Neurohydrodynamics: an engineering perspective

Bryn Martin, Ph.D.
mail@neurohydrodynamics.com
Neurohydrodynamics and Medical Technology Laboratory and
Laboratory of Hemodynamics and Cardiovascular Technology at the
Swiss Federal Institute of Technology, EPFL
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Outline

- Motivation
- Neurohydrodynamics: anatomy & physiology
  - Intracranial space (CSF, blood & brain)
  - Blood vessels
  - Brain and spinal cord
- Current concepts in craniospinal pathologies
- Current diagnostic and imaging trends in neurohydrodynamics

Motivation

- neurohydrodynamics play a role in craniospinal pathologies (and cerebrovascular)

Craniospinal disorder	**Prevalence (USA)**
Hydrocephalus	1 in 500
Chiari malformation	1 in 1,000
Spina bifida	1 in 1,500
Tethered cord	1 in 4,000
Syringomyelia	1 in 8,000
Spinal cord tumor	3,200 / yr. diagnosed
Brain tumor	195,000 / year diagnosed

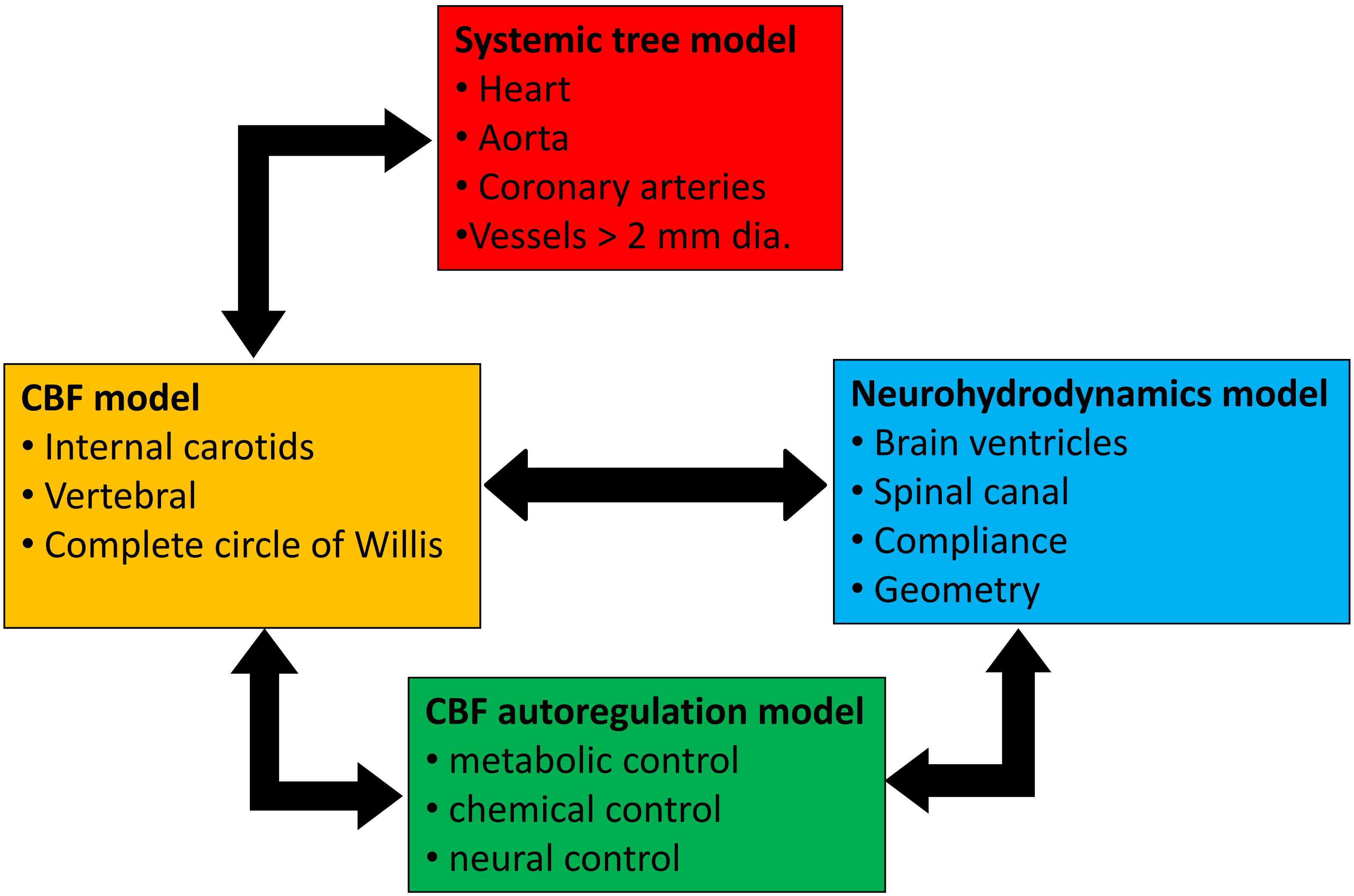
ninds.nih.gov/disorders/

Neurohydrodynamics research

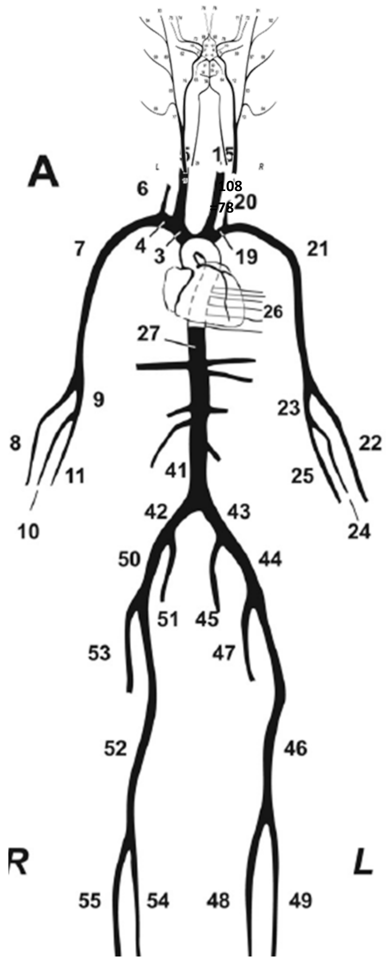
Goals

1. Identify mechanical forces that could play a role in craniospinal disorders.
2. Provide quantitative tools for craniospinal disorder assessment.

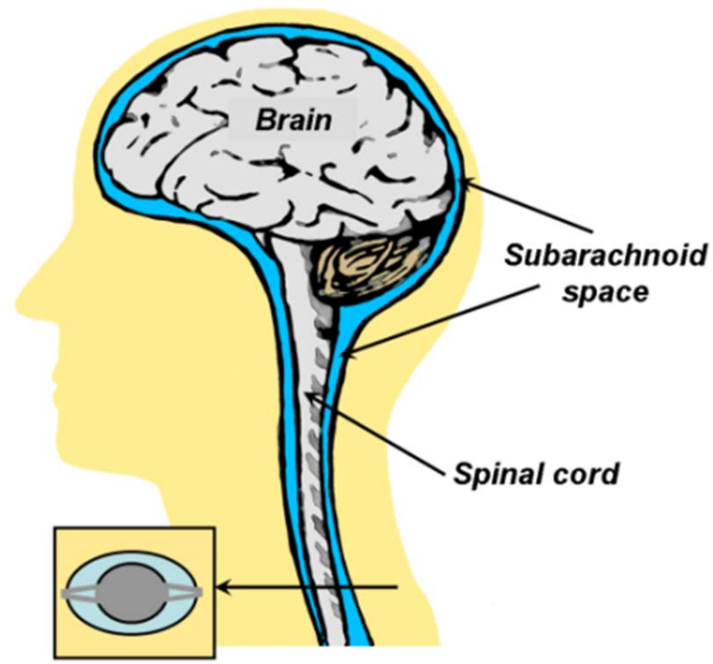
The big picture



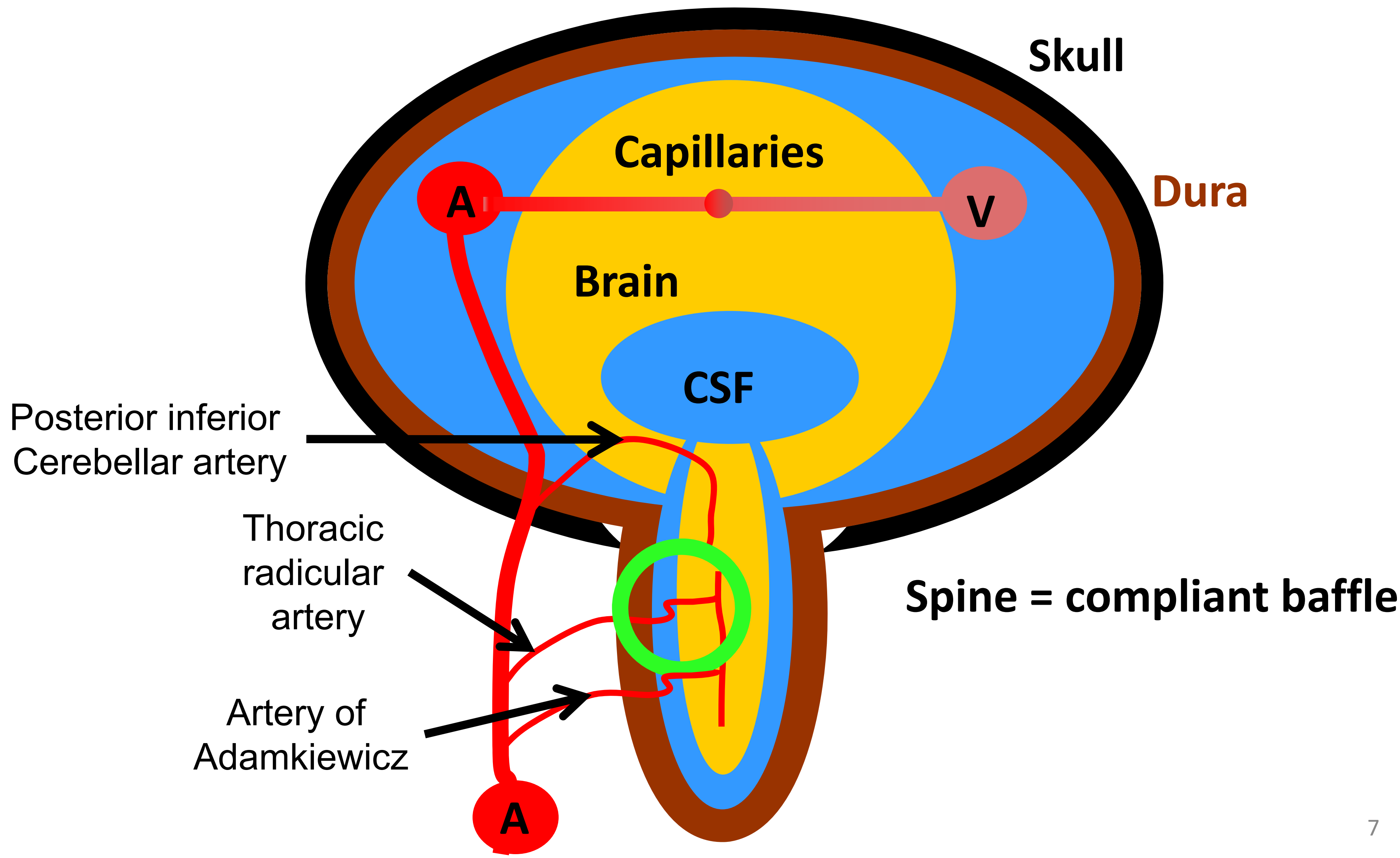
Systemic Tree model



Cerebrospinal Fluid model

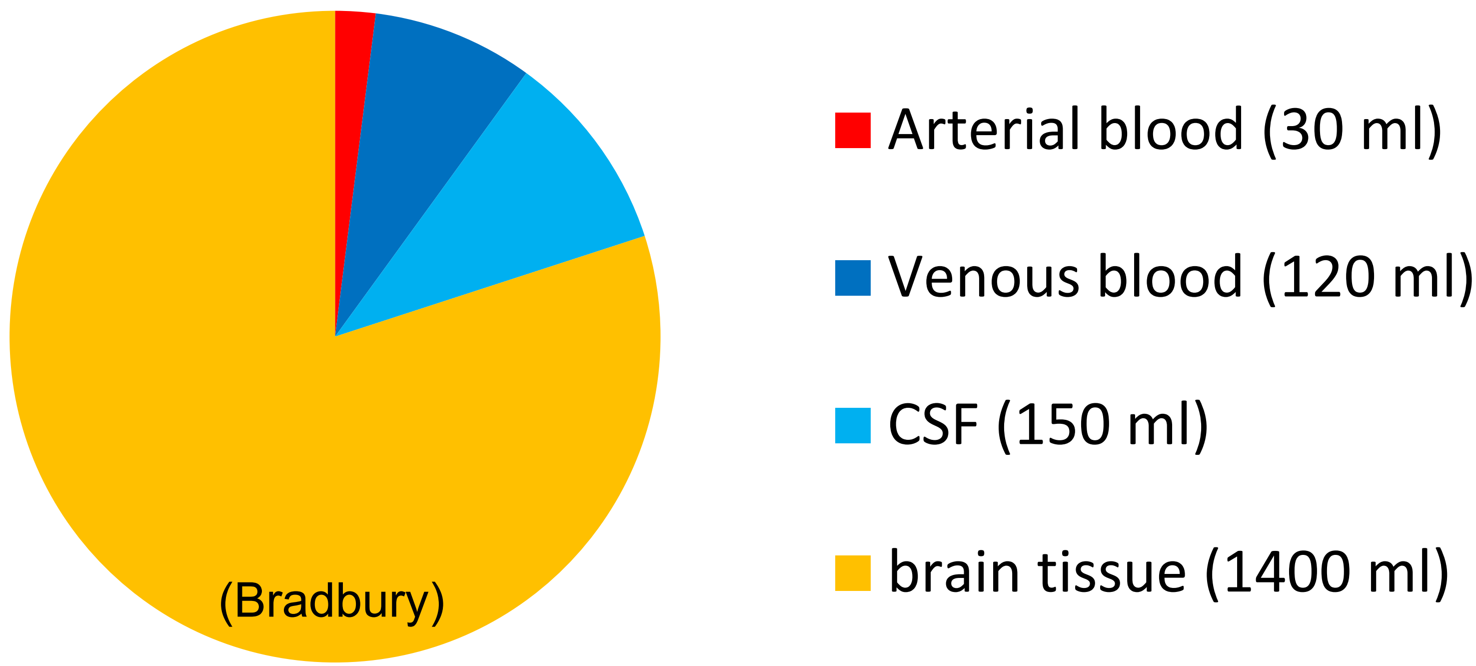


Mechanical perspective of CSF and cardiovascular system



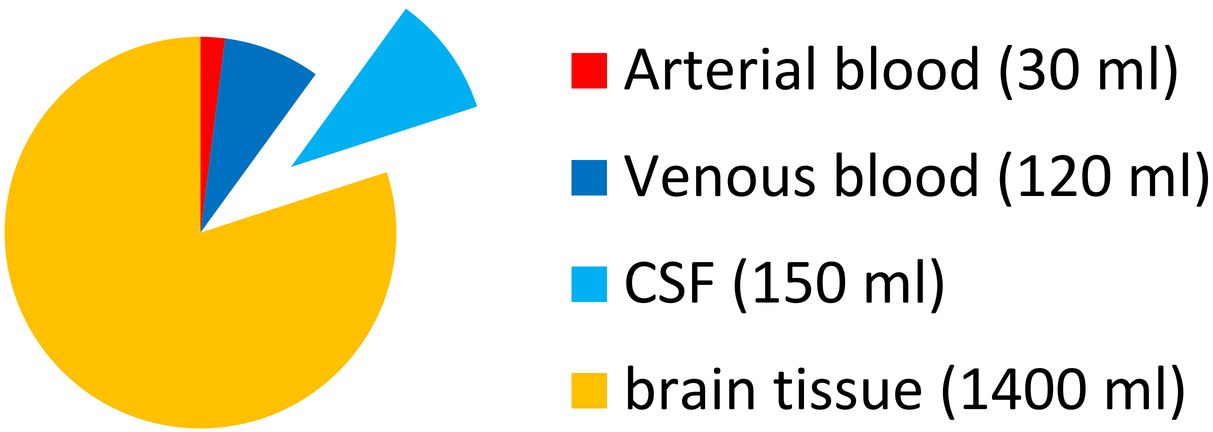
The intracranial space (CSF, blood & brain)

- A 1700 ml "control volume" (Monroe-Kelly)



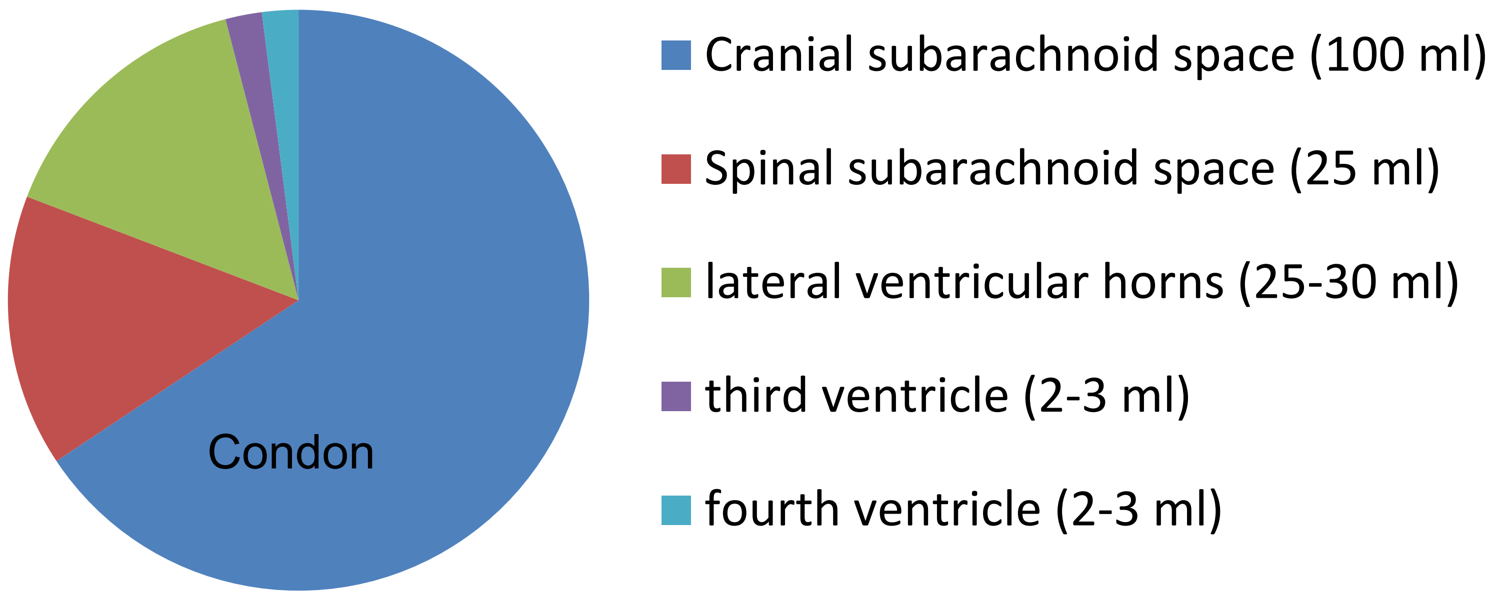
Kelly, G. (1824). "An account of the appearances observed in the dikssection of two of three individuals presumed to have perished in the storm of the 3rd, and whose bodies were deiscovered in the vicinity of the Leith on the morning of the 4th of November 1821, with some reflections on the pathology of the brain." Trans Med Chir Sci Edinb **1**:: 84–169.
Monroe, A. (1783). "Observations on the structure and function of the nervous system." Edinburgh: Creech & Johnson.
Bradbury, M. W. B. (1979). The concept of a blood-brain barrier. Chichester ; New York, Wiley.

Cerebrospinal fluid: CSF



Volumetric distribution of CSF

- μ = 0.01 g/cm*s, ρ = 1.0 g/cm, plasma (Blmfld)
- Provides buoyancy to brain



Condon, B., J. Patterson, et al. (1986). "Use of magnetic resonance imaging to measure intracranial cerebrospinal fluid volume." Lancet **1**(8494): 1355-7.
Bloomfield, I. G., I. H. Johnston, et al. (1998). "Effects of proteins, blood cells and glucose on the viscosity of cerebrospinal fluid." Pediatr Neurosurg **28**(5): 246-51.

Production and absorption of CSF

Production

- Choroid plexus 0.3-0.7 ml/min (Guyton)
- Replaced about 3-4 times each day

Absorption

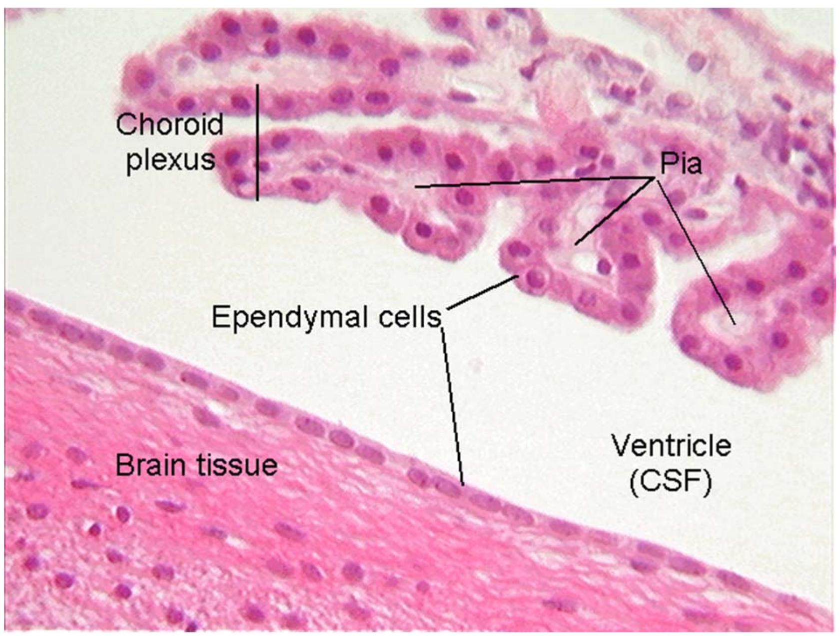
- arachnoid granulations (AG) at SSS (Gray).
- # of AG varies with age
- (50 at 0-9 / 250 at 60 / <10 at 90 yrs.) (Ikshm)

Gray, H., P. L. Williams, et al. (1995). Gray's anatomy : the anatomical basis of medicine and surgery. New York, Churchill Livingstone.
Guyton, A. C. and J. E. Hall (2006). Textbook of medical physiology. Philadelphia, Elsevier Saunders.
Ikushima, I., Y. Korogi, et al. (1999). "MRI of arachnoid granulations within the dural sinuses using a FLAIR pulse sequence." Br J Radiol **72**(863): 1046-51.

