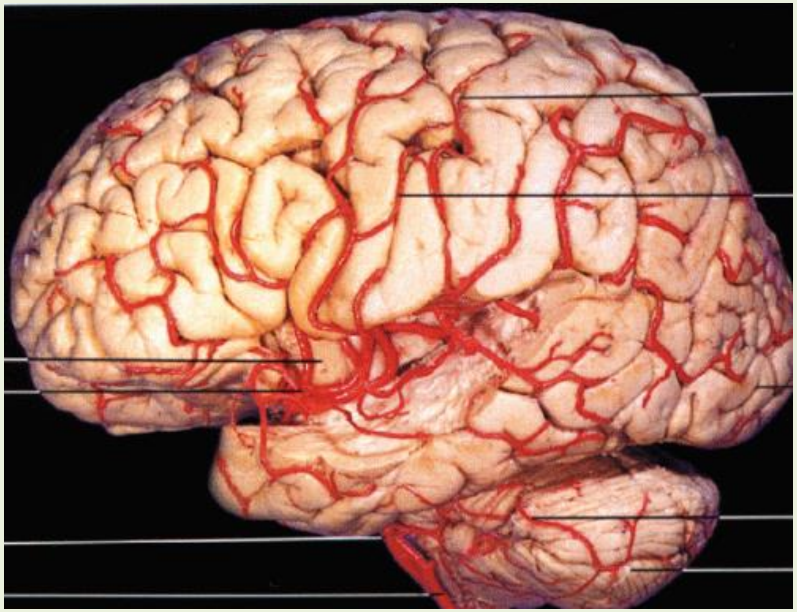
2. Cerebral blood flow and Metabolism



Impact Factor

Impact Factor: 5.457*
Rank:
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2009 Journal Citation Report (Thomson Reuters, 2010)

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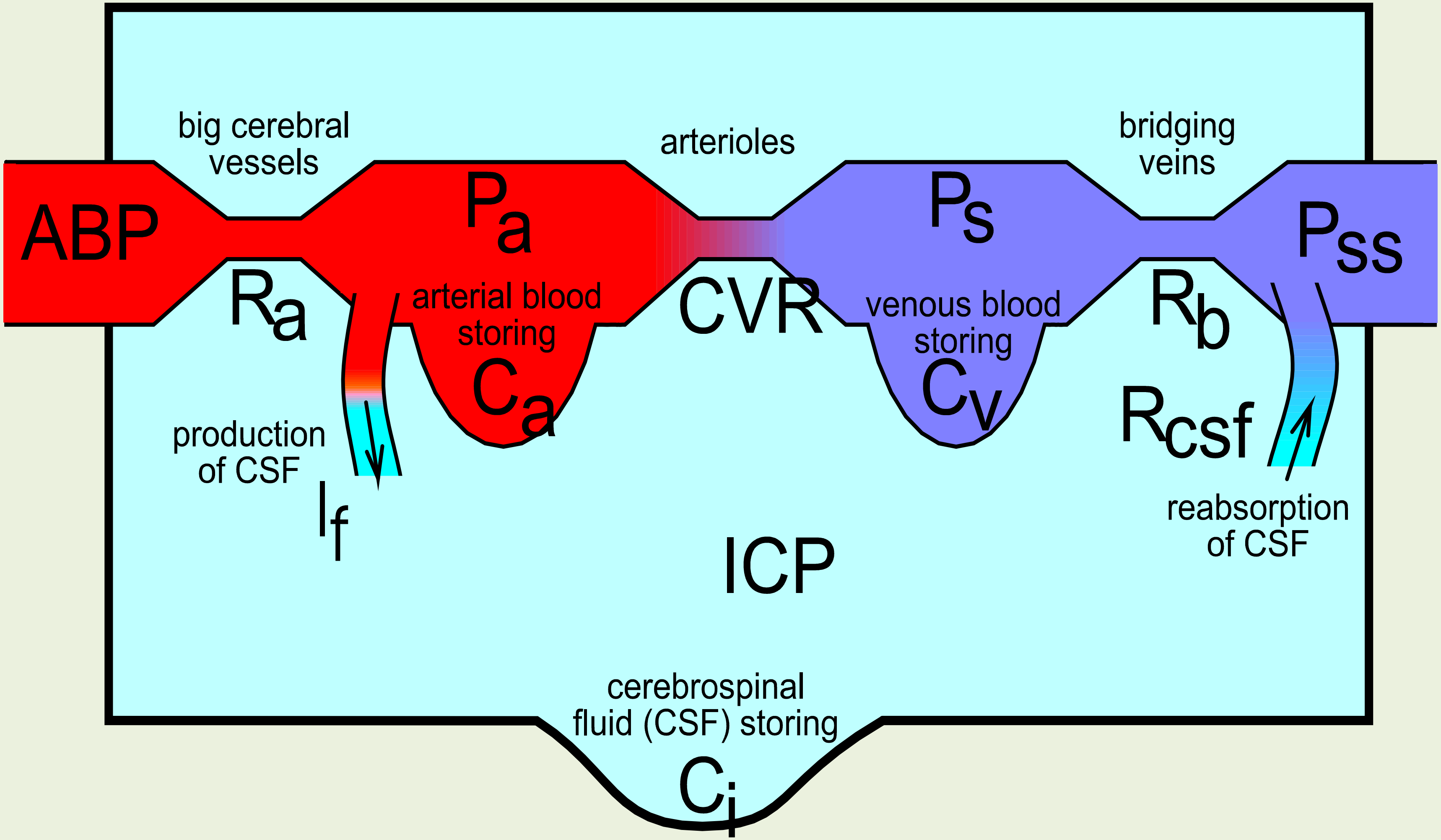
BIOSIS

