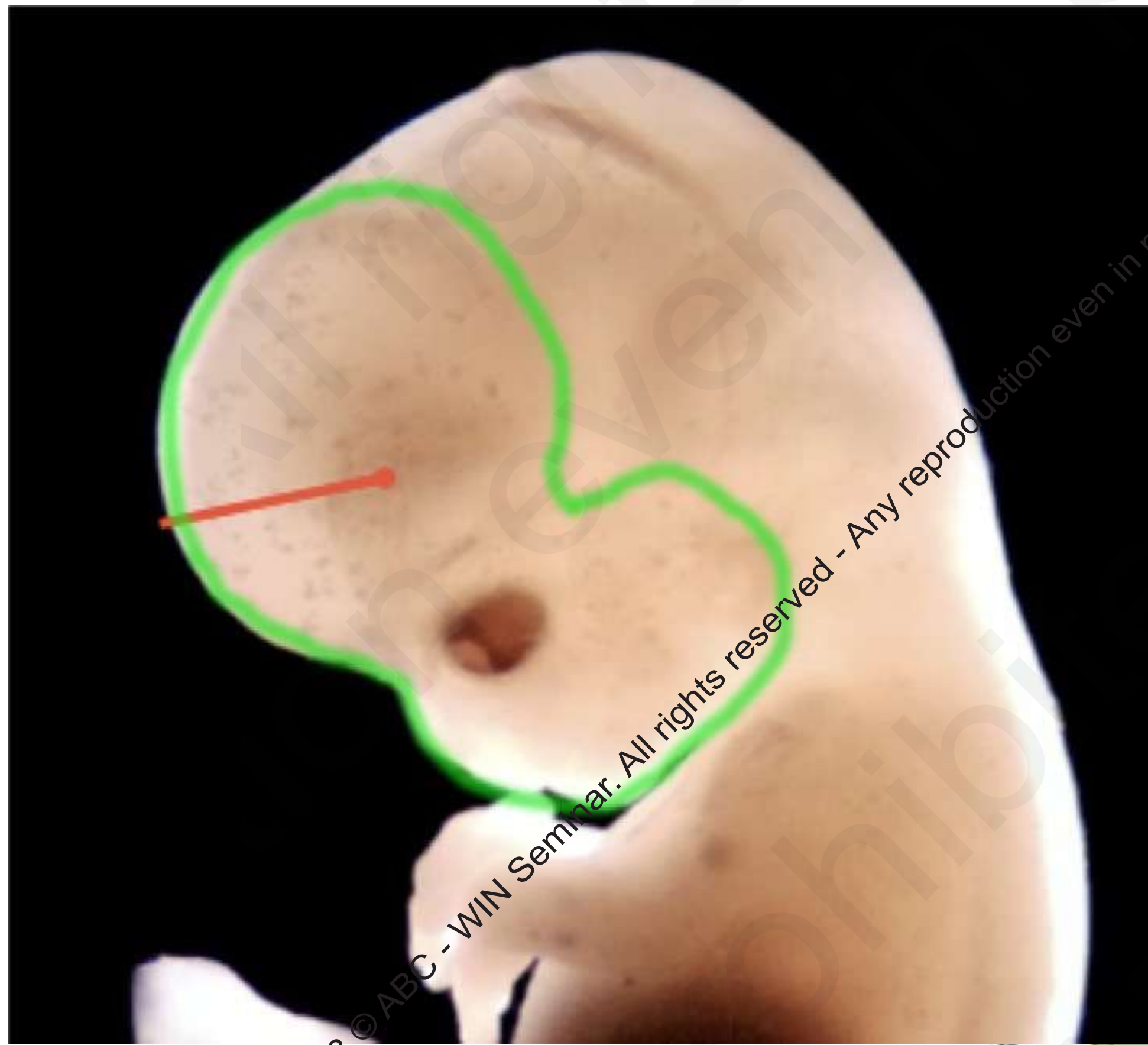
Date of Birth: 1952/02/17, Female
Patient ID: 3510265
Exam ID: 27062006130715
Exam date: 2006/06/27
Rot: 94
Ang: -16
Head side
Subtraction

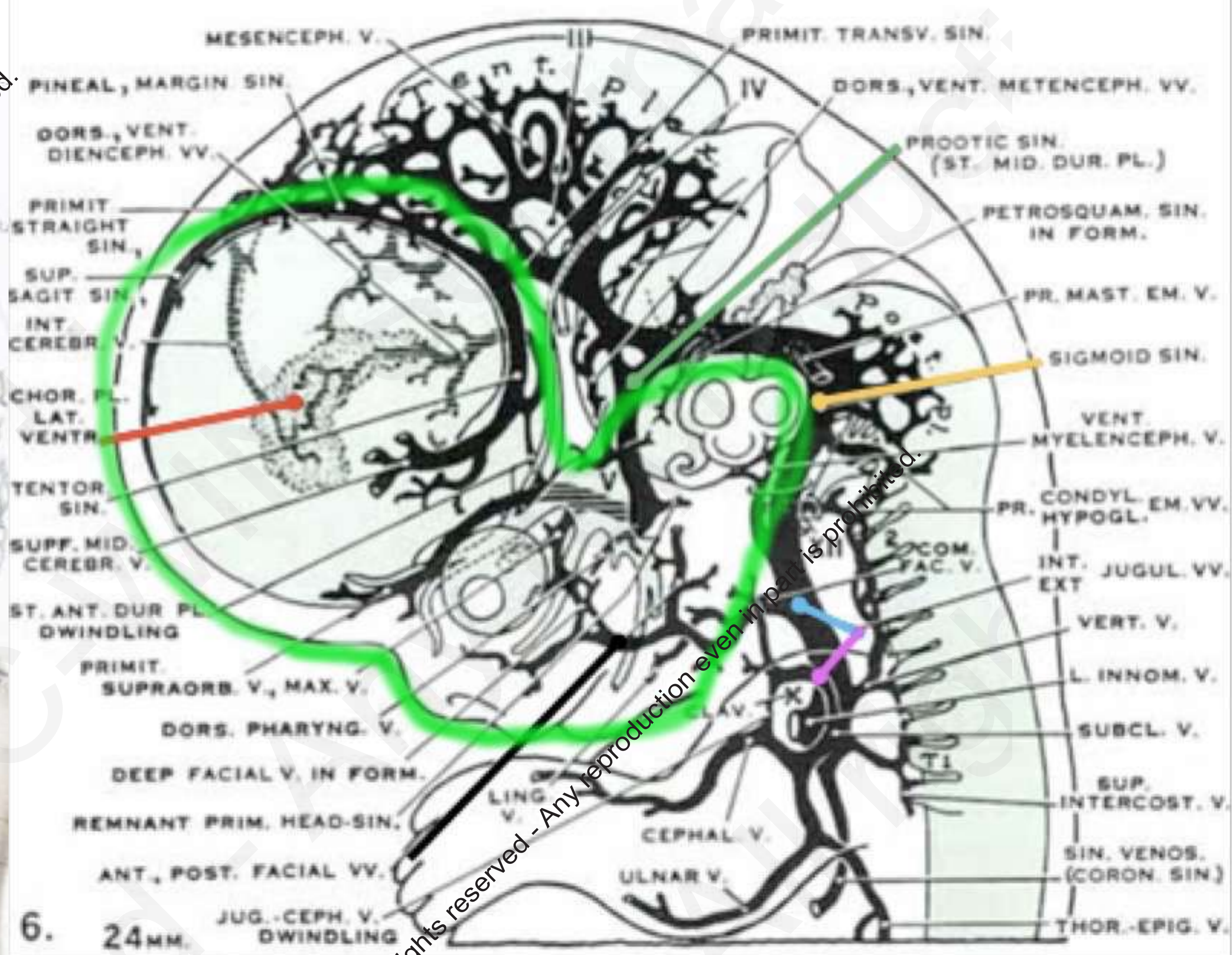
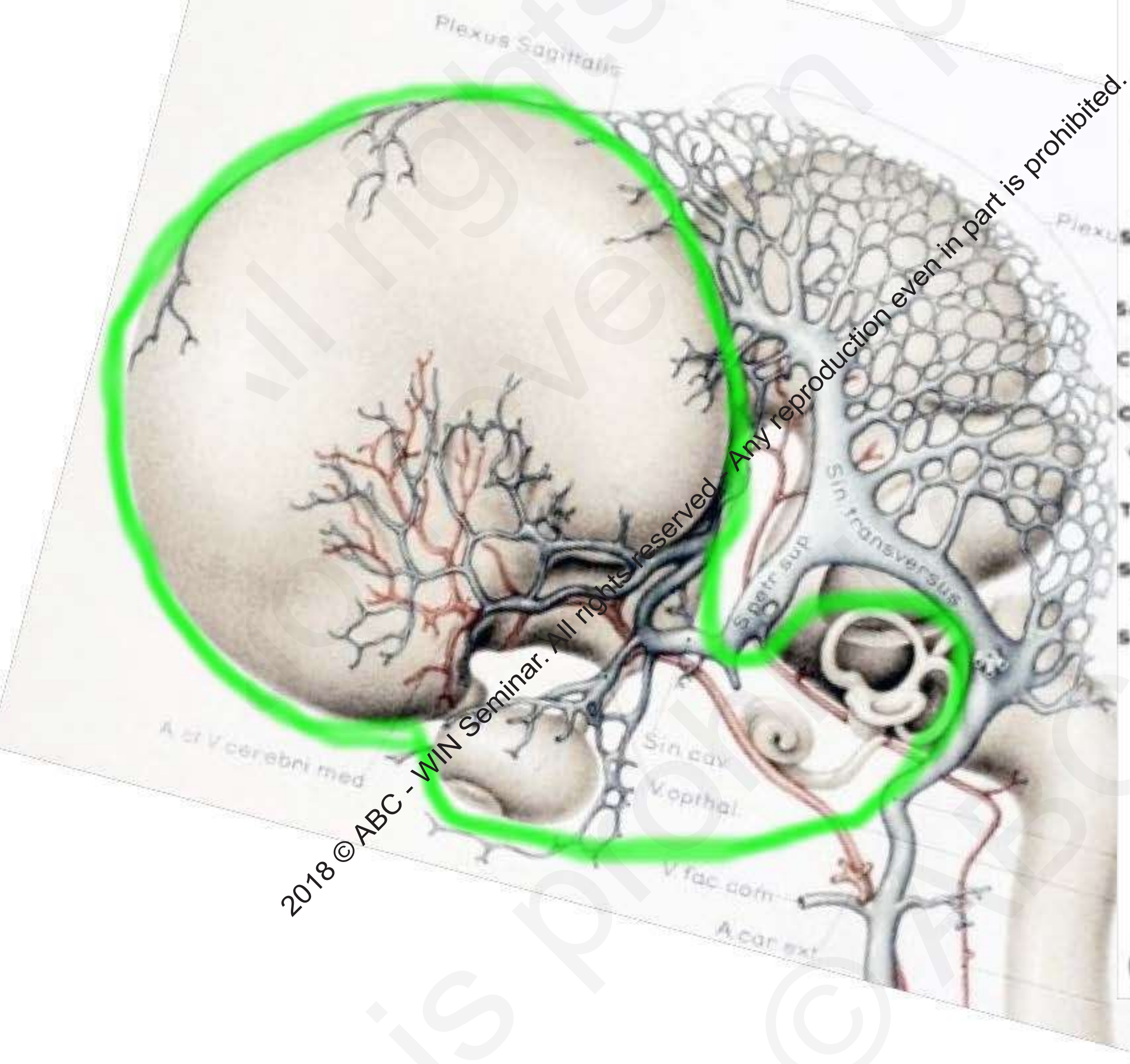


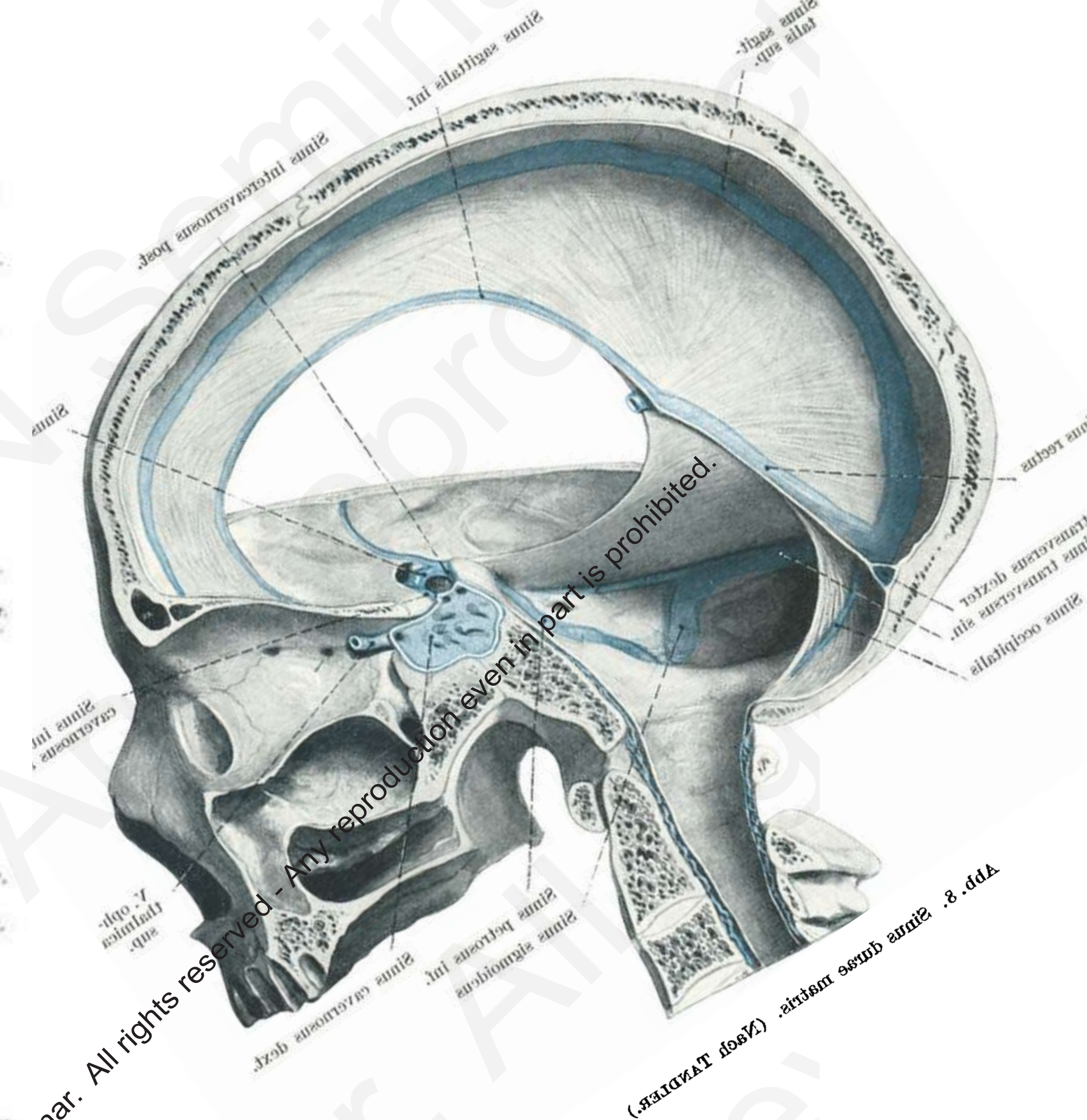
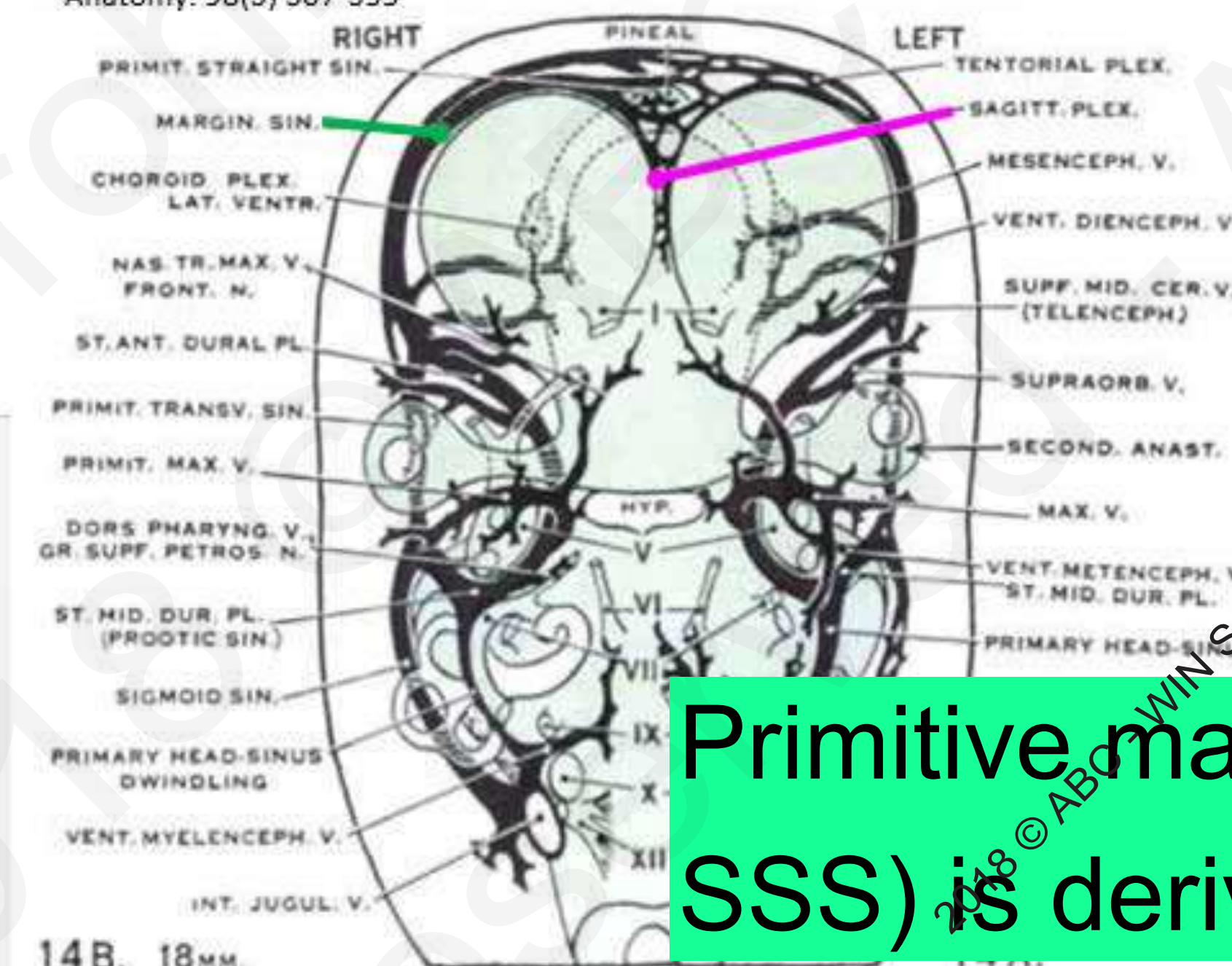


direct duro-leptomeningeal venous connections



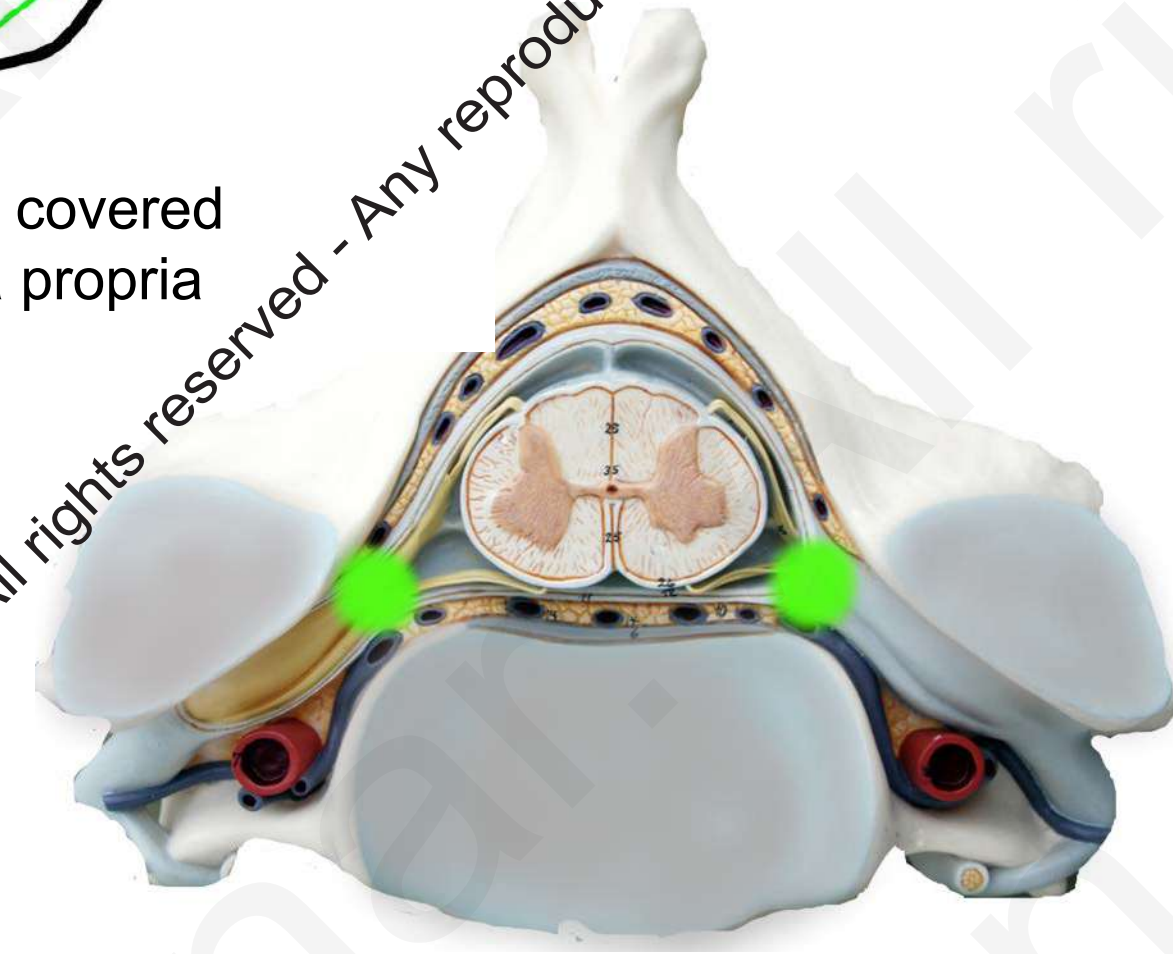
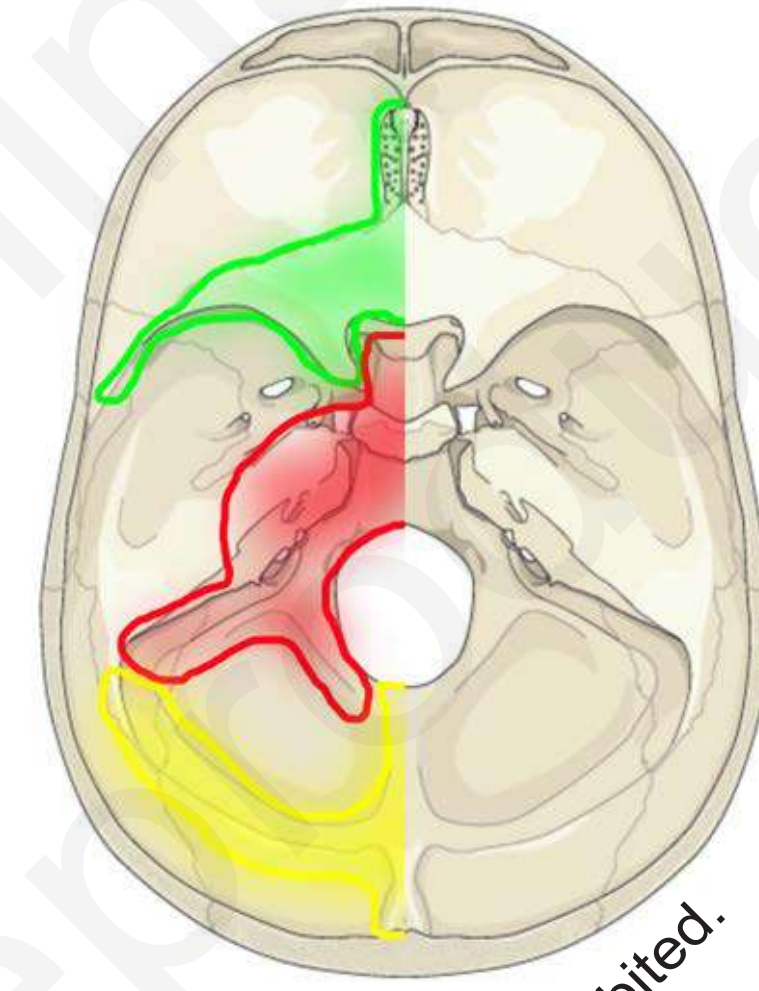
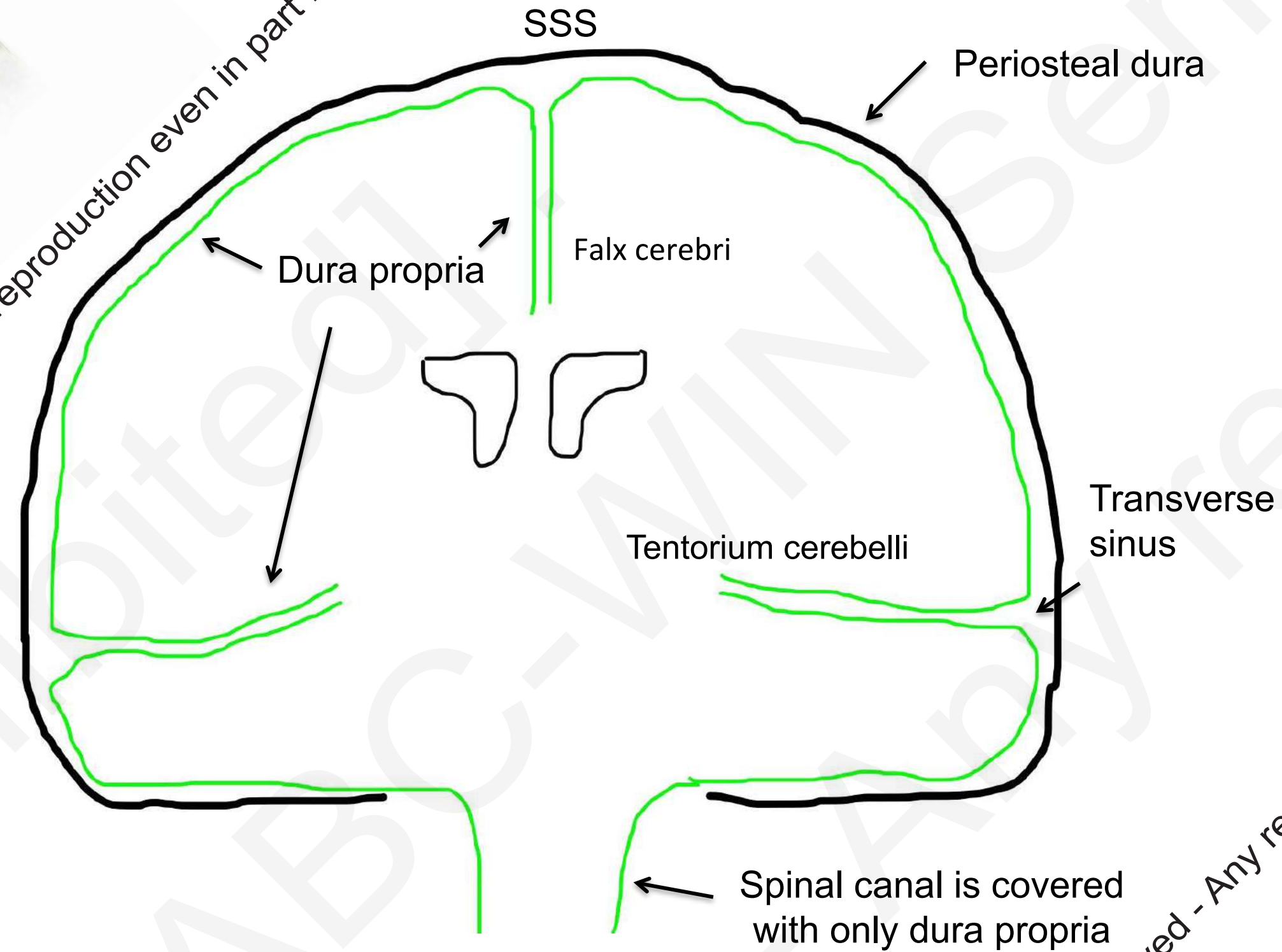
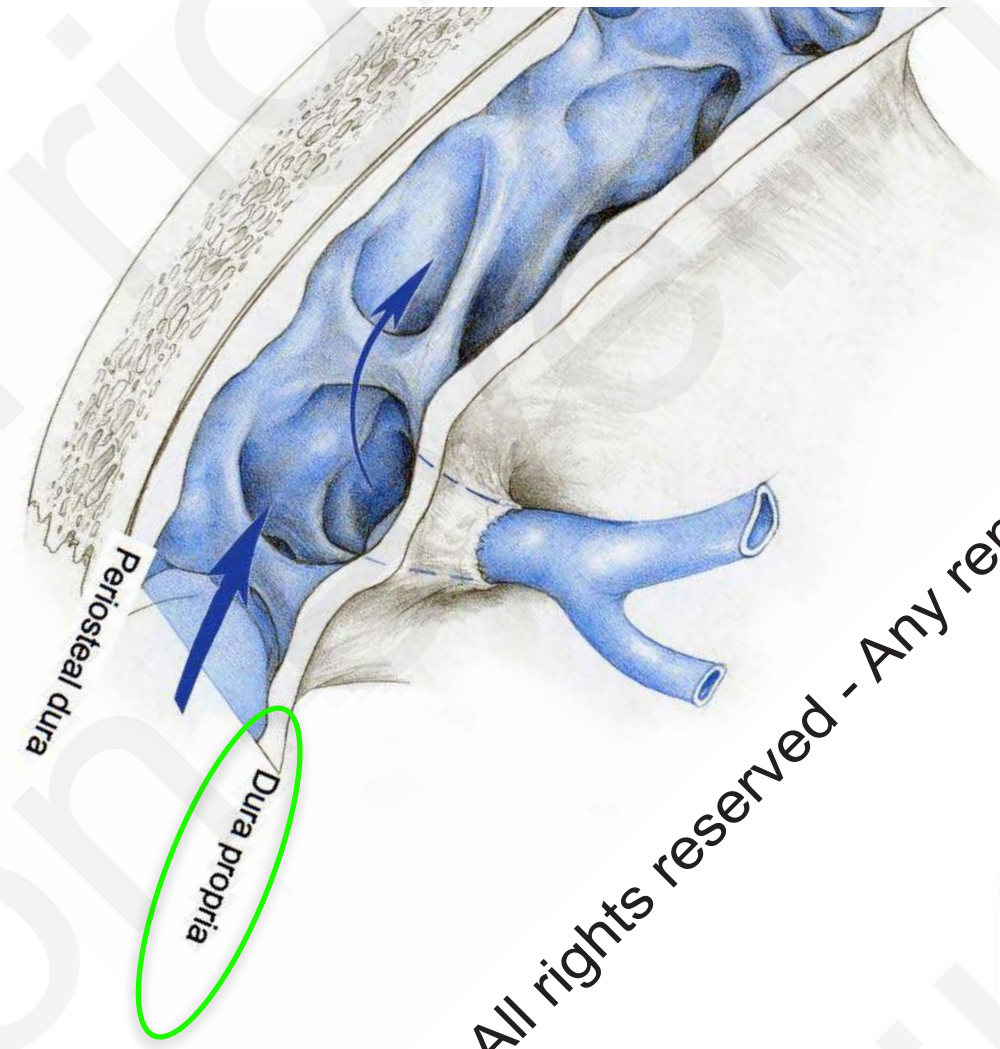