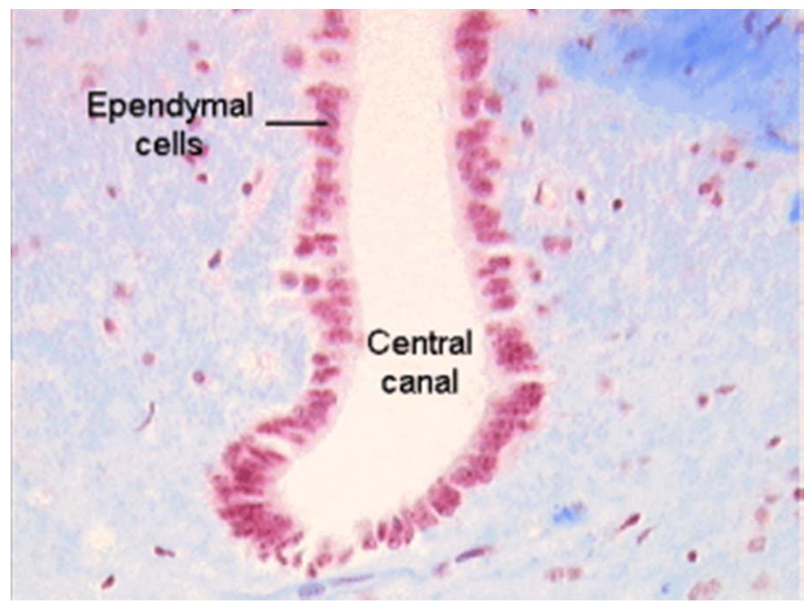
Ependymal cells produce CSF

- Cell wall thickness ~10-20 um
- Ependymal cells have a column or cube shape

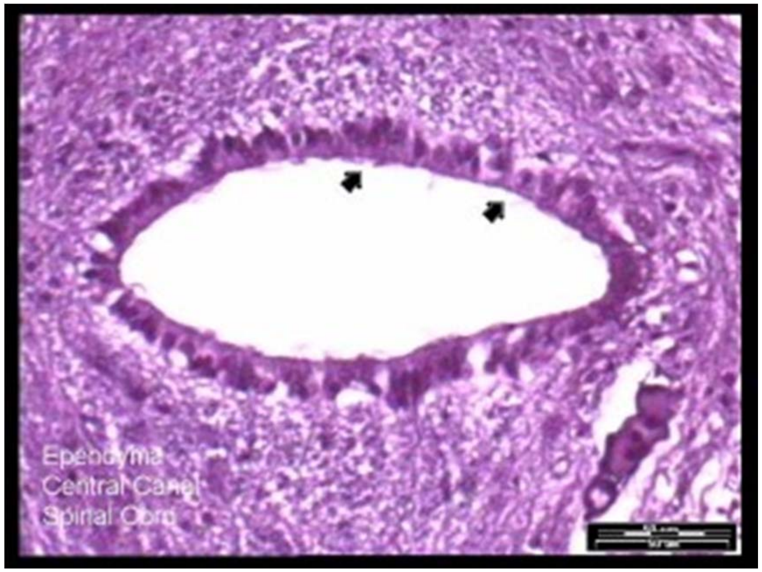
Choroid plexus

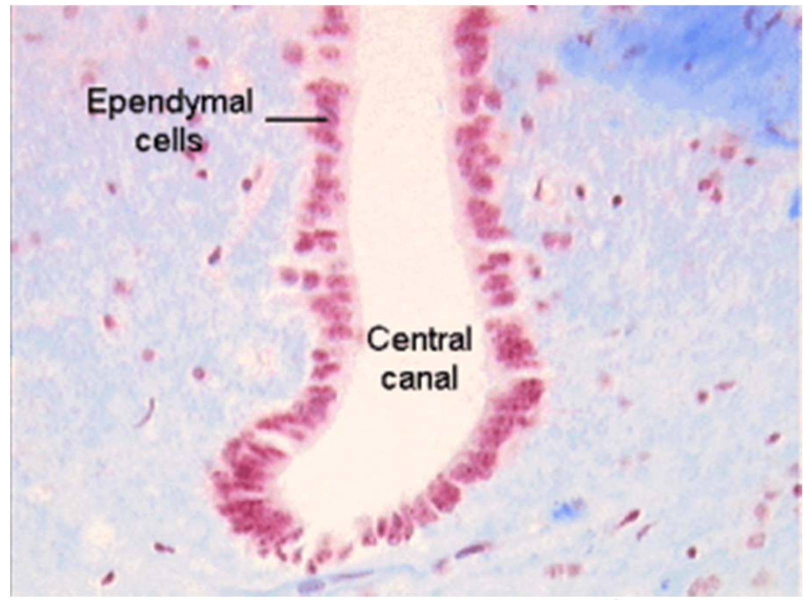


Central canal



More about ependymal cells

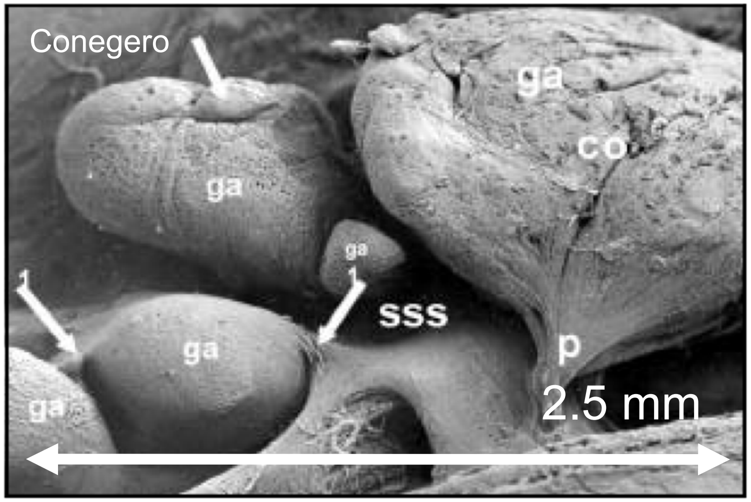


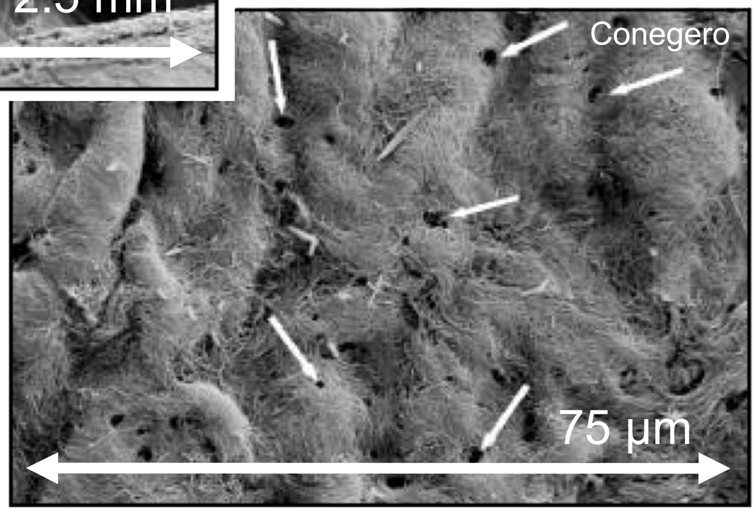


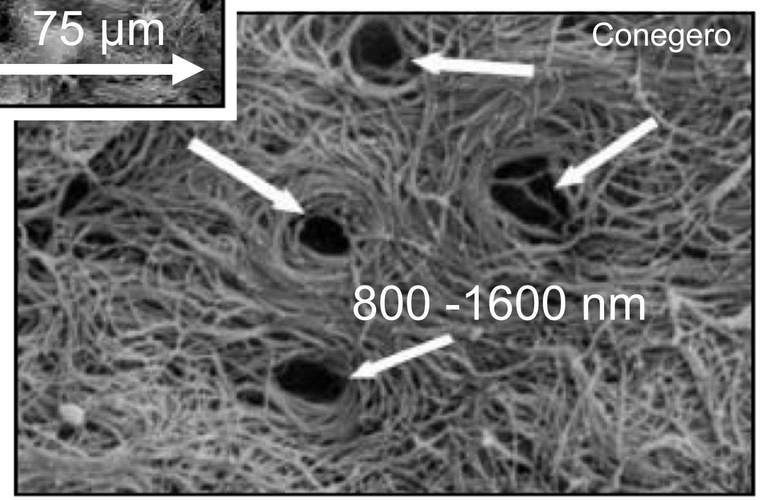
These cells have cilia (like little arms/tails) that help to move the spinal fluid. These cells tend to have a cube or column shape.

Scientists still aren't sure as to all of the functions of the ependymal cell. They do know for sure that it creates and directs spinal fluid, but they still believe more functions are undiscovered.

CSF is absorbed through the arachnoid granulations

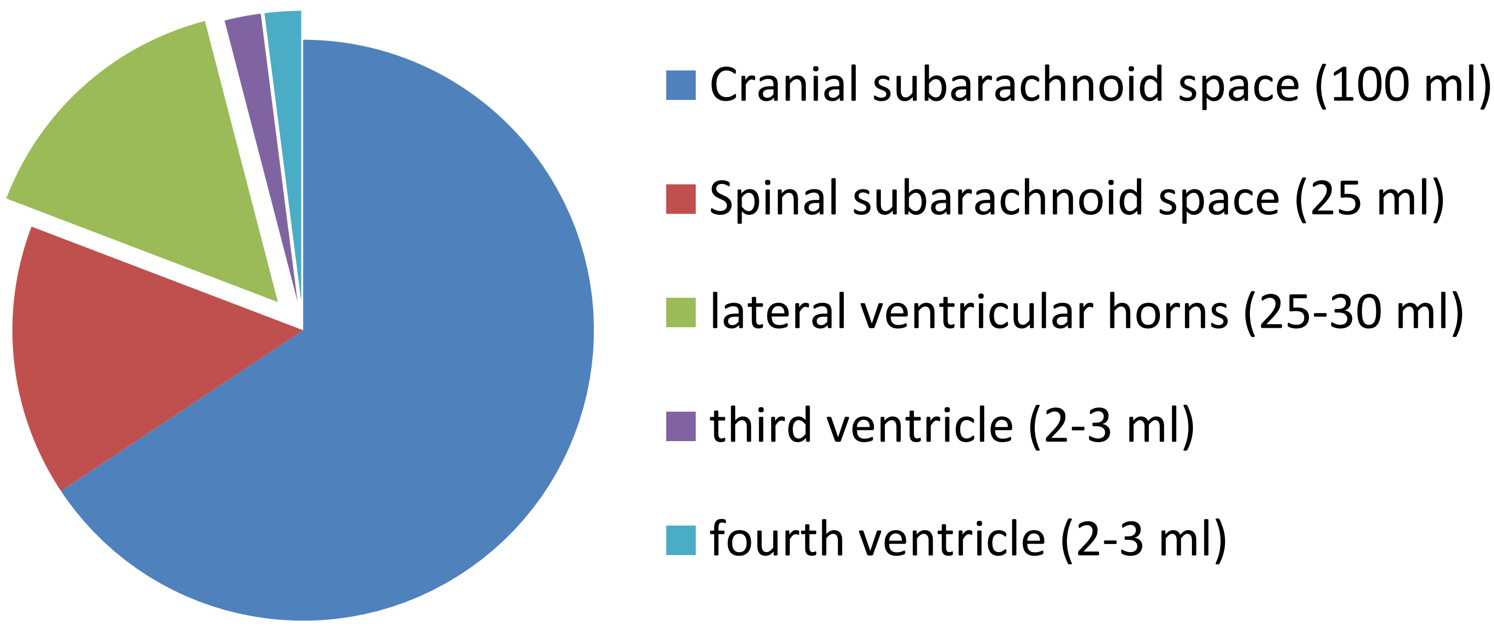






Conegero, C. I. and R. P. Chopard (2003). "Tridimensional architecture of the collagen element in the arachnoid granulations in humans: a study on scanning electron microscopy." Arq Neuropsiquiatr **61**(3A): 561-5.

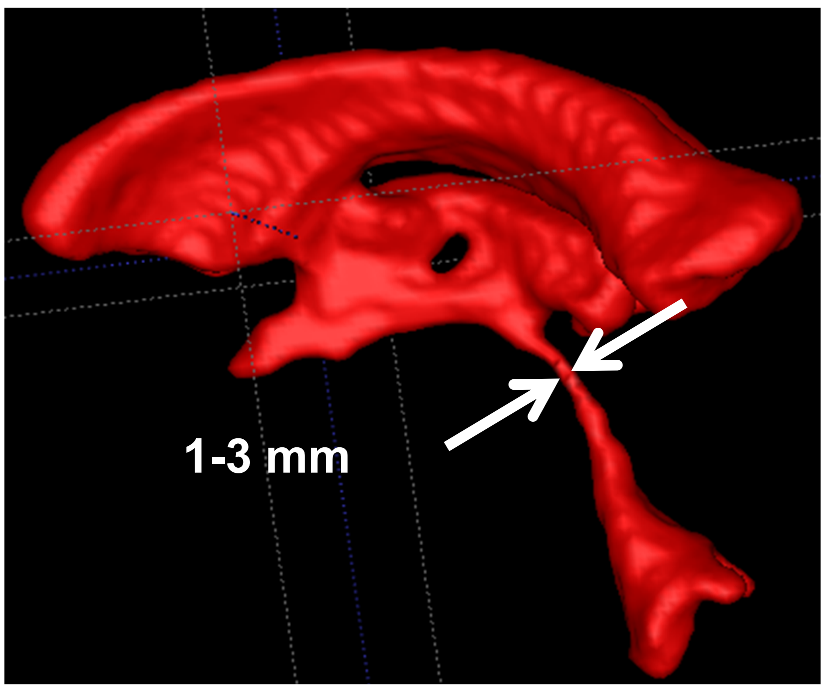
Lateral, 3rd, and 4th Ventricles

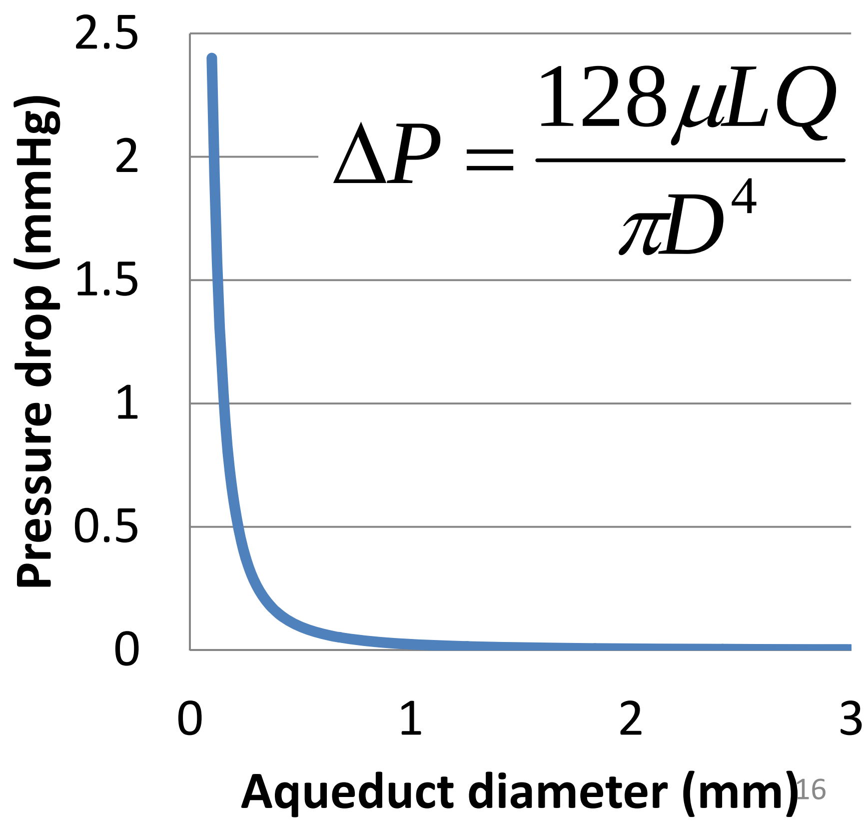


Ventricle geometry

- aqueduct of Sylvius provides greatest hydraulic resistance to CSF flow

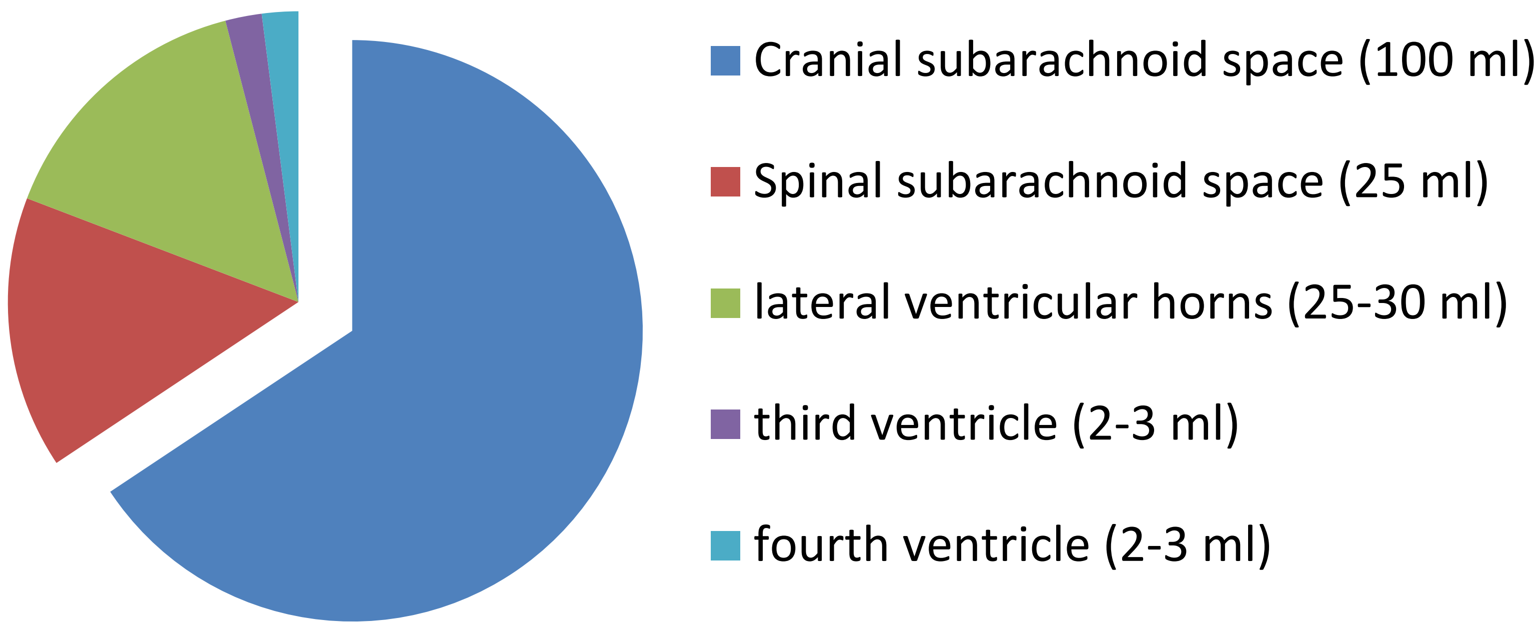
3D ventricle reconstruction





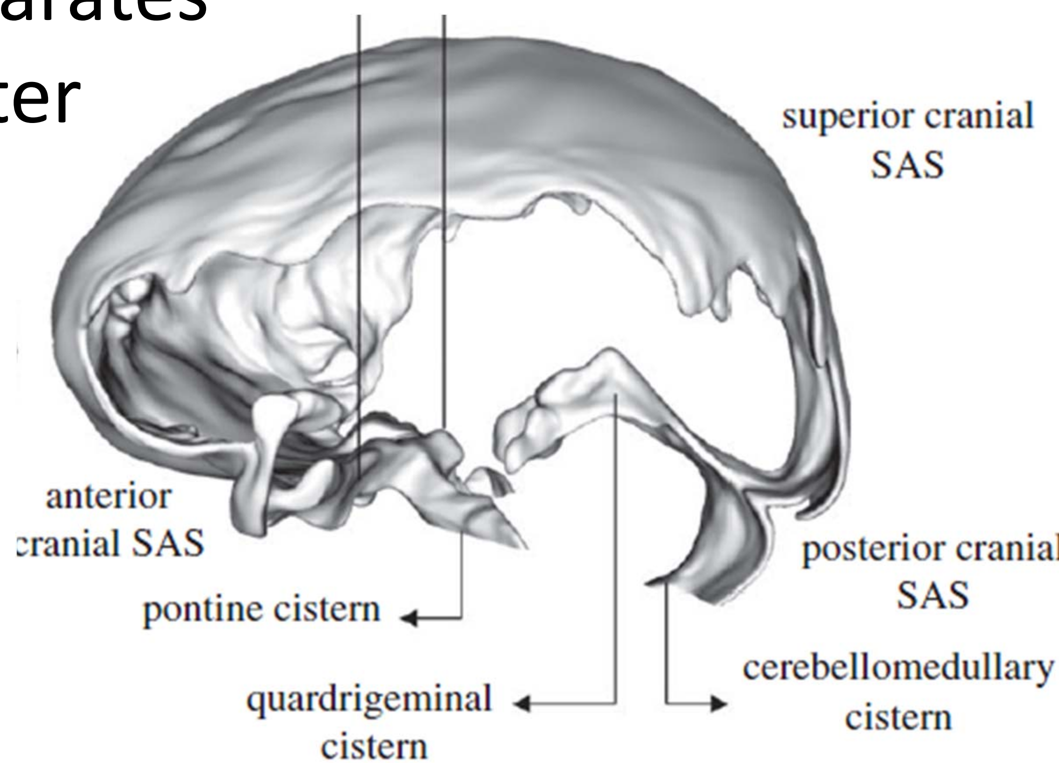
$$\Delta P = \frac{128 \mu L Q}{\pi D^4}$$

Cranial subarachnoid space



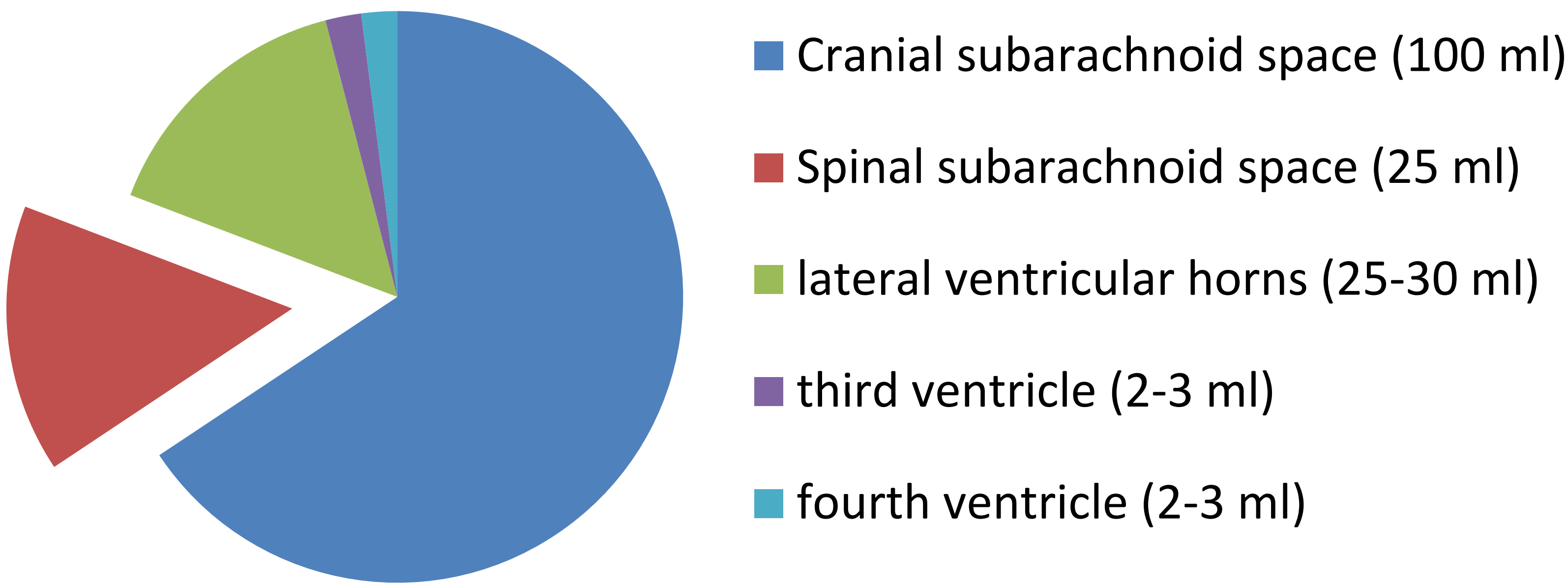
Cranial subarachnoid space

- 100 ml total volume
- 2-9 mm space separates pia/arachnoid mater



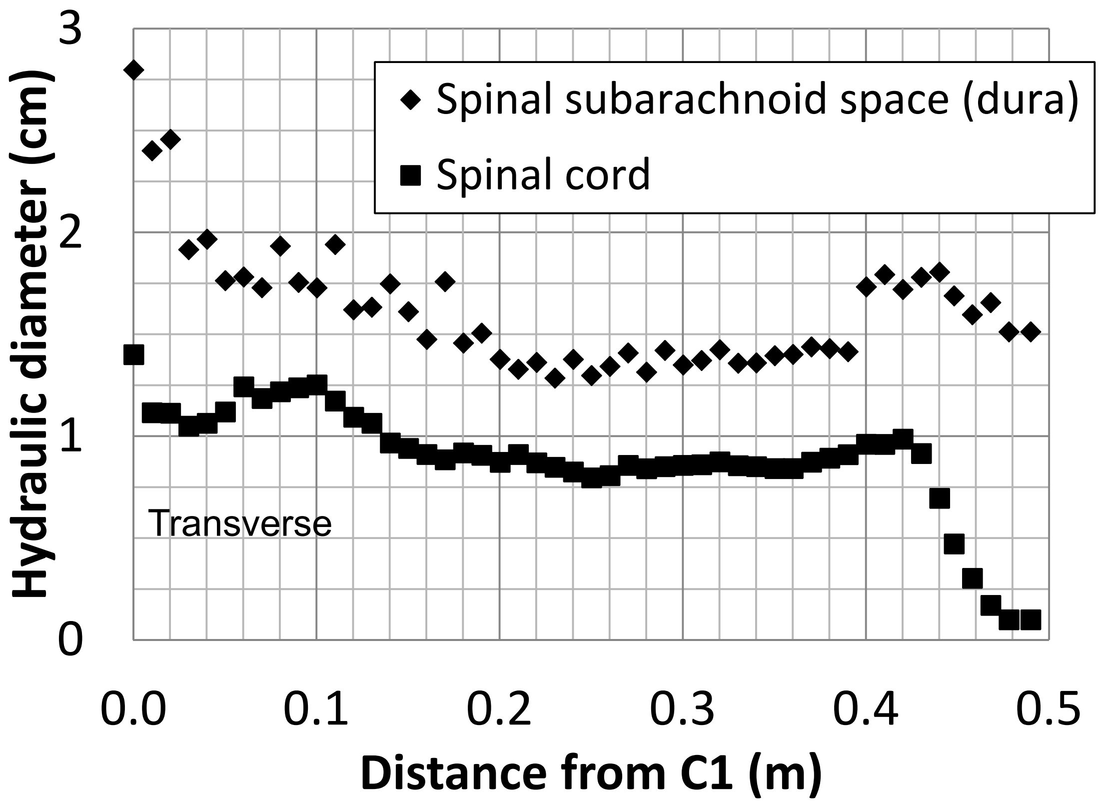
Gupta, S., M. Soellinger, et al. "Cerebrospinal fluid dynamics in the human cranial subarachnoid space: an overlooked mediator of cerebral disease. I. Computational model." J R Soc Interface **7**(49): 1195-204.

Spinal subarachnoid space



Spinal subarachnoid space

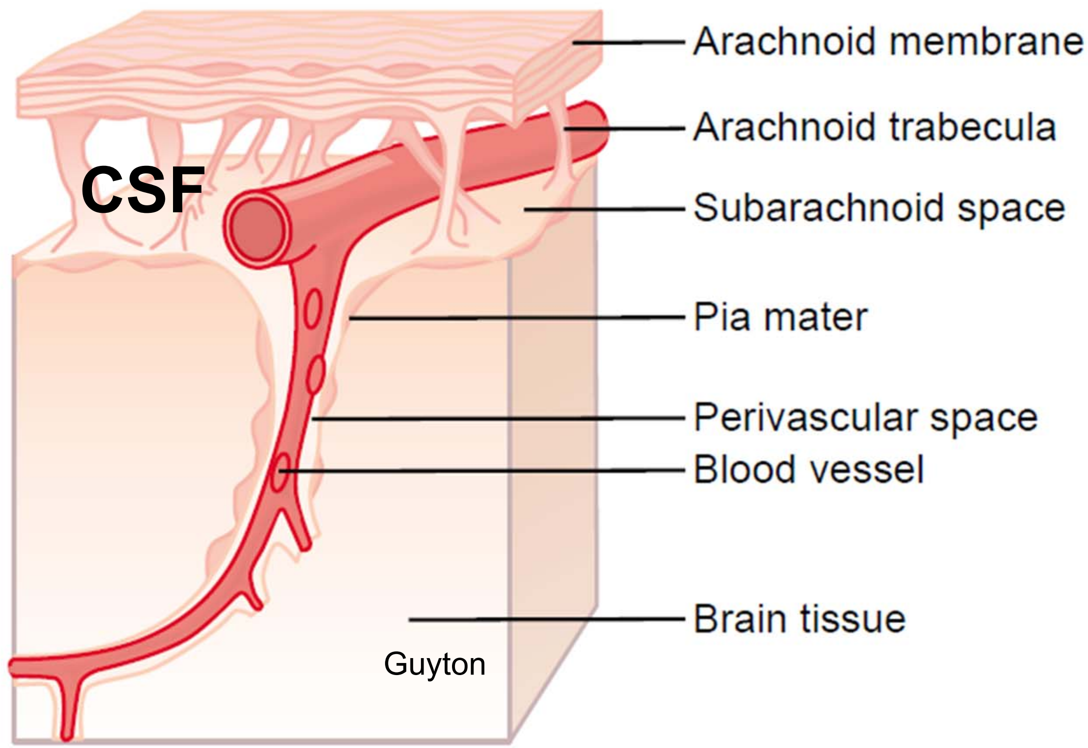
- 25 ml total volume
- 3 mm “doughnut” of space



3D reconstruction of spinal SAS

The subarachnoid space is porous

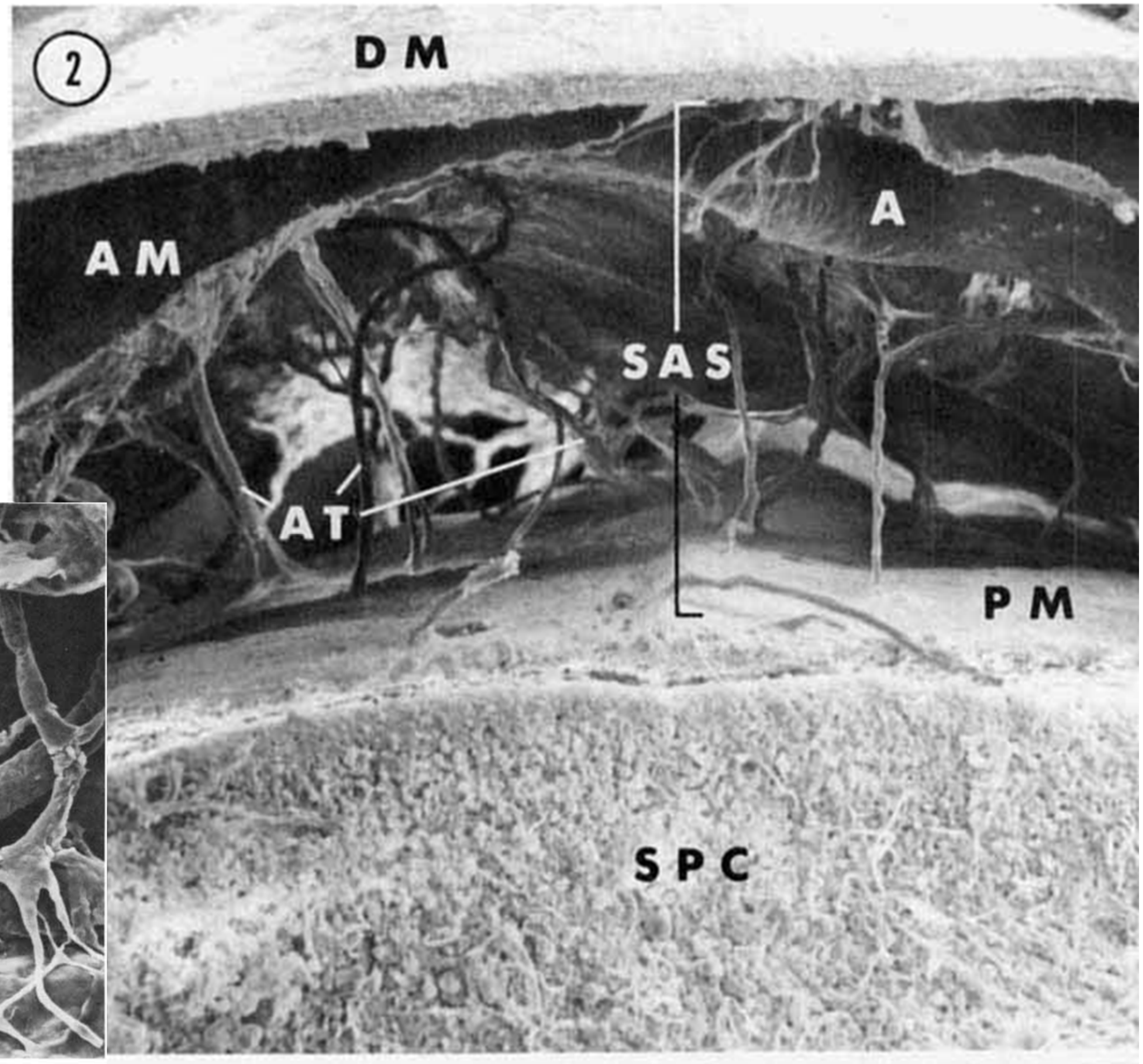
- Arachnoid trebeculae have 30 μm dia. (Gupta)
- Anisotropic porosity (void fraction?)

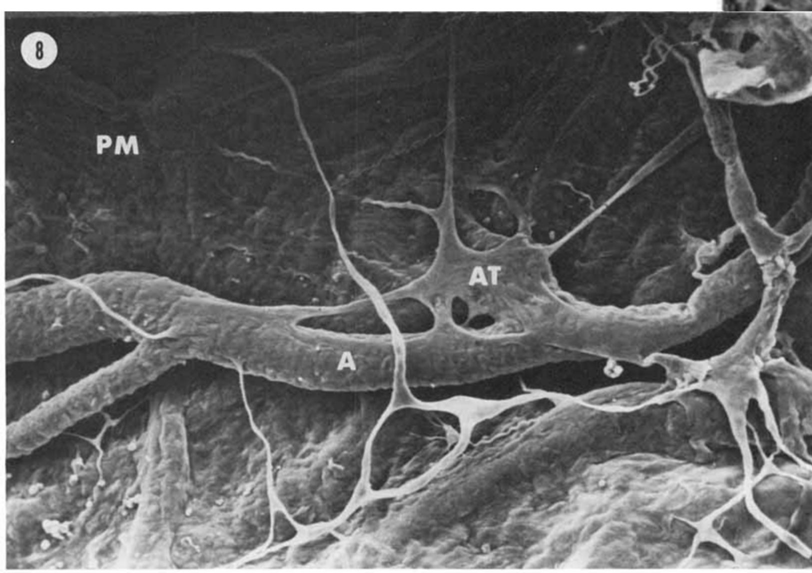


Gupta, S., M. Soellinger, et al. (2009). "Three-dimensional computational modeling of subject-specific cerebrospinal fluid flow in the subarachnoid space." J Biomech Eng **131**(2): 021010.
Guyton, A. C. and J. E. Hall (2006). Textbook of medical physiology. Philadelphia, Elsevier Saunders.

Arachnoid trabeculae

(2) Spinal meninges and subarachnoid space. A view of the cut end of the spinal cord **(SPC)** shows the pia mater **(PM)** lying directly upon the surface of the cord. Arachnoid trabeculae **(AT),** continuous with the pia, extend to the arachnoid mater **(AM)** and to an artery **(A)** above. The separation of the arachnoid mater from the thick dura mater **(DM)** is an artifact of preparation. The subarachnoid space **(SAS)** separates the arachnoid from the pia. *x* 140.

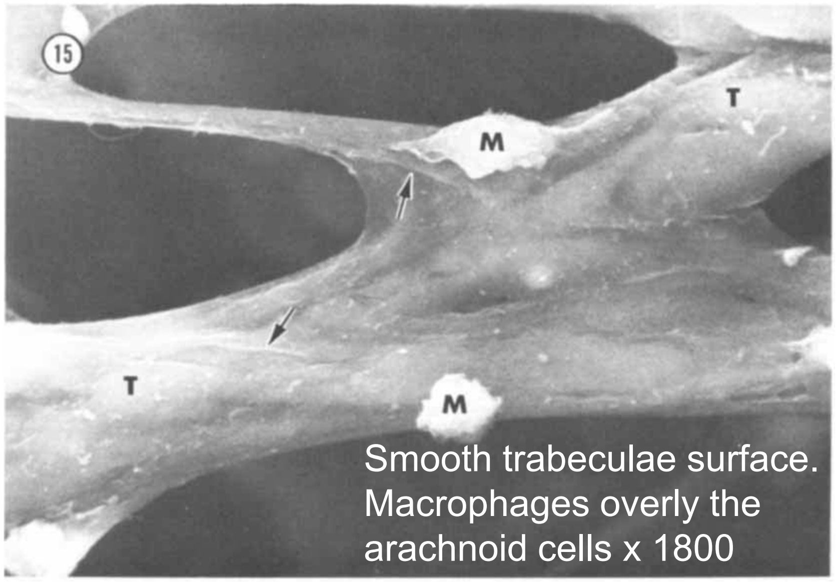




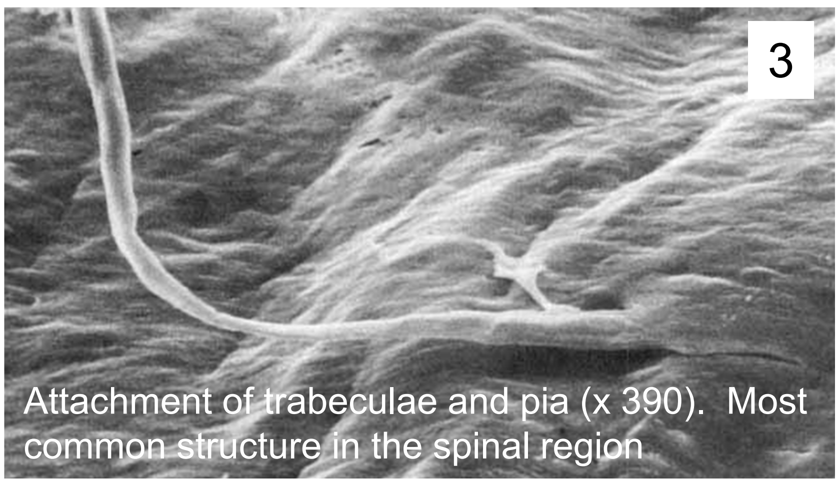
(1) Allen, D. J. and F. N. Low (1975). "Scanning electron microscopy of the subarachnoid space in the dog. III. Cranial levels." The Journal of comparative neurology **161**(4): 515-539.

(2) Cloyd, M. W. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. I. Spinal cord levels." The Journal of comparative neurology **153**(4): 325-368.

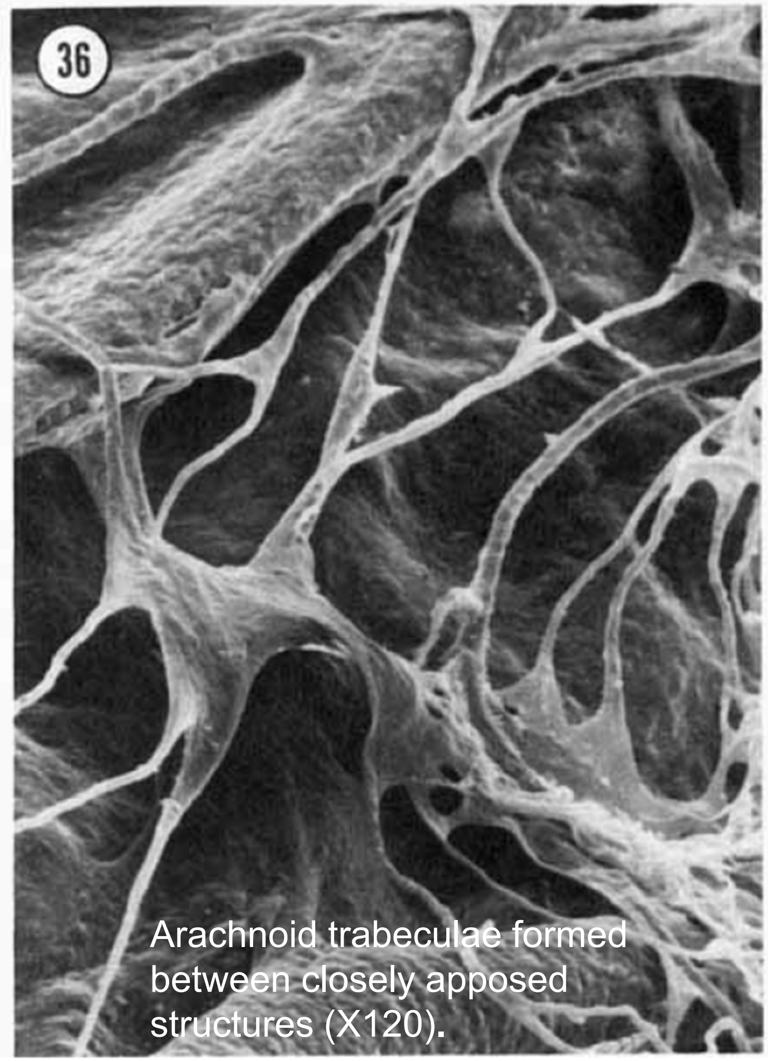
Trabeculae microstructure



Smooth trabeculae surface. Macrophages overly the arachnoid cells x 1800



Attachment of trabeculae and pia (x 390). Most common structure in the spinal region

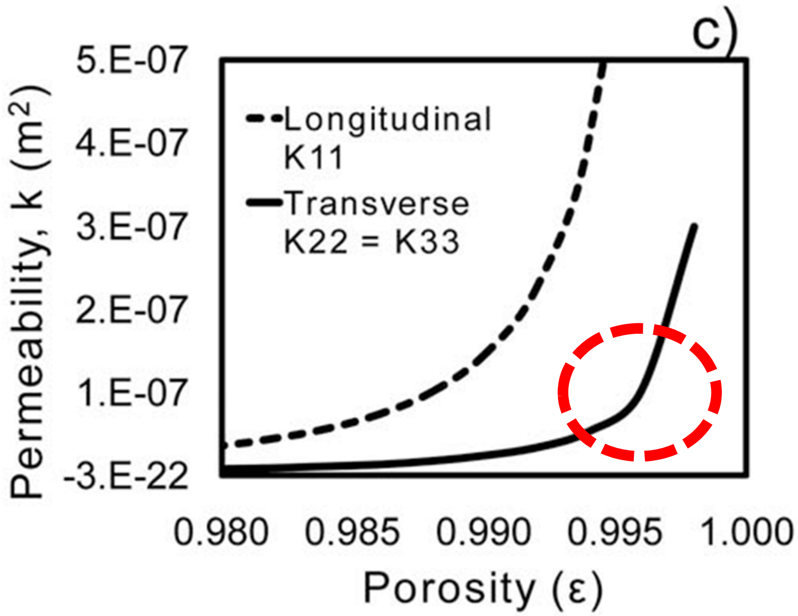


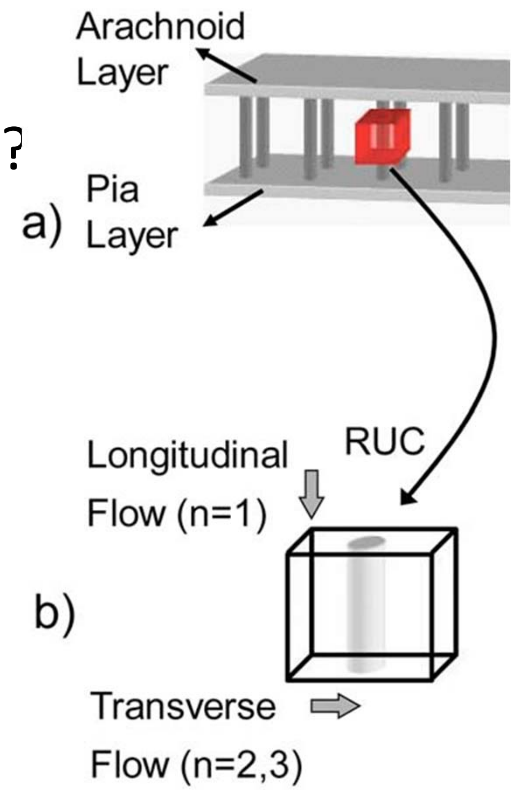
Arachnoid trabeculae formed between closely apposed structures (X120).

(15) Malloy, J. J. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. II. Spinal nerve exits." The Journal of comparative neurology **157**(1): 87-107.
(36,3) Cloyd, M. W. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. I. Spinal cord levels." The Journal of comparative neurology **153**(4): 325-368.

Analytical expression for porosity

- Westhuizen and DuPlessis analytical expression for longitudinal and transverse permeability
- For trabecular fiber radius, *r*
- Subarachoind space porosity ε (*in vivo* = ????





Transverse

$$\frac{k_{11}}{r^2} = \frac{\varepsilon^2 \cdot (\pi + 2.157 \cdot (1-\varepsilon))}{48 \cdot (1-\varepsilon)^2},$$

Longitudinal

$$\frac{k_{22}}{r^2} = \frac{k_{33}}{r^2} = \frac{\pi \cdot \varepsilon \cdot (1-\sqrt{1-\varepsilon})^2}{24 \cdot (1-\varepsilon)^{3/2}}$$

Gupta, S., M. Soellinger, et al. (2009). "Three-dimensional computational modeling of subject-specific cerebrospinal fluid flow in the subarachnoid space." J Biomech Eng **131**(2): 021010.

CSF pressure
(steady state and pulsatile components)

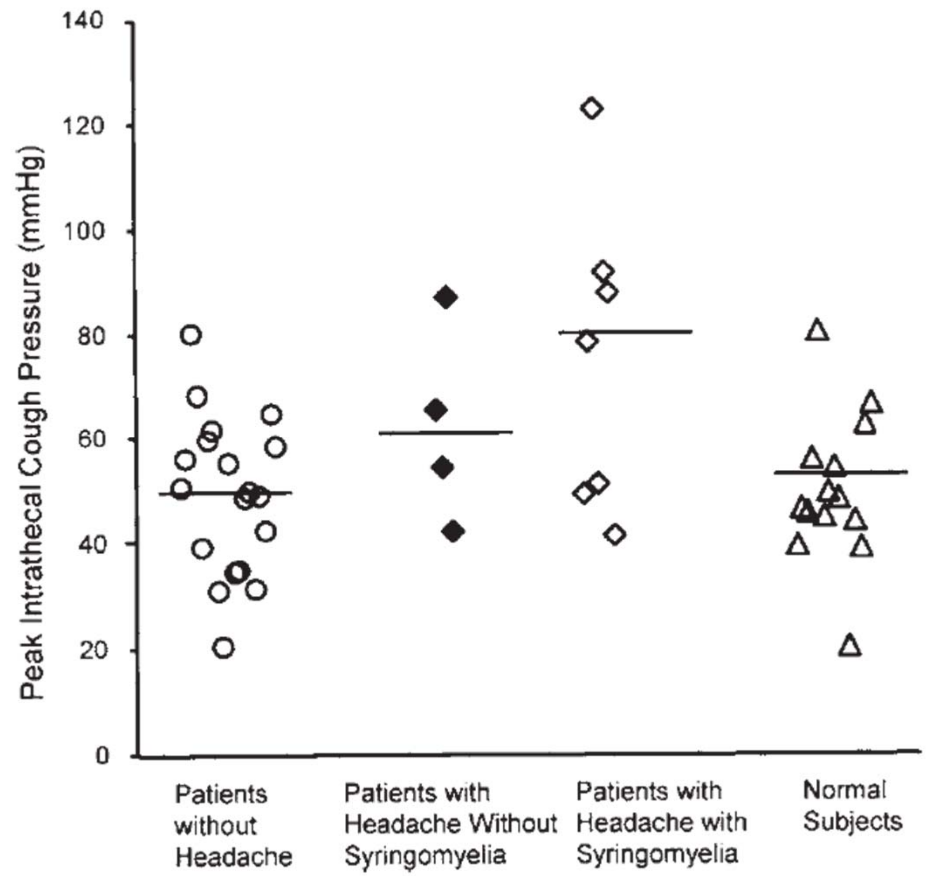
Steady state CSF pressure

- ICP is 7-15 mmHg in supine (Ghajar, Czsnk.)
- 0-10 mmHg in vertical position (Ghjar, Czsnk.)
- Only small pressure gradients exist (<<1 mmHg)

Ghajar, J. (2000). "Traumatic brain injury." Lancet **356**(9233): 923-9.
Czosnyka, M., Z. Czosnyka, et al. (2004). "Cerebrospinal fluid dynamics." Physiol Meas **25**(5): R51-76.
Czosnyka, M. and J. D. Pickard (2004). "Monitoring and interpretation of intracranial pressure." J Neurol Neurosurg Psychiatry **75**(6): 813-21.

CSF pressure during coughing

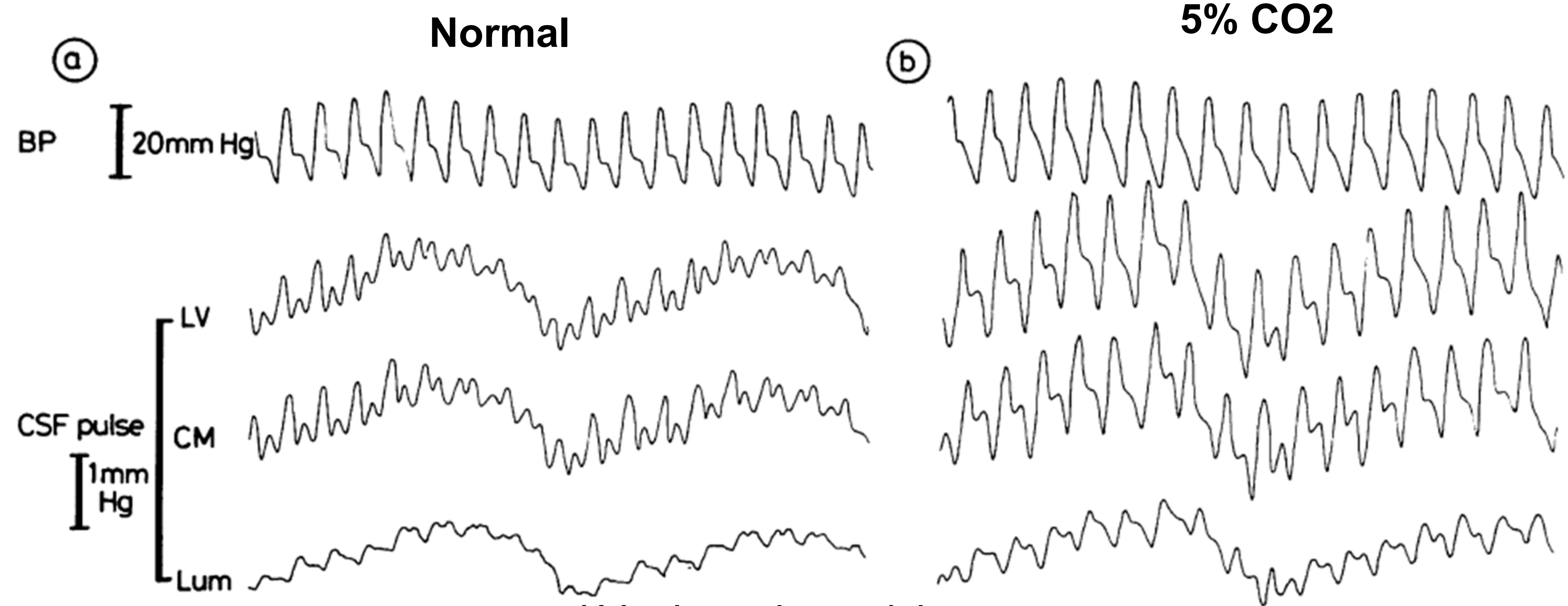
- High spikes in CSF pressure are possible
- ~ 55 mmHg!
- Higher in patients with syringomyelia (Sansur)



Sansur, C. A., J. D. Heiss, et al. (2003). "Pathophysiology of headache associated with cough in patients with Chiari I malformation." J Neurosurg **98**(3): 453-8.

CSF pressure and flow pulsations are in the ventricular system and subarachnoid space

- ~ 0.5-1 mmHg in healthy adult

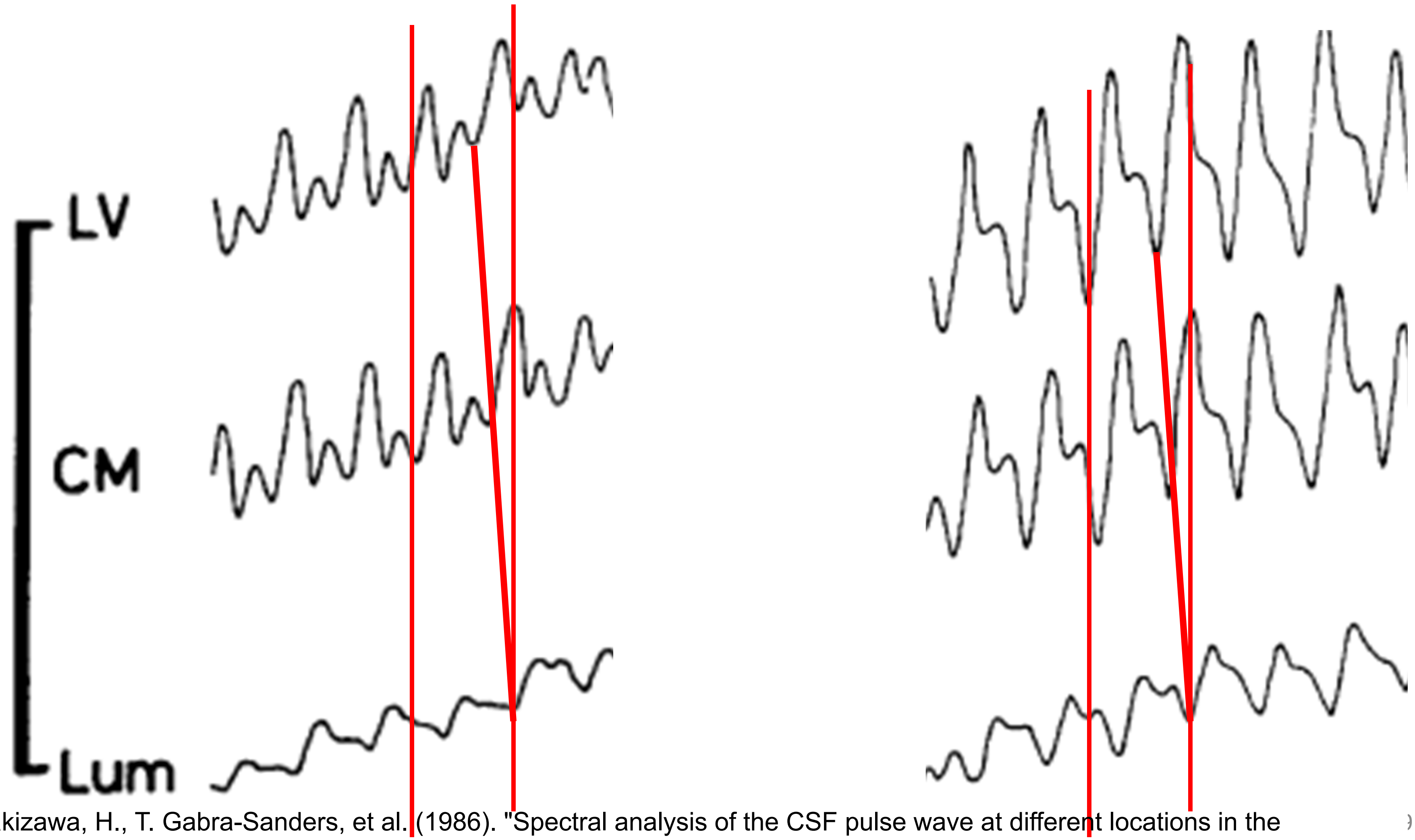


LV = lateral ventricle
CM = cisterna magna
Lum = lumbar sss

Takizawa, H., T. Gabra-Sanders, et al. (1986). "Spectral analysis of the CSF pulse wave at different locations in the craniospinal axis." J Neurol Neurosurg Psychiatry **49**(10): 1135-41.