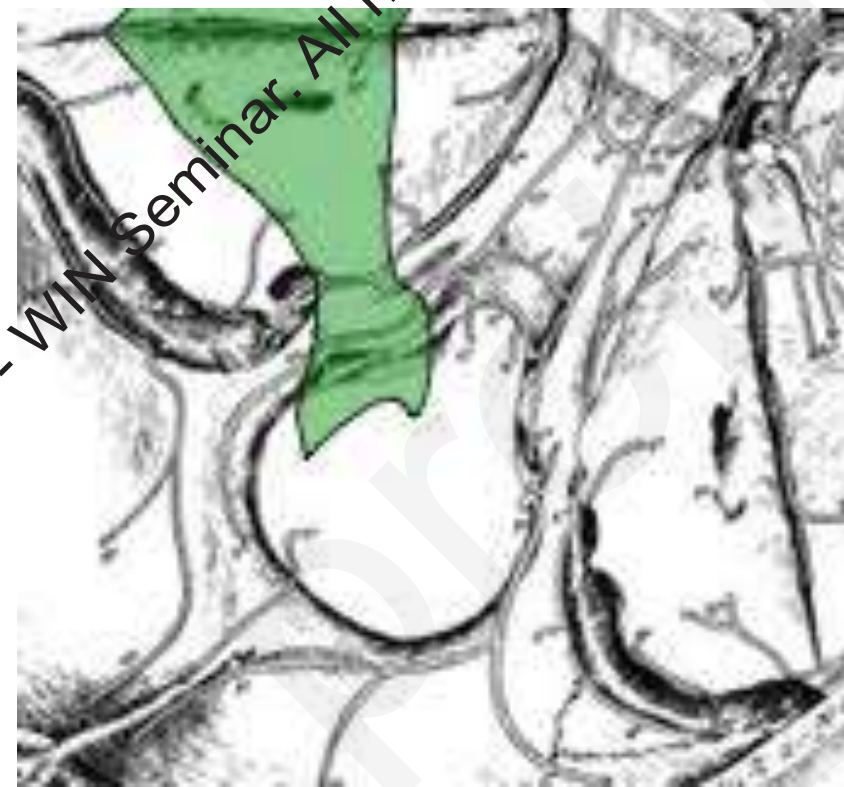
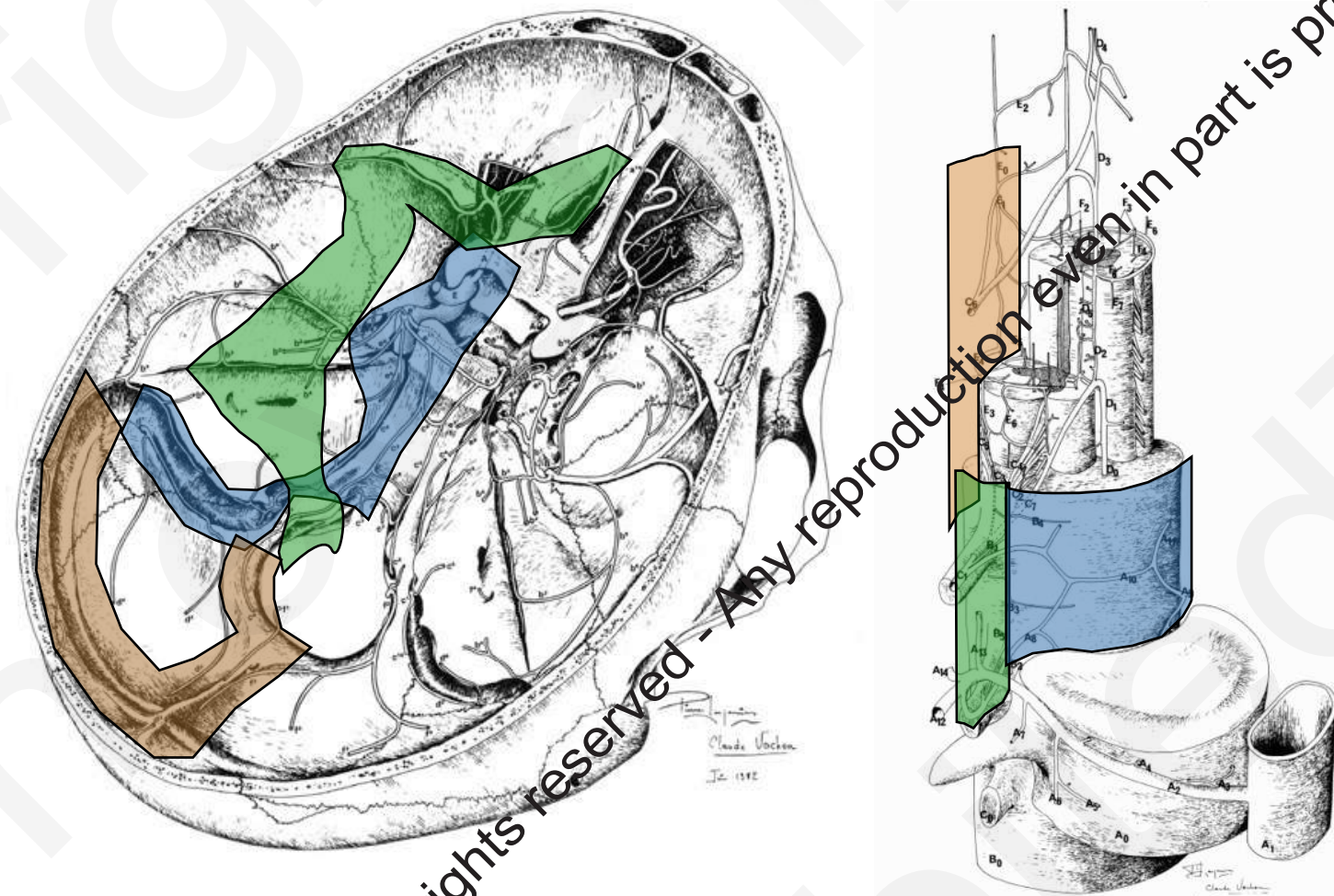
Primitive marginal sinus (future's falx and SSS) is derived from neural crest.

The pathologies on the surface of falco-tentorial region can be considered as the neurocristopathy.



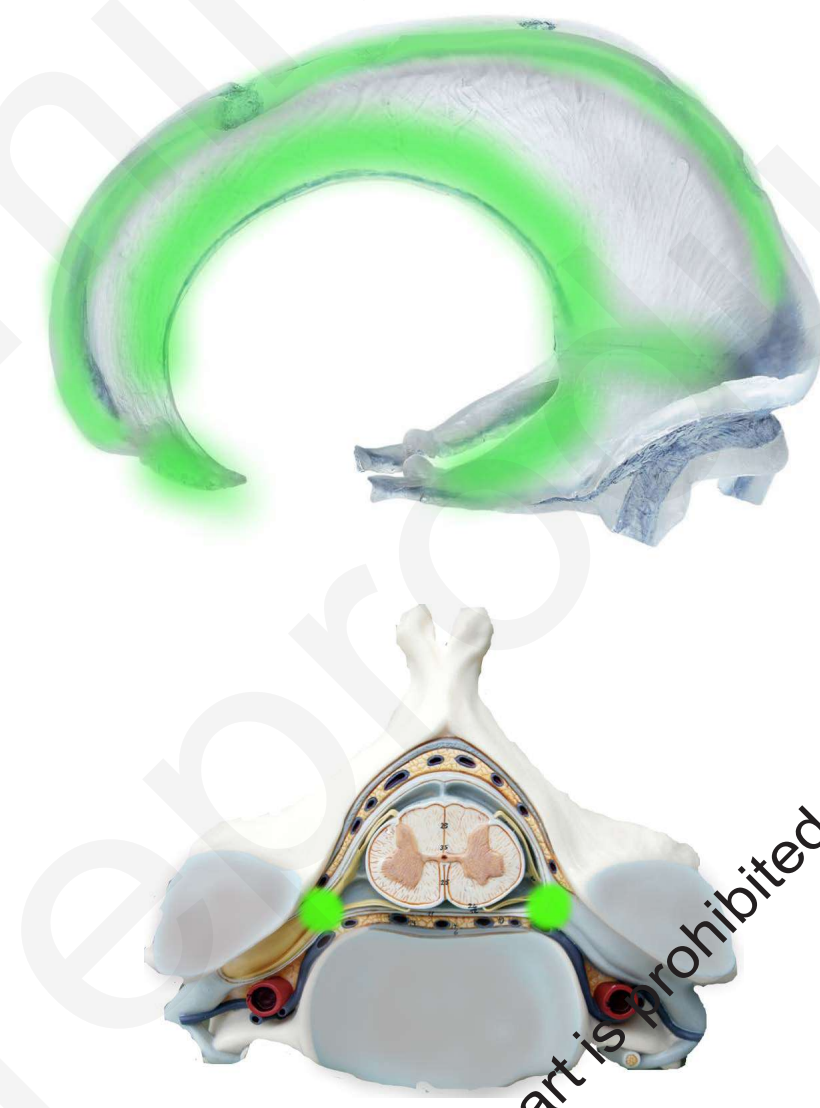
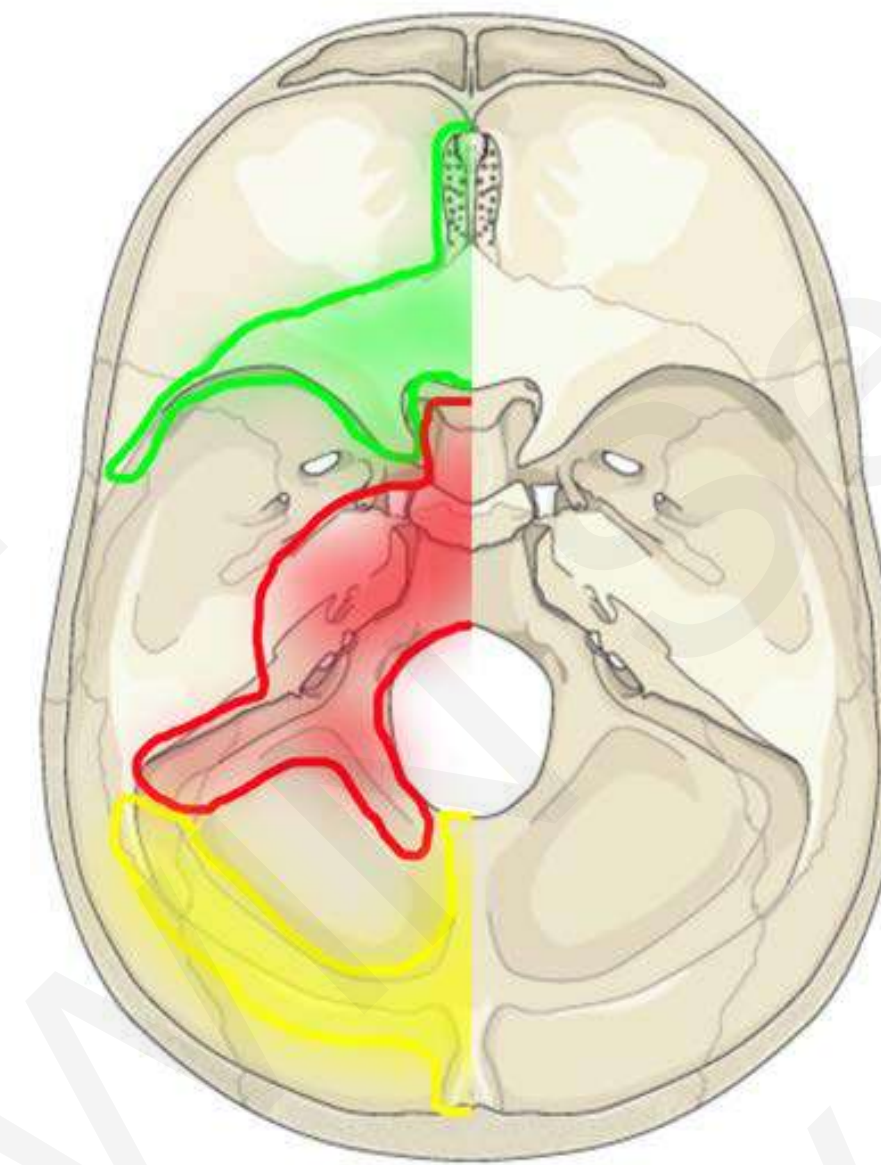
■ FT group: Falx, tent of the cerebellum and lateral surface of spinal canal group derived from neural crest cells

Discussion based on embryology

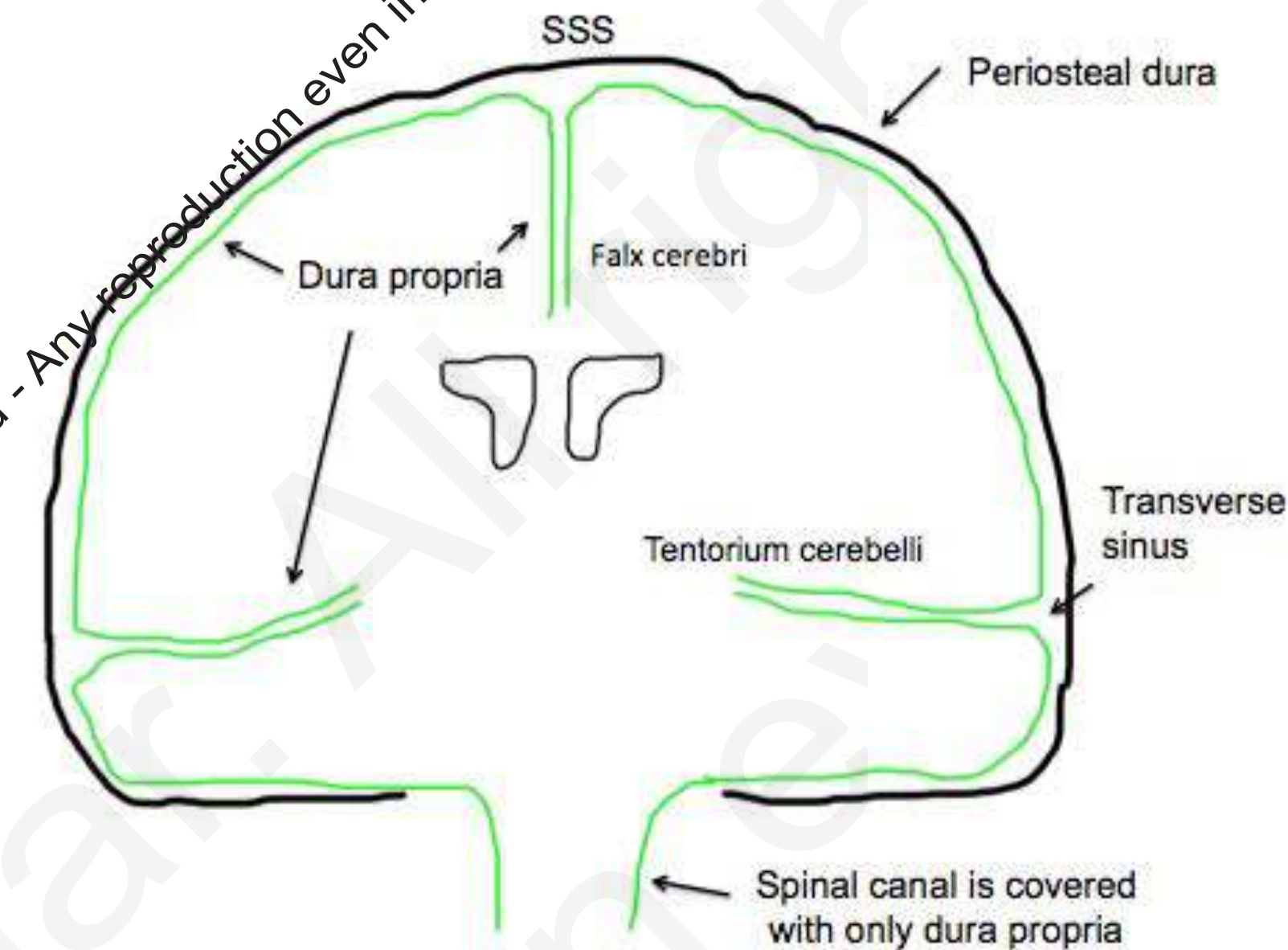


ACC, olfactory groove,
lateral spinal

Geibprasert S et al. 2008



ACC, Cavernous,
sigmoid



Tanaka M, 2016

Summary 1

1. Dural membrane on the falx, tentorium cerebelli, olfactory groove and spinal cord are derived from neural crest.

2. Dural AVFs associated with neural crest have always pial cortical venous reflux and character of demographic with male predominant.

3. Falco-tentorial, olfactory groove and spinal cord DAVFs can be considered as the neurocristopathy with aggressive clinical course.

Embryological Consideration of Dural Arteriovenous Fistulas

Michihiro TANAKA¹

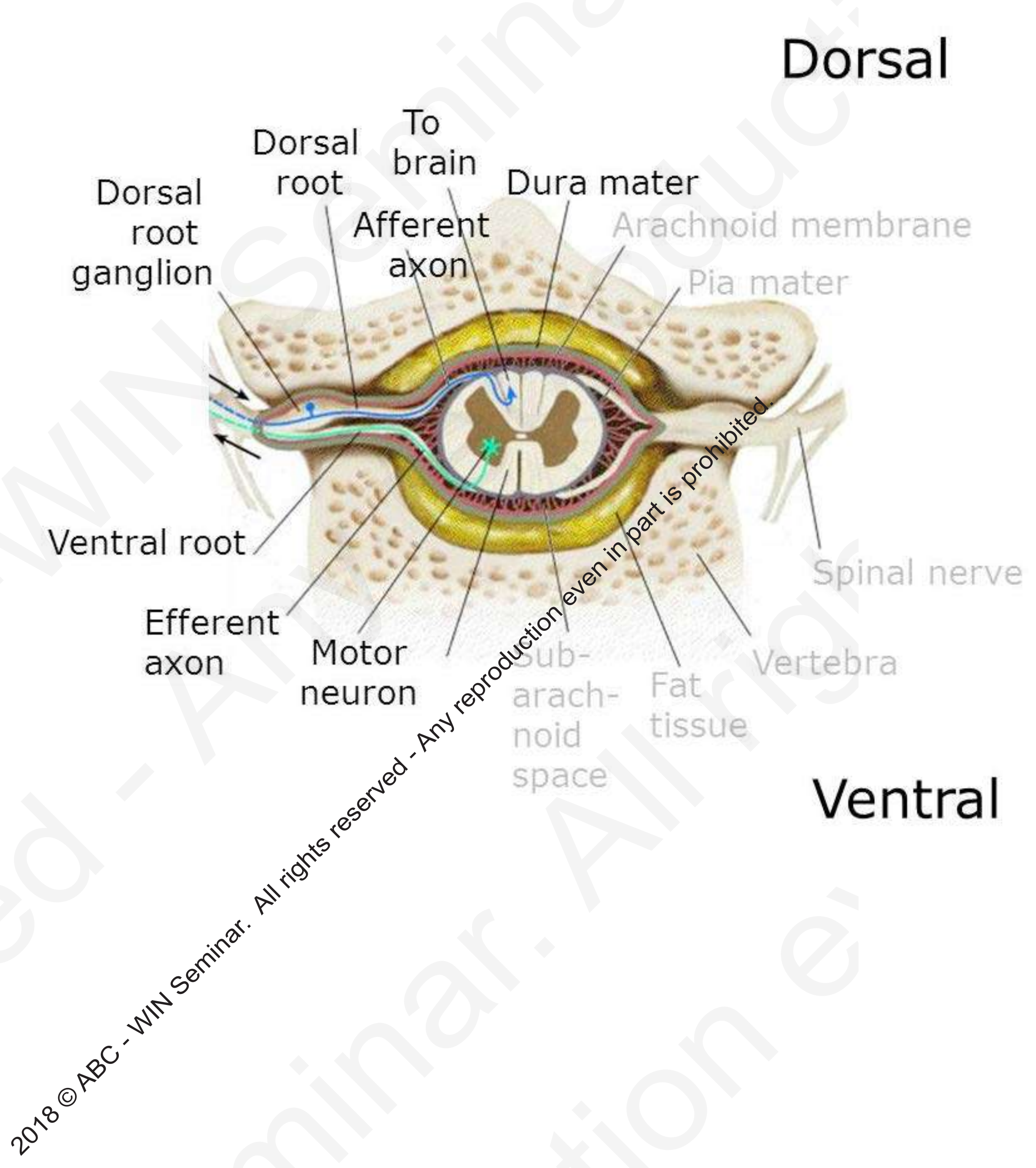
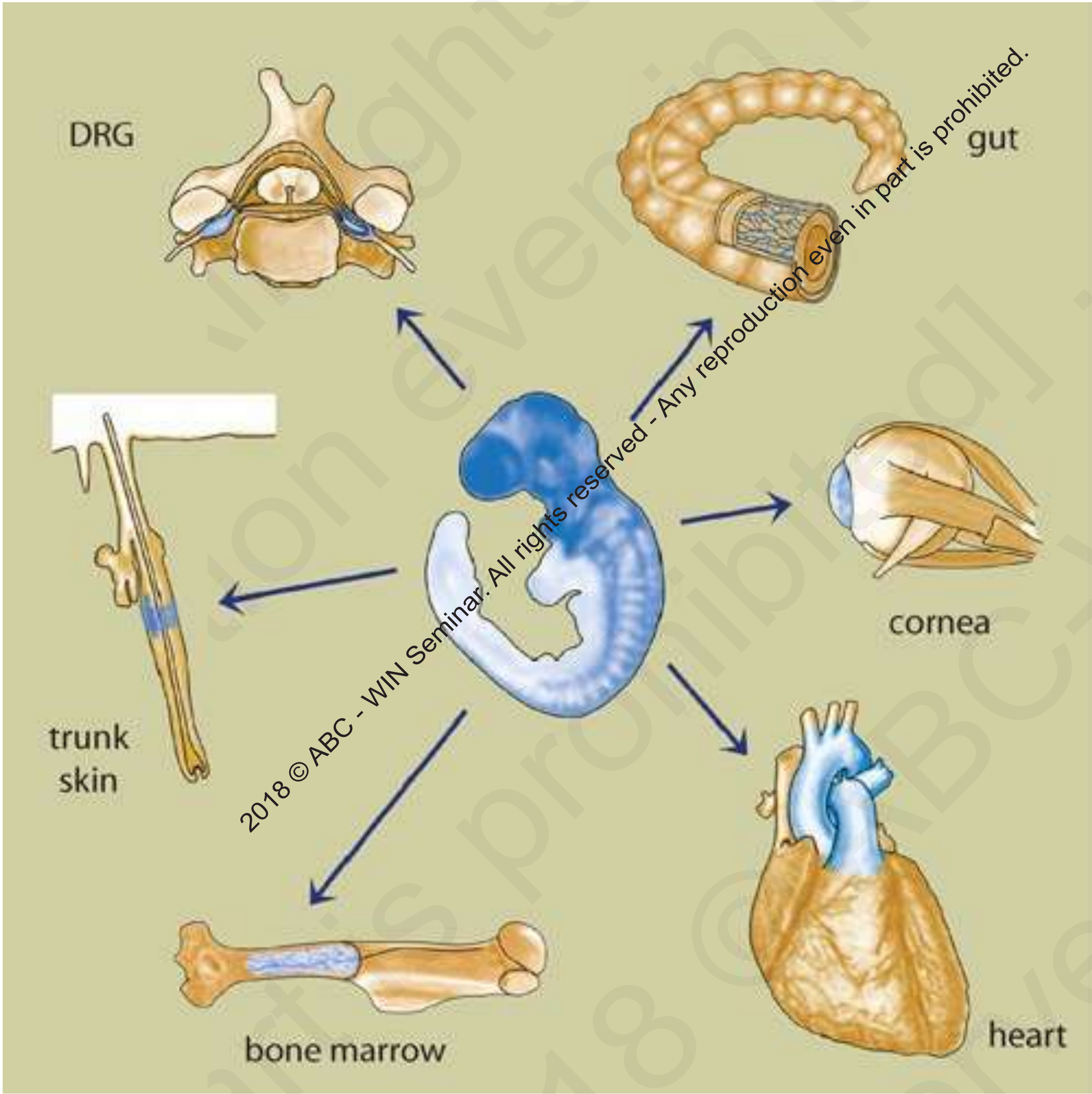
¹Department of Neurosurgery, Kamada Medical Center, Kamogawa City, Chiba, Japan

Abstract

The topographical distribution of dural arteriovenous fistulas (DAVFs) was analyzed based on the embryological anatomy of the dural membrane. Sixty-six consecutive cases of intracranial and spinal DAVFs were analyzed based on the angiography, and each shunt point was identified according to the embryological bony structures. The area of dural membranes was categorized into three different groups: a ventral group located on the endochondral bone (VE group), a dorsal group located on the membranous bone (DM group) and a falco-tentorial group (FT group) located in the falx cerebri, tentorium cerebelli, falx cerebelli, and diaphragm sellae. The FT group was designated when the dural membrane was formed only with the dura propria (meningeal layer of the dura mater) and not from the endosteal dura. Cavernous sinus, sigmoid sinus, and anterior condylar confluence was categorized to VE group, which had a female predominance, more benign clinical presentations, and a lower rate of cortical and spinal venous reflux. Transverse sinus, confluence, and superior sagittal sinus belonged to the DM group. Olfactory groove, falx, tent of the cerebellum, and nerve sleeve of spinal cord were categorized to the FT group, which presented later in life and which had a male predominance, more aggressive clinical presentations, and significant cortical and spinal venous reflux. The DAVFs was associated with the layers of the dural membrane characterized by the two different embryological bony structures. The FT group was formed only with the dura propria as an independent risk factor for aggressive clinical course and hemorrhage of DAVFs.