CSF pulse comes from the brain

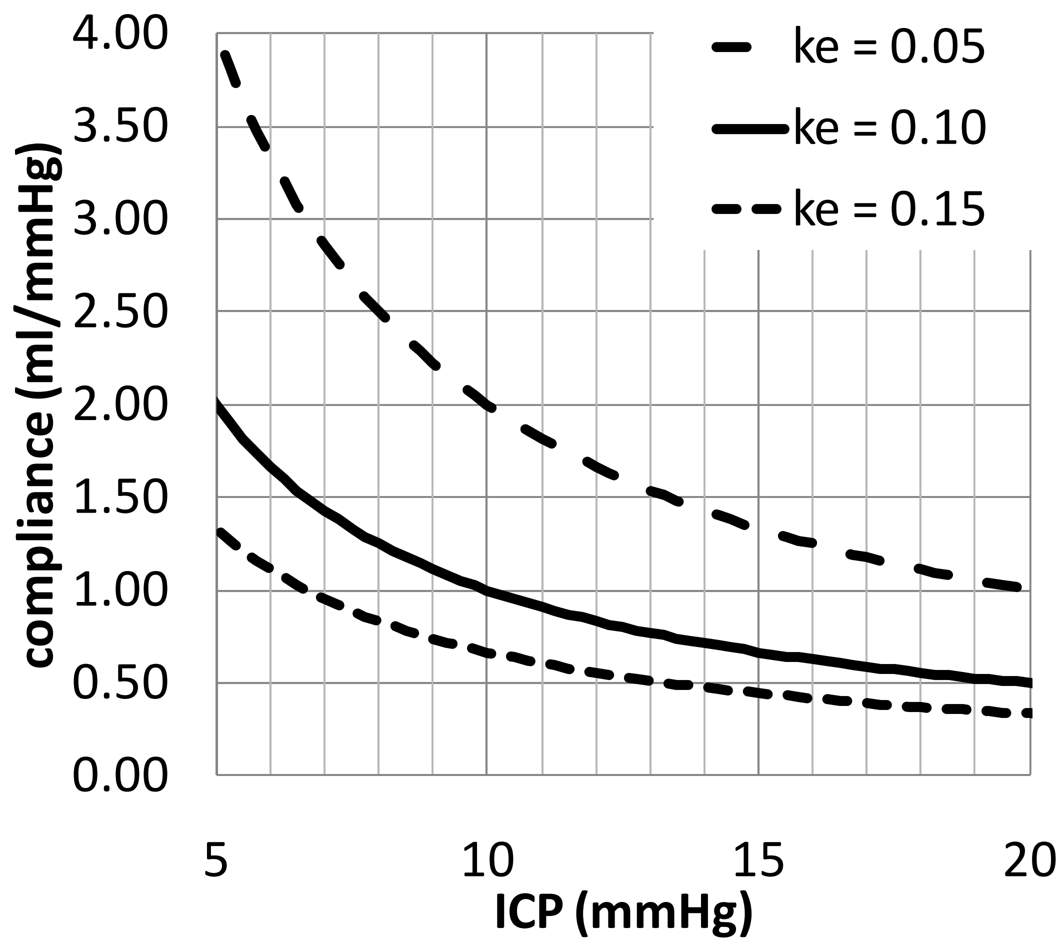
- PWV from figure = 2.5 m/s [0.5/(1/5)]



Takizawa, H., T. Gabra-Sanders, et al. (1986). "Spectral analysis of the CSF pulse wave at different locations in the craniospinal axis." J Neurol Neurosurg Psychiatry **49**(10): 1135-41.

CSF pressure pulsation amplitude is dependent on craniospinal compliance

- C=dV/dP
- (Arterial compliance is 1-5 ml/mmHg)

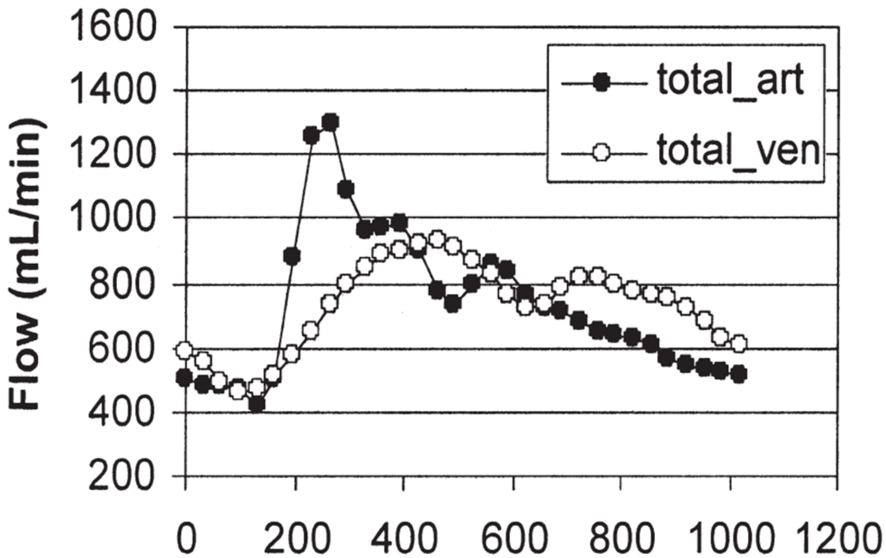


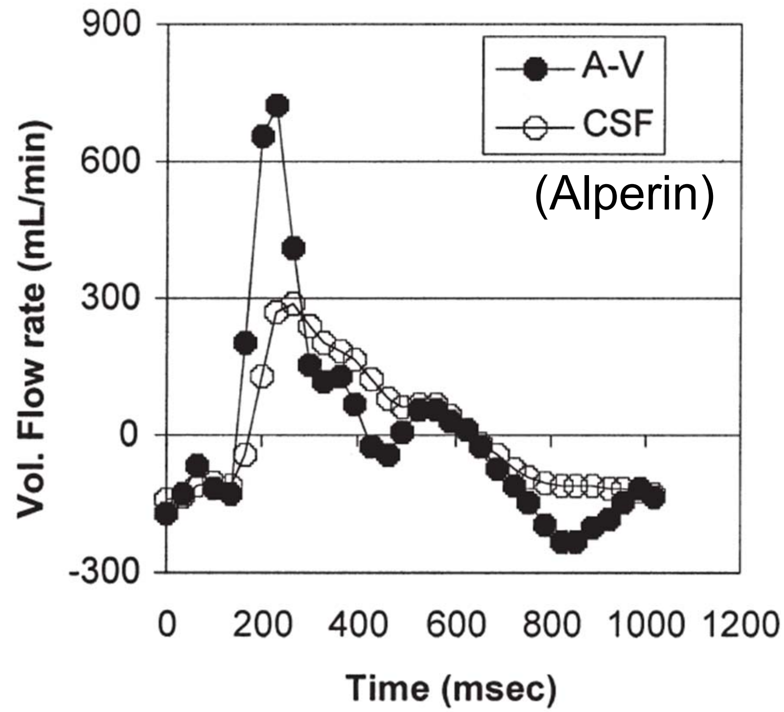
$$C_{ic} = 1/(k_E P_{ic})$$

Ursino M: A mathematical study of human intracranial hydrodynamics. Part 1--The cerebrospinal fluid pulse pressure. *Ann Biomed Eng* 1988, 16:379-401.

CSF flow pulsations

CSF flow pulsations come from cerebral blood flow pulsations

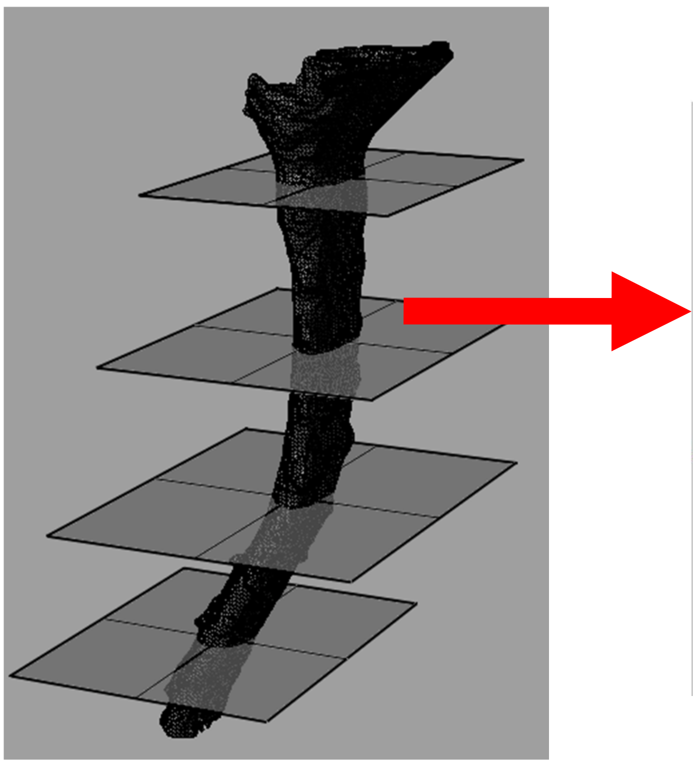




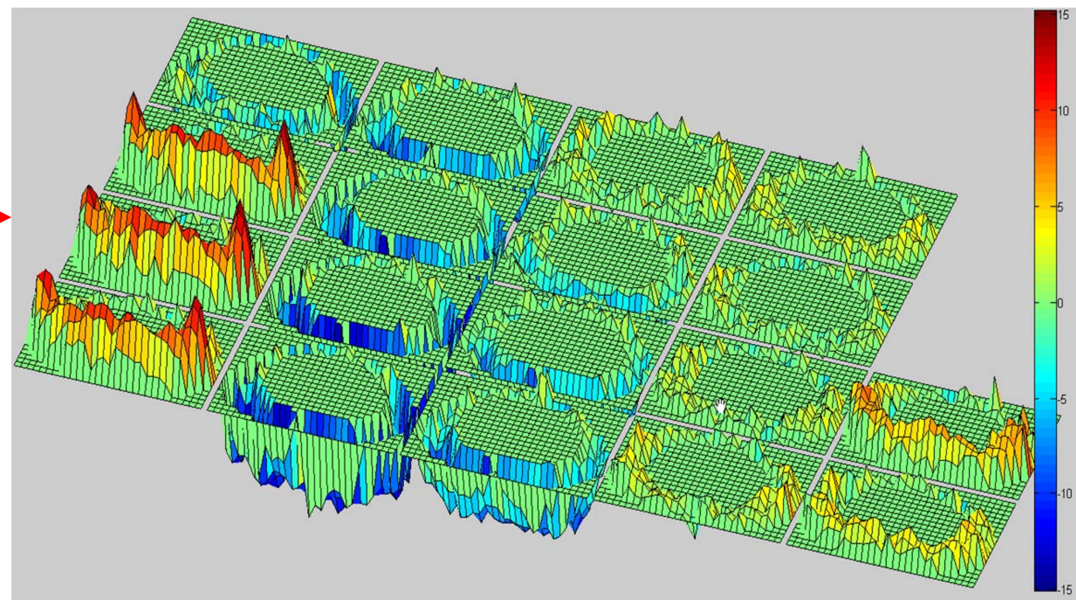
Alperin, N., A. Sivaramakrishnan, et al. (2005). "Magnetic resonance imaging-based measurements of cerebrospinal fluid and blood flow as indicators of intracranial compliance in patients with Chiari malformation." J Neurosurg **103**(1): 46-52.
Baledent, O., C. Gondry-Jouet, et al. (2004). "Relationship between cerebrospinal fluid and blood dynamics in healthy volunteers and patients with communicating hydrocephalus." Invest Radiol **39**(1): 45-55.
Baledent, O., M. C. Henry-Feugeas, et al. (2001). "Cerebrospinal fluid dynamics and relation with blood flow: a magnetic resonance study with semiautomated cerebrospinal fluid segmentation." Invest Radiol **36**(7): 368-77.

CSF pulsations are present throughout the subarachnoid space

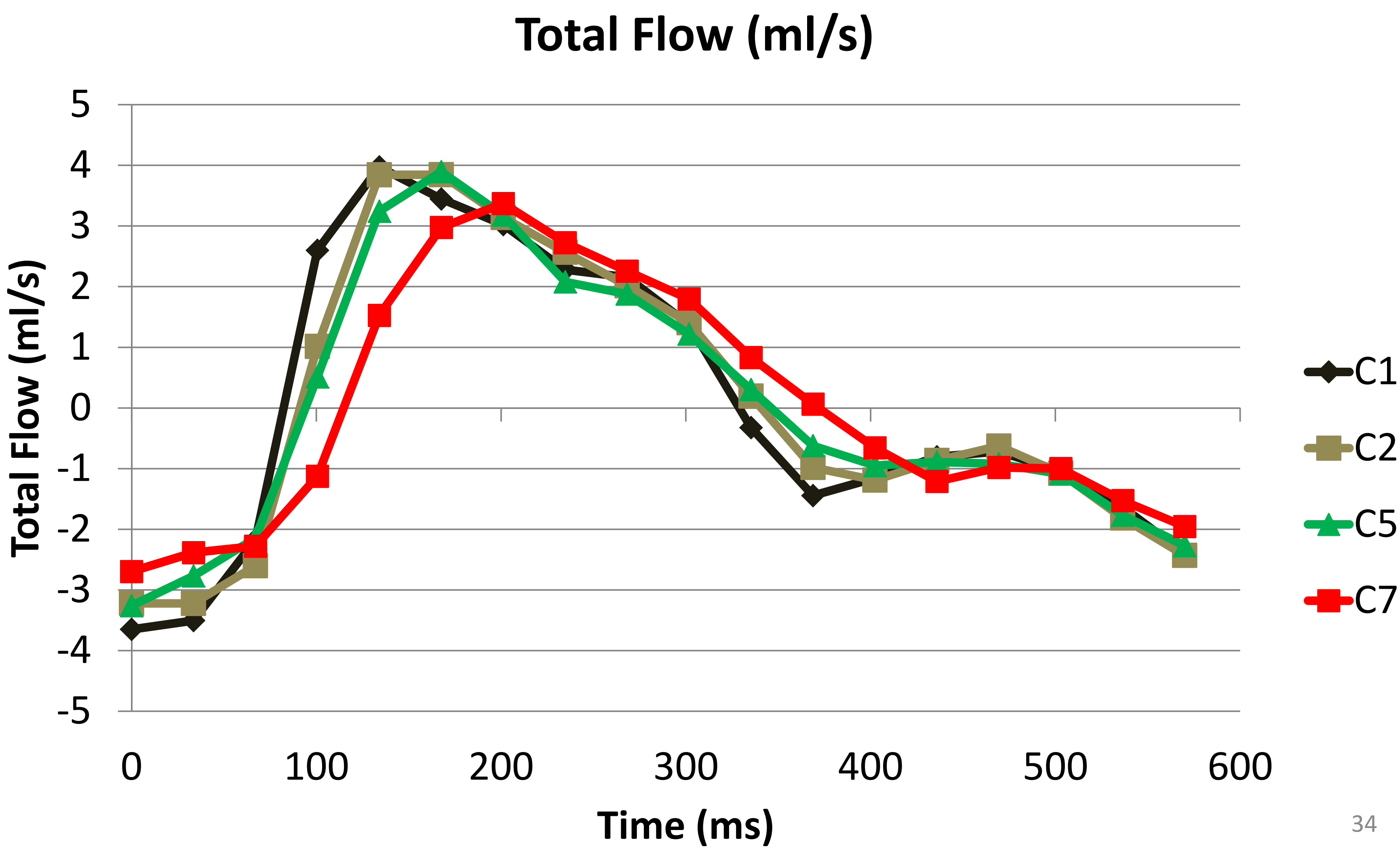
- ~ Zero net flow



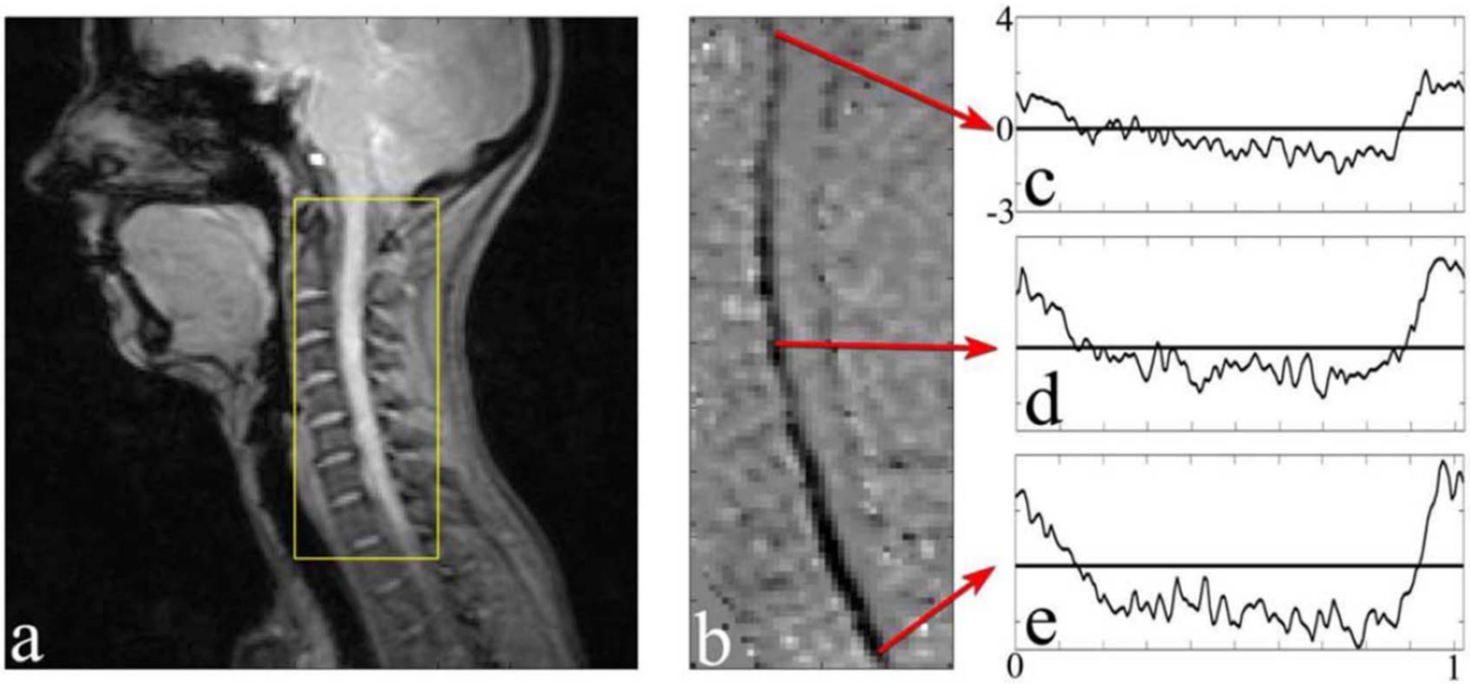
CSF flow around spinal cord at Different time points in the cardiac cycle



The spinal CSF pulsation decreases in the caudal direction



The CSF pulse travels down the spinal subarachnoid space

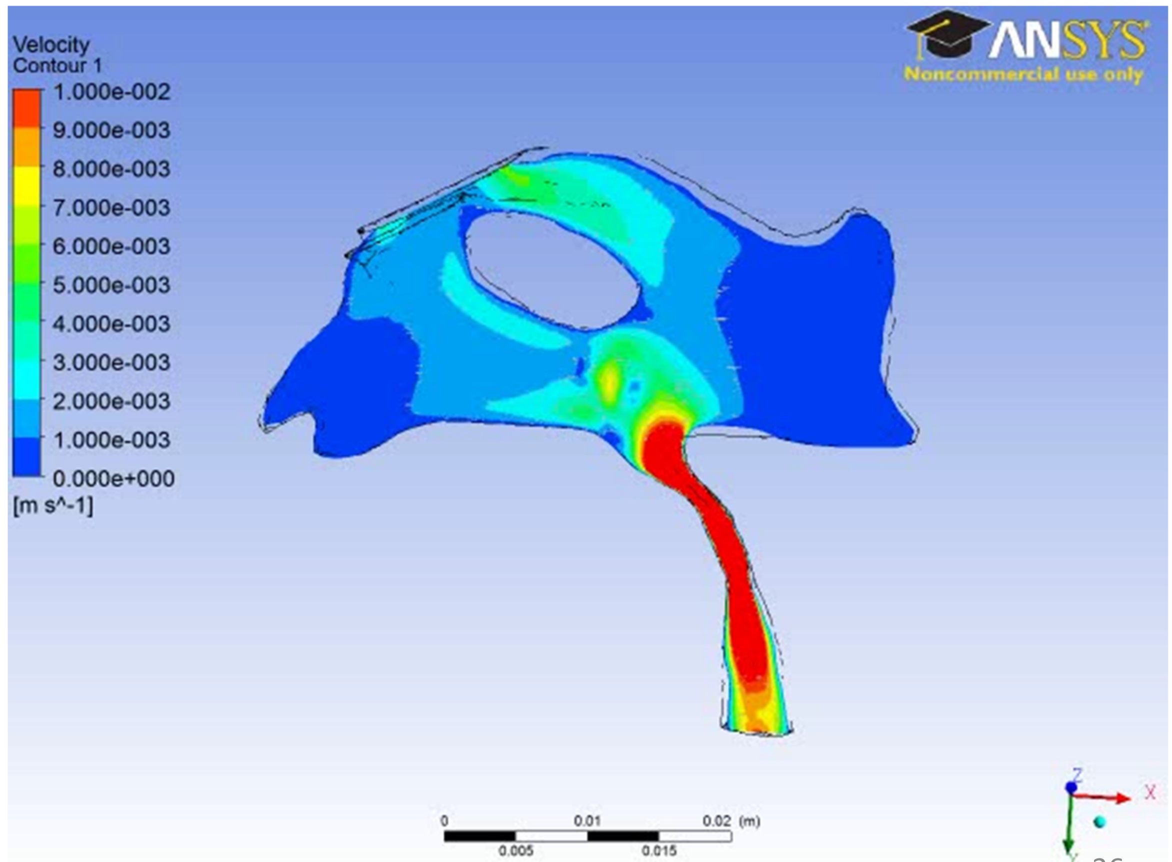


- Wave propagation velocity of ~ 4.6 m/s
- Related to craniospinal compliance

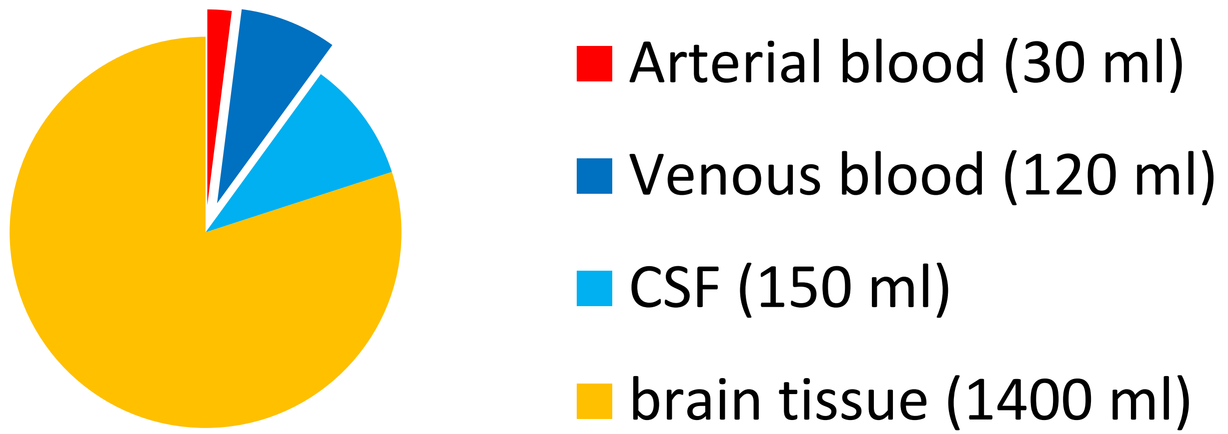
Kalata, W., B. Martin, et al. (2009). "MR Measurement of Cerebrospinal Fluid Velocity Wave Speed in the Spinal Canal." IEEE Trans Biomed Eng.

The largest CSF velocities occur in the aqueduct of Sylvius

- 5-40 mm/s

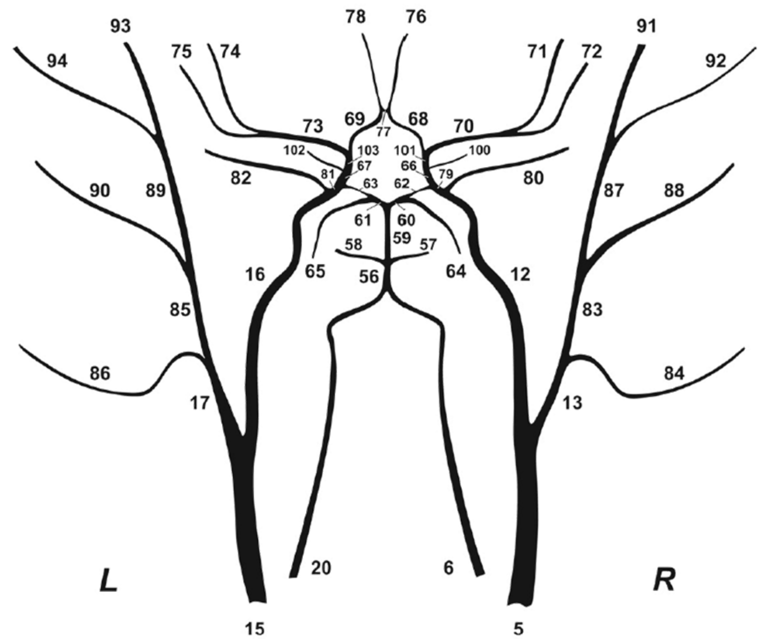


Blood
(cerebral and spinal cord)



Cerebral blood flow is modified by the CSF system

- Transmural pressure acts on vessels from CSF
- Perfusion pressure is related to venous pressure (and abdominal pressure)
- ICP = 1.5mmHg + venousP
- 50 ml/min of blood

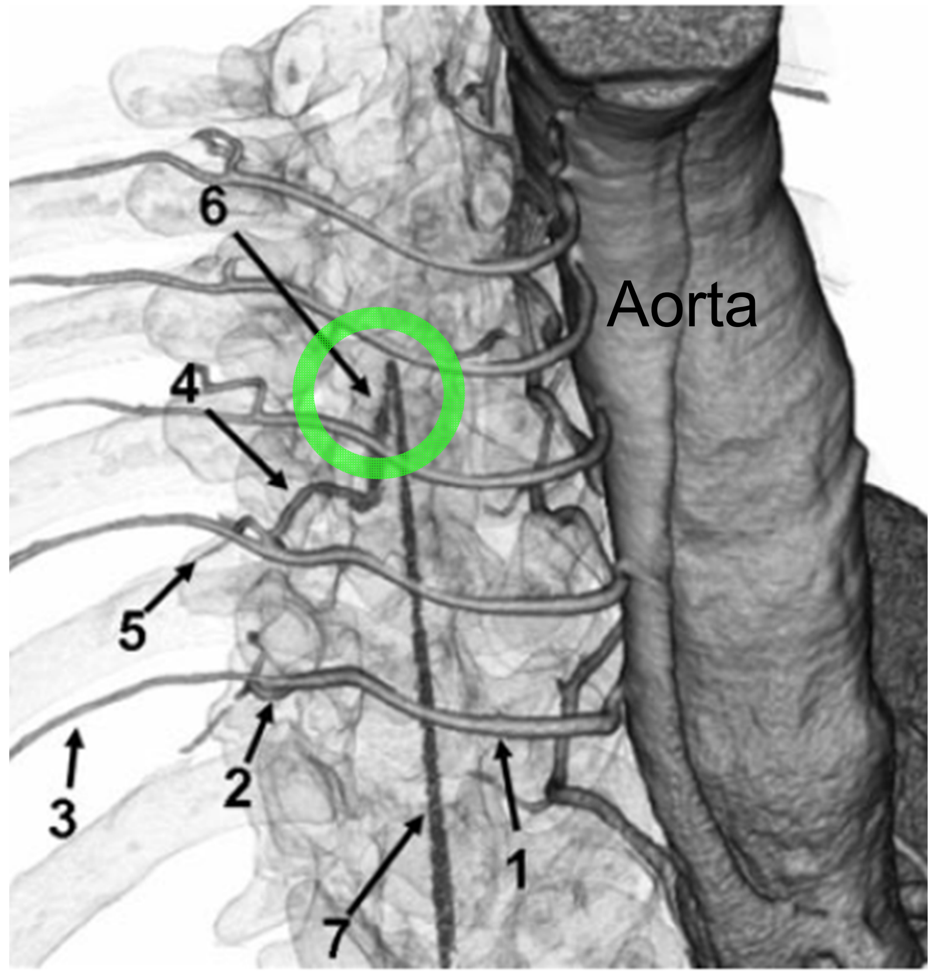


Reymond, P., F. Merenda, et al. (2009). "Validation of a one-dimensional model of the systemic arterial tree." Am J Physiol Heart Circ Physiol **297**(1): H208-22.

Spinal cord arteries

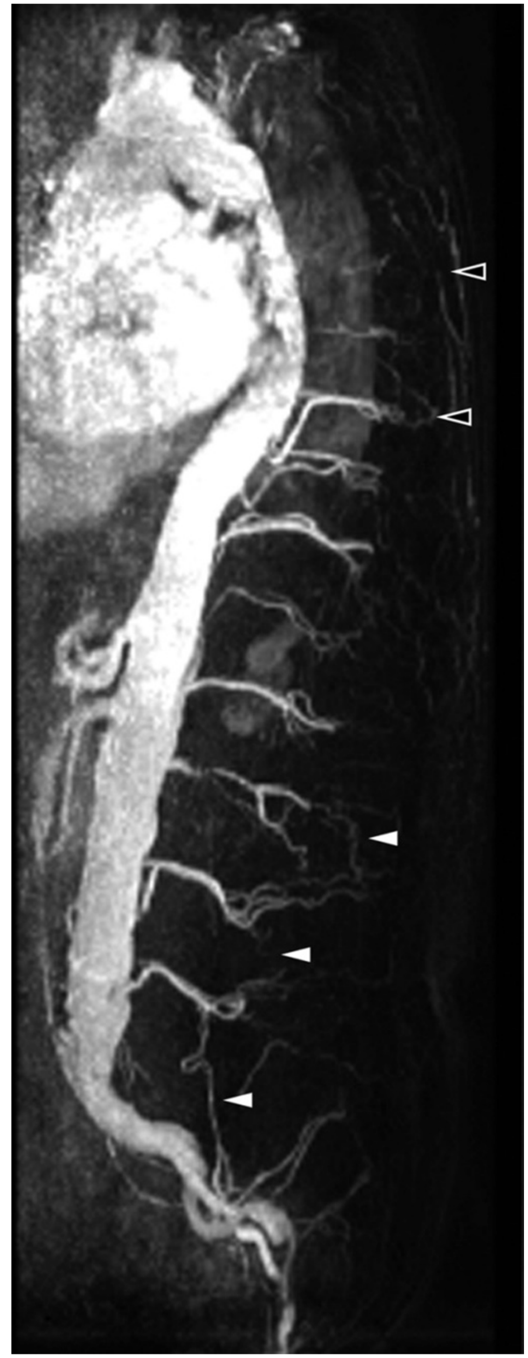
- There is a lot of anatomical variation in SC blood supply

1. Intercostal artery
2. Posterior inter. art. branch
3. Anterior inter. art. branch
4. Radiculomedullary art.
5. Muscular branch
6. Artery of Adamkiewicz
7. Anterior spinal artery (ASA)



Uotani, K., N. Yamada, et al. (2008). "Preoperative visualization of the artery of Adamkiewicz by intra-arterial CT angiography." AJNR Am J Neuroradiol **29**(2): 314-8.

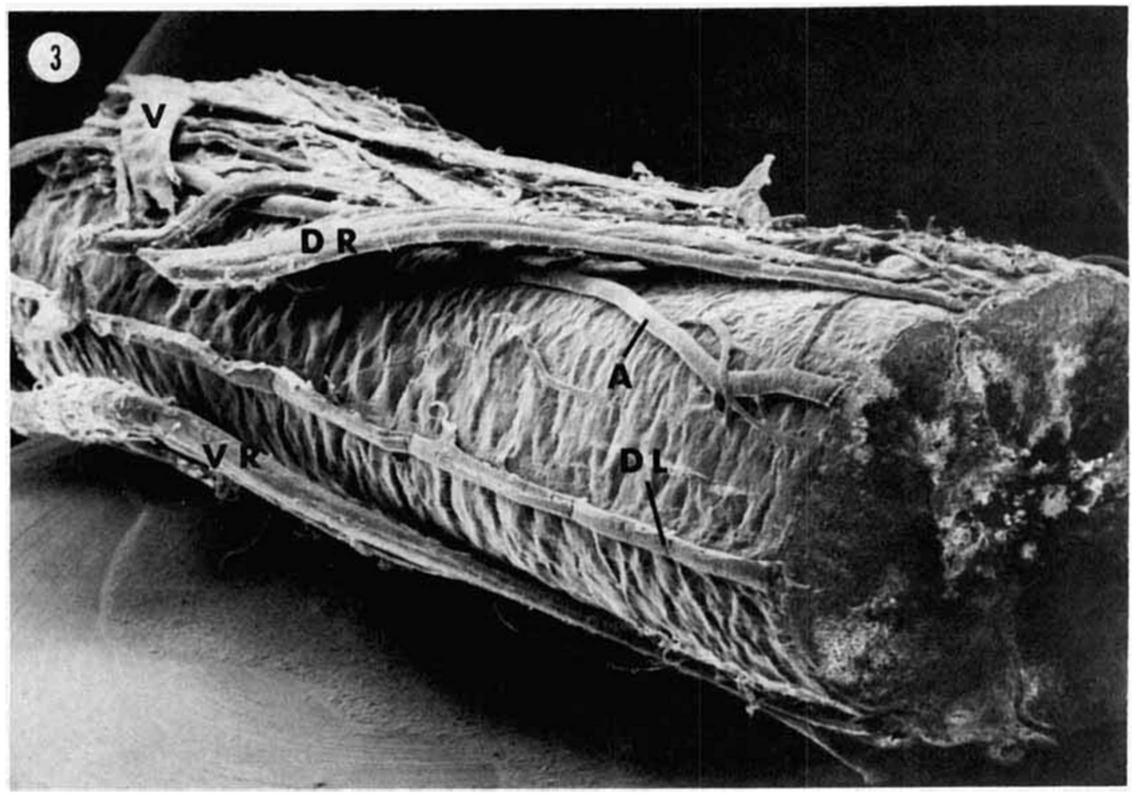
More on spinal cord blood supply



Backes WH, Nijenhuis RJ, Mess WH, Wilmink FA, Schurink GW, and Jacobs MJ. Magnetic resonance angiography of collateral blood supply to spinal cord in thoracic and thoracoabdominal aortic aneurysm patients. *Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter* 48: 261-271, 2008.

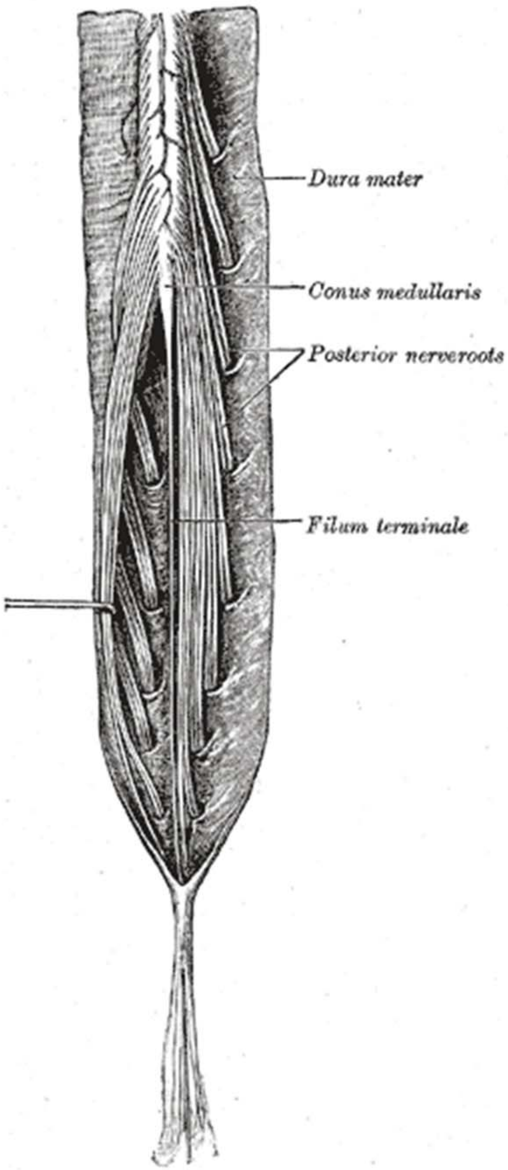
Spinal cord gross anatomy

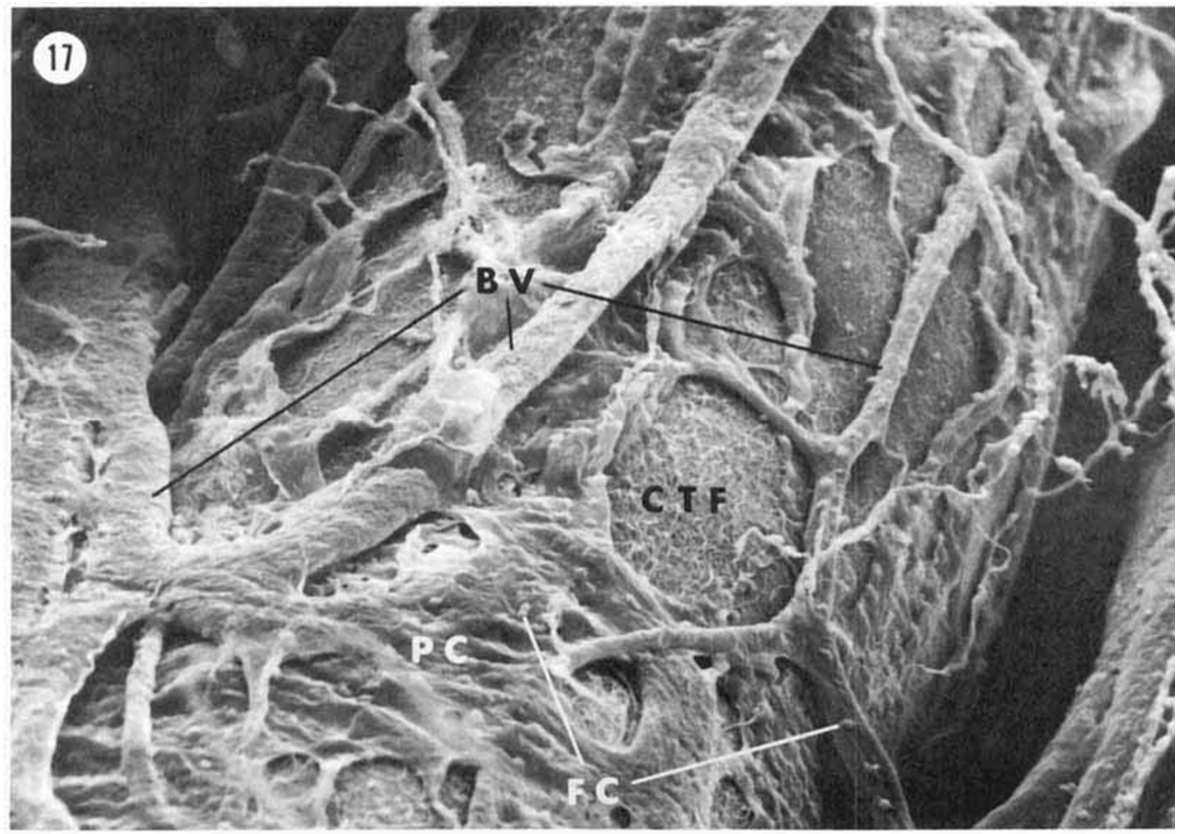
Section of lumbar spinal cord. The dura-arachnoid has been removed to expose pial and root sheath surfaces. Dorsal **(DR)** and ventral **(VR)** nerve roots have been cut proximal to their exit through the duraarachnoid. **A** denticulate ligament **(DL)** extends along the lateral side of the cord. Arteries **(A)** and veins **(V)** lie on the pial surface. x ***28.***



(3) Cloyd, M. W. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. I. Spinal cord levels." The Journal of comparative neurology **153**(4): 325-368.

Spinal cord microstructure at conus

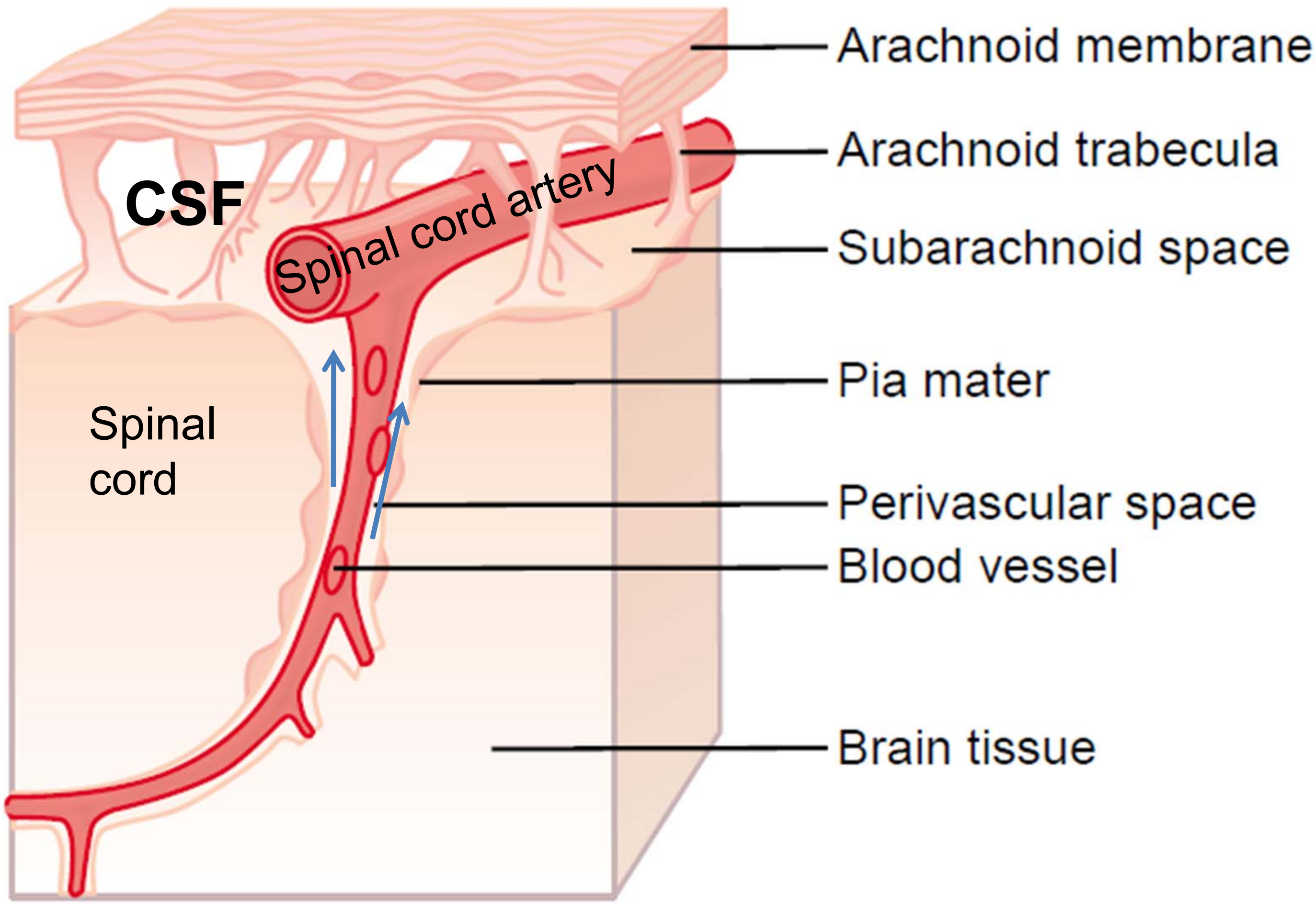




Spinal pia at the conus medullaris region. Here the cellular layer of the pia (PC) is highly fenestrated. Large areas lack **a** surface cellular layer, with the result **that** connective tissue fibers (CTF) are exposed to the subarachnoid space. A network of blood vessels (BV) is intimately associated with the pia mater. Free cells (FC) can be observed. x 140.

(3) Cloyd, M. W. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. I. Spinal cord levels." The Journal of comparative neurology **153**(4): 325-368.

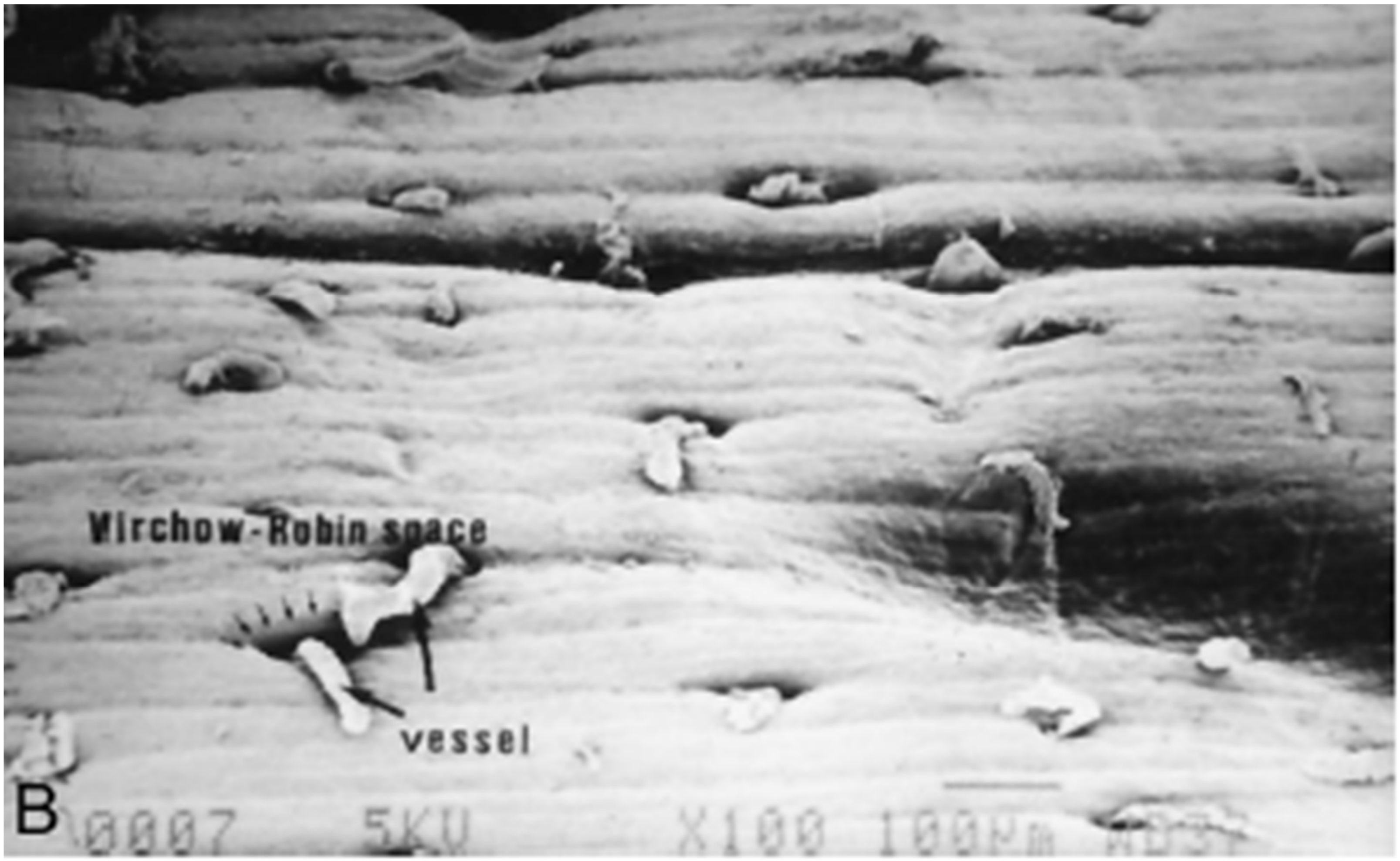
Perivascular spaces



- Spinal cord perivascular spaces are a "specialized lymphatic system" (Guyton et al.)

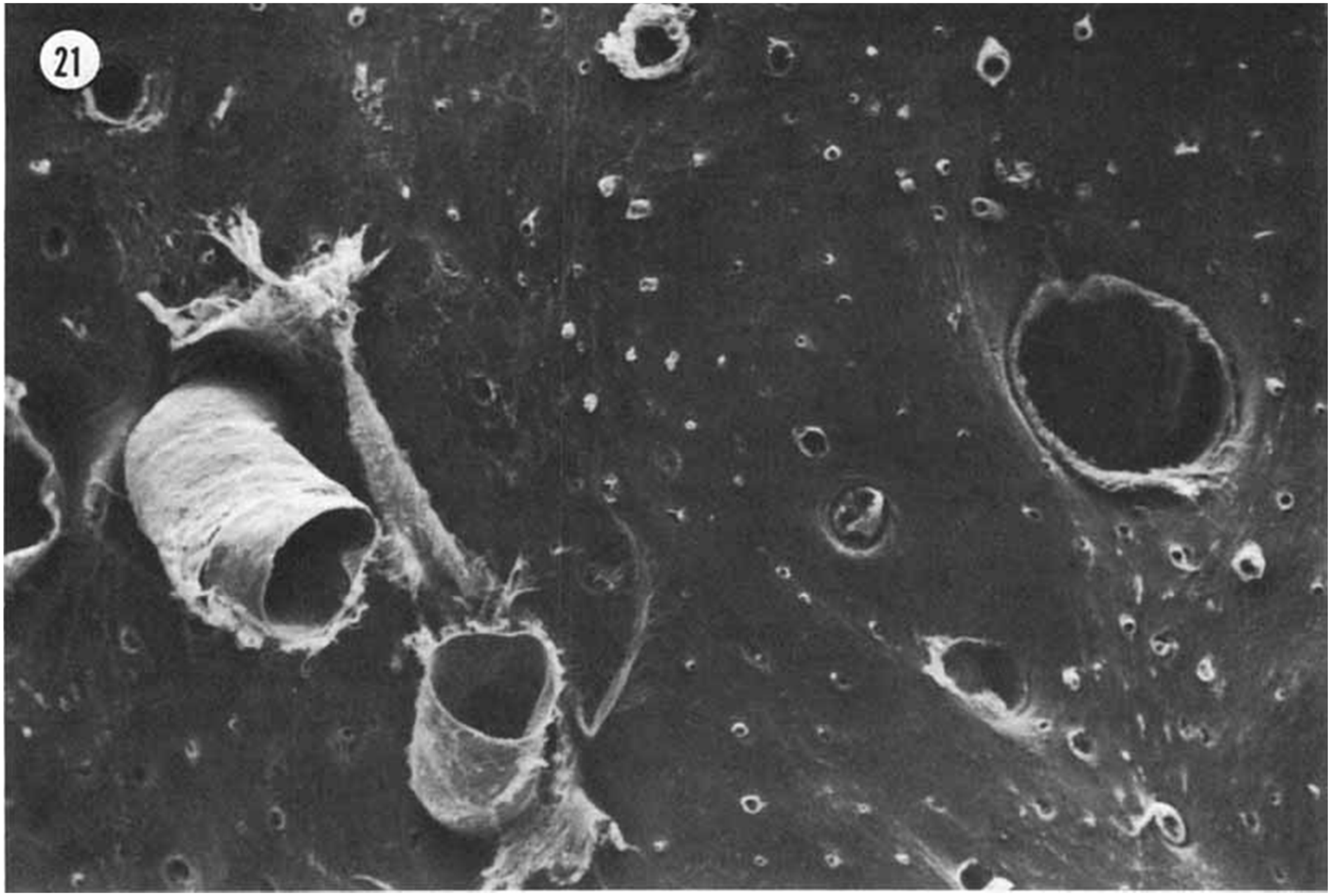
Guyton, A. C. and J. E. Hall (2006). Textbook of medical physiology. Philadelphia, Elsevier Saunders.

Arterioles entering spinal cord



Yoshizawa, H. (2002). "Presidential address: pathomechanism of myelopathy and radiculopathy from the viewpoint of blood flow and cerebrospinal fluid flow including a short historical review." Spine (Phila Pa 1976) **27**(12): 1255-63.

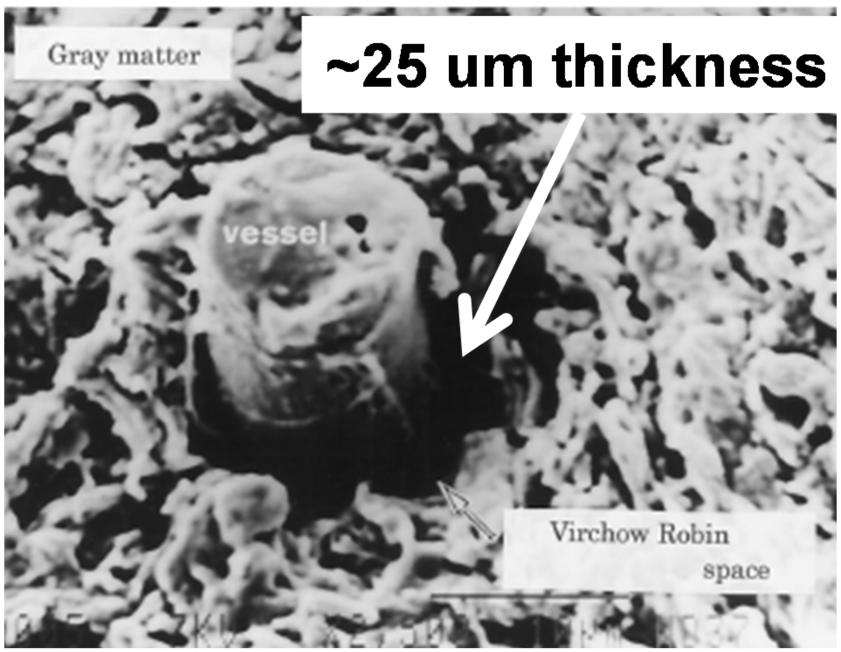
Arterioles entering brain surface

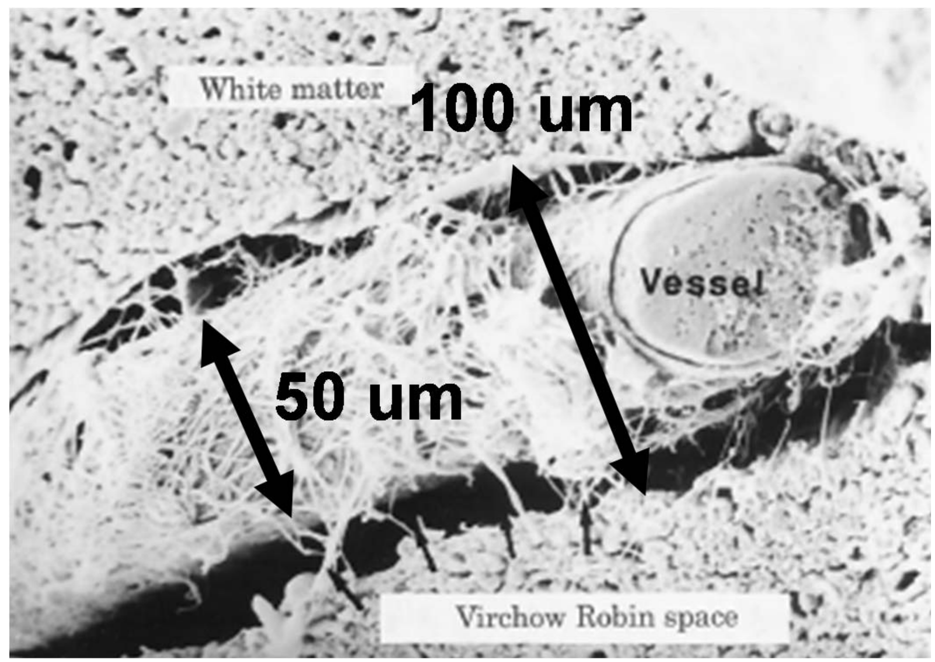


Allen, D. J. and F. N. Low (1975). "Scanning electron microscopy of the subarachnoid space in the dog. III. Cranial levels." The Journal of comparative neurology **161**(4): 515-539.