Key words: dural arteriovenous fistulas, dura propria, osteal dura, endochondral bone, membranous bone





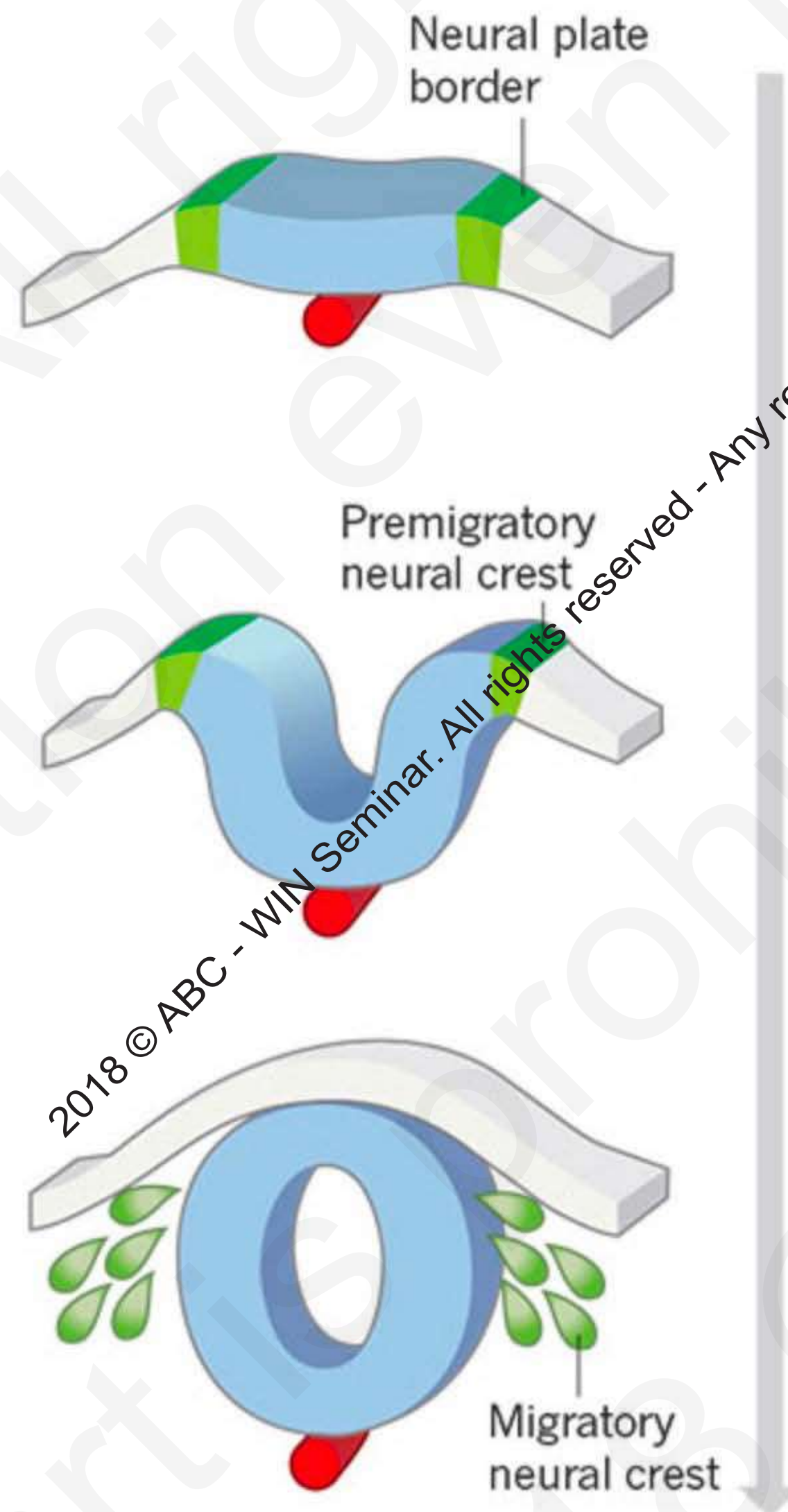


Spinal DAVF

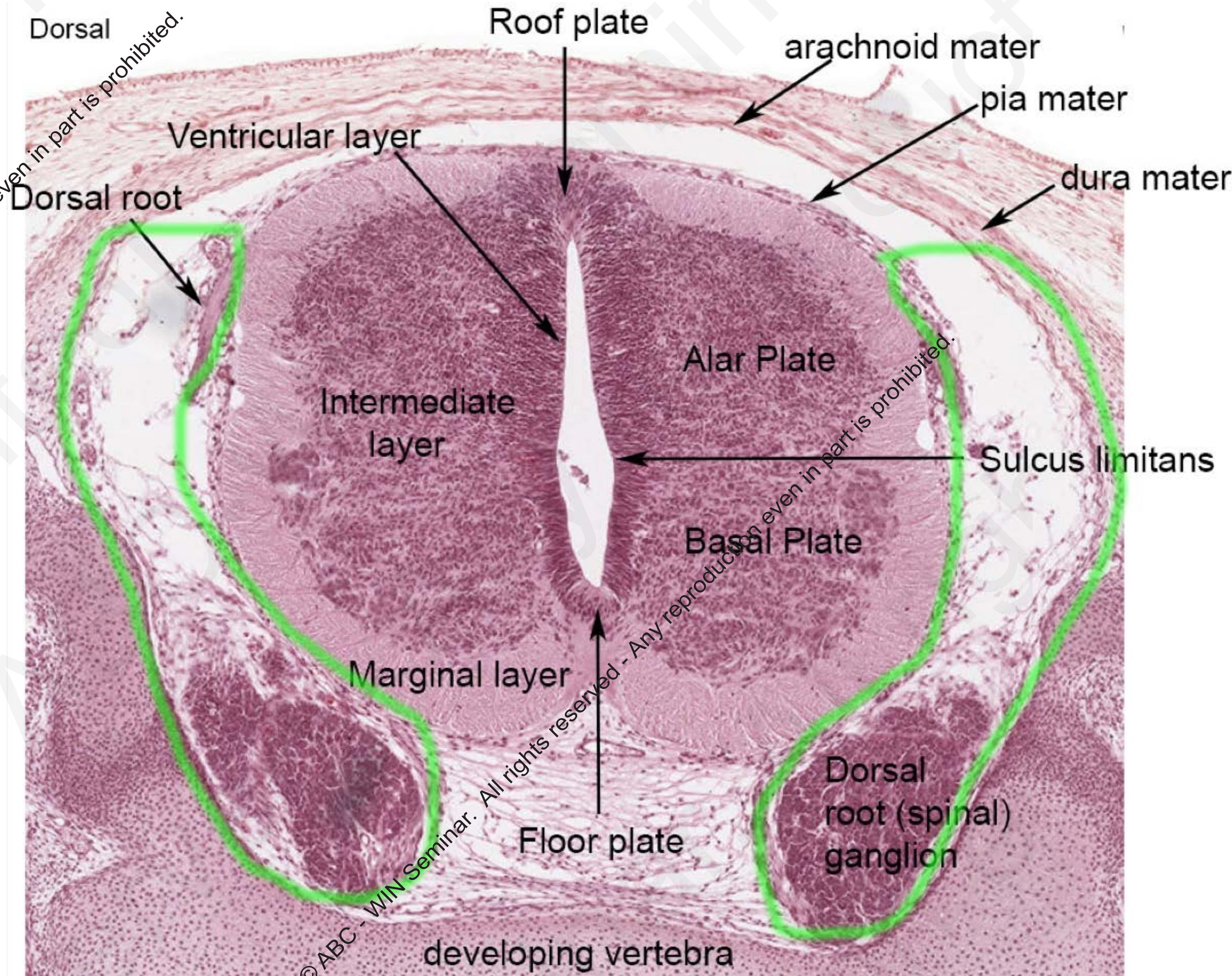
Why posterior spinal vein is always dilated rather than anterior spinal vein ?

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a Vertebrate neural crest development

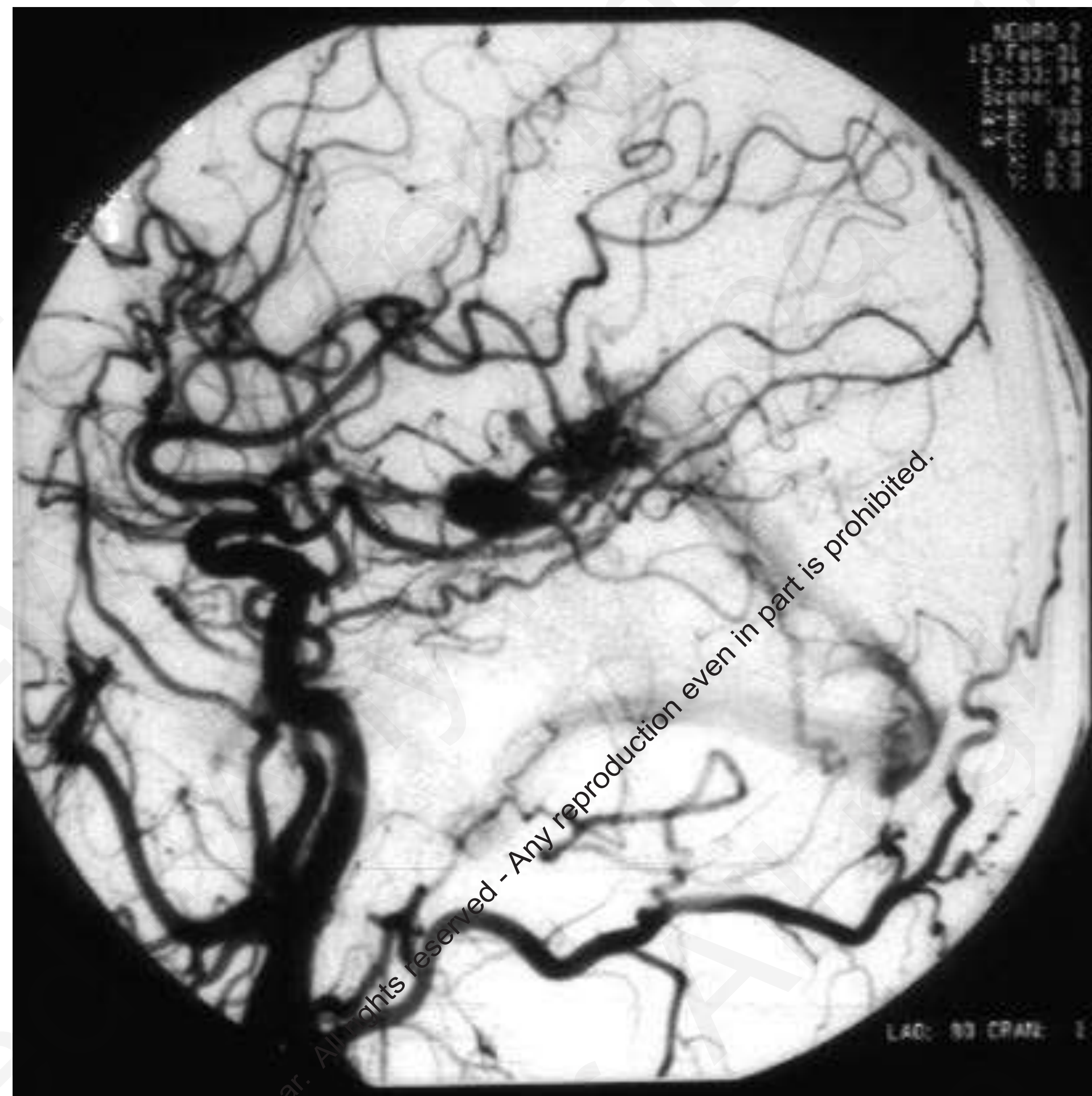
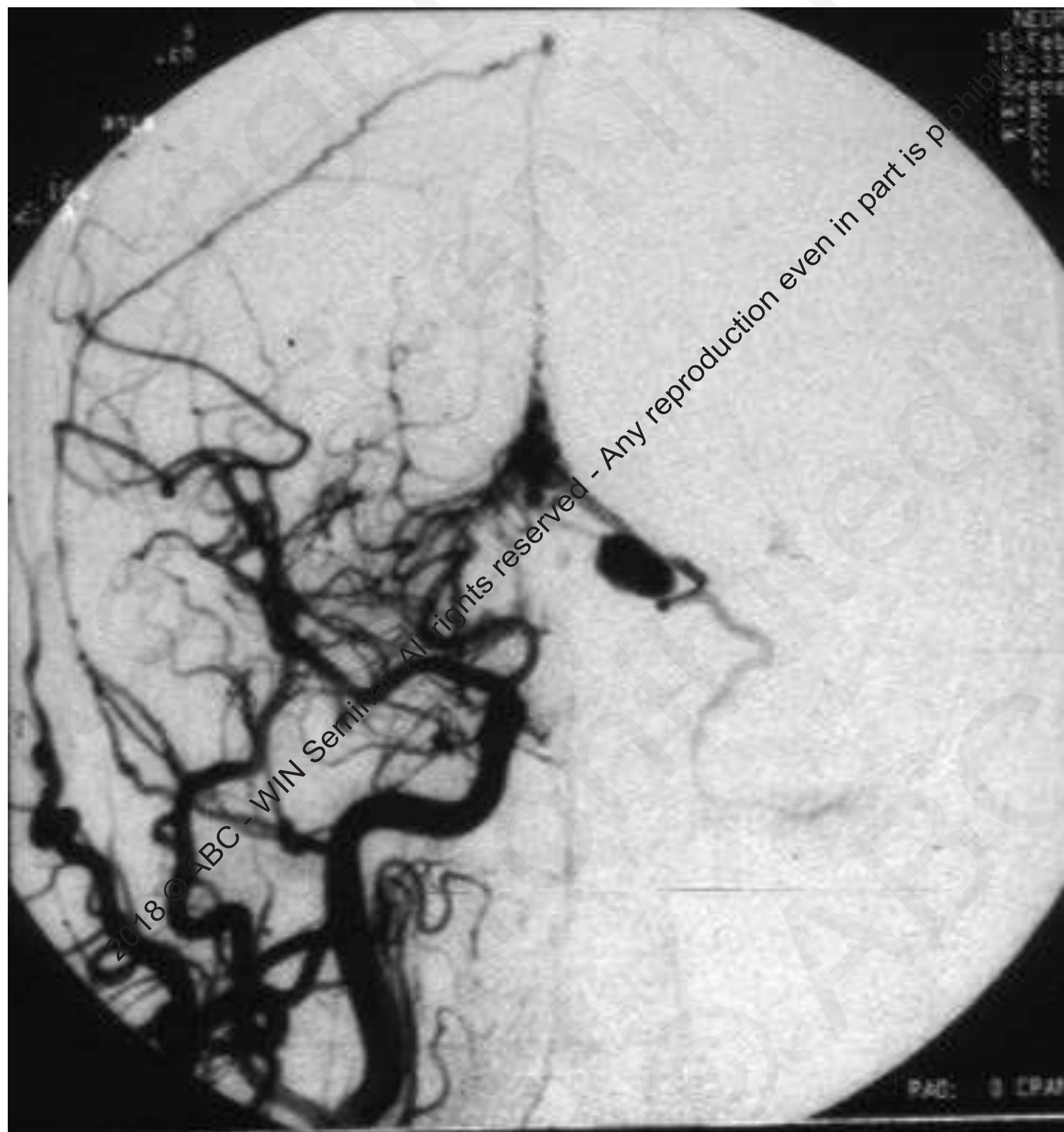


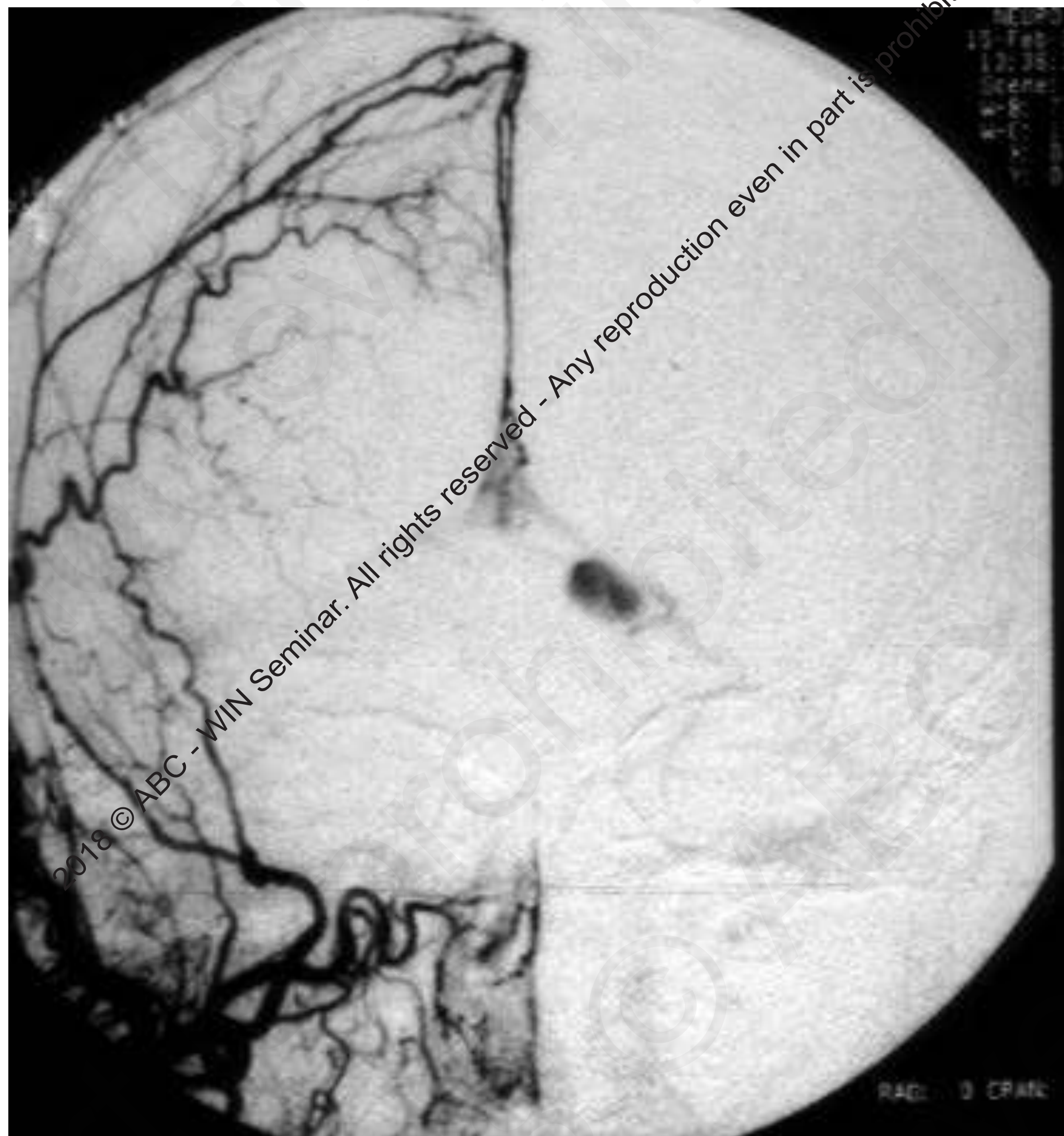
Green SA, Simoes-Costa M, Bronner ME.
Nature. 2015 Apr 23;520(7548):474-82.

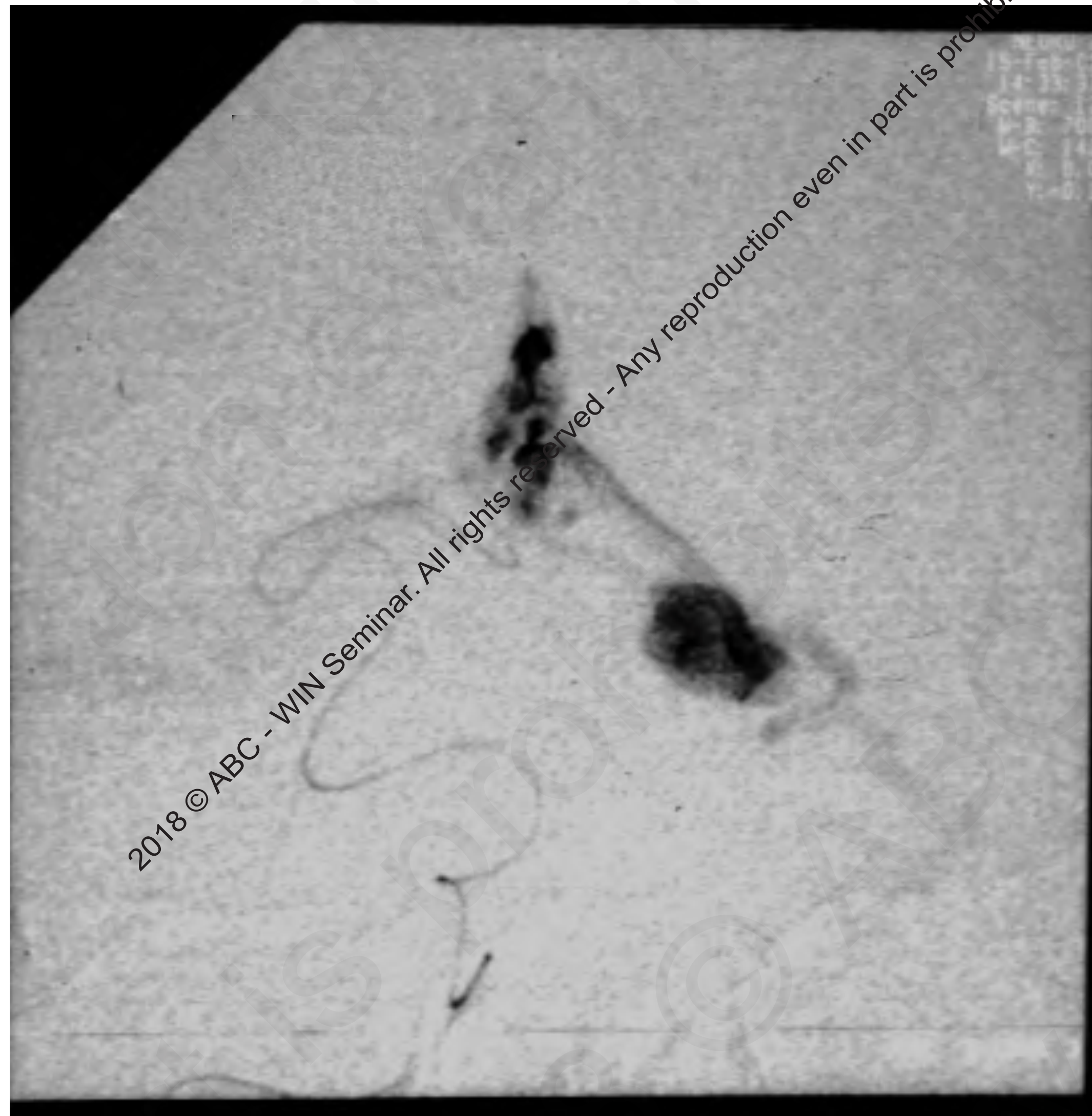


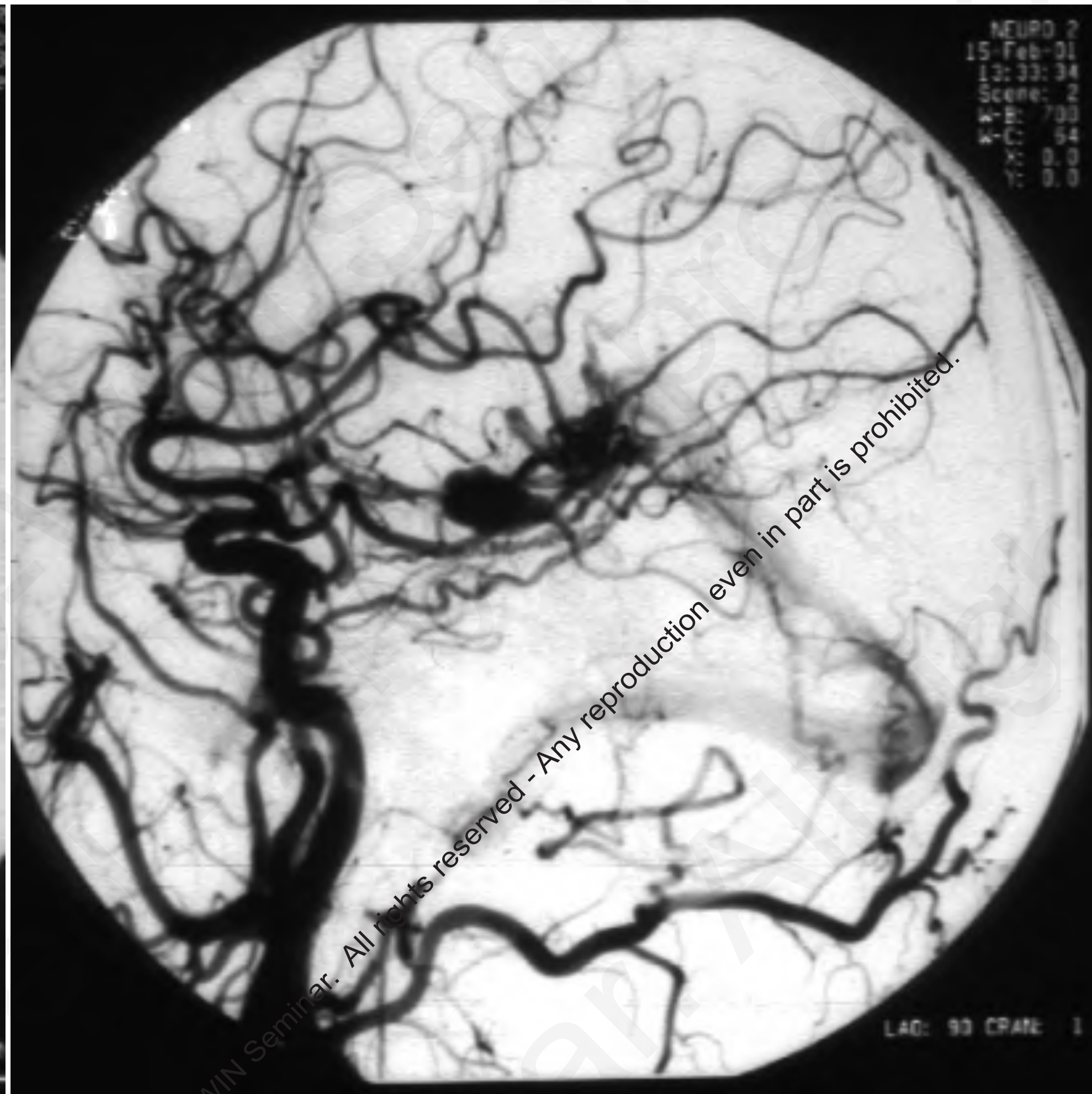
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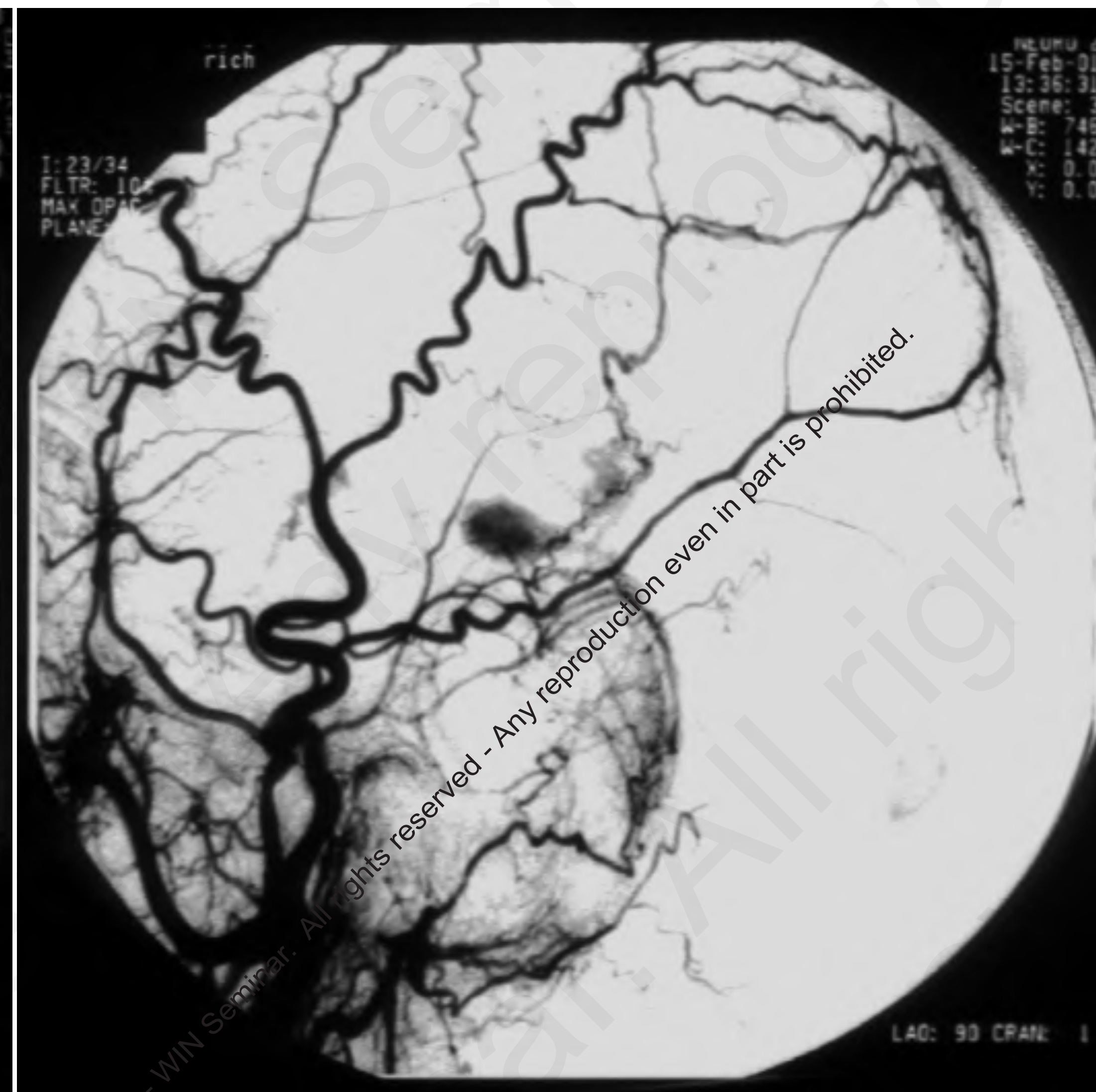
Embryo@8 week