Spinal cord perivascular space (detailed)

"…the subpial space and the perivascular space communicate with the subarachnoid space via the fenestrae of the superficial layer of the pia mater. When horseradish peroxidase is injected into the subarachnoid space, it infiltrates gradually from the surface into the spinal cord over time from a few minutes to 1 hour, but reaches the interior of the spinal cord rapidly through the perivascular spaces." (Yoshizawa 2002)



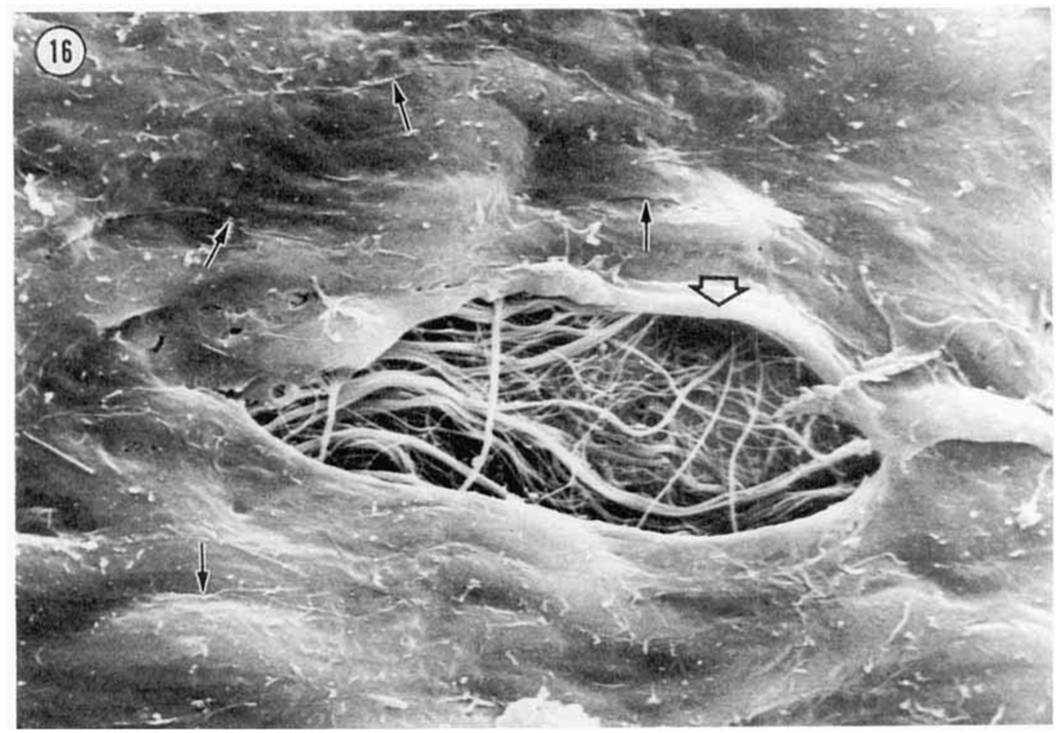


Yoshizawa, H. (2002). "Presidential address: pathomechanism of myelopathy and radiculopathy from the viewpoint of blood flow and cerebrospinal fluid flow including a short historical review." Spine (Phila Pa 1976) **27**(12): 1255-63.

Pia matter fenestration

Fenestration in spinal pia mater. Fenestrations of various sizes are common in the pial surface. This moderate sized fenestration results from a lack of surface pial cells. Pial connective tissue fibrils are revealed through the fenestration. The fibers are of various diameters and most appear to be arranged in the same direction. The smallest fibers are more random in arrangement. The edge of the fenestration **is** thickened (large arrow). The edges **of** flat pial cells (small arrows), and numerous microvilli can be observed. x 1,400. (Cloyd)

Interstitial brain fluid and CSF are nearly homogenous in composition due to the permeability of the pia mater (Guyton)



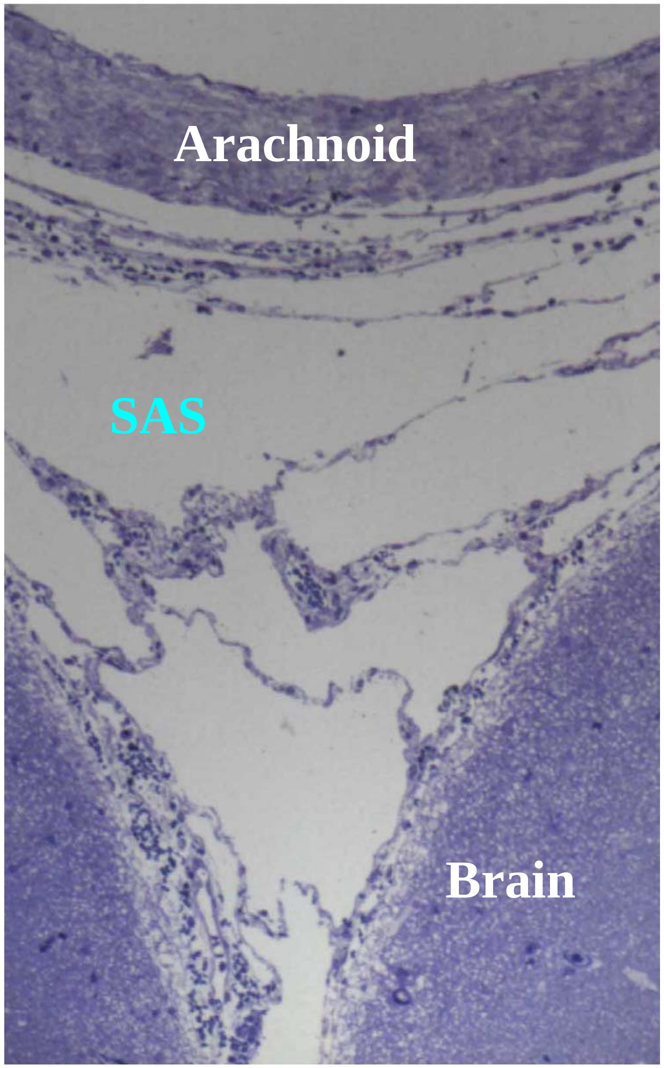
(3) Cloyd, M. W. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. I. Spinal cord levels." The Journal of comparative neurology **153**(4): 325-368.

Pia mater microstructure

View of transected spinal pia mater. The cut end of spinal cord (SPC) and its pia mater (PM) illustrates the arrangement of pial connective tissue fibers. There appear to be two layer of fibers. The first is a surface lamella (large arrows) which is covered by a smooth cellular lining facing the subarachnoid space. This delicate cellular lining is easily lacerated during preparation (small arrow). The connective tissue fibers in the surface lamella appear closely packed and are arranged longitudinal to the axis of the spinal cord. The second layer of connective tissue fibers lies deeper in the pial connective tissue space and is considerably thicker. The fibers of this layer for the most part either run longitudinal or circumferential to the cord. Some fibers are grouped into large bundles. x 320.

(3) Cloyd, M. W. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. I. Spinal cord levels." The Journal of comparative neurology **153**(4): 325-368.

Human Subarachnoid Space (SAS)



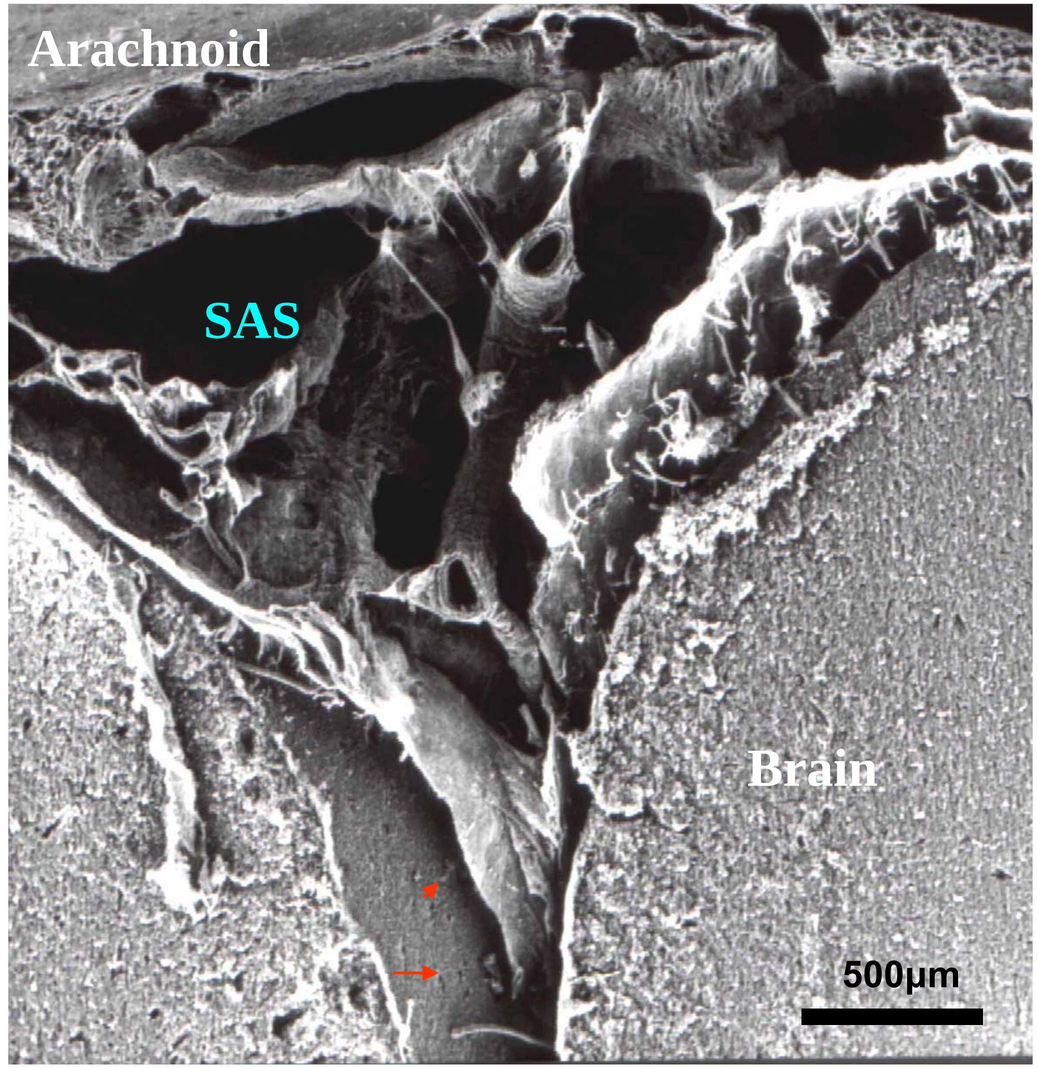
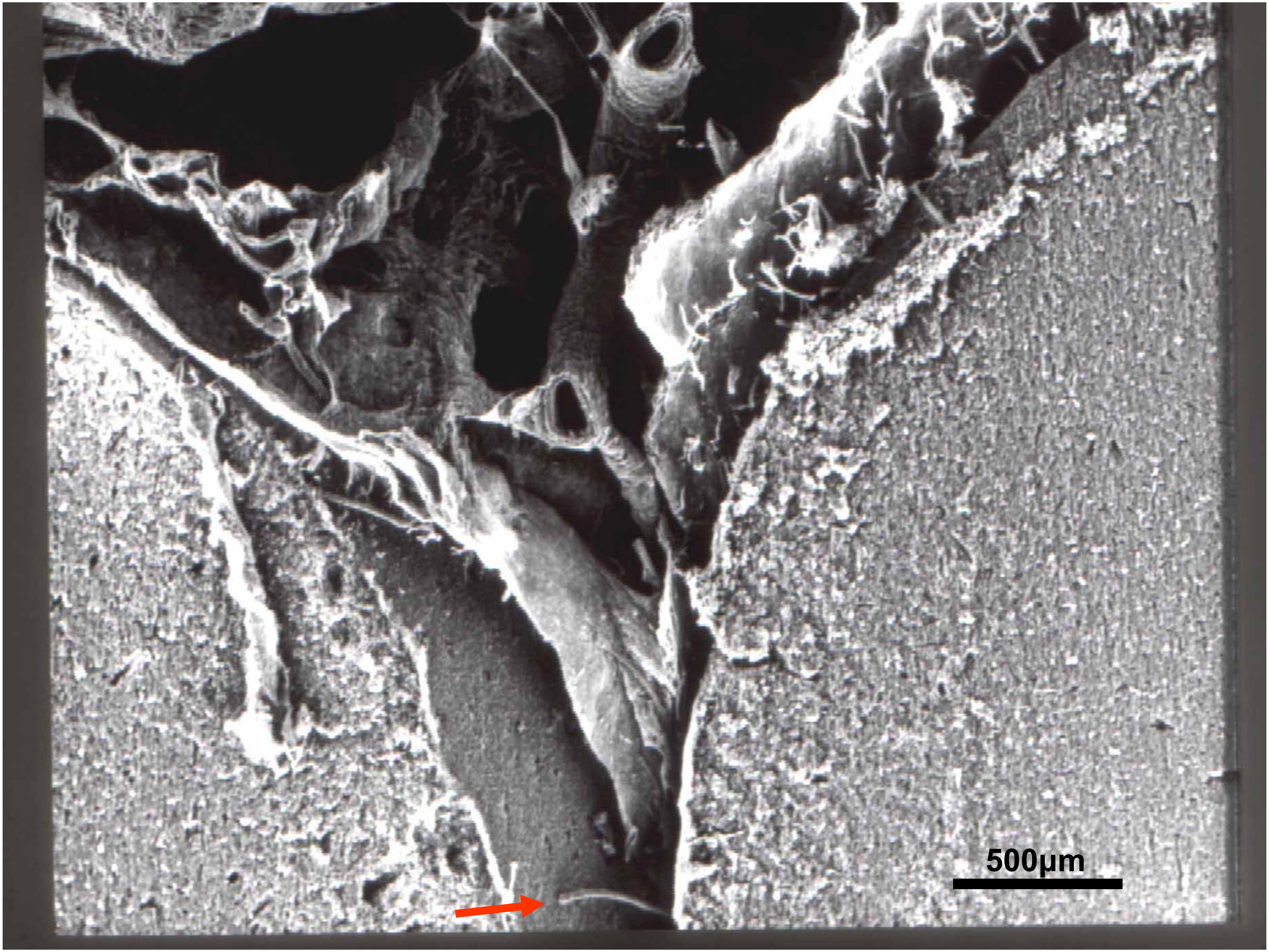
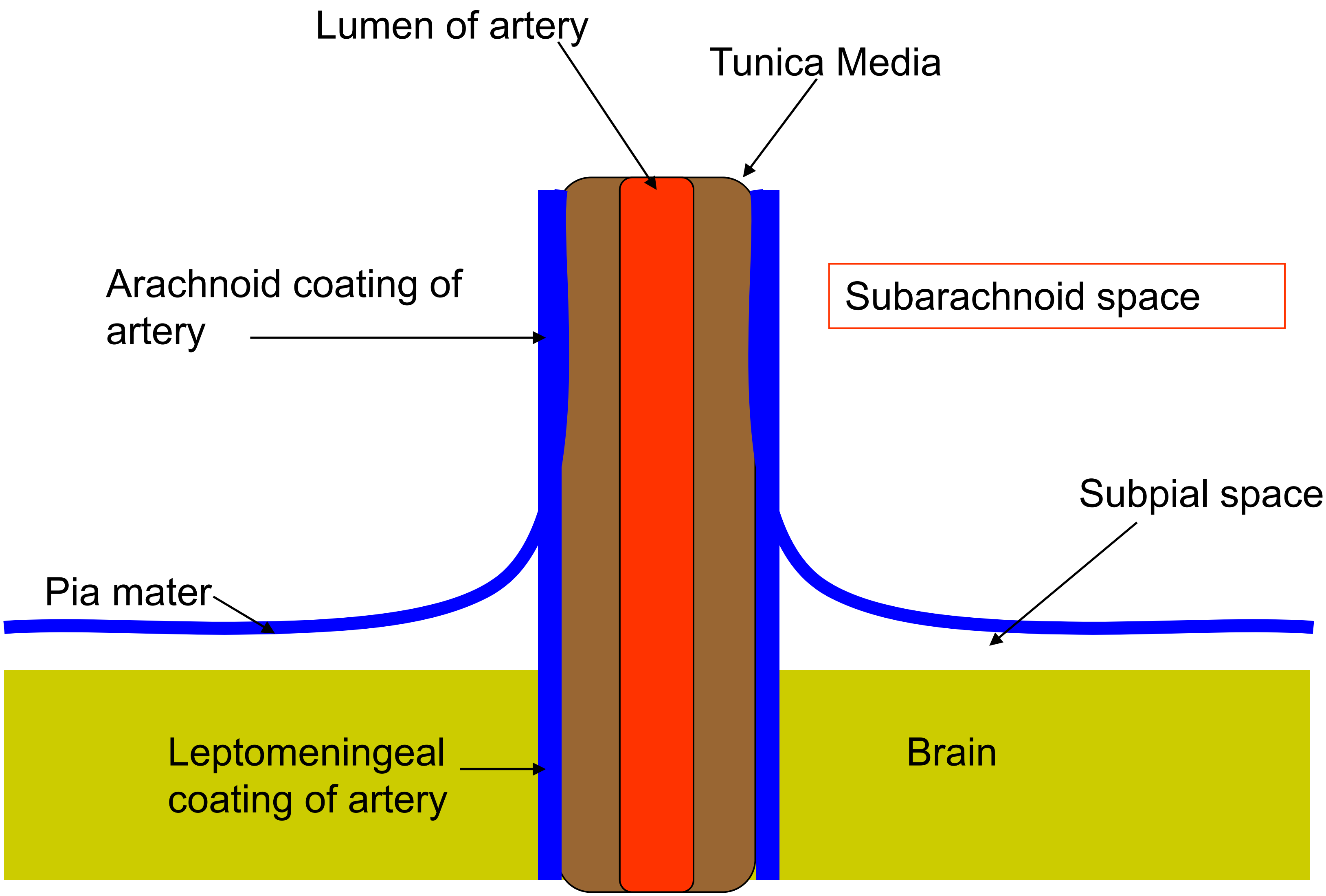


Figure from: Margaret Hutchings

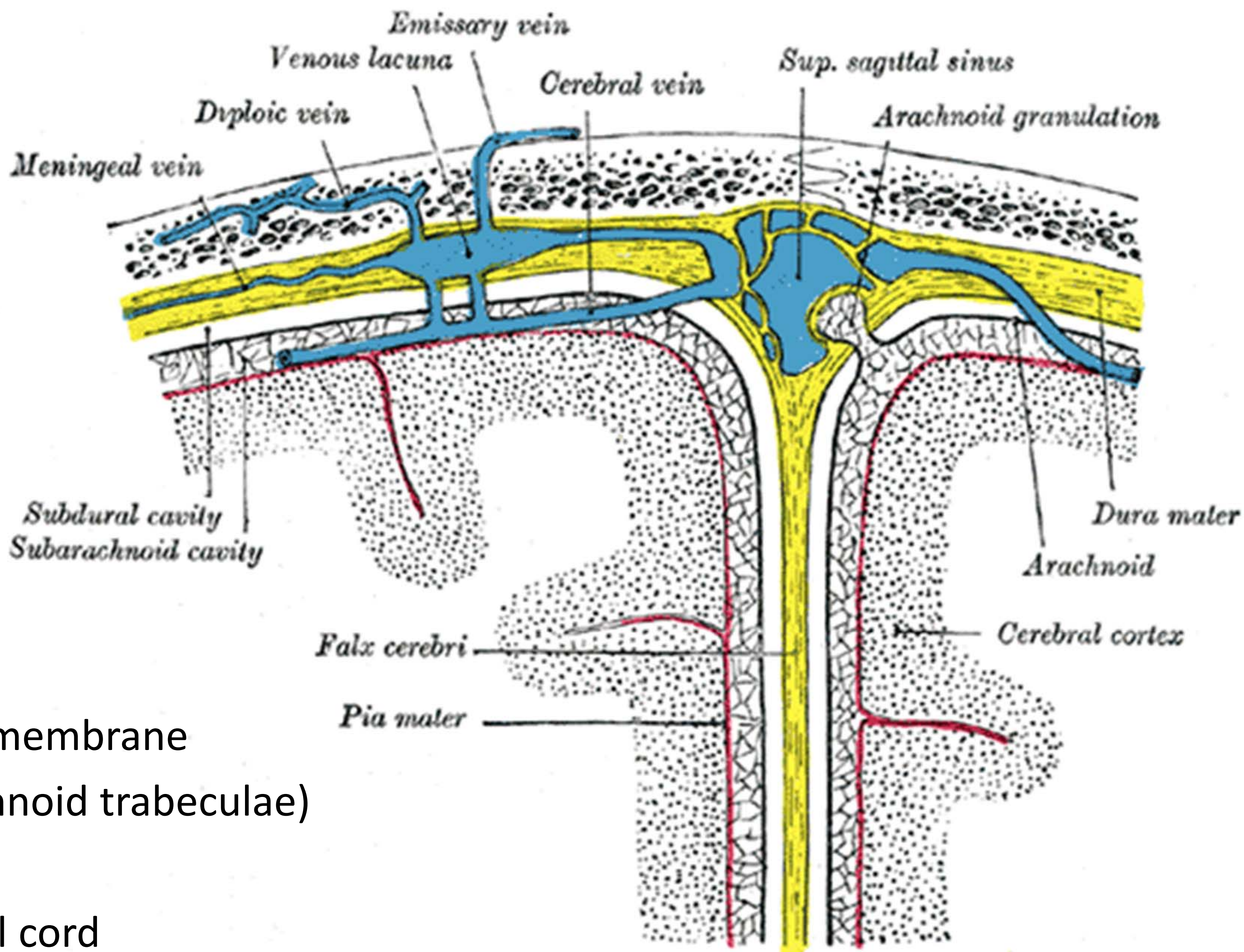

500µm



Arrangements of the Leptomeninges at the surface of the cerebral cortex (Hutchings and Weller 1986)(Zhang and Weller 1990)

Hutchings M, and Weller RO. Anatomical relationships of the pia mater to cerebral blood vessels in man. *Journal of Neurosurgery* 65: 316-325, 1986.
Zhang ET, Inman CB, and Weller RO. Interrelationships of the pia mater and the perivascular (Virchow-Robin) spaces in the human cerebrum. *J Anat* 170: 111-123, 1990.

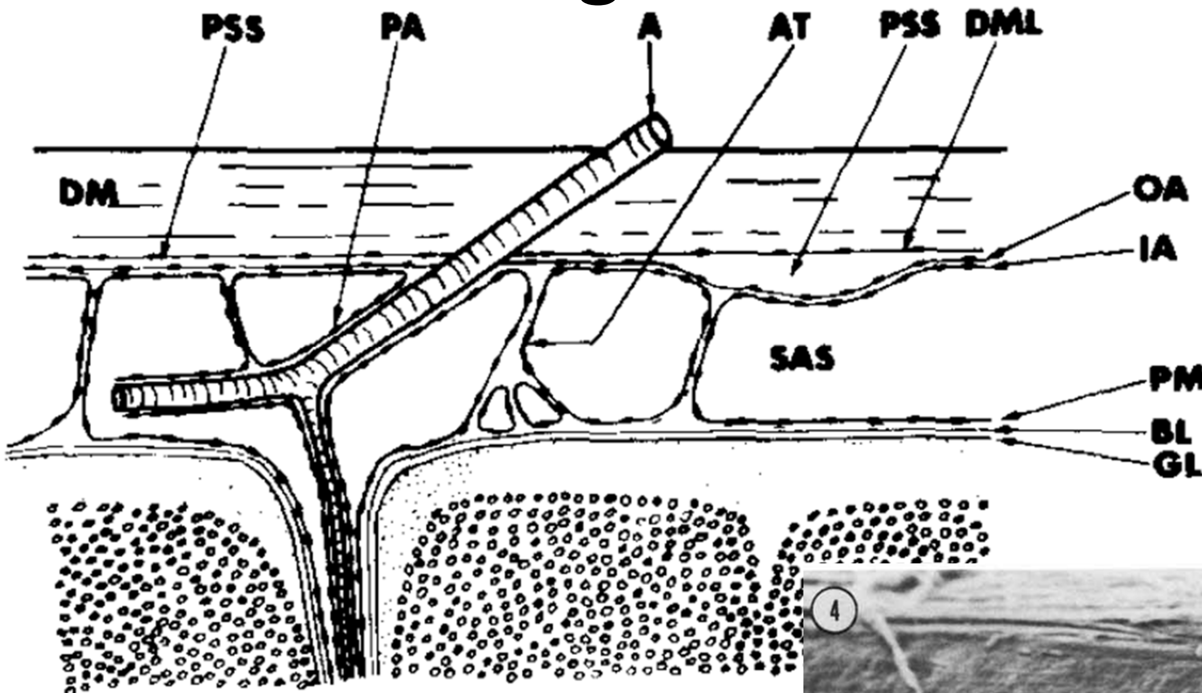
Meninges (layers) of the CNS

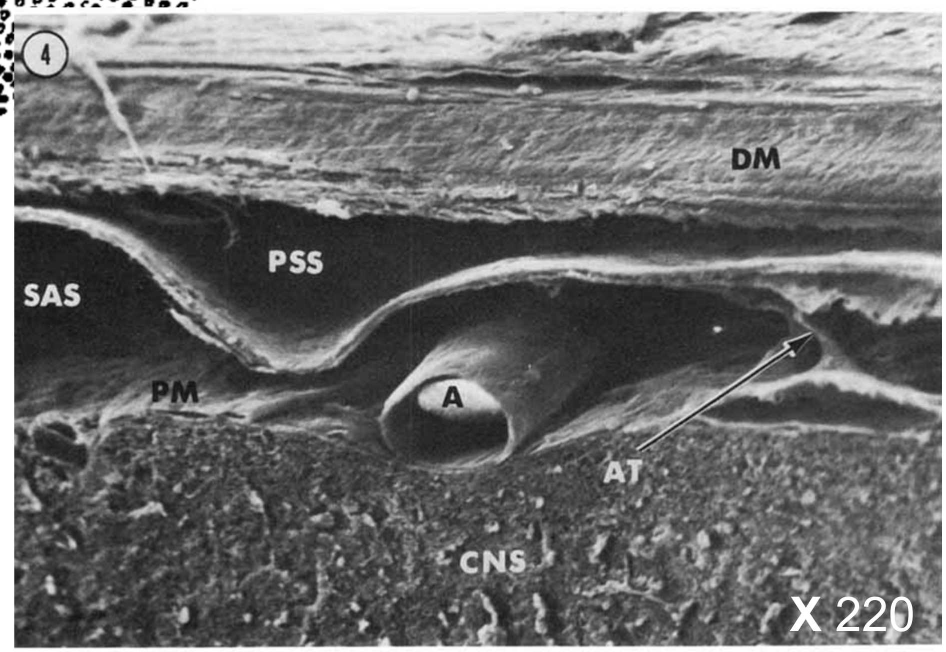


Outer to inner:

1. Skull
2. Dura mater
3. Arachnoid membrane
4. (CSF / arachnoid trabeculae)
5. Pia mater
6. Brain/spinal cord

Cranial meninges and subarachnoid space

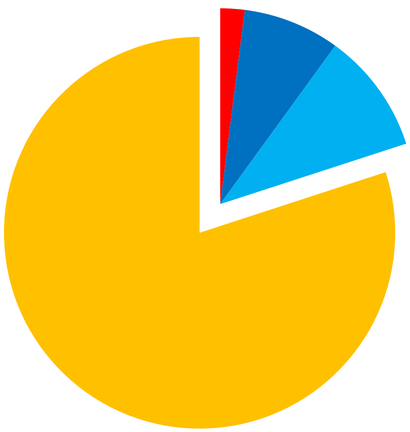




PSS, potential subdural space
DM, dura mater
PA, pia-arachnoid / leptomeninges
A, blood vessels
AT, arachnoid trabeculae
DML, inner suface of dura mater
OA, outer arachnoid (facing dura mater
IA, inner arachnoid (facing subarachnoid space
PM, pia mater
BL, basal lamina
GL, glia limitans

Allen, D. J. and F. N. Low (1975). "Scanning electron microscopy of the subarachnoid space in the dog. III. Cranial levels." The Journal of comparative neurology **161**(4): 515-539.