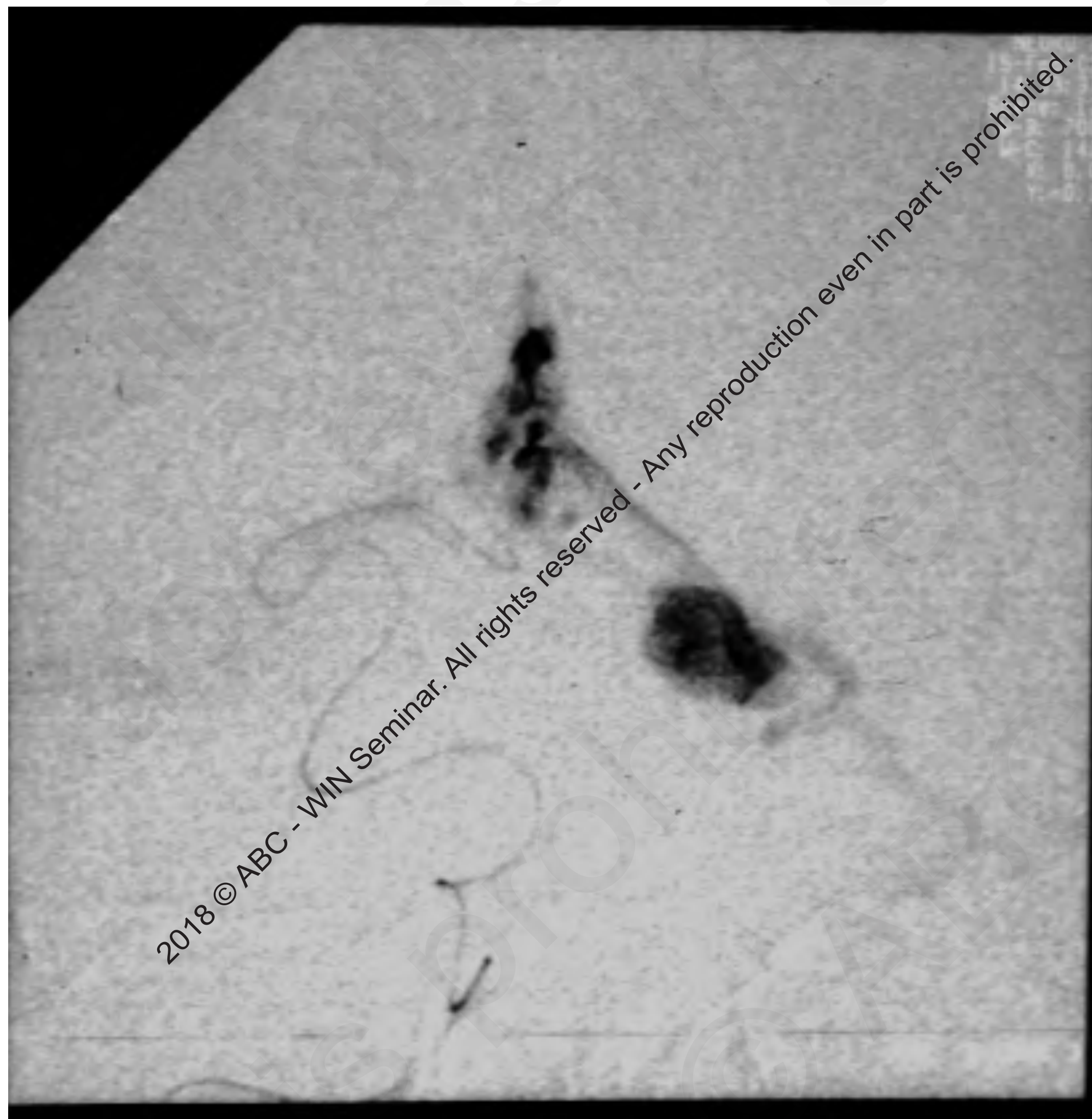


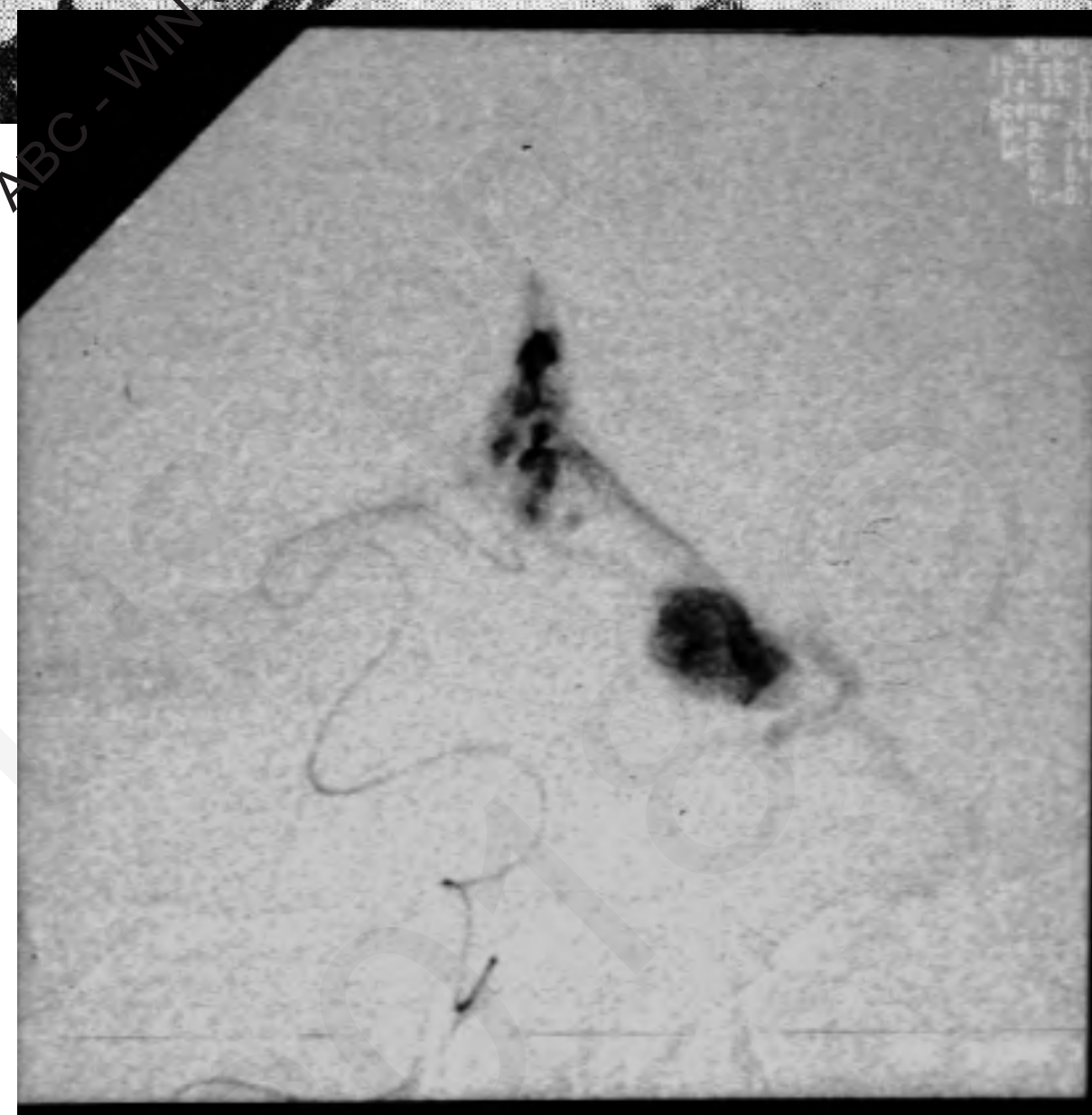
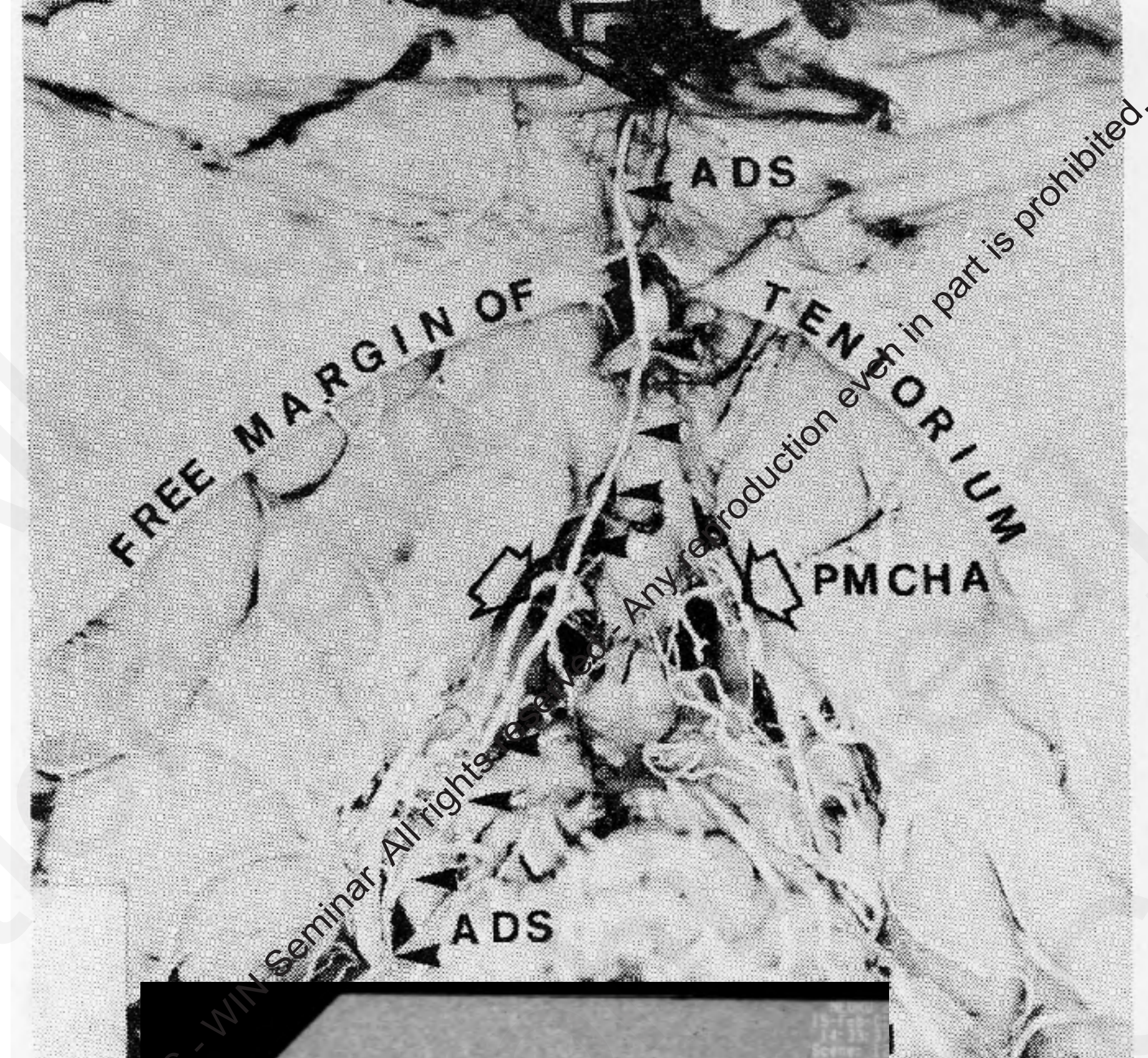




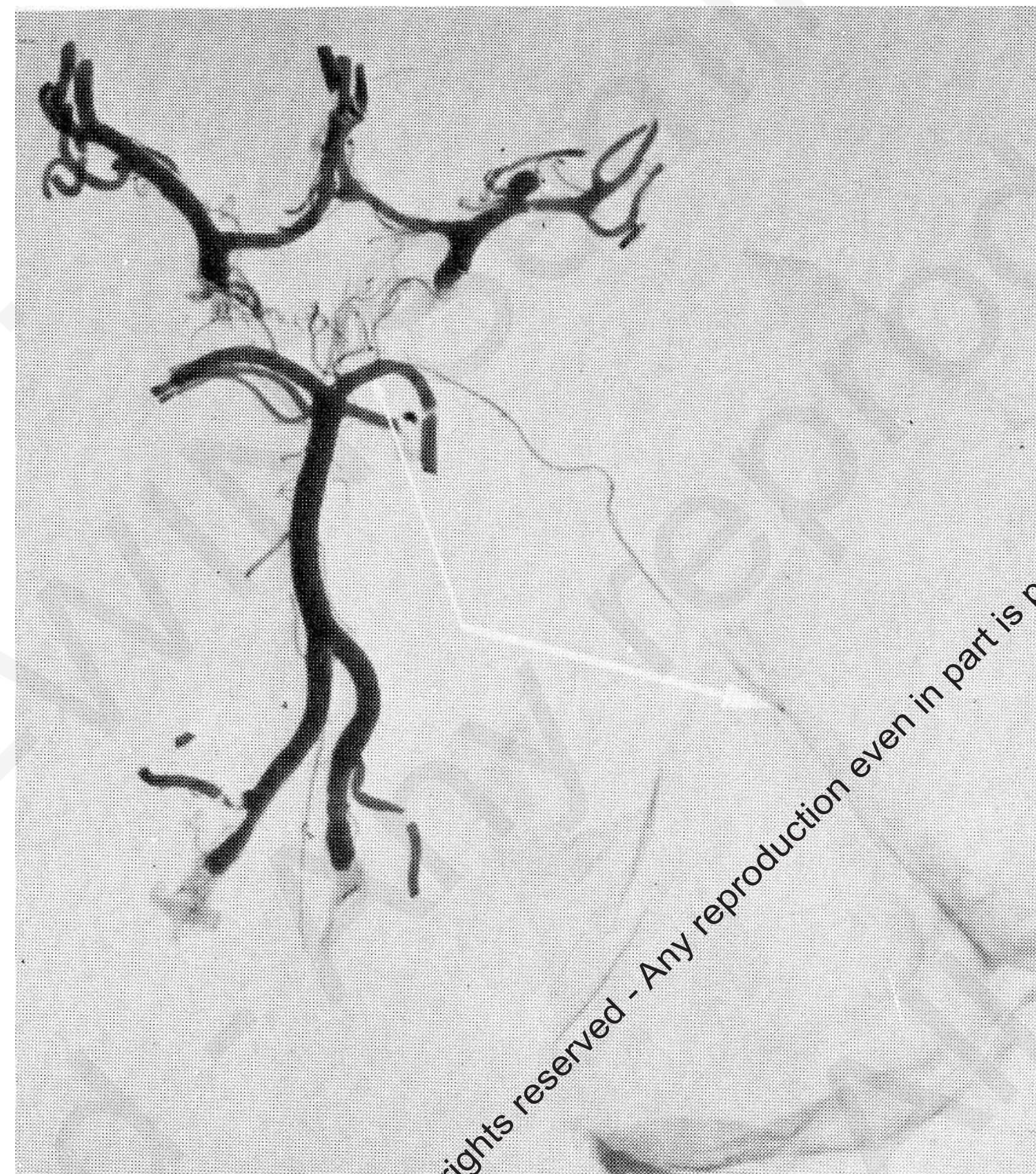


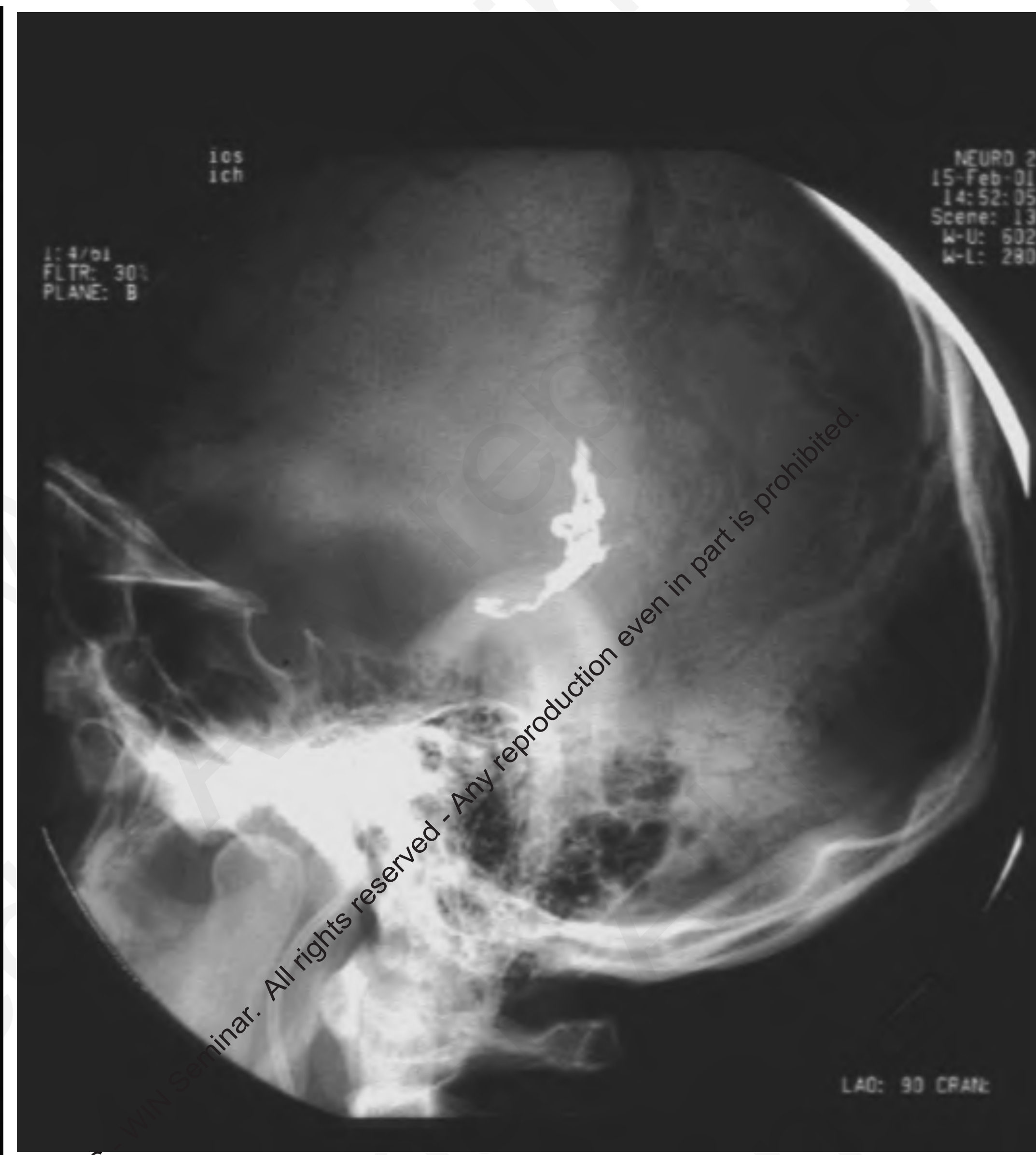
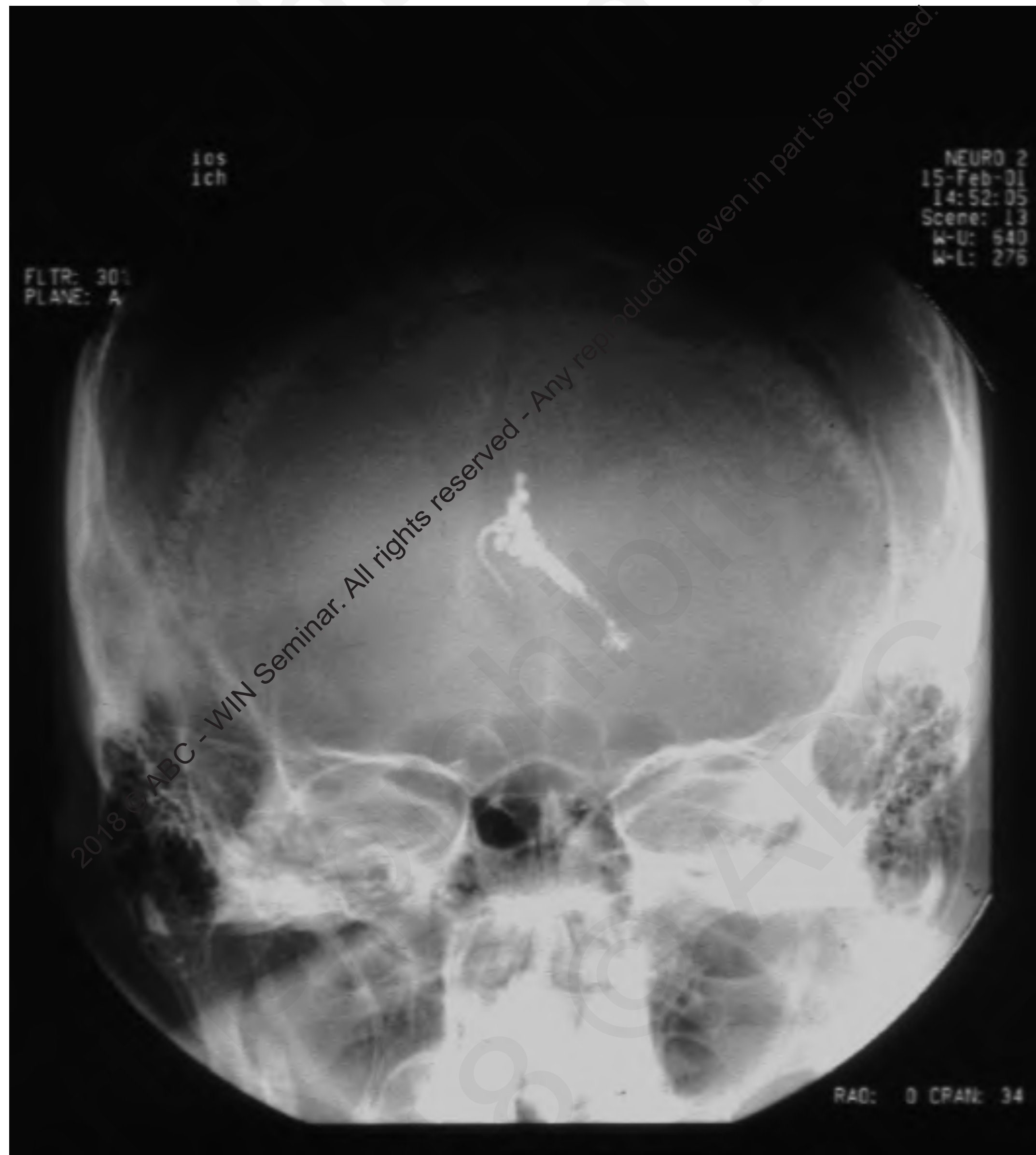






Aretery of Davidoff-Schechter





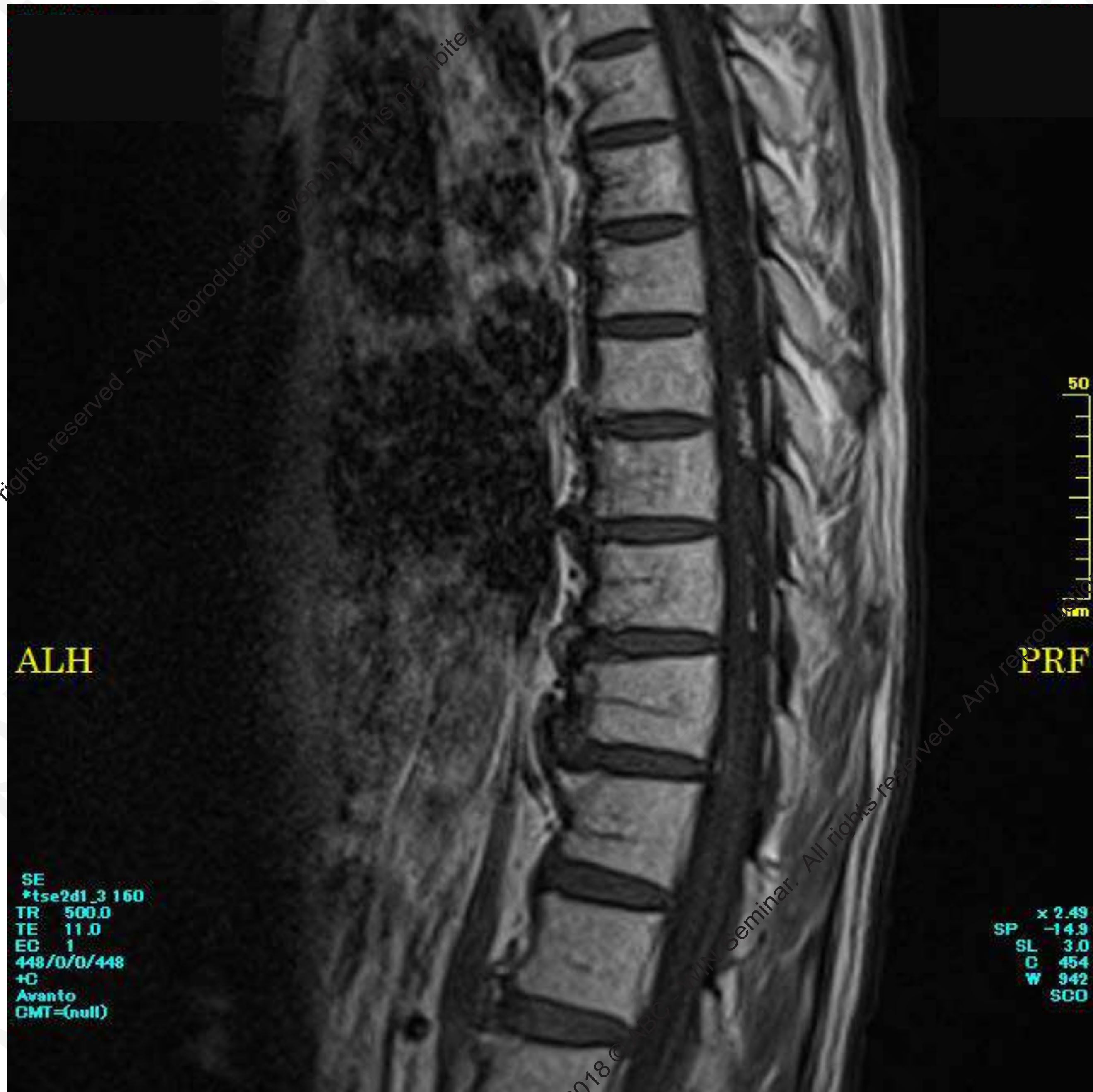
A 64 year-old-man presented with progressive paraplegia with bladder and rectal disturbance.



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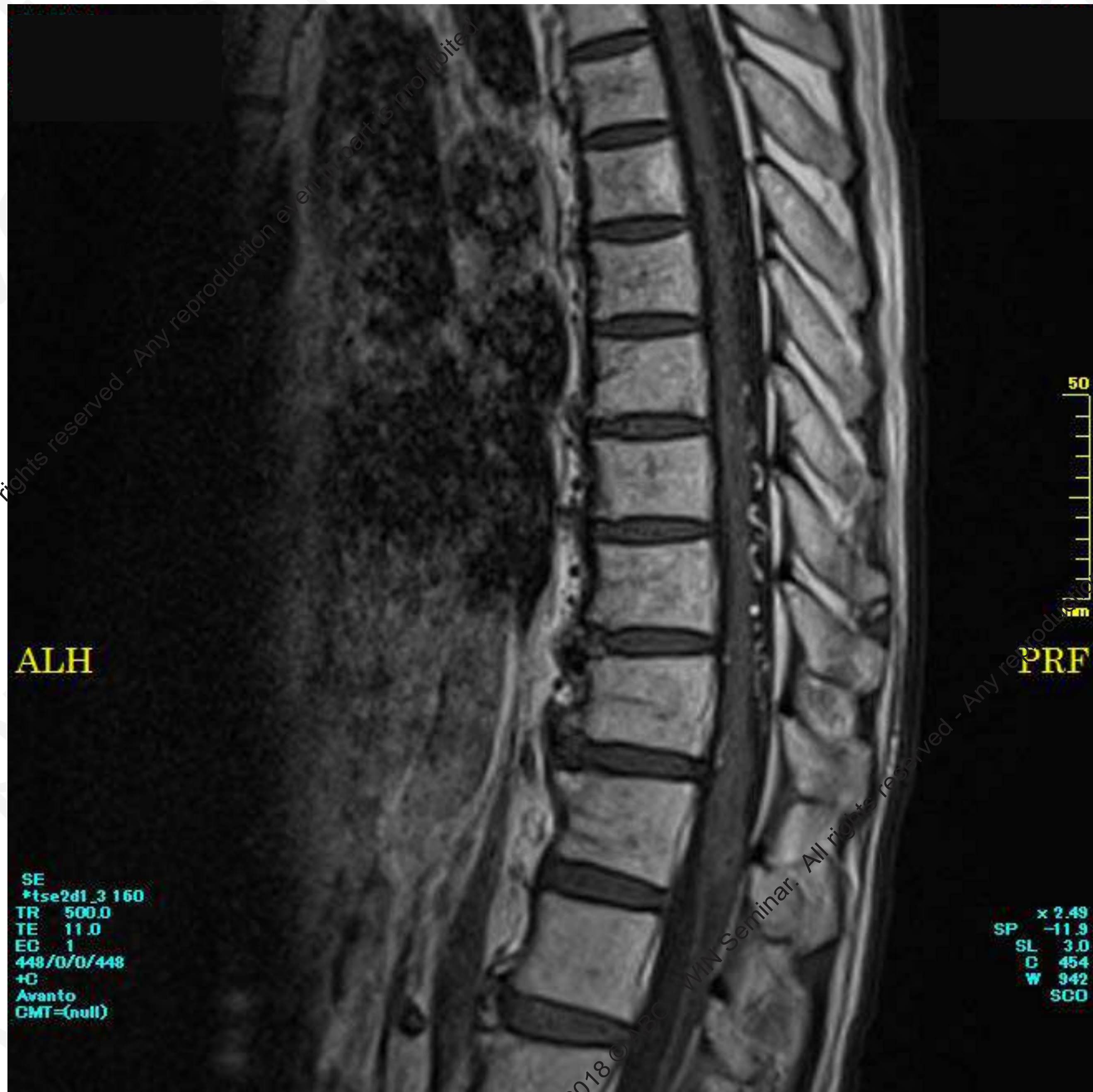
ALH

PRF

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TE 11.0
EC 1
448/0/0/448
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SP -14.9
SL 3.0
C 454
W 942
SGO

50
cm



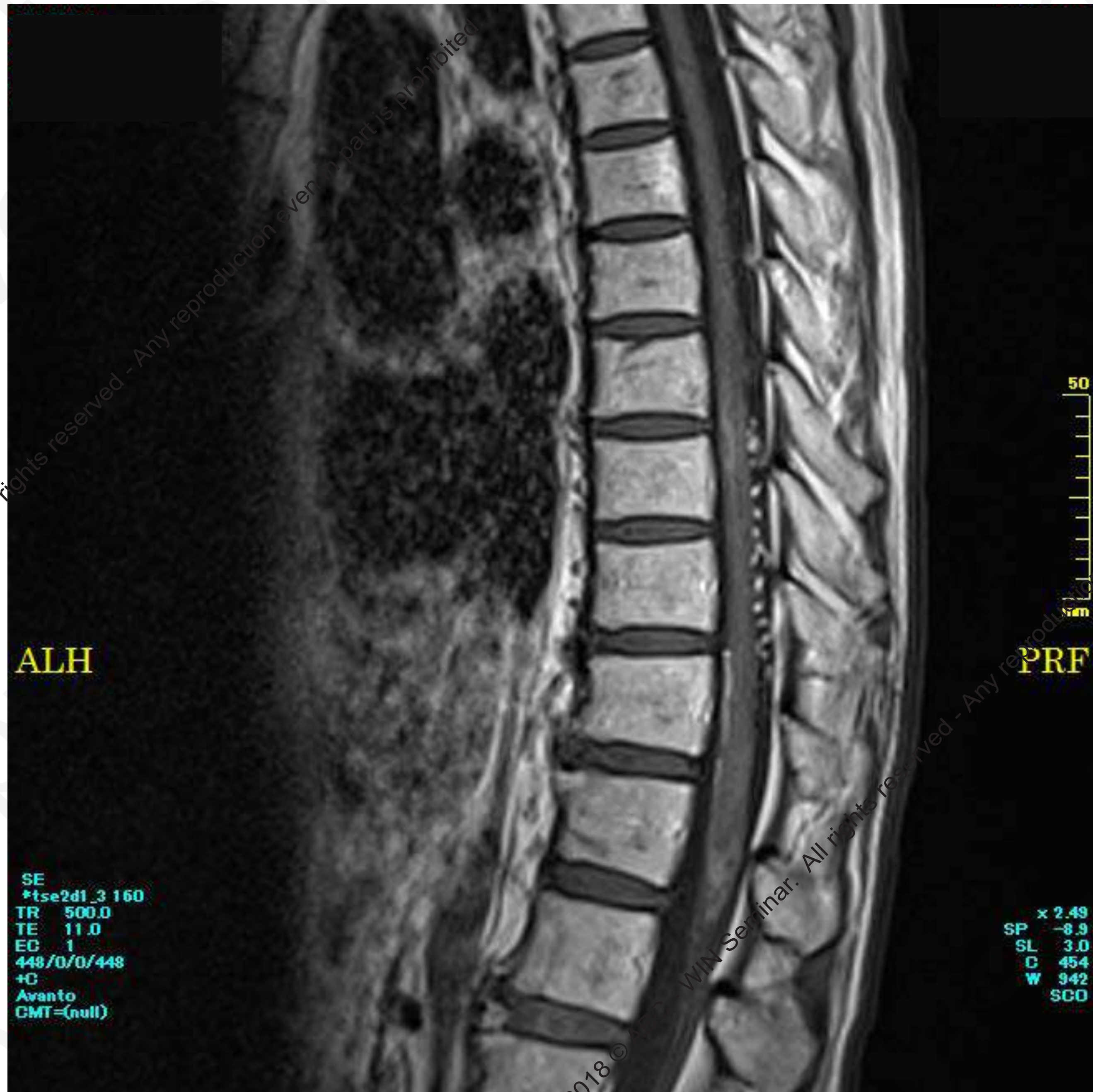
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Avanto
CMT=(null)

x 2.49
SP -11.9
SL 3.0
C 454
W 942
SGO

50
cm



07225514 Patient ID: 07225514
1952/03/17 Date of Birth: 1952/03/17, Male
2016/01/27 Date: 2016/01/27
10:48 AM Date: 2016/01/27
Run 9015 - Frame 1 / 512

Rot: AP
Ang:

Head Side



Run Number: 5013
Volume Type: 3DRA
Run Date: 2016/01/27
Run Time: 11:40:26
Cube Size: 147.06 mm



07225514 Patient ID: 07225514
1952/03/17 Date of Birth: 1952/03/17, Male
2016/02/09 Date: 2016/02/09
1:16 PM Date: 2016/02/09
Run 9030 - Frame 1 / 545

Rot: AP
Ang:

Head Side

Run Number: 5020
Volume Type: XperCT
Run Date: 2016/02/09
Run Time: 15:17:58
Cube Size: 104.56 mm



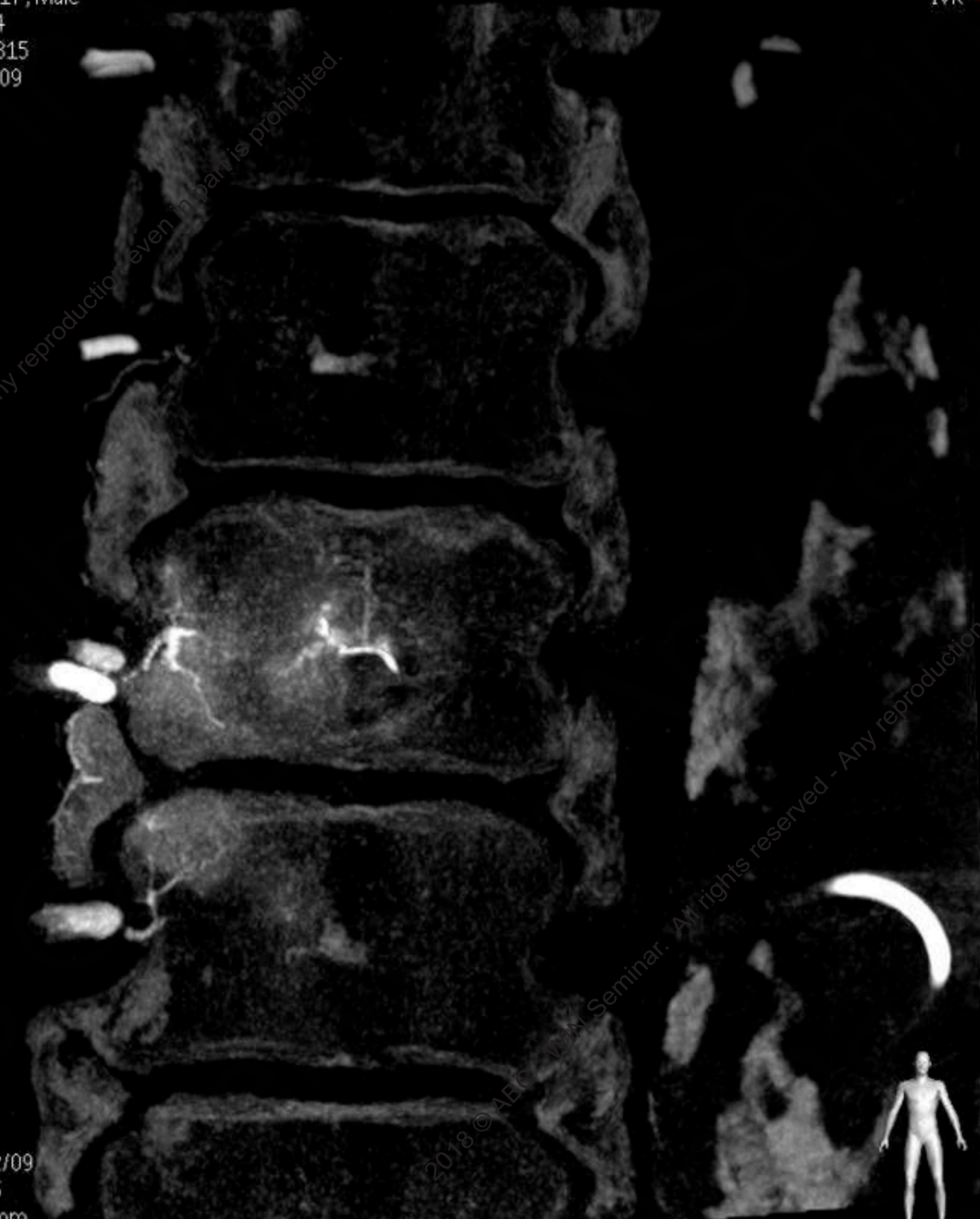
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20160209D: 6A27143815
1:16 PM Date: 2016/02/09
Run 9033 - Frame 1 / 145

Rot: AP
Ang:

Head Side

Zoom 100%

Run Number: 5027
Volume Type: XperCT
Run Date: 2016/02/09
Run Time: 16:00:06
Cube Size: 104.56 mm





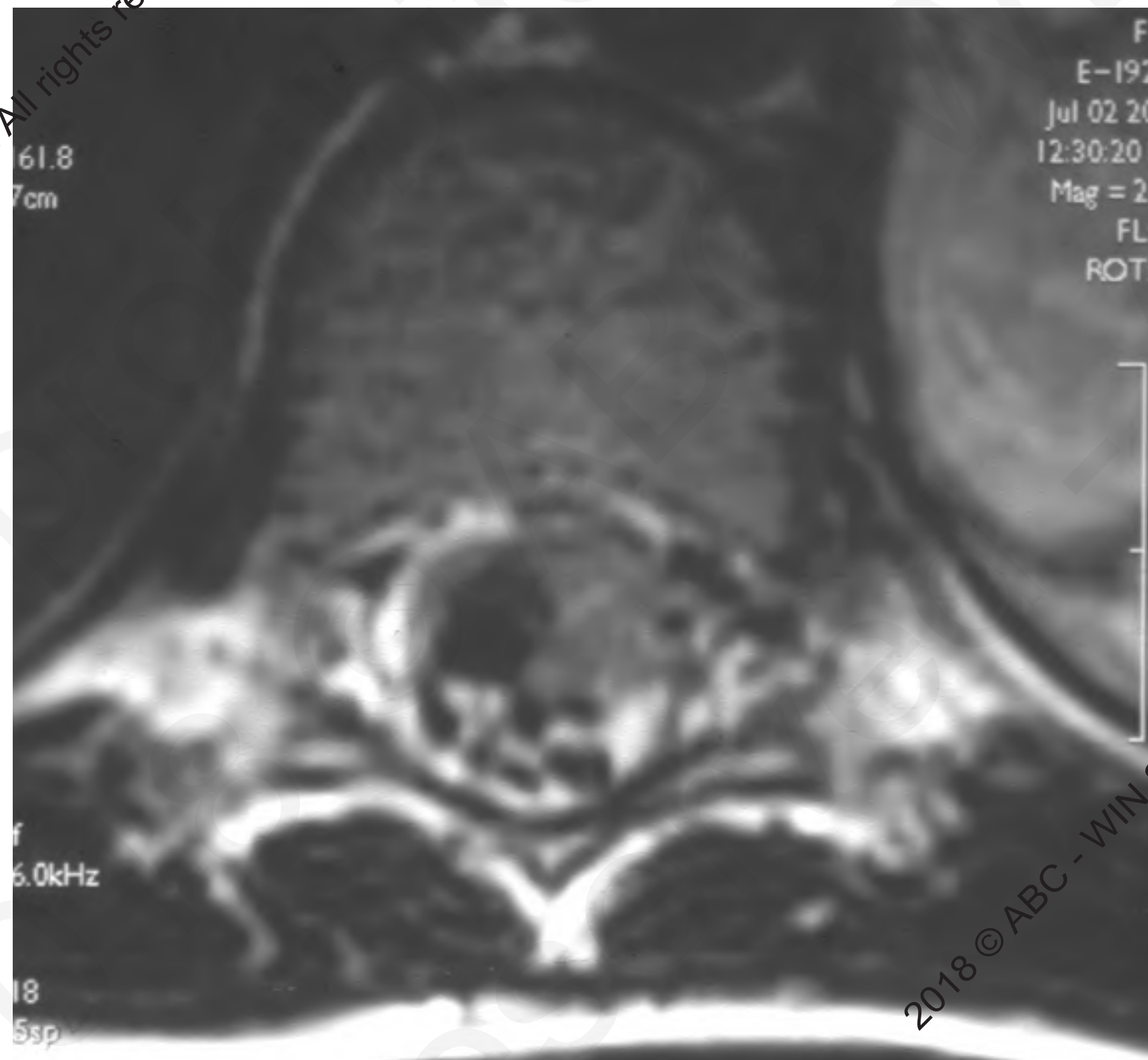
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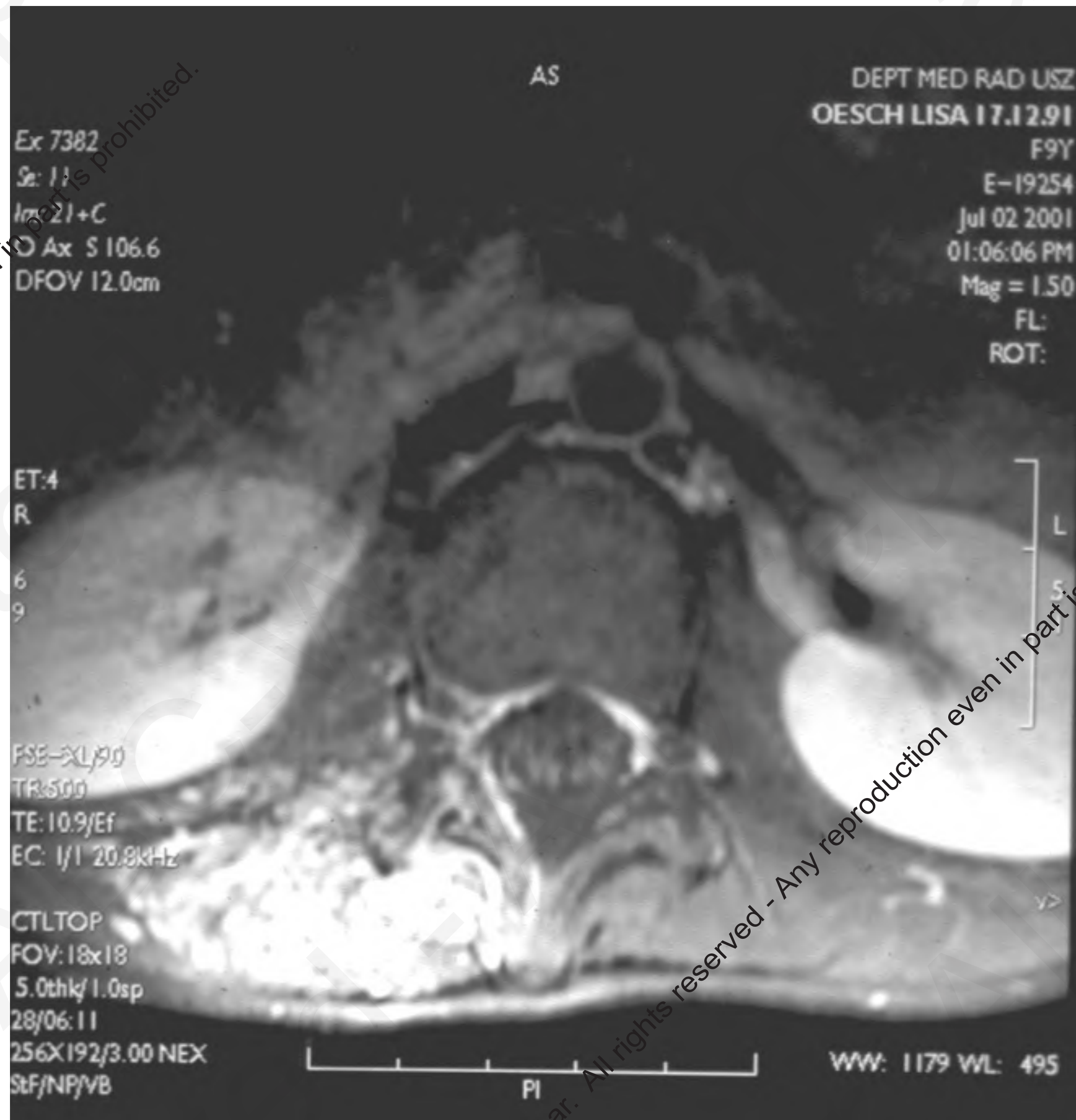
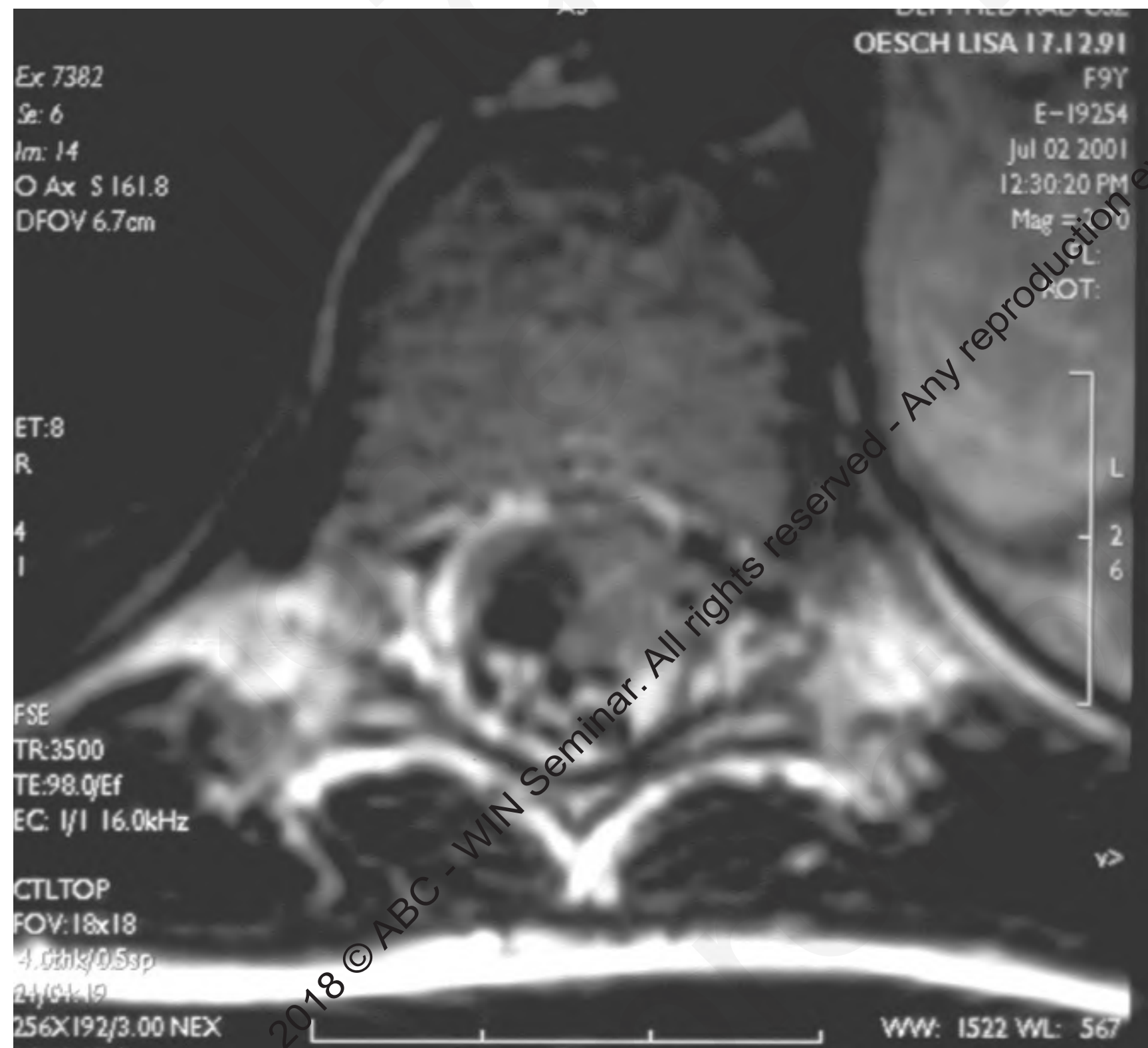


Post@72hr

What causes Cobb syndrome?

The cause of Cobb syndrome is not completely understood. It is believed that somatic mutations in the neural crest or mesoderm are responsible for its development fairly early in the development of the embryo .

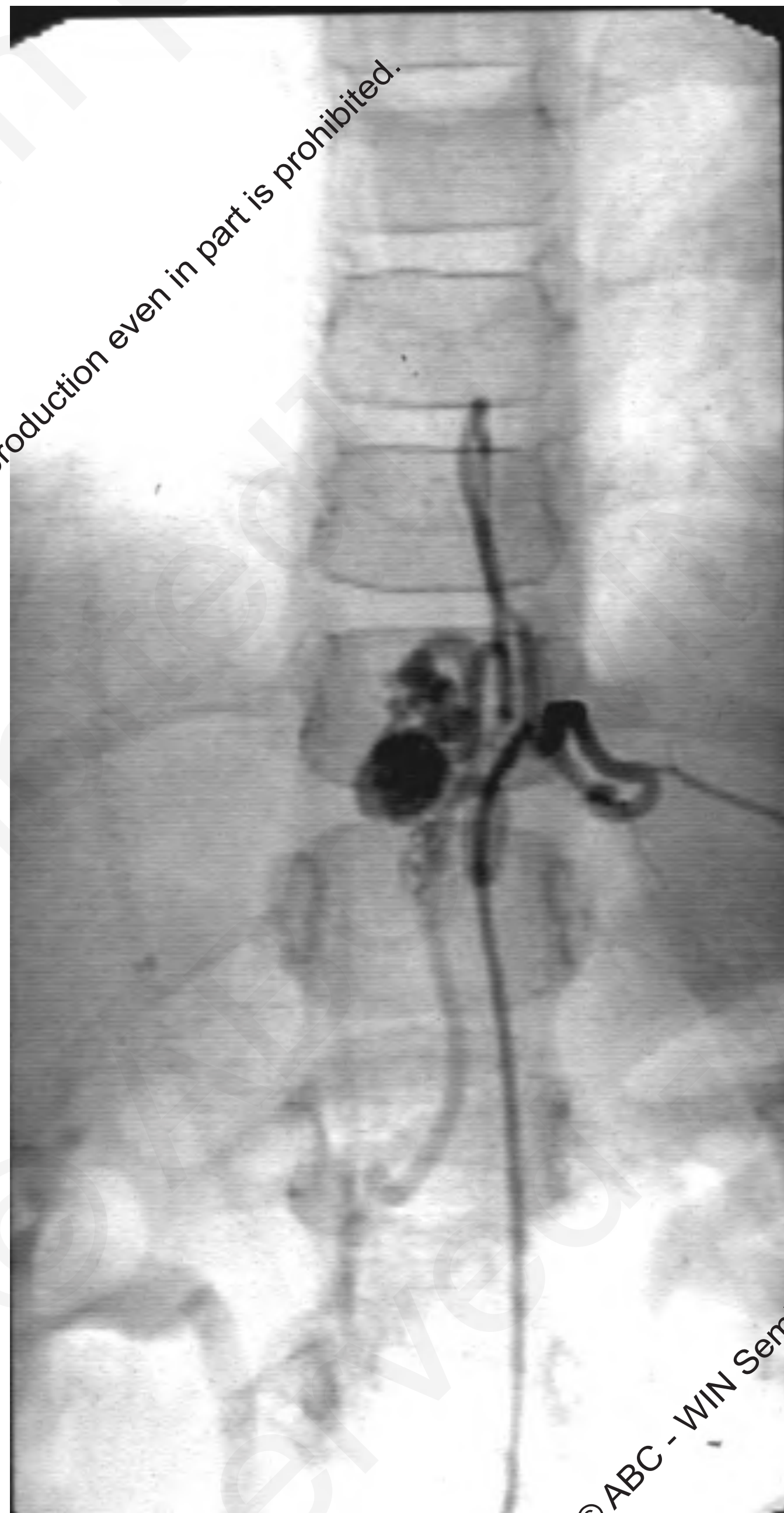




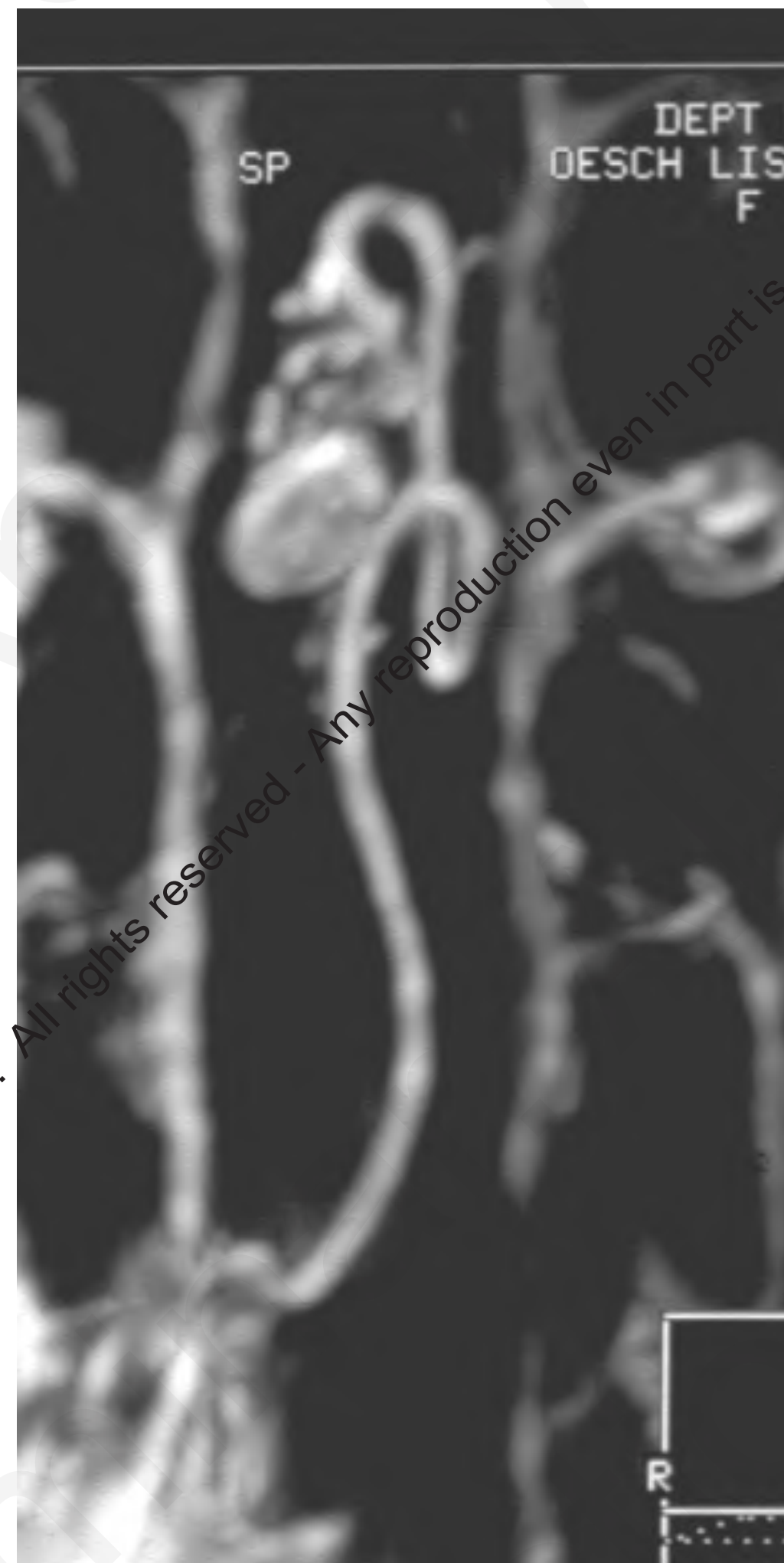
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Lt.T11