Brain and spinal cord anatomy



- Arterial blood (30 ml)
- Venous blood (120 ml)
- CSF (150 ml)
- brain tissue (1400 ml)

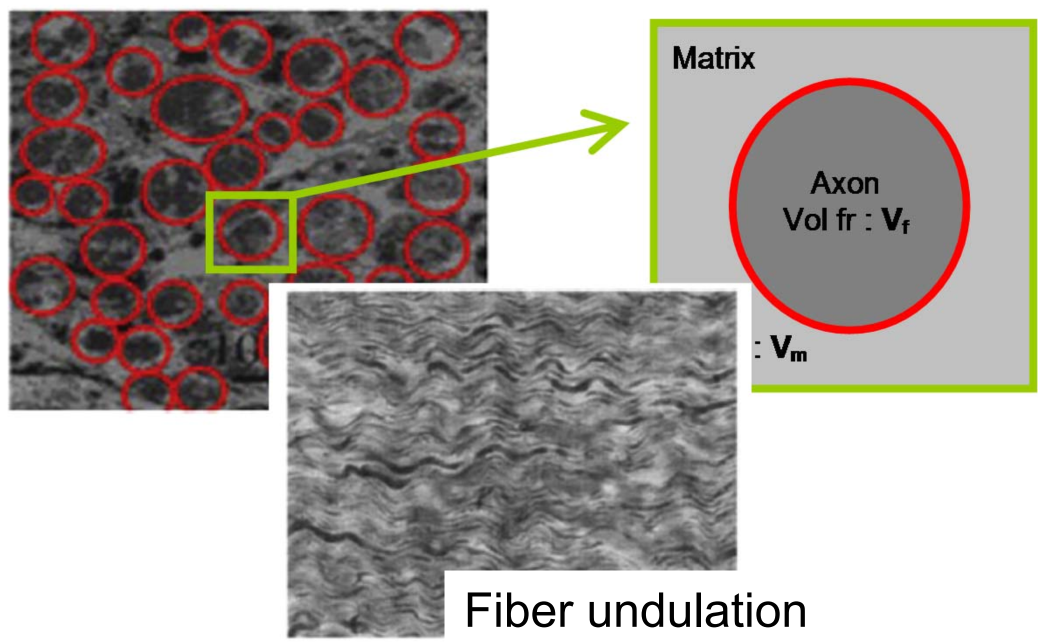
The brain has highly complex mechanical properties

- Anisotropic white matter
- Isotropic grey matter
- Viscoelastic throughout
- Shear modulus *10-10,000* Pa (lower in white)
- Porous (Nicholson)
  - 10x smaller in direction of fibers

Nicholson, C. and E. Syková (1998). "Extracellular space structure revealed by diffusion analysis." Trends in Neurosciences **21**(5): 207-215.
Pierpaoli, C. and P. J. Basser (1996). "Toward a quantitative assessment of diffusion anisotropy." Magnetic Resonance in Medicine **36**(6): 893-906.

Fiber tract geometry

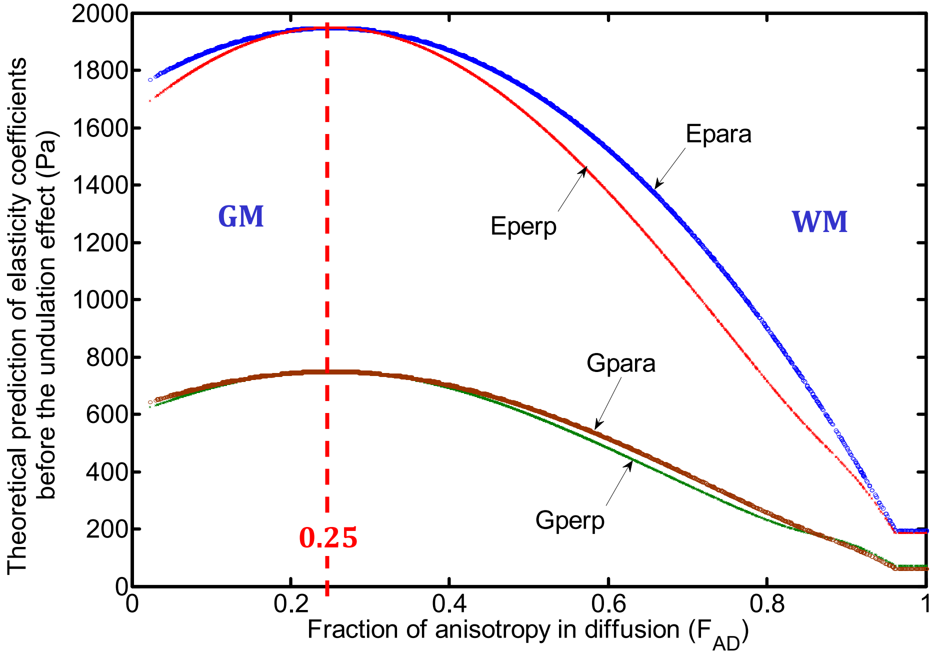
- ~ 15% fiber undulation results in a complex non-linear elasticity



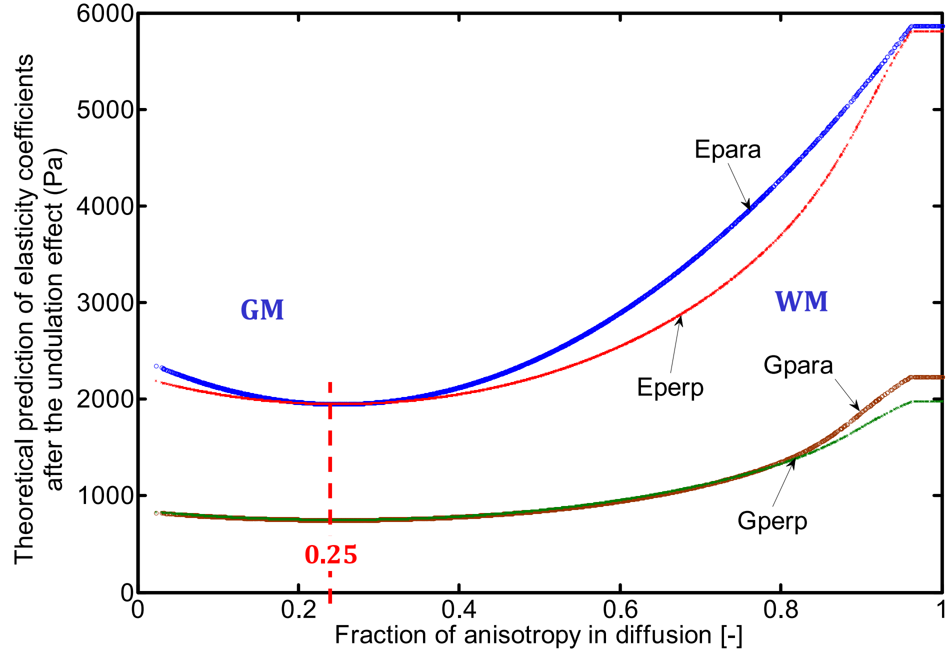
Bain, A. C., D. I. Shreiber, et al. (2003). "Modeling of Microstructural Kinematics During Simple Elongation of Central Nervous System Tissue." Journal of Biomechanical Engineering **125**(6): 798-804.
Karami, G., N. Grundman, et al. (2009). "A micromechanical hyperelastic modeling of brain white matter under large deformation." Journal of the Mechanical Behavior of Biomedical Materials **2**(3): 243-254.

Effect of fiber undulation could be to make two separate elasticity regimes

Regime 1: <15% stretch



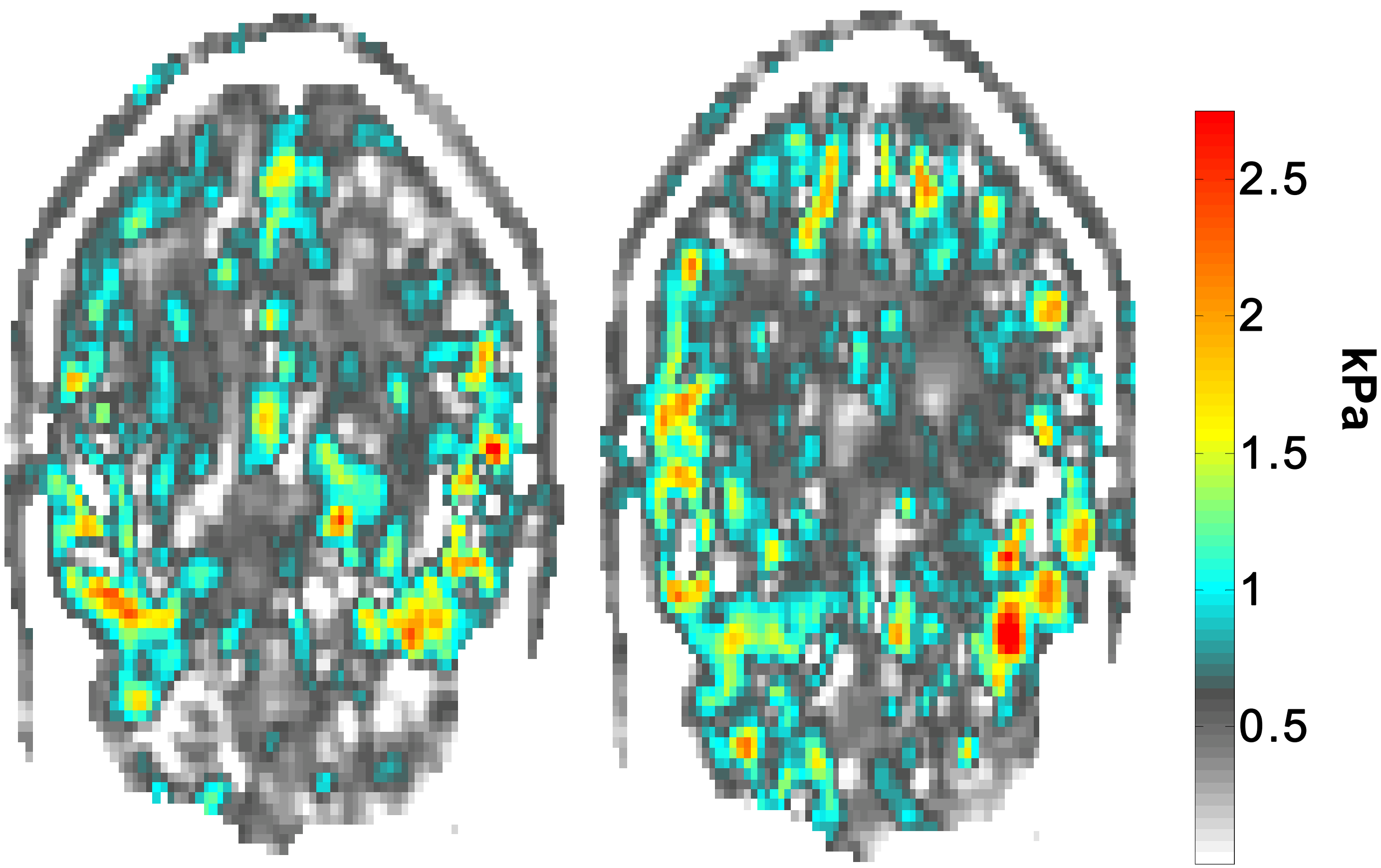
Regime 2: >15% stretch



Unpublished, K. Shahim, Bryn A. Martin, J.-M. Drezet, R. Sinkus, J.-F. Molinari, S. Momjian, “Evolution of brain parenchyma elastic properties in the development of normal pressure hydrocephalus,” (submitted, January 2011).

Magnetic resonance elastography for material properties of brain

Shear moduli parallel (left) and perpendicular (right) to fiber tracts



Green, M. A., L. E. Bilston, et al. (2008). "In vivo brain viscoelastic properties measured by magnetic resonance elastography." NMR in Biomedicine 21(7): 755-764.

Spinal cord nerve roots

- Various types in different regions of the SC

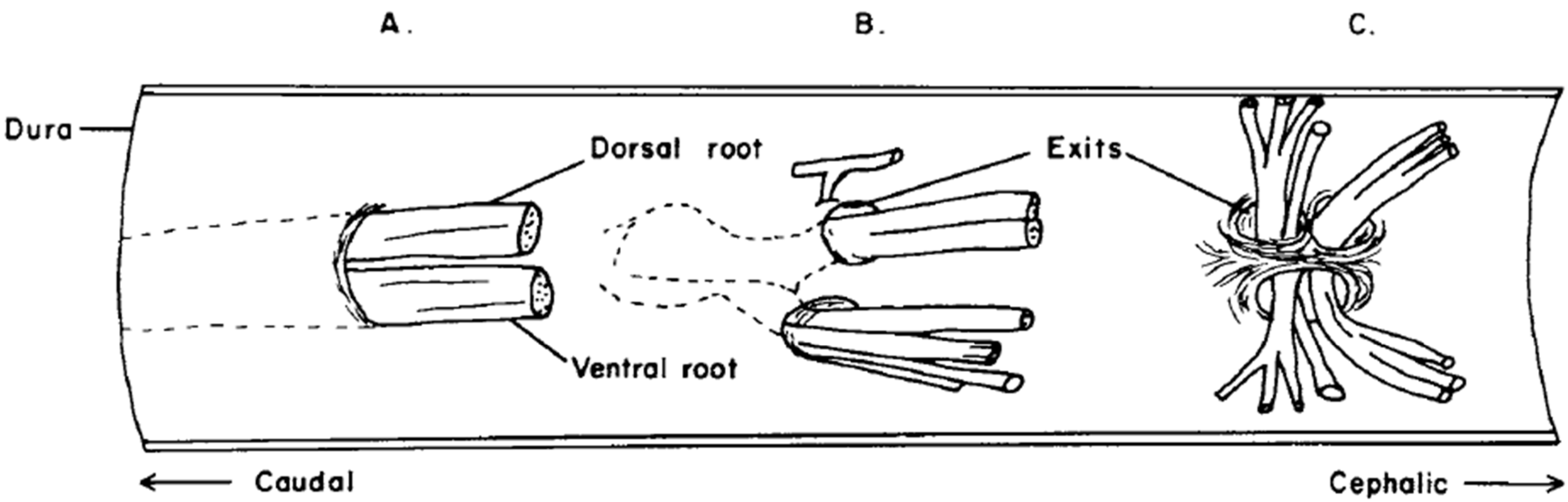


Fig. 1 *Nerve root exits.* A is a single exit of the tvpe found in lower lumbar and sacral levels. B is a typical double exit from the thoracic region and C a more complicated type from the lower cervical region. Drawn from laboratory observations.

Malloy, J. J. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. II. Spinal nerve exits." The Journal of comparative neurology **157**(1): 87-107.

Spinal cord nerve roots

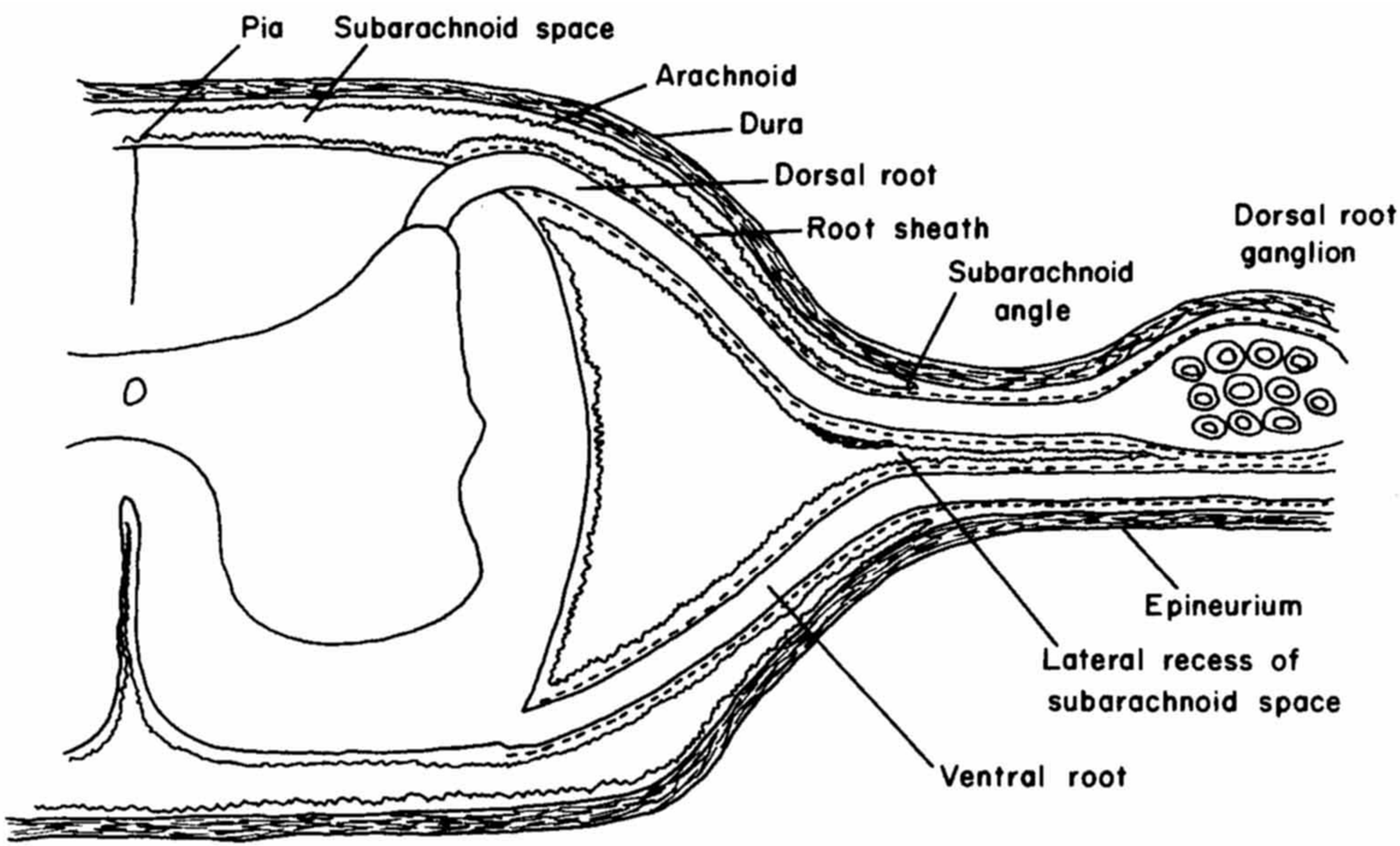
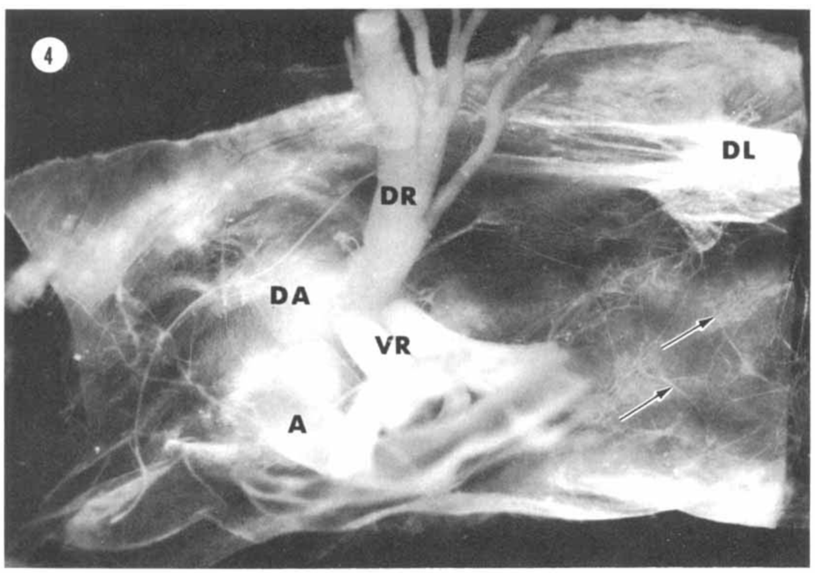


Figure redrawn and modified from McCabe and Low ('69) and Himango and Low ('71) by: Malloy, J. J. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. II. Spinal nerve exits." The Journal of comparative neurology **157**(1): 87-107.

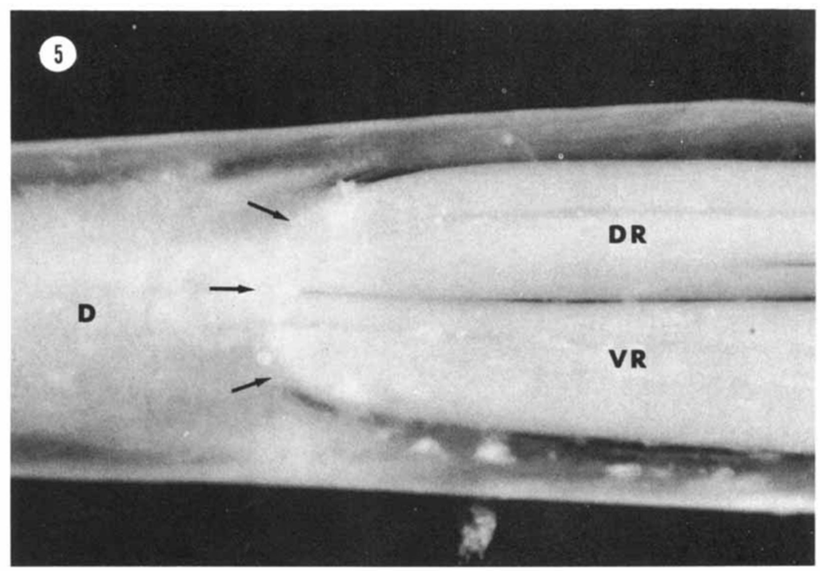
Nerve root anatomy

The dorsal root **(DR)** and ventral root **(VR)** converge on one another and pass through the dura-arachnoid **(DA)** by means of a single exit. The cerebrospinal artery **(A)** enters the subarachnoid space cephalic to the ventral root. An attachment **of** the denticulate ligament **(DL)** is located caudally and is slightly dorsal to the nerve exit. Numerous arachnoid trabeculae (arrows) can be seen in this **35** mm light micrograph. x **15.**

Cervical nerve root



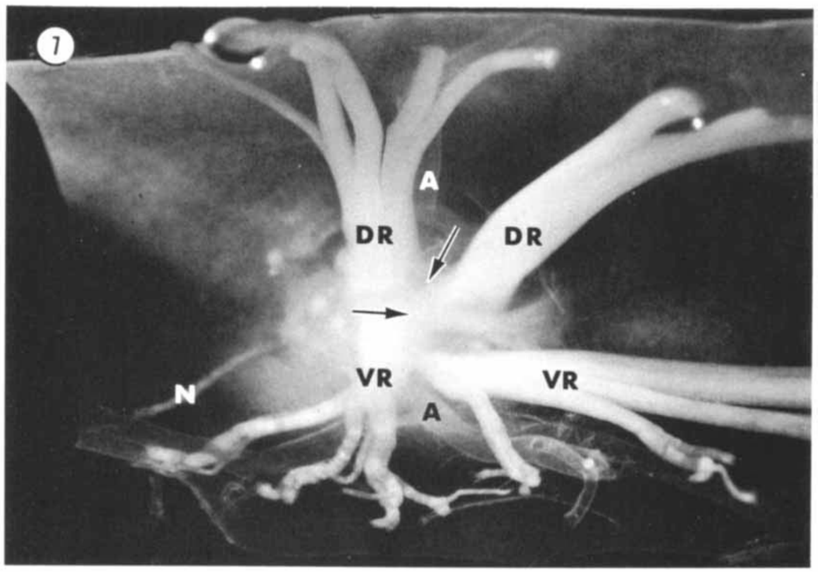
Lumbar nerve root



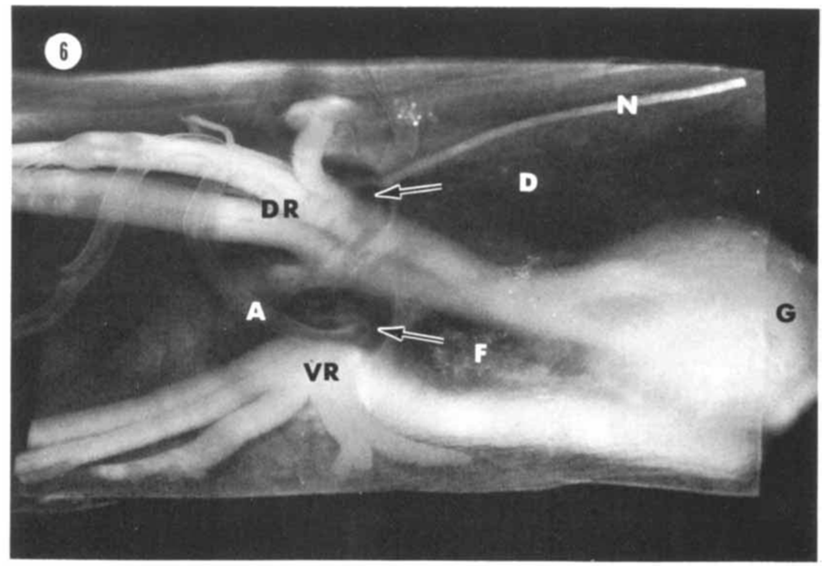
Malloy, J. J. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. II. Spinal nerve exits." The Journal of comparative neurology **157**(1): 87-107.