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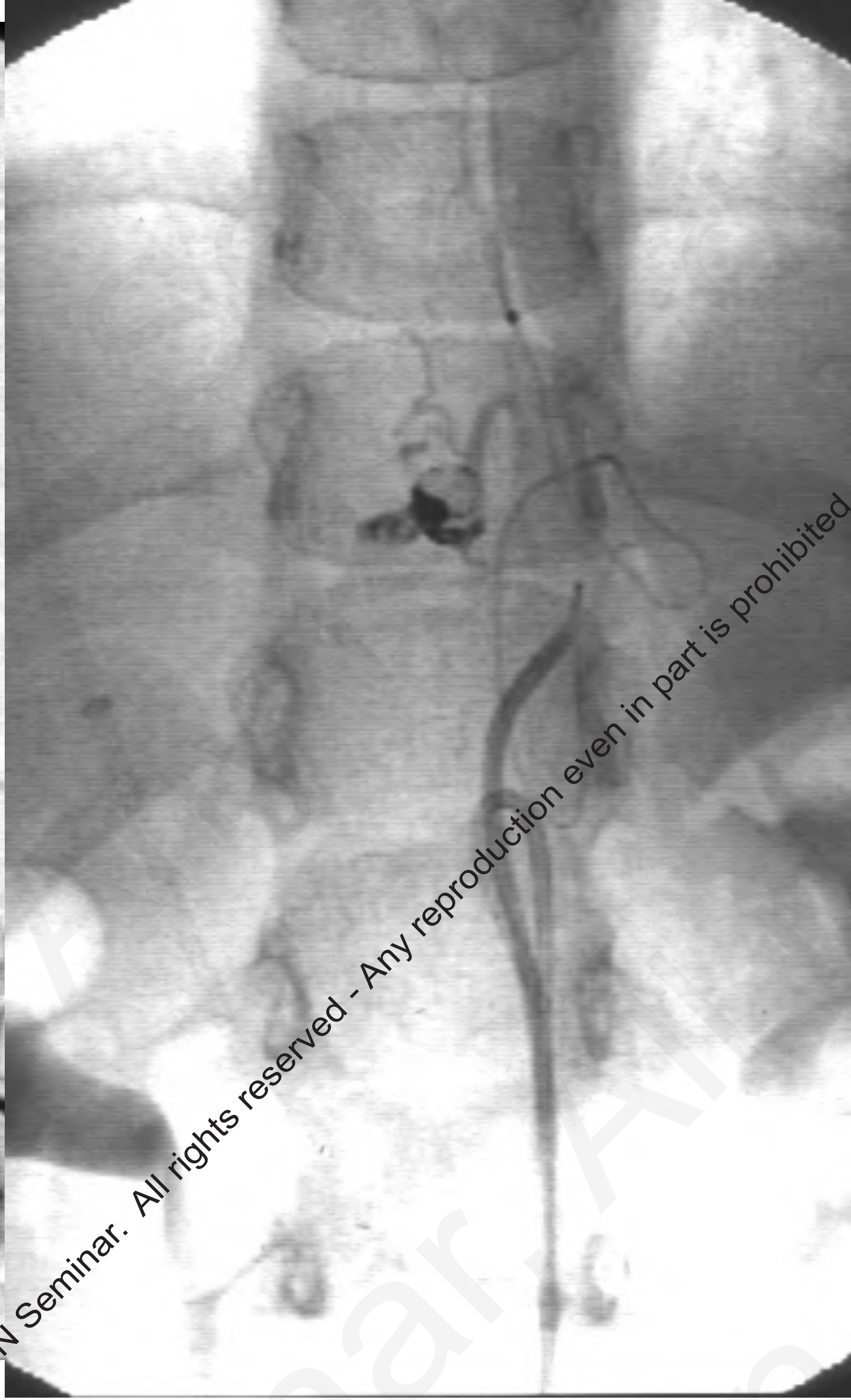


DEPT M OESCH LIS F
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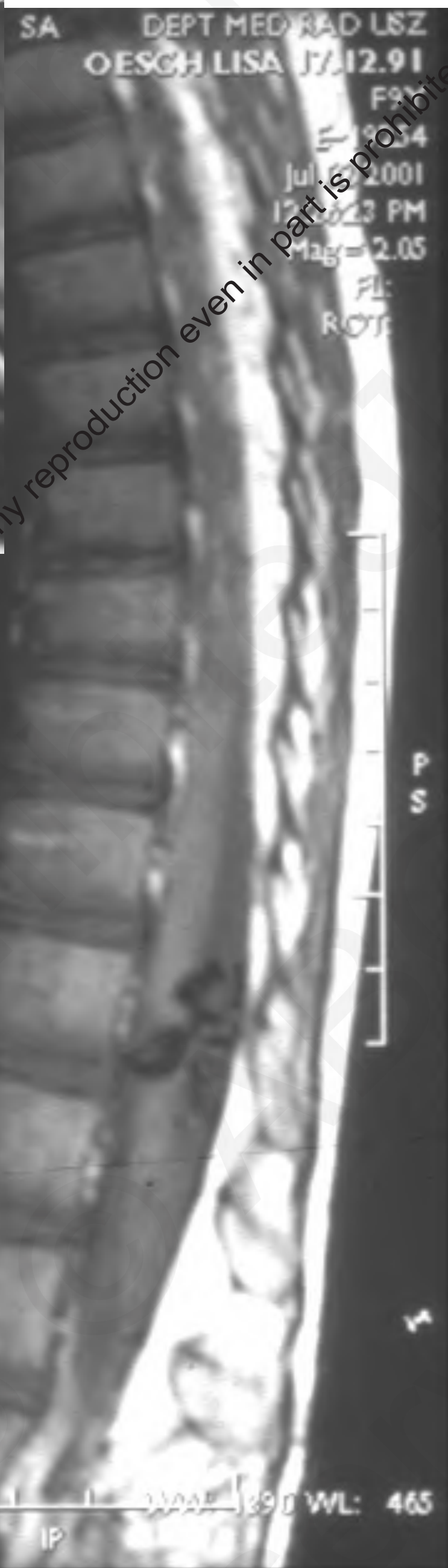
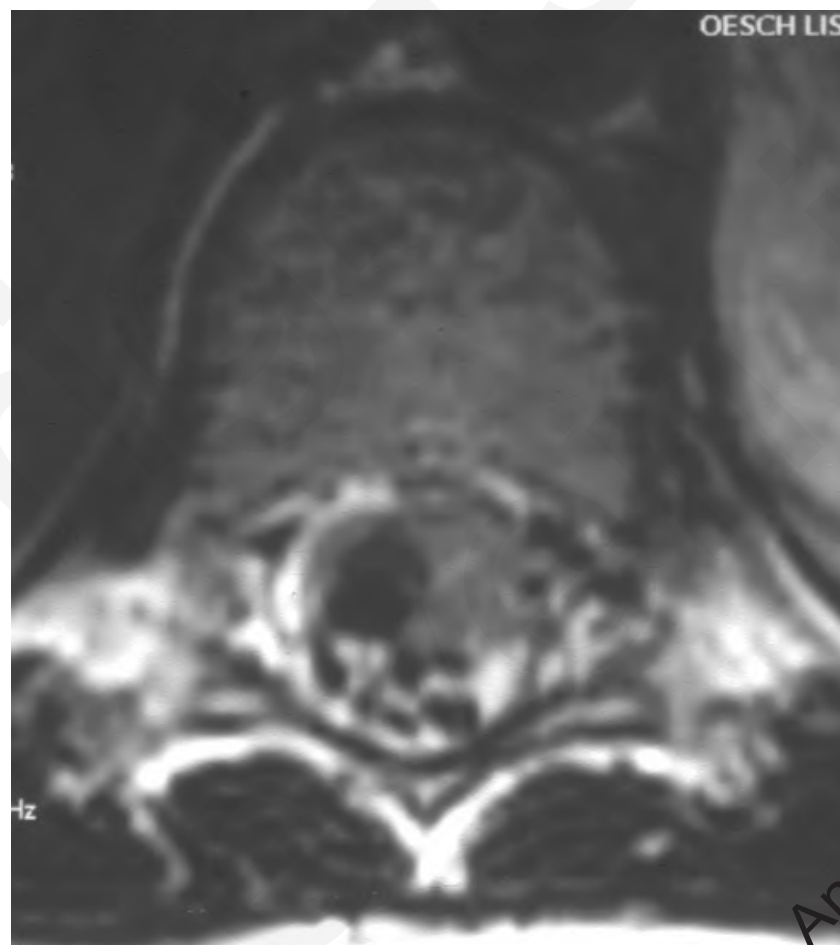


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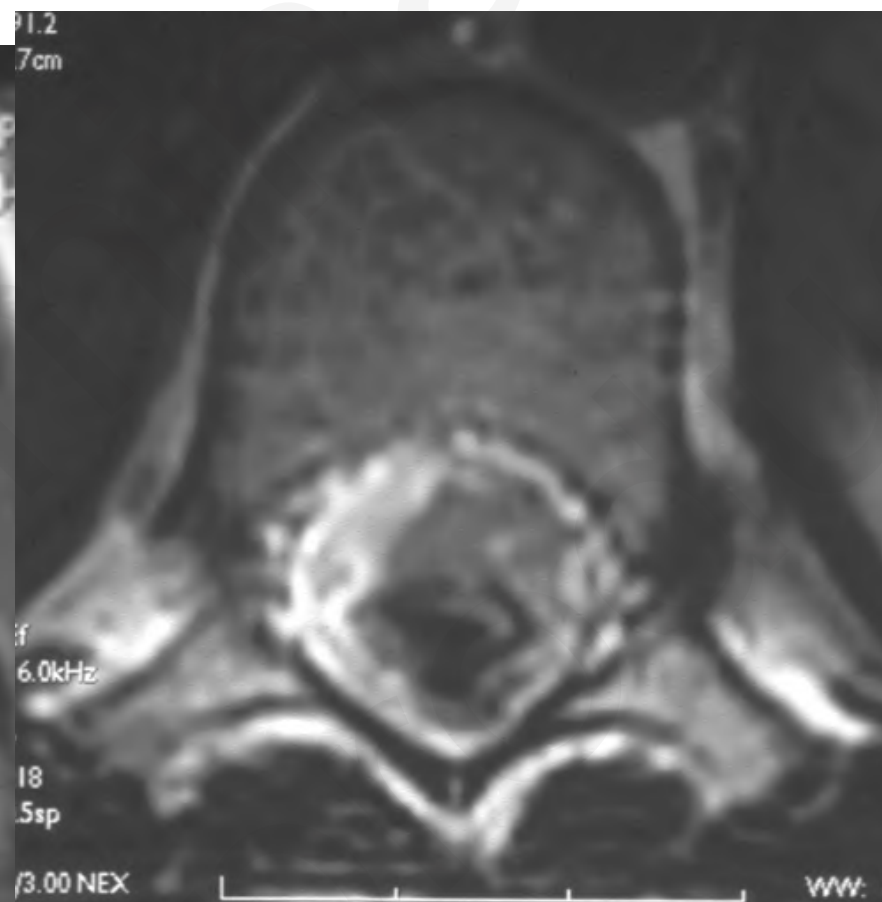


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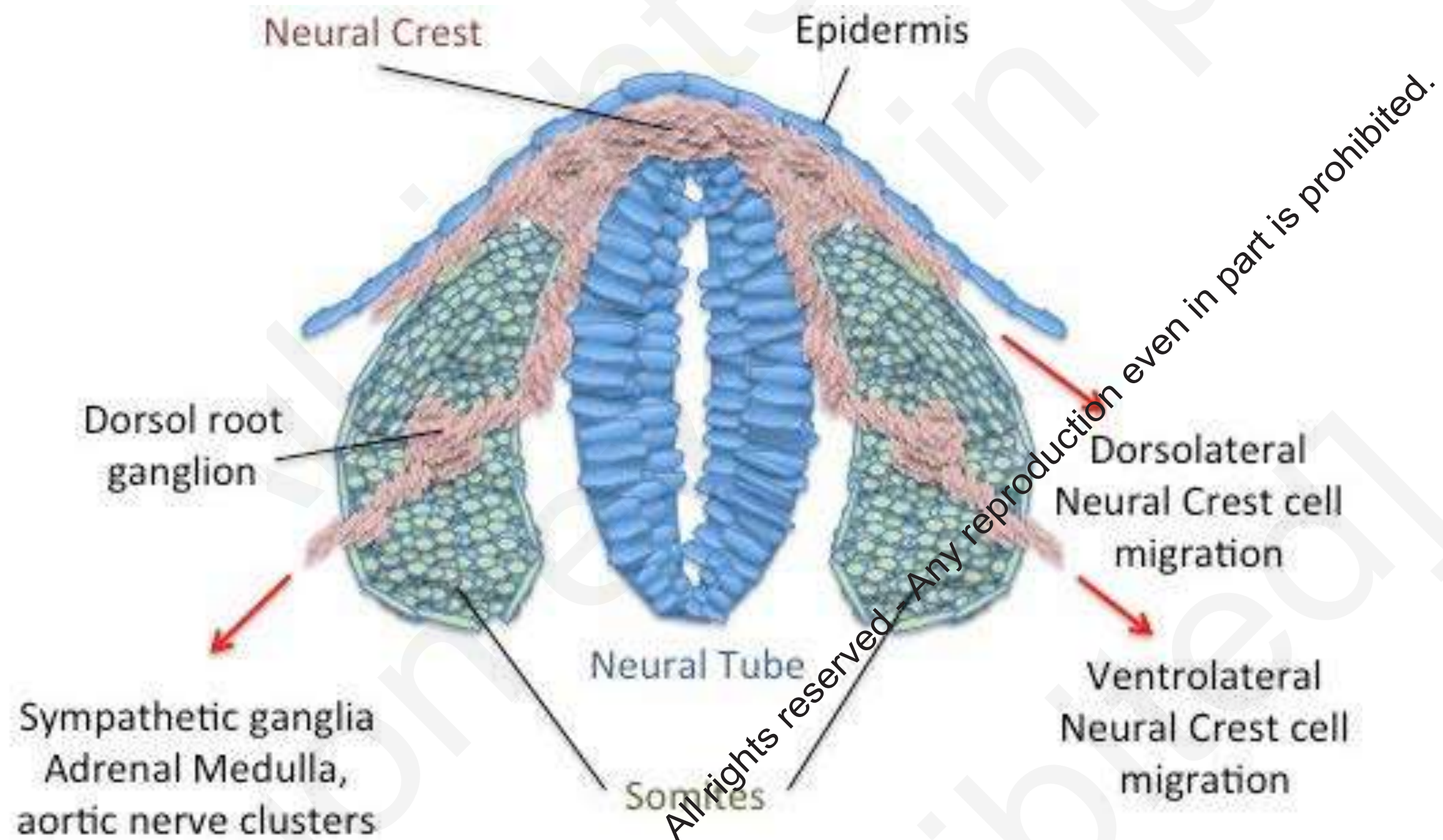




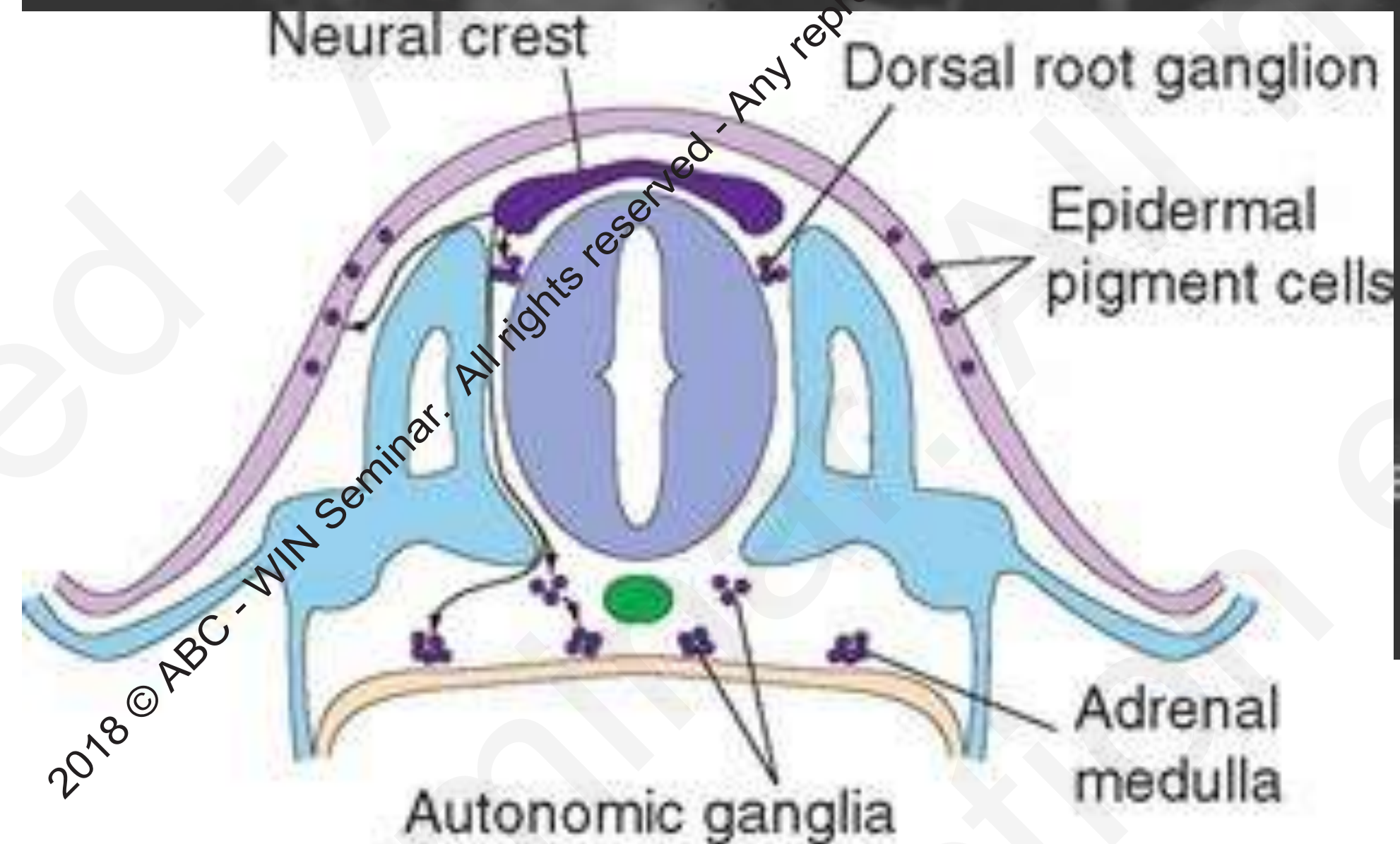
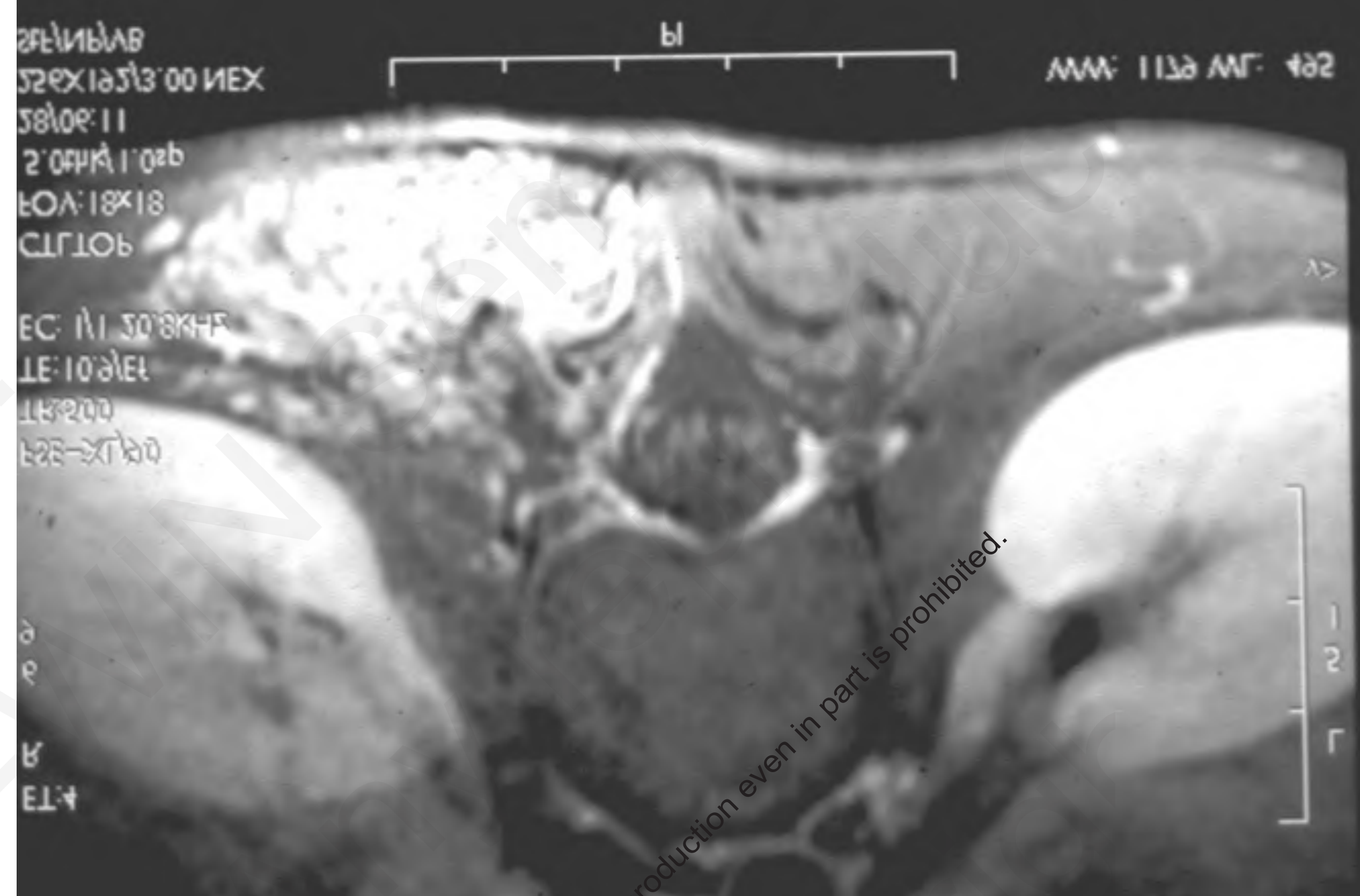
Pre



Post



Cobb syndrome is associated with the migration of neural crest pericyte.



Neurocristopathy

The neural crest (NC) is a transient, embryologic structure that was first found by a famous anatomist Wilhelm His in 1868.

NC is called the fourth germ layer and is characteristic to the vertebrates phylogenetically. Neural crest cells (NCCs) are pluripotent and give rise to a variety of derivatives after migration in early embryogenesis, such as neurons, glia, cartilage, connective tissue, pigment cells, and adrenal cells.

It was proposed to call the diseases of NC origin as neurocristopathy (crista = crest, ridge), which is divided into dysgenetic and neoplastic forms.

Canadian pediatric pathologist Bolande proposed that diseases of NC should be called "neurocristopathy" in 1974.

Neurocristopathy was further classified into dysgenetic and neoplastic forms.

Dysgenetic neurocristopathy, for example, includes congenital melanotic nevi, cafe au lait spots, albinism, Pierre Robin syndrome, Treacher Collins syndrome, facial clefting syndrome, and Hirschsprung's disease,

The neoplastic form is typified by neuroblastoma, pheochromocytoma, carotid body tumor, paraganglioma, peripheral neuroectodermal tumor, and meningioma.

Treacher Collins syndrome as a neurocristopathy mutation p.Lys643GlufsX38 (c.1927dupG) in the TCOF1 gene

SKELETAL DERIVATIVES OF BRANCHIAL ARCHES

I. MANDIBULAR ARCH

ARCH - forms

a) BONES OF MIDDLE EAR

(malleus, incus, also ant. lig. of malleus);

b) STRUCTURES ASSOCIATED WITH MANDIBLE

sphenomandibular lig., (Meckel's cartilage, framework of mandible)

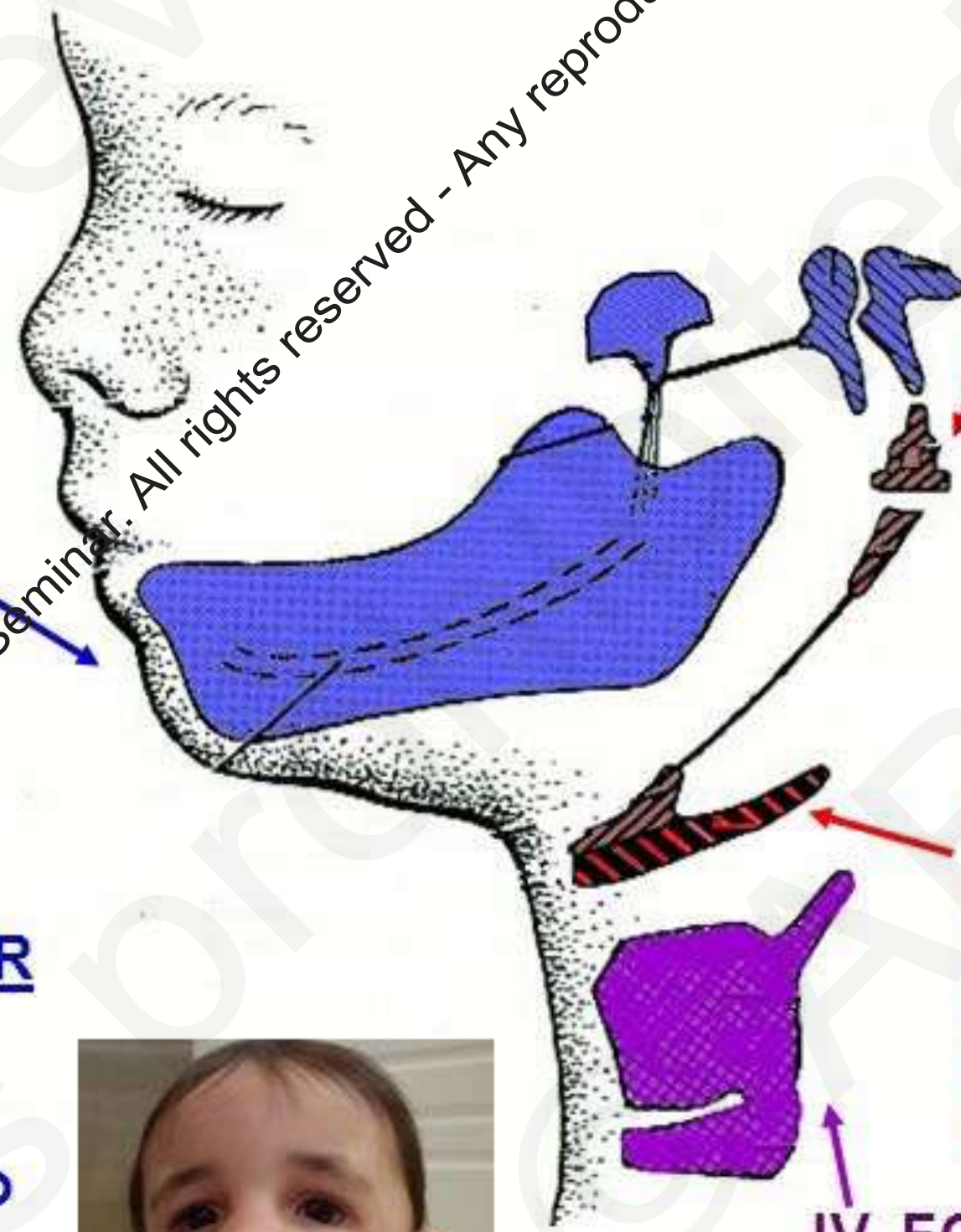
note: FIRST ARCH SYNDROME (TREACHER COLLINS)

- genetic disorder; Neural crest cells do not migrate into Arch 1:

- mandibular hypoplasia
- **conductive hearing loss**
- facial malformation



TREACHER COLLINS SYNDROME



II. HYOID ARCH

a) ONE BONE OF MIDDLE EAR (stapes); also

b) STYLOID PROCESS and stylohyoid lig.

c) part of HYOID BONE (upper half of body of hyoid bone)

III. THIRD ARCH - REST OF HYOID BONE - lower half of body of hyoid

IV. FOURTH ARCH - cartilages of larynx

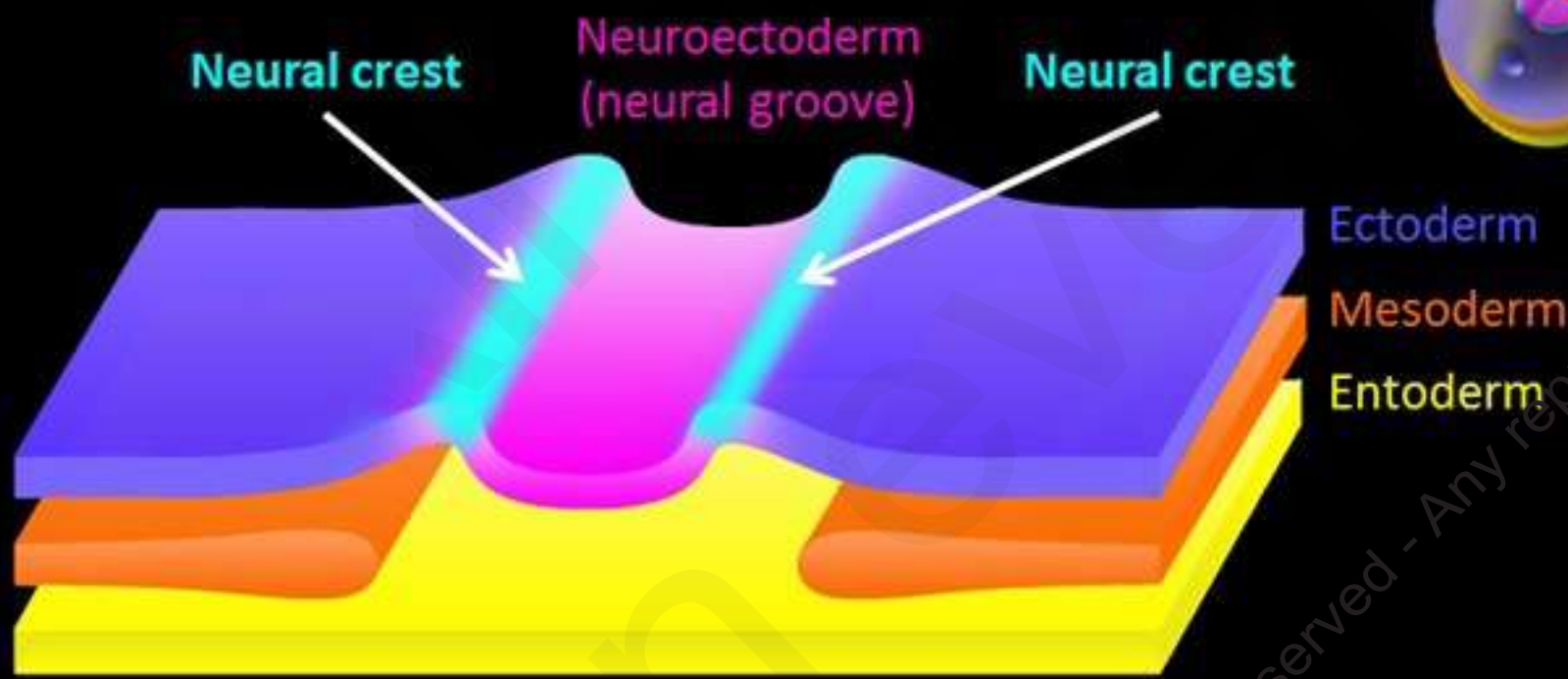


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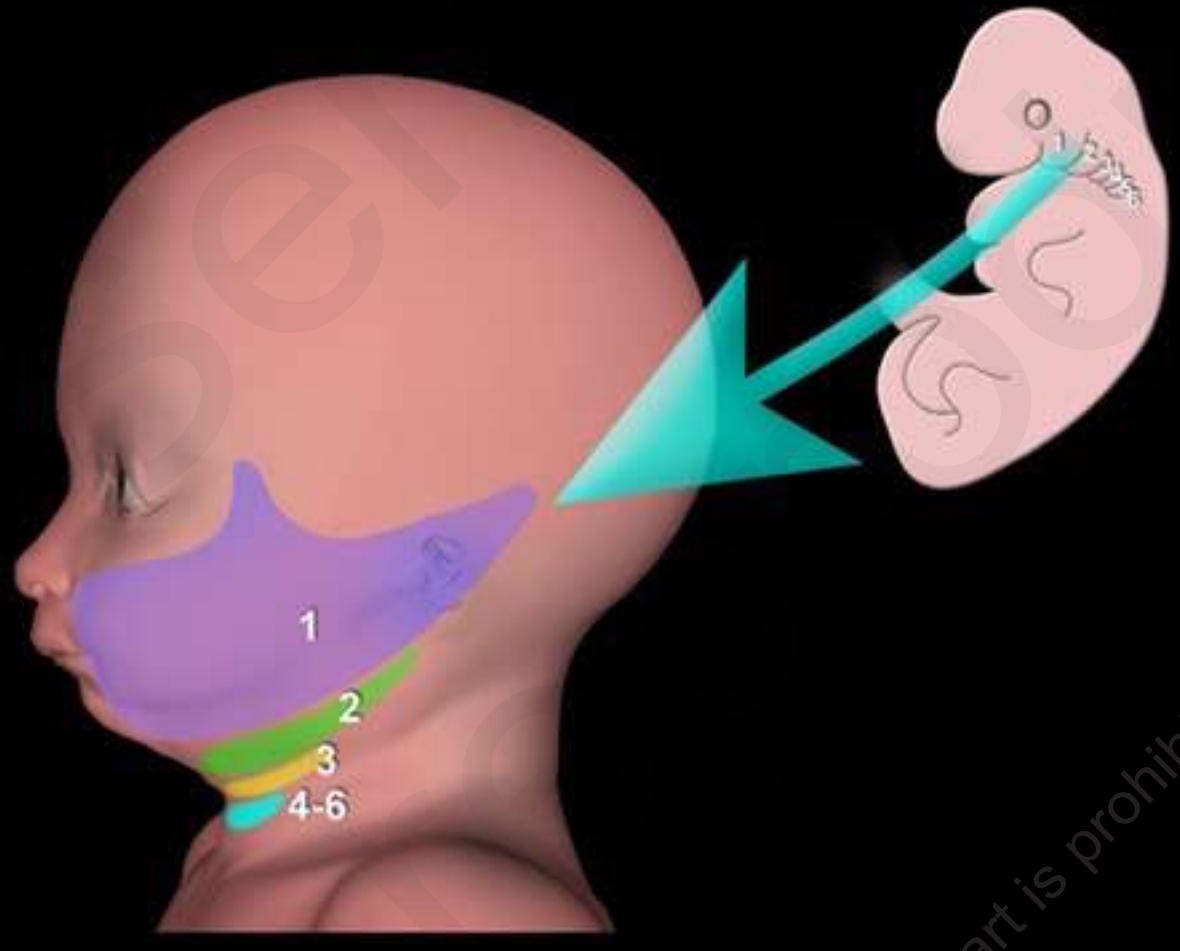


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Population of **neural crest cells** migrates to many areas of embryonic body to differentiate to various structures including **pharyngeal arches**, which are a base for formation of some **facial, cervical, laryngeal and pharyngeal structures**.



Decreased amount of migrating cells to the **first and second pharyngeal arches** leads to **malformations of mandibulofacial and auricular areas** typical for Treacher – Collins syndrome.



Mutation of TCOF1 gene

↓ Treacle phosphoprotein

↑ p53 and activation of proapoptotic genes

↑ neuroepithelial apoptosis of neural crest cells

Normal TCOF1 gene – **normal** amount of migrating cells from neural crest area

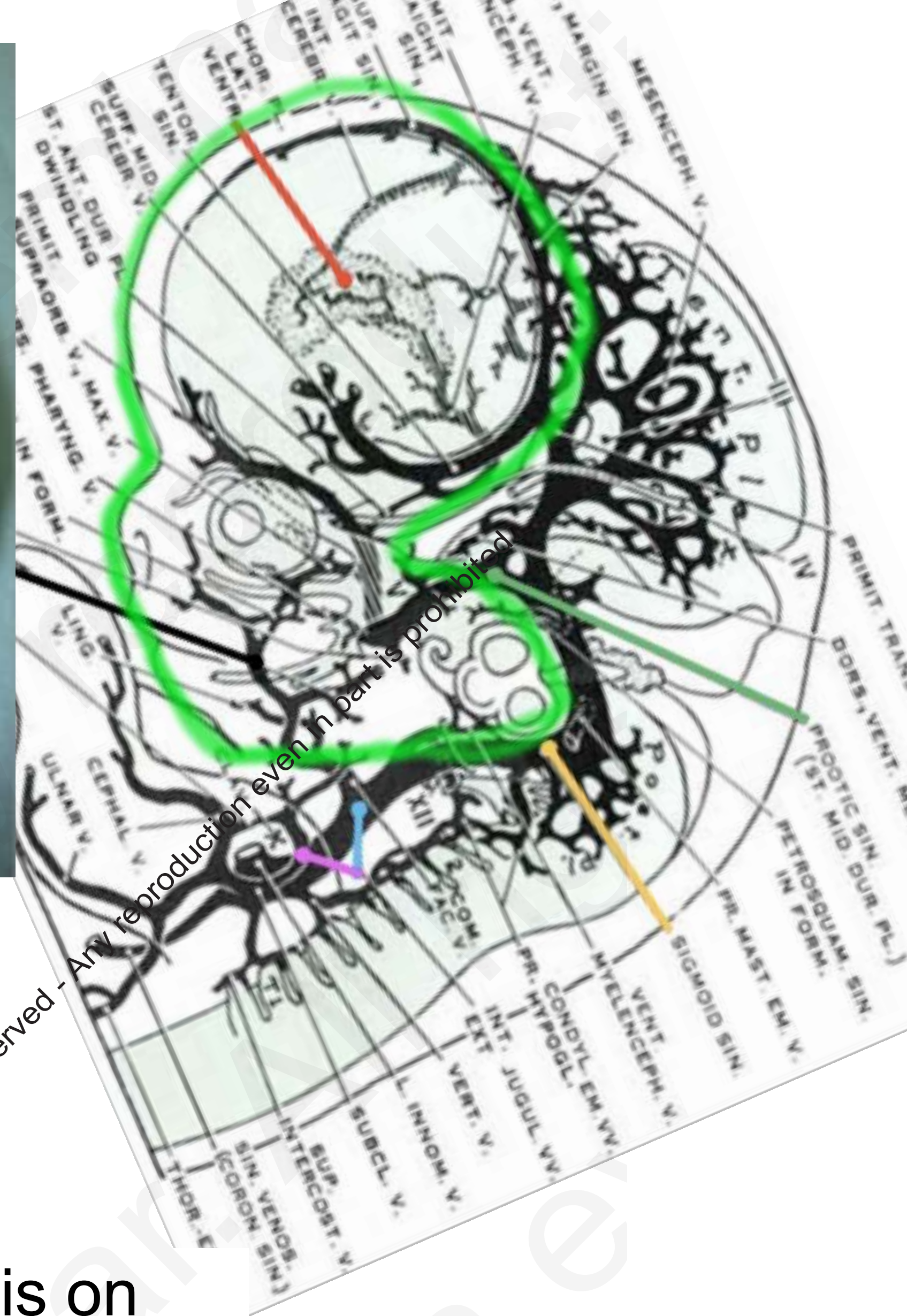
Mutation of TCOF1 gene – **decreased** amount of migrating cells from neural crest area

Down-slanting „antimongoloid“ palpebral fissures

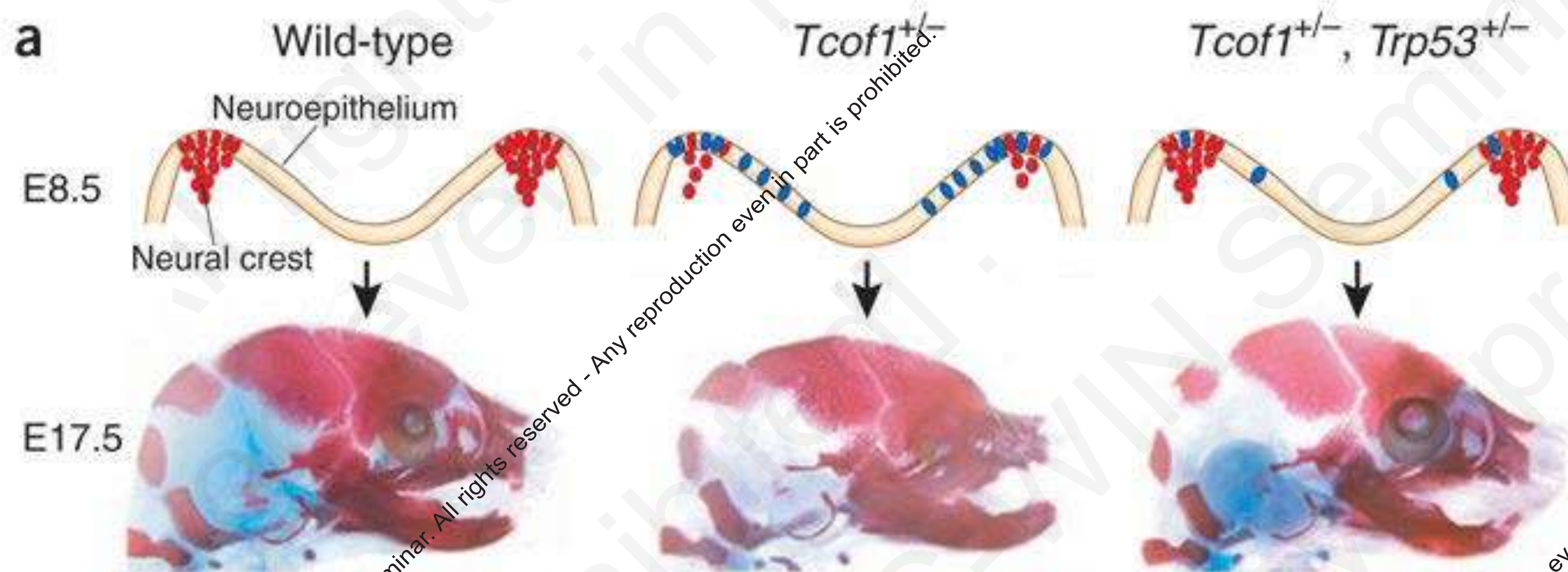
Coloboma of the lower lid

Microtia, malformed ears

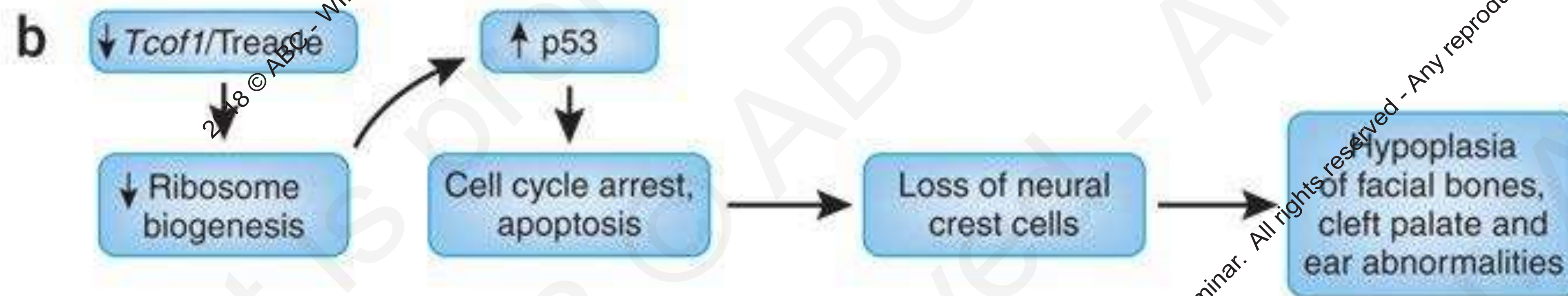
Macrostomia
Micro/retrognathia
Cleft palate



Treacher Collins syndrome has potential risk of dysgenesis on the falco-tentorial region as a neurocristopathy.



Right panel shows rescue of most apoptosis in the neuroepithelium, normal neural crest migration and normal bone structure in $Tcof1^{+/-}$ mice lacking one copy of $Trp53$.



Flow diagram of the current model of the pathogenesis of Treacher Collins syndrome.

Segmental neurovascular syndromes in children.

The concept of segmental vascular syndromes with different, seemingly unrelated, diseases is based on the embryology of the neural crest and the mesoderm migration of cells that share the same metameric origin.

Migrating patterns of these cells link the brain, the cranial bones, and the face on the same side.

A somatic mutation developing in the region of the neural crest or the adjacent cephalic mesoderm before migration can, therefore, be postulated to produce arterial or venous metameric syndromes, including **PHACES**, **CAMS**, **Cobb syndrome**, and **Sturge-Weber syndrome**.

Although these diseases may be rare, their relationships among each other and their postulated linkage with the development of the neural crest and the cephalic mesoderm may shed light on the complex pathology and etiology of various cerebral vascular disorders.

The PHACE acronym refers to the association of:

Posterior fossa anomalies- Includes Dandy-Walker malformation, cerebellar hypoplasia or agenesis as well as other central nervous system (CNS) abnormalities

Hemangiomas- segmental facial

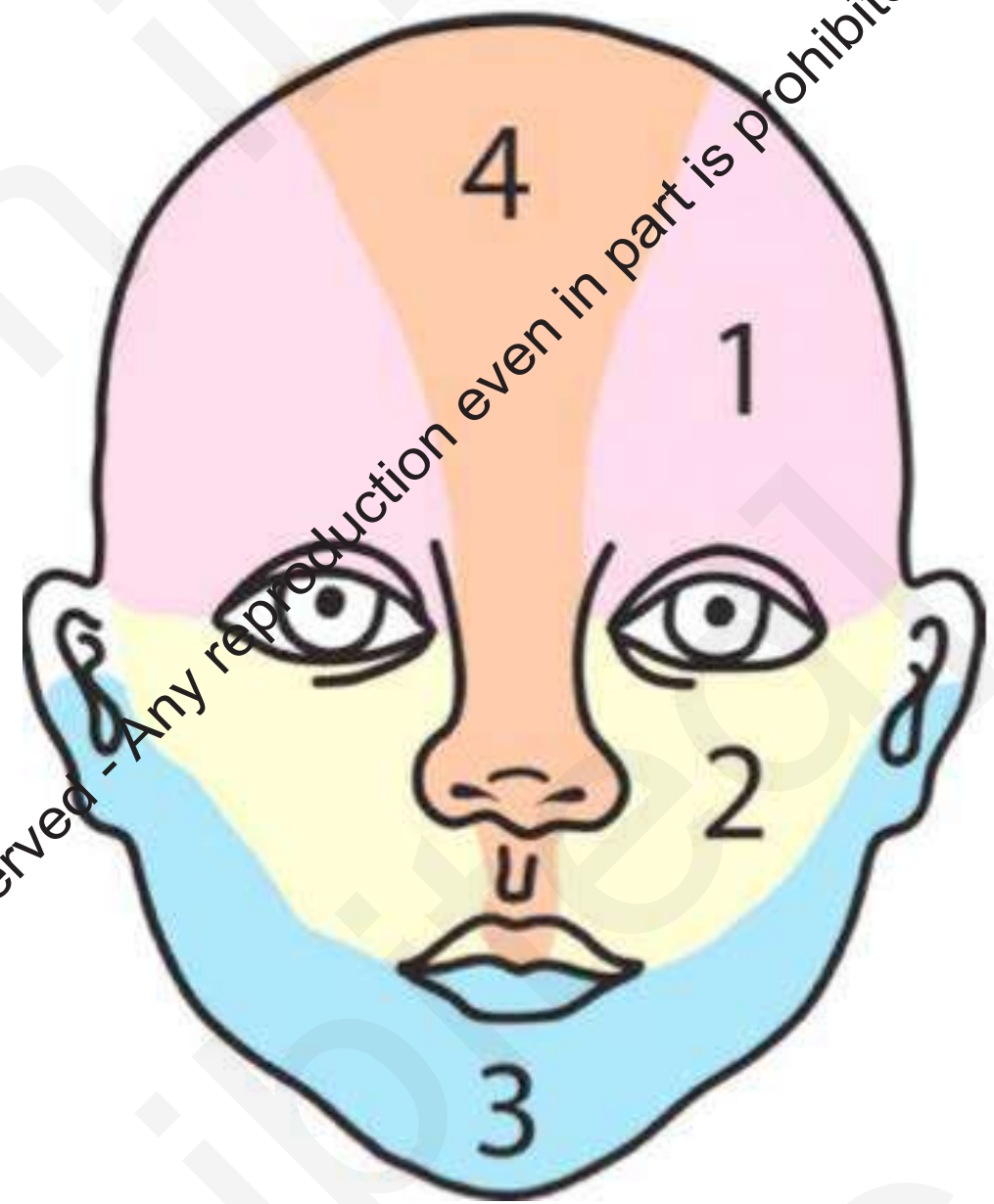
Arterial cerebrovascular anomalies- agenesis, aneurysms, occlusion or anomalies of arteries or persistence of fetal circulation

Cardiac abnormalities and Coarctation of the Aorta- structural heart defects and/or coarctation, aneurysm or aberrant anatomy of the aorta or the vessels that arise from the aorta

Eye abnormalities- persistent fetal vasculature and morning glory disc anomalies, microphthalmia, optic nerve hypoplasia and other ocular abnormalities

This is not an all-inclusive list. Recently, a review detailed findings in each of the above categories that can be associated with PHACE and defined consensus criteria to diagnose PHACE syndrome.

PHACE syndrome should be suspected clinically whenever a newborn exhibits a segmental hemangioma greater than 5 cm of the face and/or scalp. Subtle skin changes involving the skin overlying the sternum or above the umbilicus can also be a clue to PHACE syndrome. These include linear scars, clefts, pits, dimples, or papules.



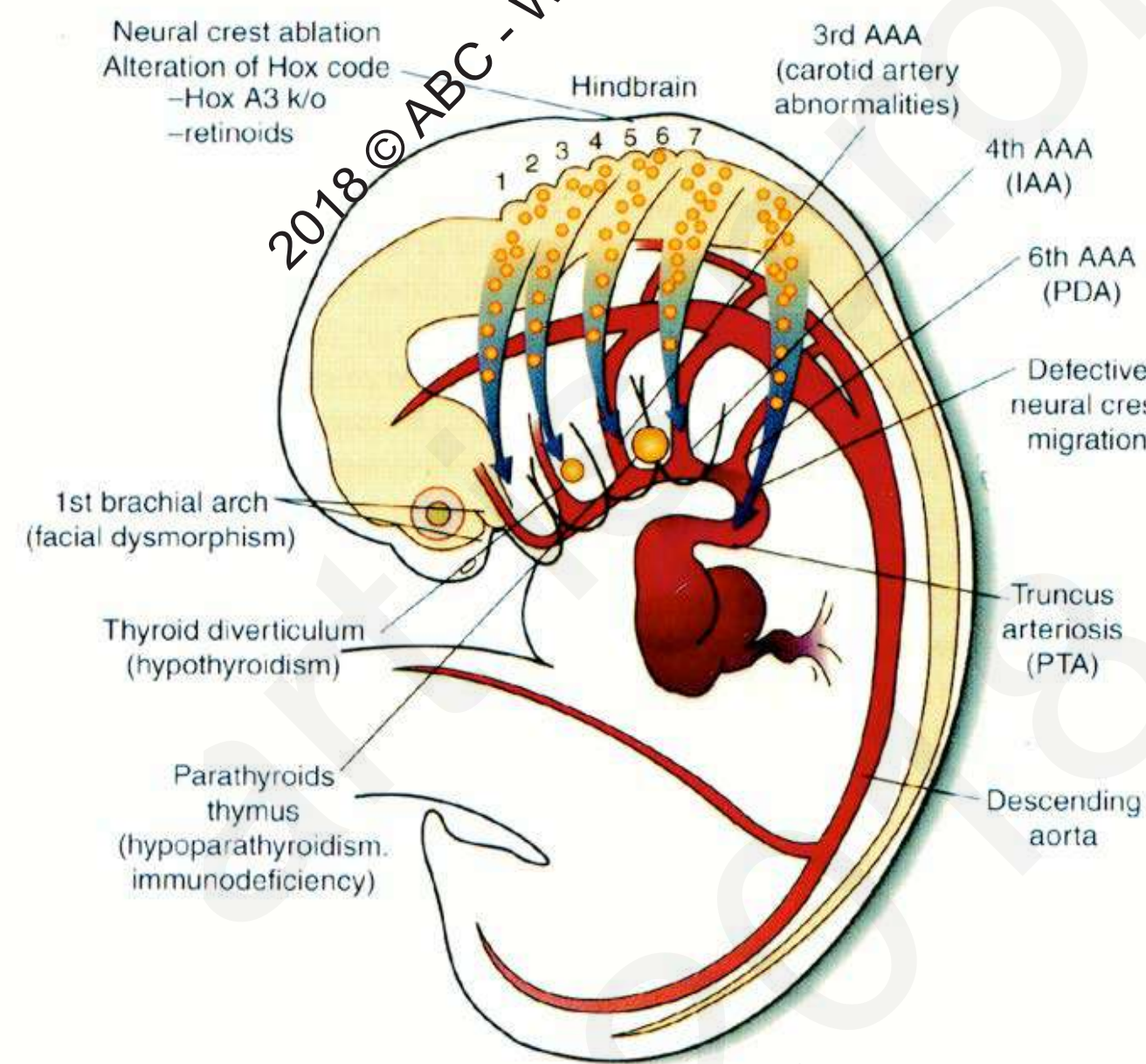
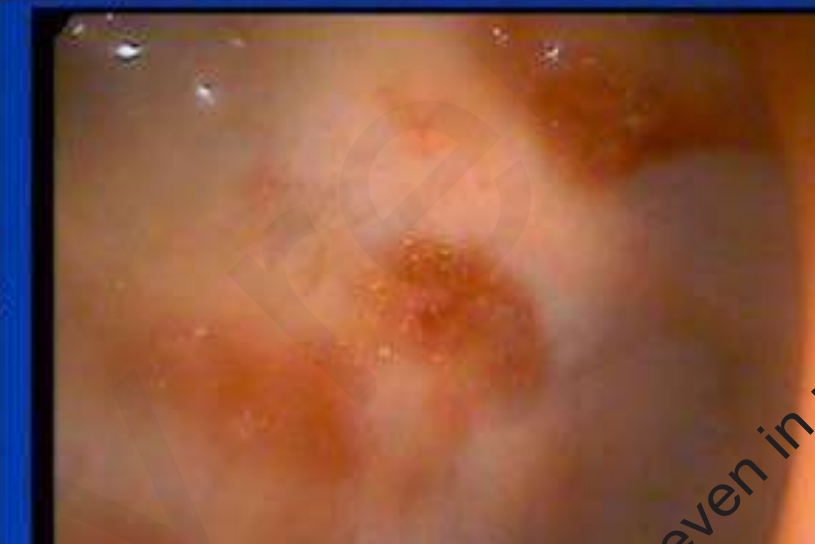
Itinteang T, et al. Primitive mesodermal cells with a neural crest stem cell phenotype predominate proliferating infantile haemangioma. J Clin Pathol (2010) 63:771–6.

In a review of 108 patients with large facial hemangiomas (images from Haggstrom), it was found that the highest risk for PHACE syndrome seems to be in patients who have hemangiomas involving the S1 and S3 segments. S4 segmental involvement also confers risk but PHACE rarely occurs with solely S4 presentations without S1 or S3 involvement. Isolated S2 involvement seems to have a lower risk of PHACE as well.