More on nerve roots

Cervical multiple exit nerve root



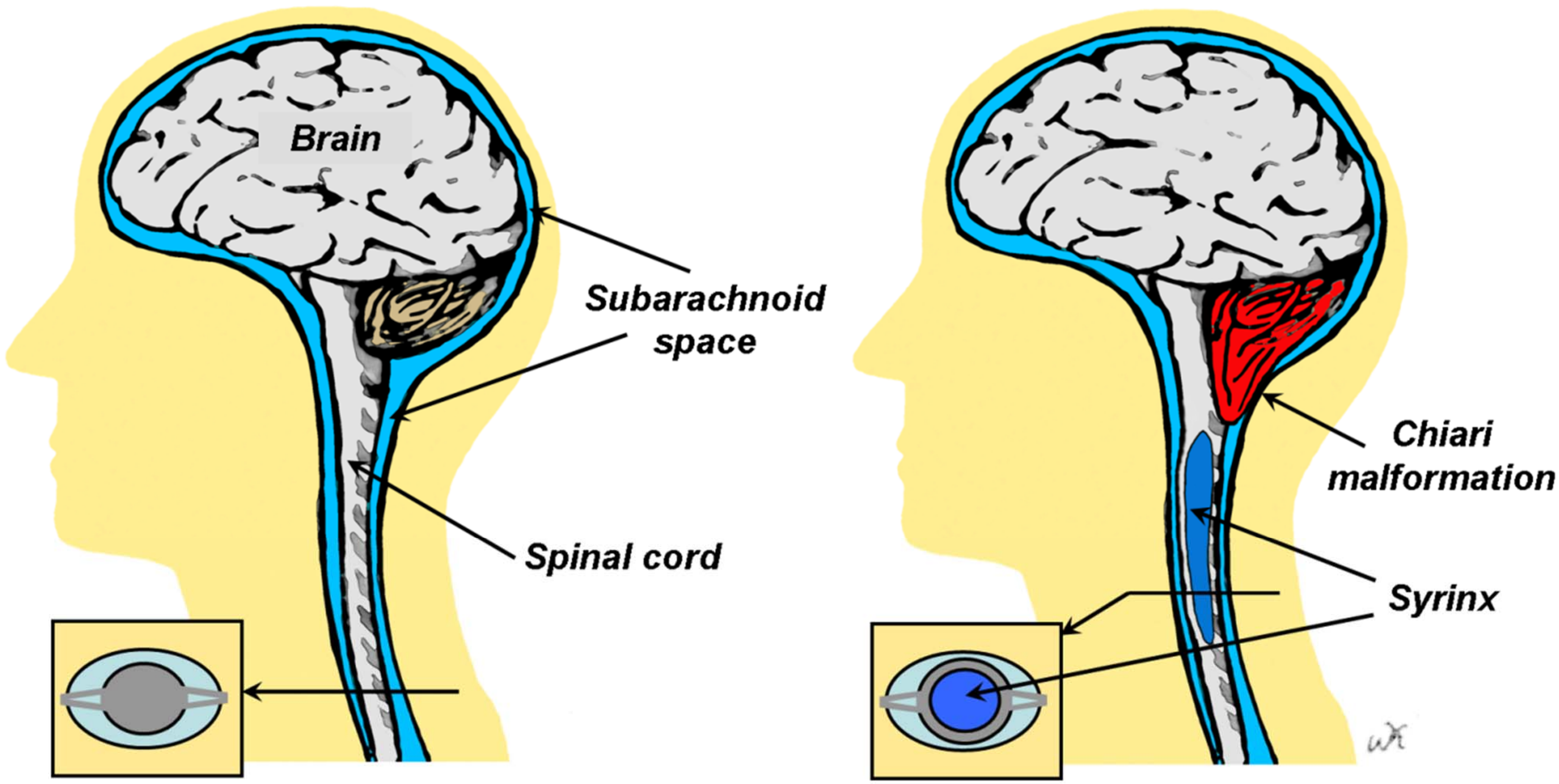
Lumbar double nerve root



Malloy, J. J. and F. N. Low (1974). "Scanning electron microscopy of the subarachnoid space in the dog. II. Spinal nerve exits." The Journal of comparative neurology **157**(1): 87-107.

Current areas of research in neurohydrodynamics

Craniospinal disorders: Chiari malformation



Could flow resistance through the craniospinal junction be an indicator of **Chiari "0"**

- Higher CSF flow resistance in Chiari patients?

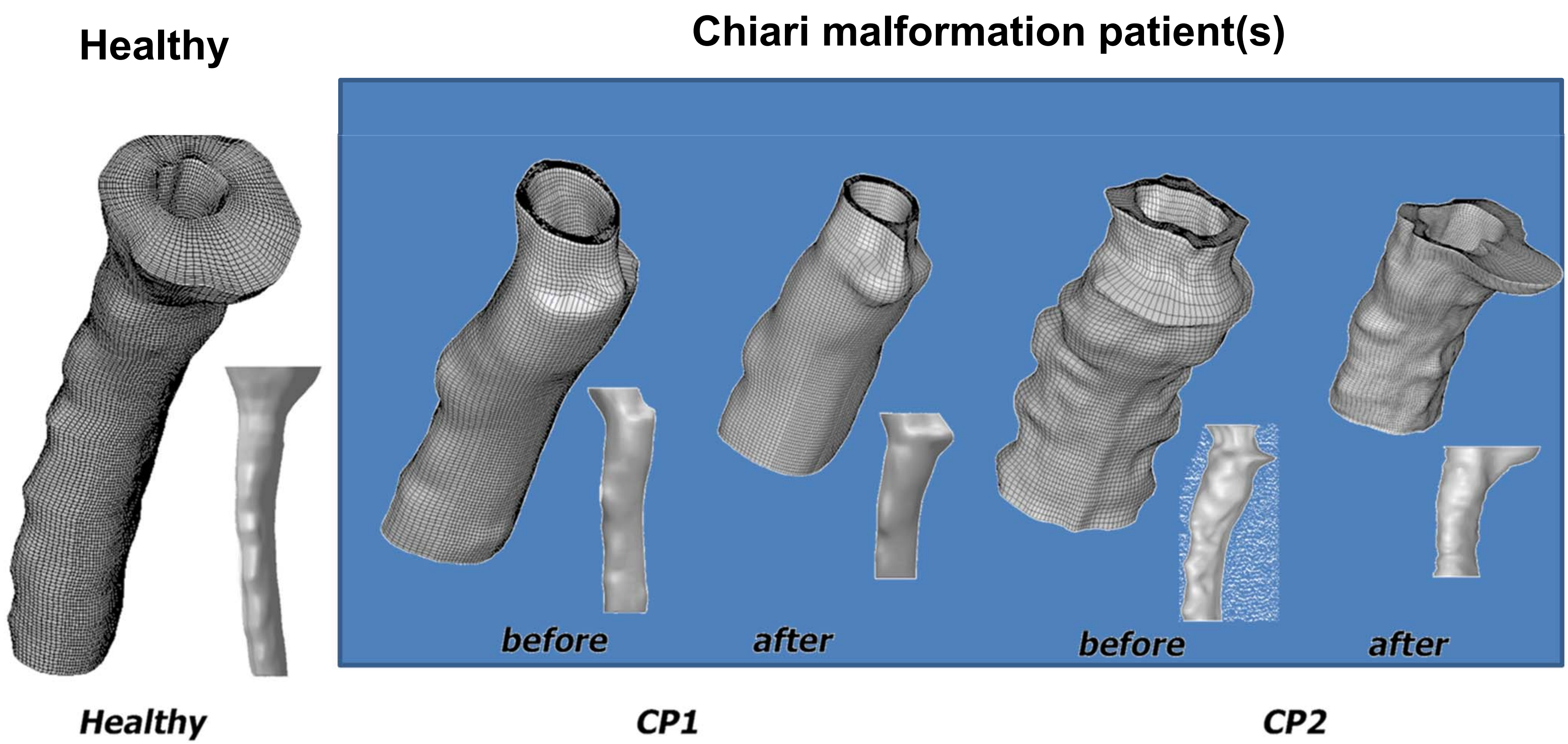


Image courtesy of Dr. Francis Loth, University of Akron, Biofluids Laboratory

Successful decompression surgery decreases flow resistance?

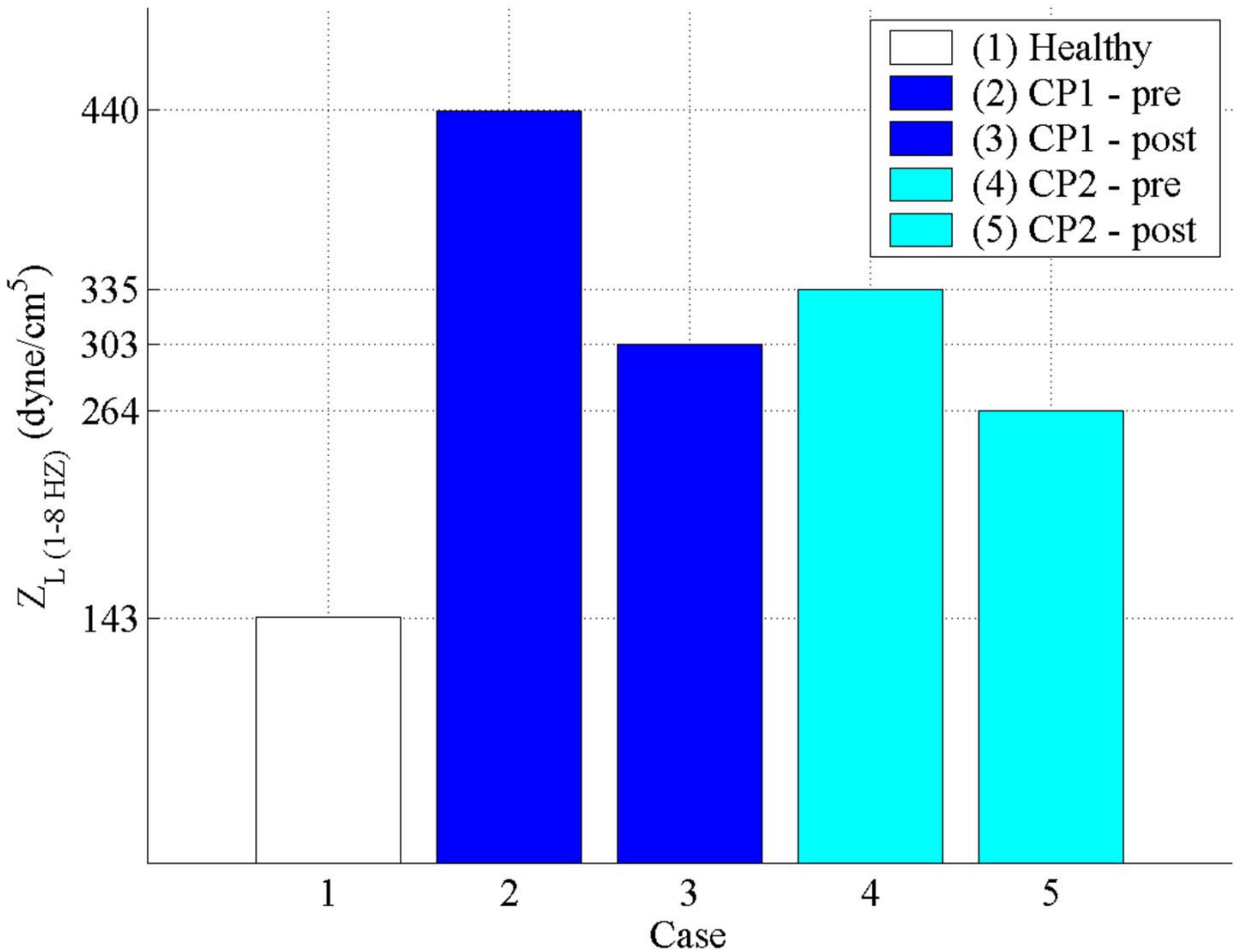
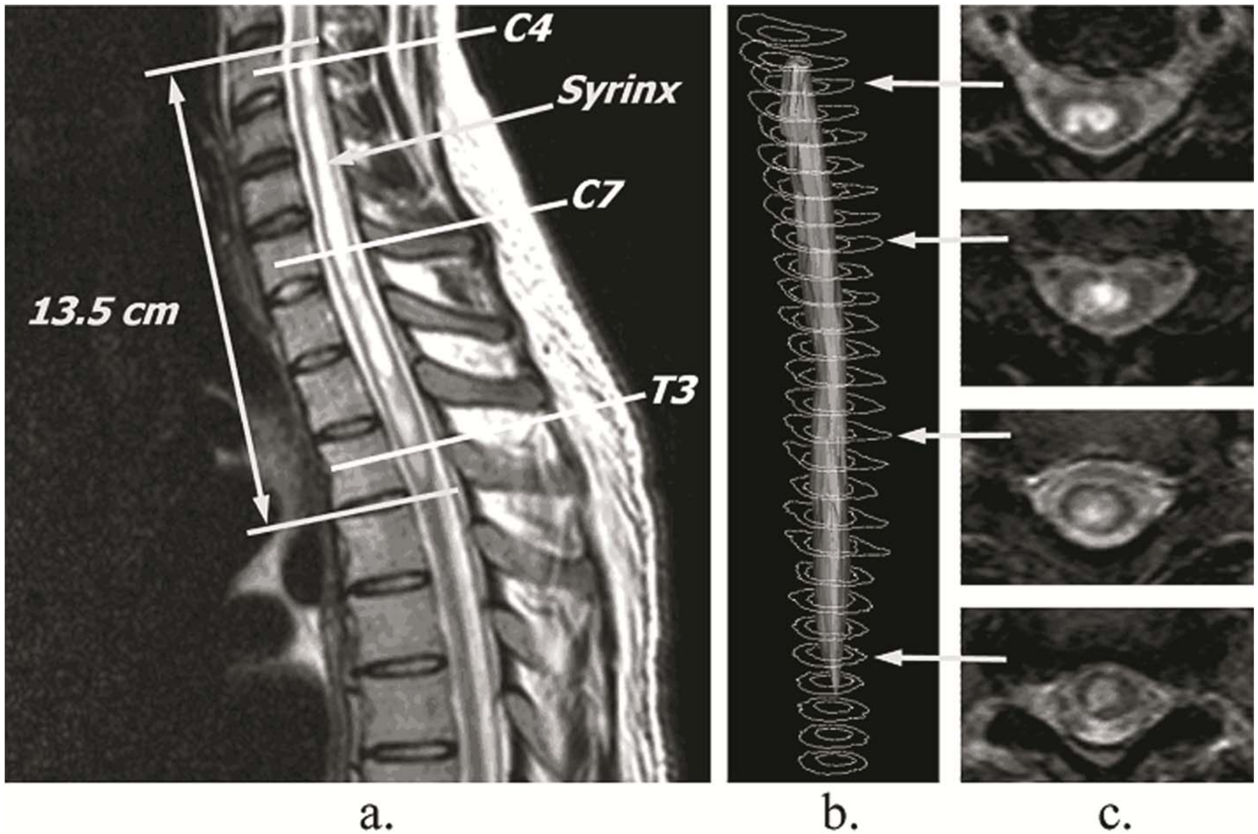


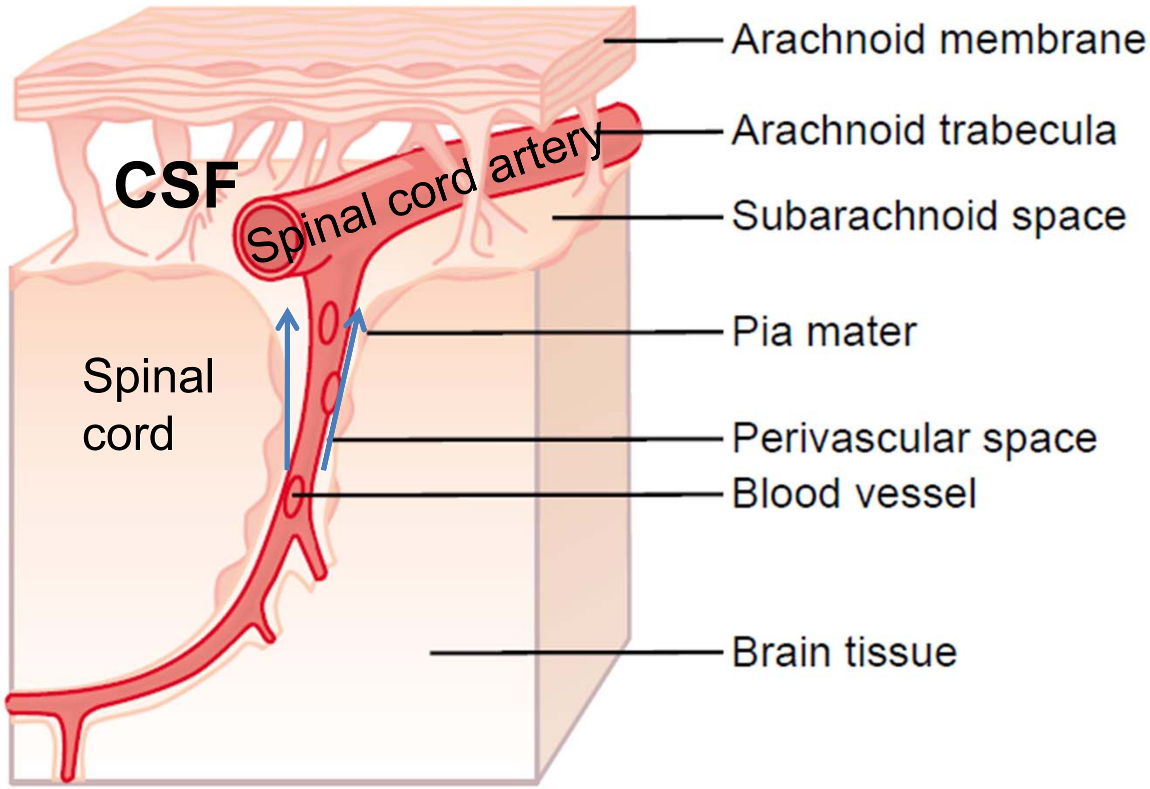
Image courtesy of Dr. Francis Loth, University of Akron, Biofluids Laboratory

Craniospinal disorders: Syringomyelia



Martin, B. A., W. Kalata, et al. (2005). "Syringomyelia hydrodynamics: an in vitro study based on in vivo measurements." J Biomech Eng **127**(7): 1110-20.
Martin, B.A., et al., *Spinal Canal Pressure Measurements in an In Vitro Spinal Stenosis Model: Implications on Syringomyelia Theories.* J Biomech Eng, 2009. **In Press**(June 2009).
Martin, B.A. and F. Loth, *The influence of coughing on cerebrospinal fluid pressure in an in vitro syringomyelia model with spinal subarachnoid space stenosis.* Cerebrospinal Fluid Res, 2009. **6**(1): p. 17.

Could the relative timing of CSF and blood pulsations help explain **syringomyelia**?

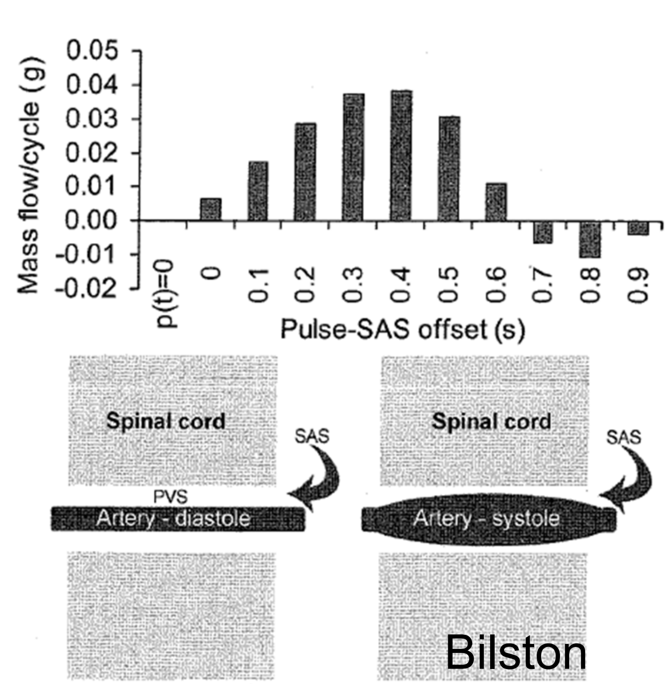


- Spinal cord perivascular spaces are a “specialized lymphatic system” (Guyton et al.)

Guyton, A. C. and J. E. Hall (2006). Textbook of medical physiology. Philadelphia, Elsevier Saunders.

Vessels entering the neural tissue could “milk” fluid in the Virchow-Robin spaces

- CSF/blood phase
- Theory (Madsen , Luciano)
- Simulation (Bilston)
- Experiments (Stoodley)



Bilston, L. E., M. A. Stoodley, et al. (2009). "The influence of the relative timing of arterial and subarachnoid space pulse waves on spinal perivascular cerebrospinal fluid flow as a possible factor in syrinx development." J Neurosurg.
Stoodley, M. A., B. Gutschmidt, et al. (1999). "Cerebrospinal fluid flow in an animal model of noncommunicating syringomyelia." Neurosurgery **44**(5): 1065-75; discussion 1075-6.
Luciano, M. and S. Dombrowski (2007). "Hydrocephalus and the heart: interactions of the first and third circulations." Cleve Clin J Med **74 Suppl 1**: S128-31.
Madsen, J. R., M. Egnor, et al. (2006). "Cerebrospinal fluid pulsatility and hydrocephalus: the fourth circulation." Clin Neurosurg **53**: 48-52.

Craniospinal disorders: Hydrocephalus

Is craniospinal compliance a missing link in **hydrocephalus** assessment?

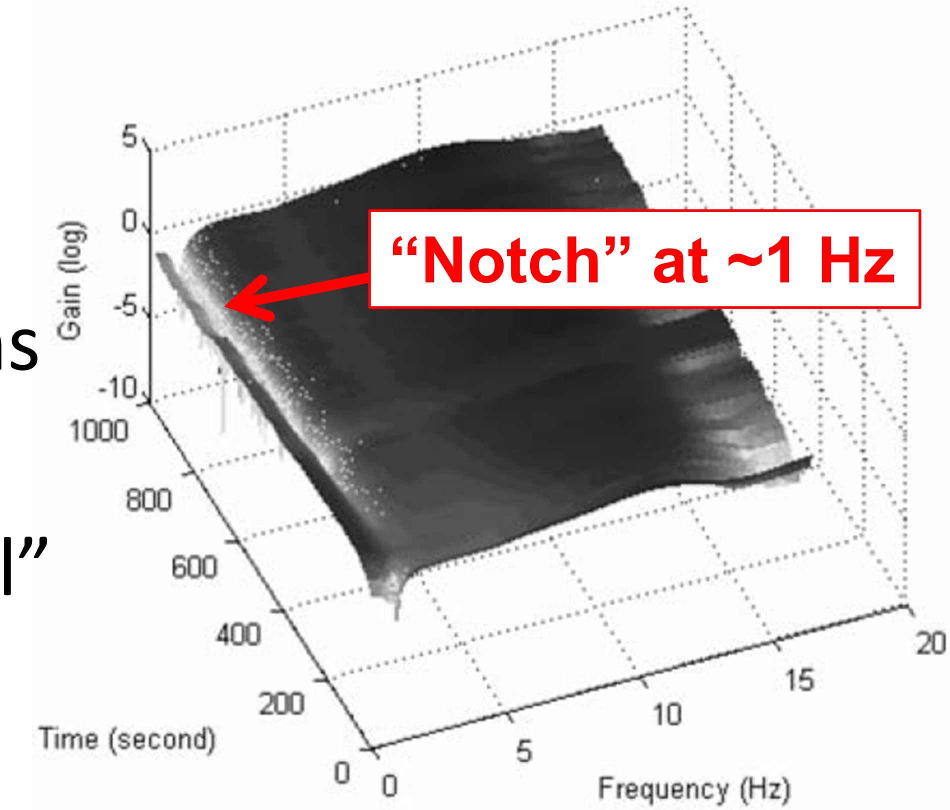
Hydrocephalus types

- Obstructive (no aqueduct)
  - Provide aqueduct with shunt
- Communicating (↑prod. or ↓absorption CSF)
  - Increase absorption with shunt
- Normal pressure (insufficient craniospinal compliance?)
  - Normal pressure, but larger ICP osc. amplitude?
  - (Eide, Czosnyka)

Eide, P. K. and A. Brean (2006). "Intracranial pulse pressure amplitude levels determined during preoperative assessment of subjects with possible idiopathic normal pressure hydrocephalus." Acta Neurochir (Wien) **148**(11): 1151-6; discussion 1156.
Eide, P. K. and W. Sorteberg (2008). "Changes in intracranial pulse pressure amplitudes after shunt implantation and adjustment of shunt valve opening pressure in normal pressure hydrocephalus." Acta Neurochir (Wien) **150**(11): 1141-7; discussion 1147.
Czosnyka, Z., N. Keong, et al. (2008). "Pulse amplitude of intracranial pressure waveform in hydrocephalus." Acta Neurochir Suppl **102**: 137-40.

Is the spine a "notch" filter to dampen CSF pressure oscillations?

- CBF → CSF
- CSF → spinal canal
- Spinal canal dampens CSF oscillations
- "cerebral Windkessel"
- (madsen, luciano)



Madsen, J. R., M. Egnor, et al. (2006). "Cerebrospinal fluid pulsatility and hydrocephalus: the fourth circulation." Clin Neurosurg **53**: 48-52.

Luciano, M. and S. Dombrowski (2007). "Hydrocephalus and the heart: interactions of the first and third circulations." Cleve Clin J Med **74 Suppl 1**: S128-31.

Craniospinal disorders: tethered spinal cord

Craniospinal disorder: pseudotumor cerebri

- To be added soon

Intrathecal drug delivery

- Drugs that enter the blood stream can not penetrate and function in the brain, but instead must be administered into the cerebrospinal fluid (Guyton)

Direct drug delivery to brain (epilepsy)

- To be added

Cerebral venous innsuficiency

Alzheimer's disease

Multiple sclerosis

Interstitial fluid movement

Current diagnostic and imaging trends in neurohydrodynamics

4DMRI

MRI pulse wave velocity

MRI elastography

MRI diffusion tensor imaging

MRI spectroscopy

More information

Neurohydrodynamics wiki research site of Dr. Bryn Martin:

- www.neurohydrodynamics.com
- Please direct questions on this presentation to: mail@neurohydrodynamics.com