Haggstrom A, et al. Pediatrics Vol120, 2010



This patient with a segmental hemangioma of the back manifested cardiac and aortic arch anomalies

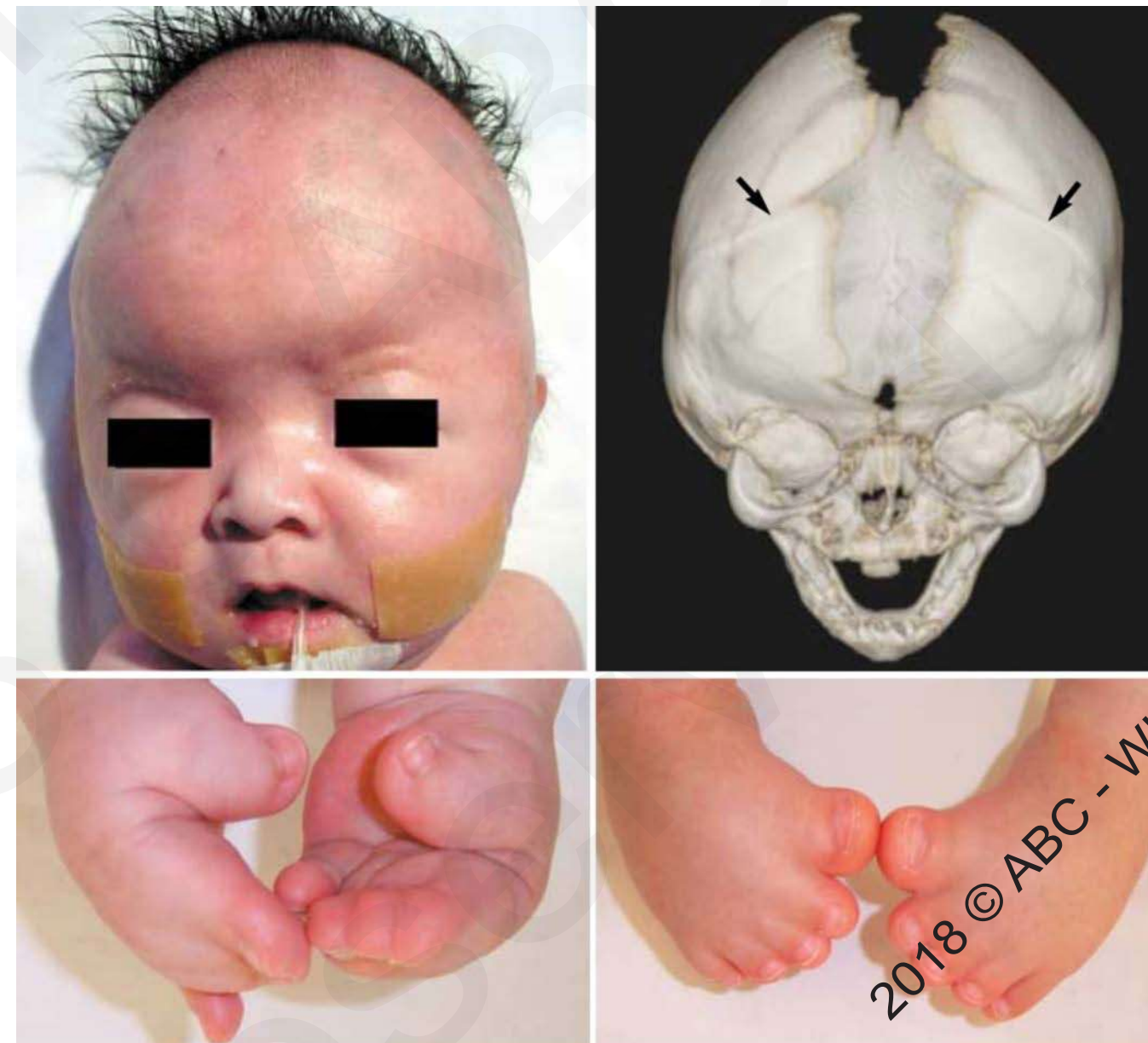
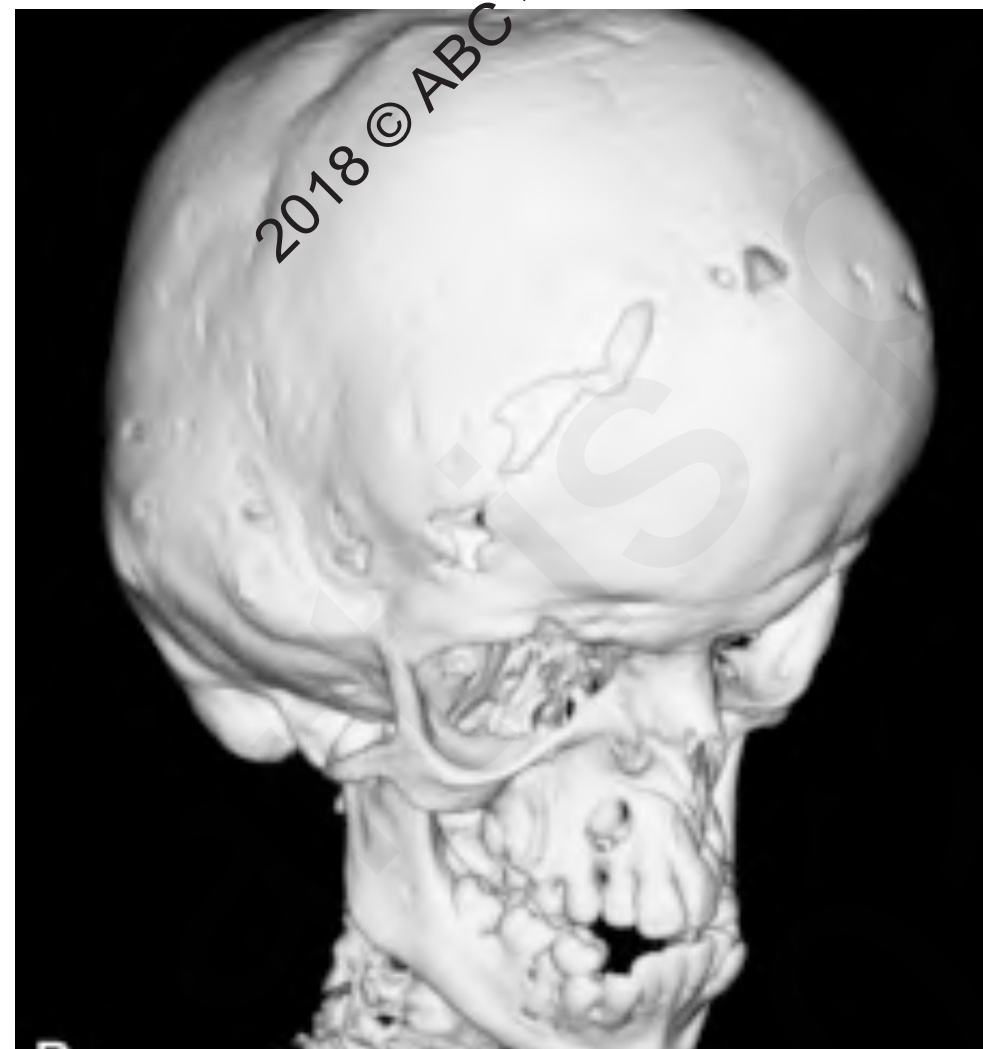


Cardio-cephalic neural crest syndrome

CRANIOSYNOSTOSIS

Craniosynostosis, the premature closure of sutures, affects approximately 1 in 2500 children and occurs in many syndromes, including **Crouzon, Apert, Pfeiffer, Muenke, and Saethre-Chotzen syndromes**

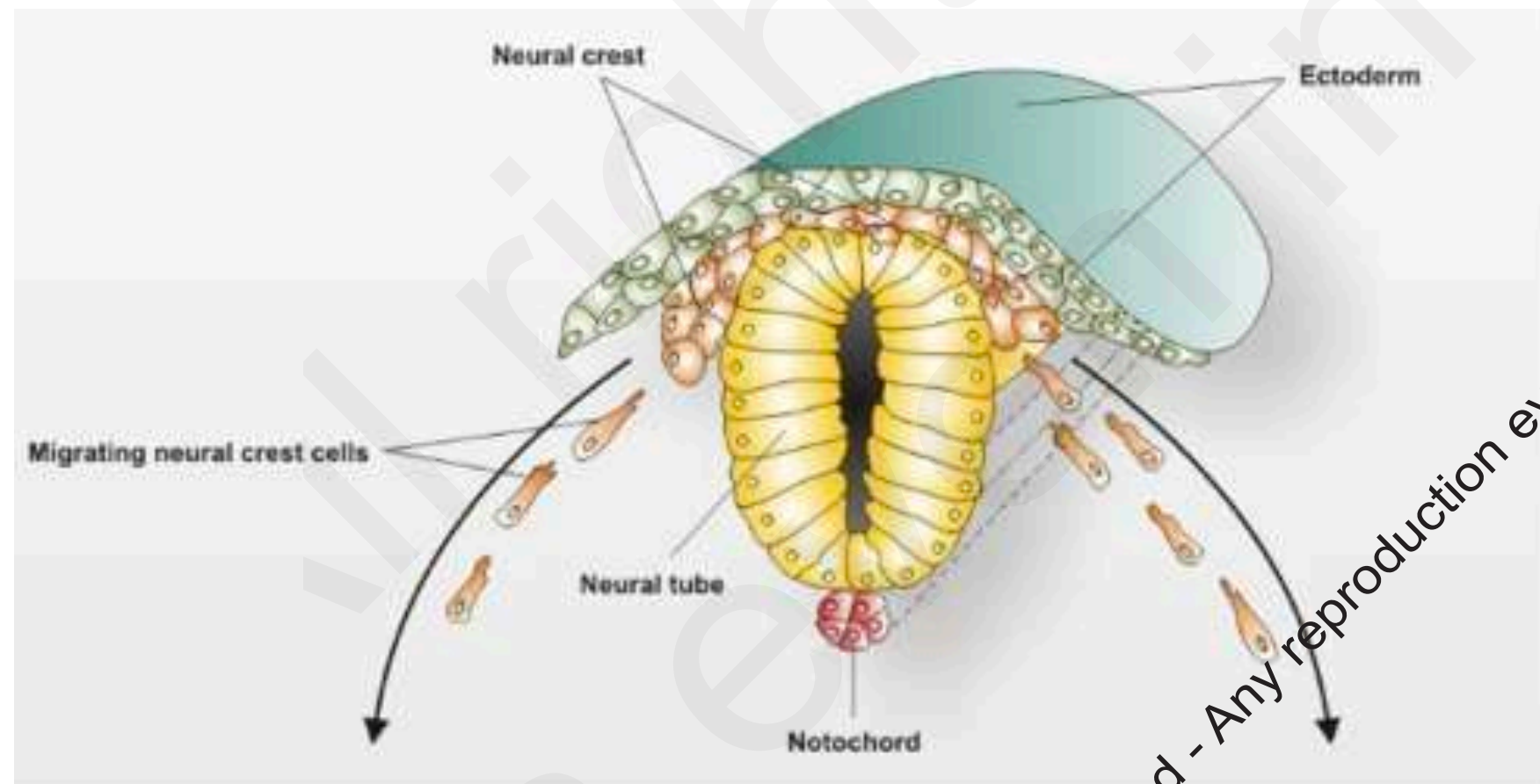
The coronal suture is derived from mesoderm and separates the neural crest cell-derived frontal bone and the mesoderm-derived parietal bone. The sagittal suture is formed from neural crest cells and separates the two mesodermally derived parietal bones.



The typical dysgenetic form includes **Hirschsprung disease, DiGeorge syndrome, coarctation of the aorta, and agenesis/ hypogenesis of the internal carotid artery (ICA)**, and the neoplastic form includes **neuroblastoma, paraganglioma, and neurofibromatosis type 1 (NF1)**.

Interestingly, it is reported that **Moyamoya** disease co-exists with Hirschsprung disease, coarctation of the aorta, and NF1.

In addition, **PHACE** syndrome may present with agenesis of the ICA, coarctation of the aorta, cardiac anomaly, and segmental facial hemangioma as well as Moyamoya disease .



neural crest origin

ICA system

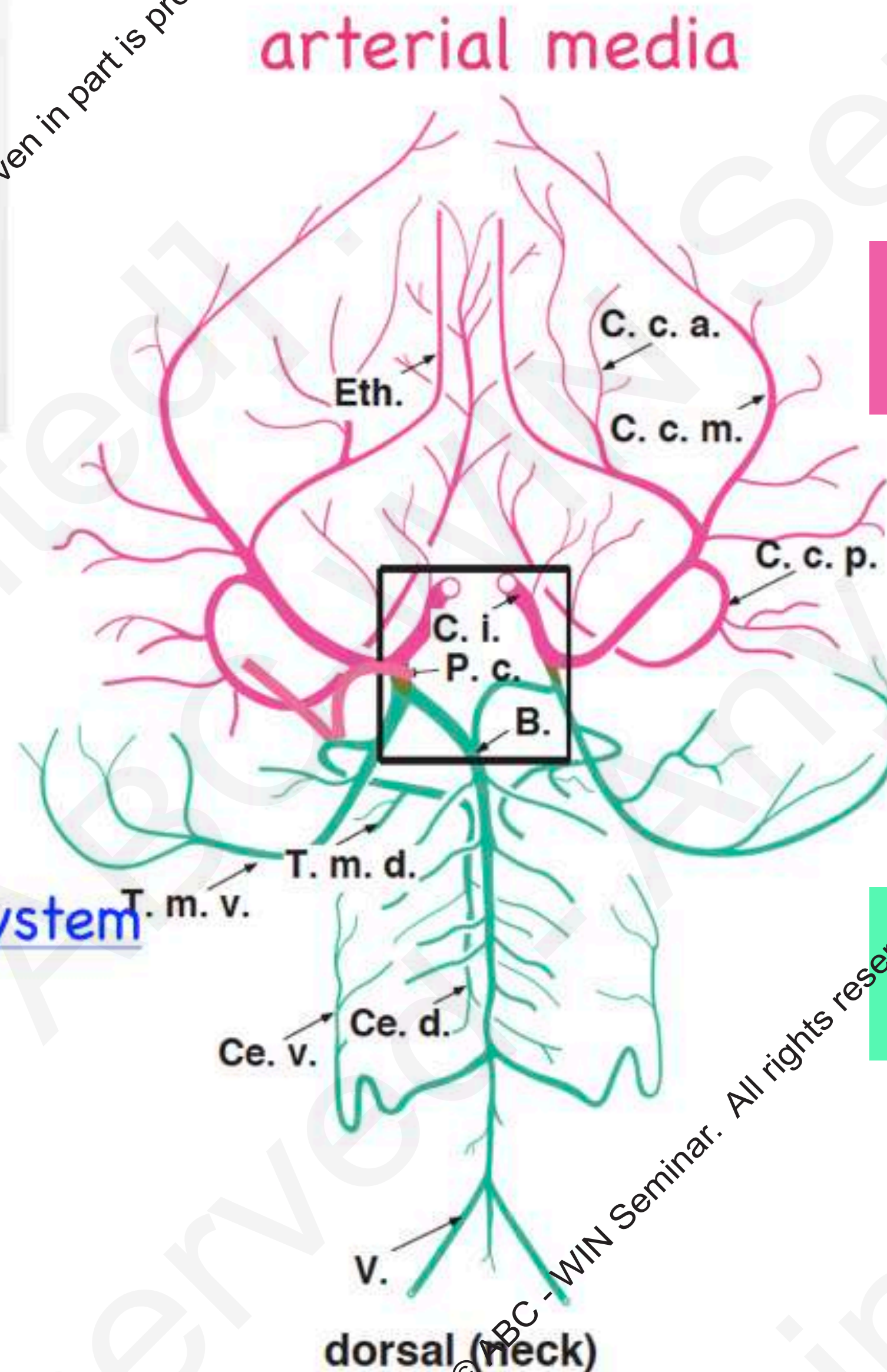
including Pcom a and entire PCA

Primitive internal carotid artery system

mesodermal origin

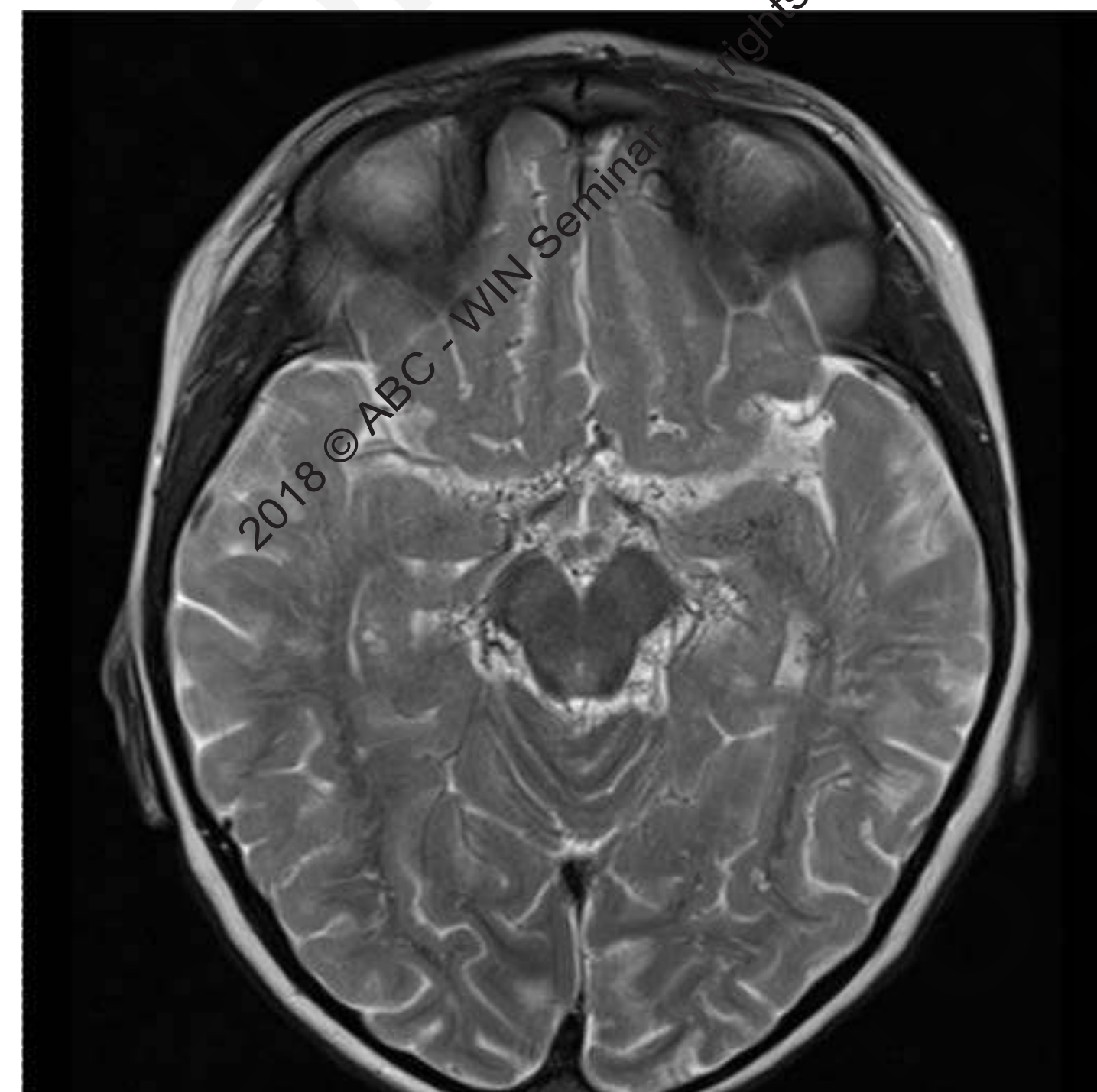
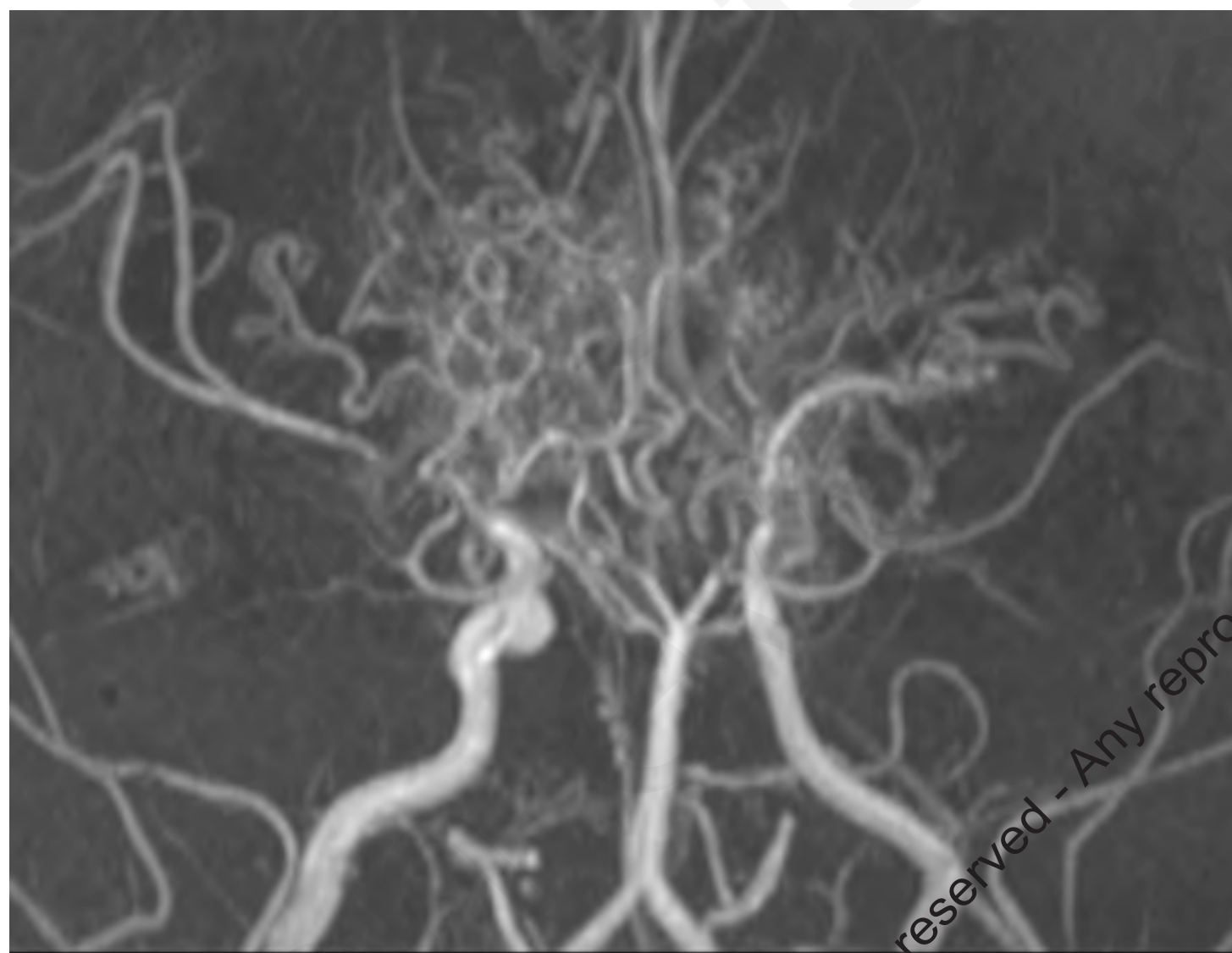
VB system

Ventral longitudinal arteries

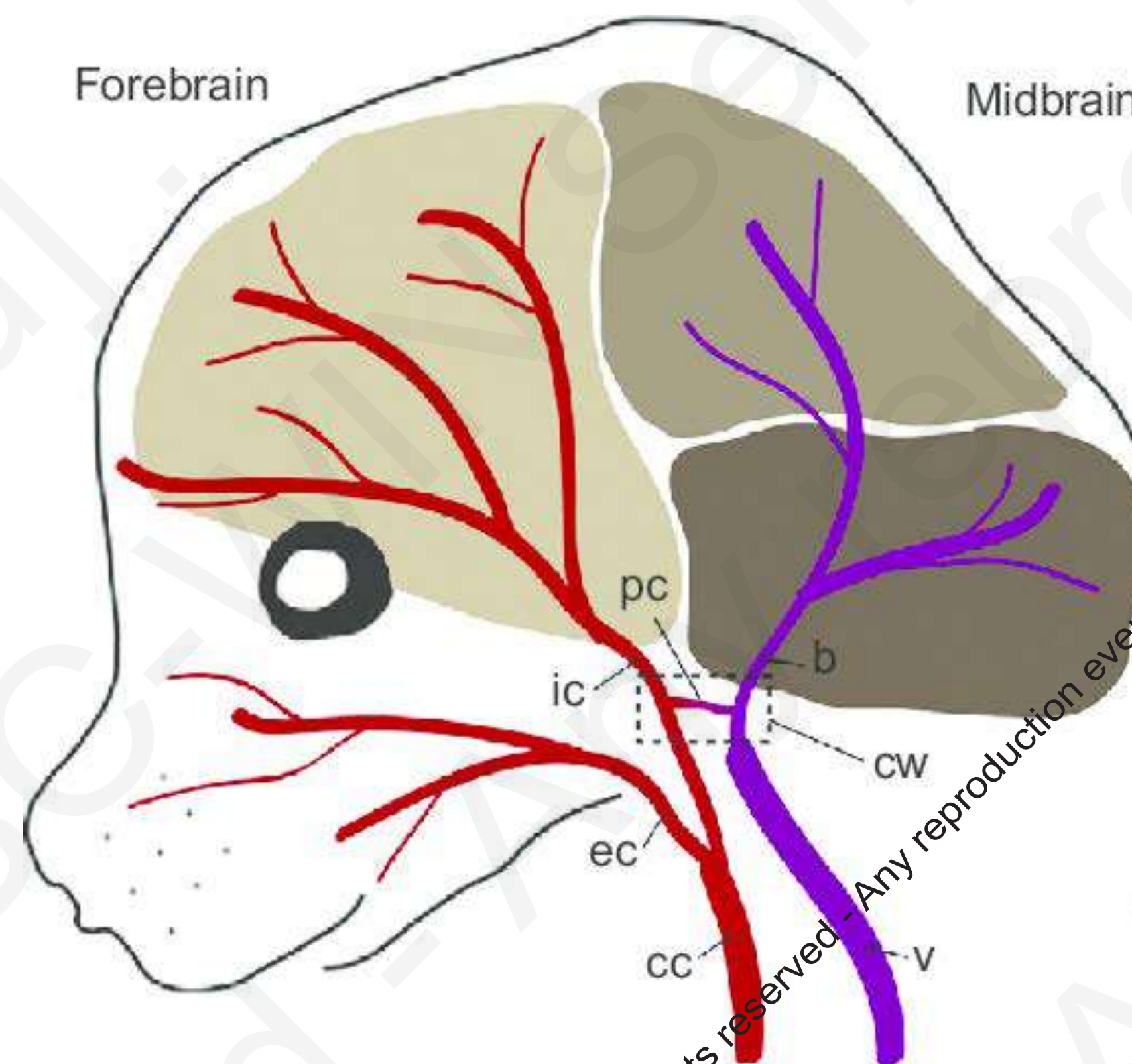


Anterior circulation is derived from neural crest

Posterior circulation is derived from mesoderm.



Moyamoya disease affects only the arterial system derived from neural crest pericytes.

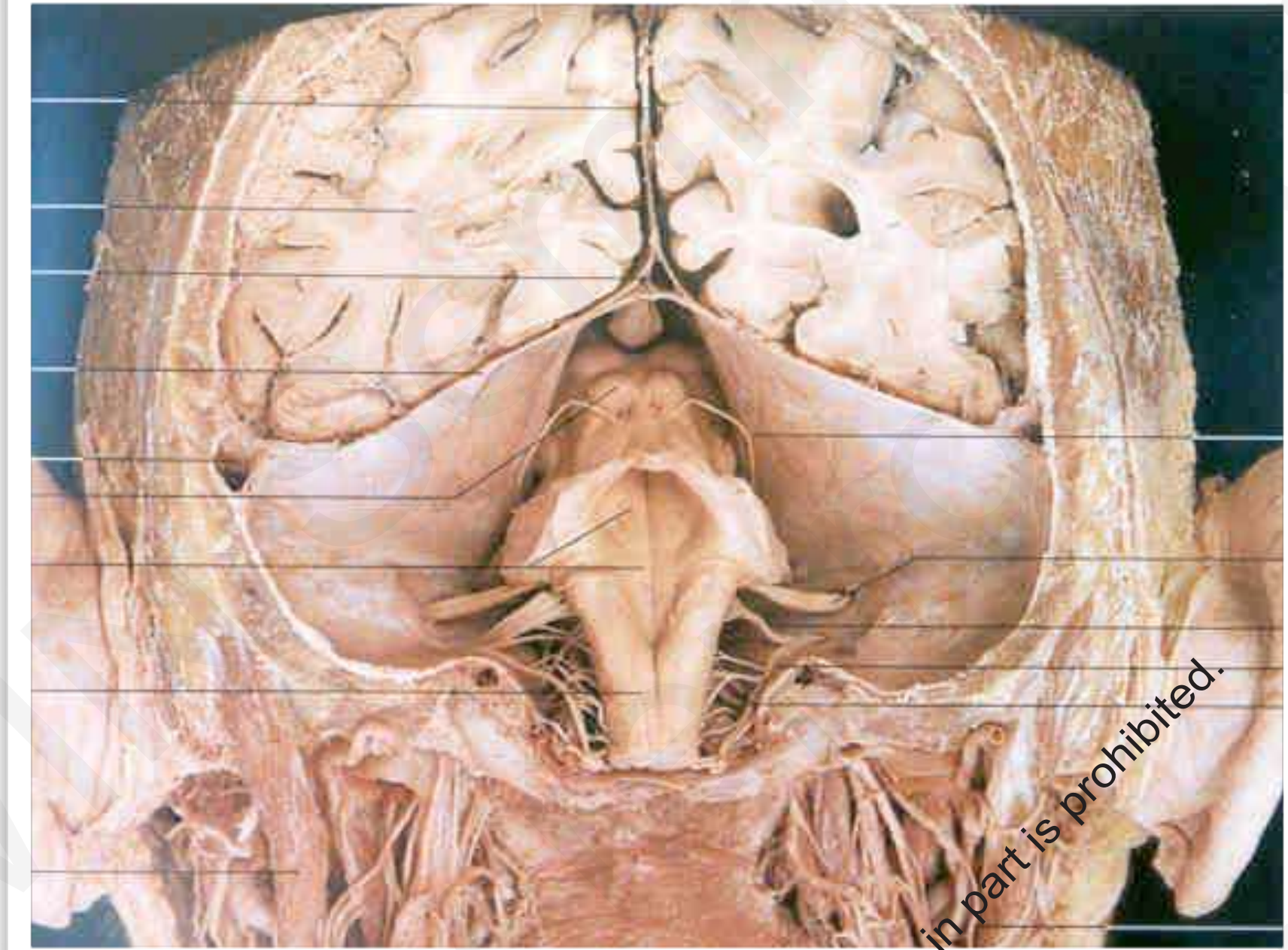


Neural crest pericytes
Mesoderm pericytes

→ Moyamoya disease is a sort of neurocristopathy.

Conclusions

1. Falx cerebri, tentorium cerebelli, olfactory groove and dura mater of spinal canal can be categorized to the same domain derived from neural crest. These dura matters consist of only dura propria (meningeal dura).
2. Falco-tentorial, olfactory groove and spinal DAVFs can be defined as the neurocristopathy that is a category of diseases associated with neural crest development.
3. A thorough knowledge of NCC may help in understanding a disease process and address these pathological issues associated with falco-tentorial dura mater.



Neural crest gives us another point of view to know underlying pathology of falco-tentorial system.



Thank you...

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