Global Model of Cerebral Blood Flow and Circulation of Cerebrospinal Fluid- Naive Model



Czosnyka M, Piechnik S, Richards HK, Kirkpatrick P, Smielewski P, Pickard JD. Contribution of mathematical modelling to the bedside tests of cerebrovascular autoregulation. Journal of Neurology, Neurosurgery, and Psychiatry 1997; 63:721-731

Blood Supply in Numbers

Blood flow through whole brain (adult) = 750-1000 ml/min
Blood flow through whole brain (adult) = 54 ml/100 g/min
Blood flow through whole brain (child) = 105 ml/100 g/min

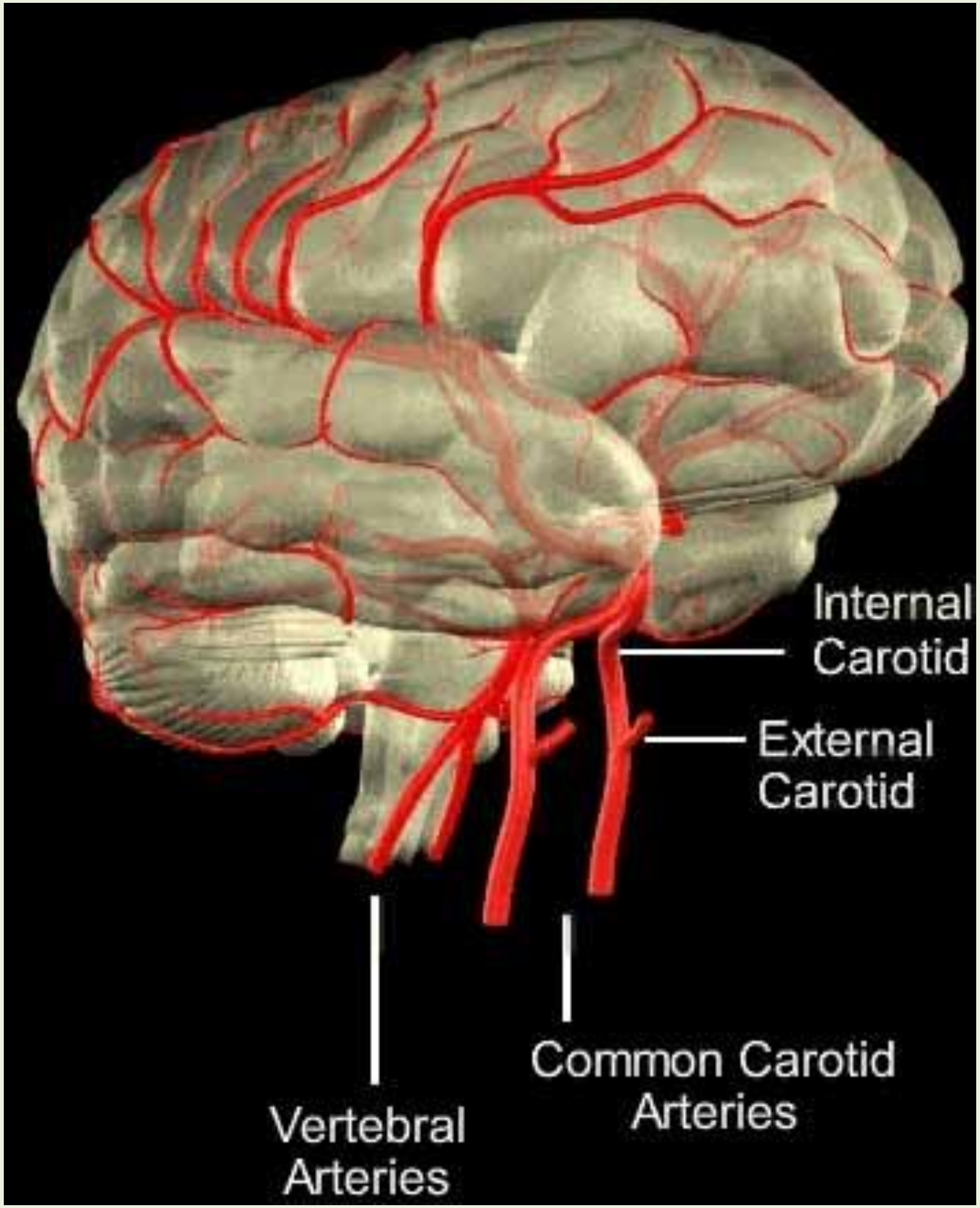
% brain utilization of total resting oxygen = 20%
% blood flow from heart to brain = 15-20% (Kandel et al., 2000)

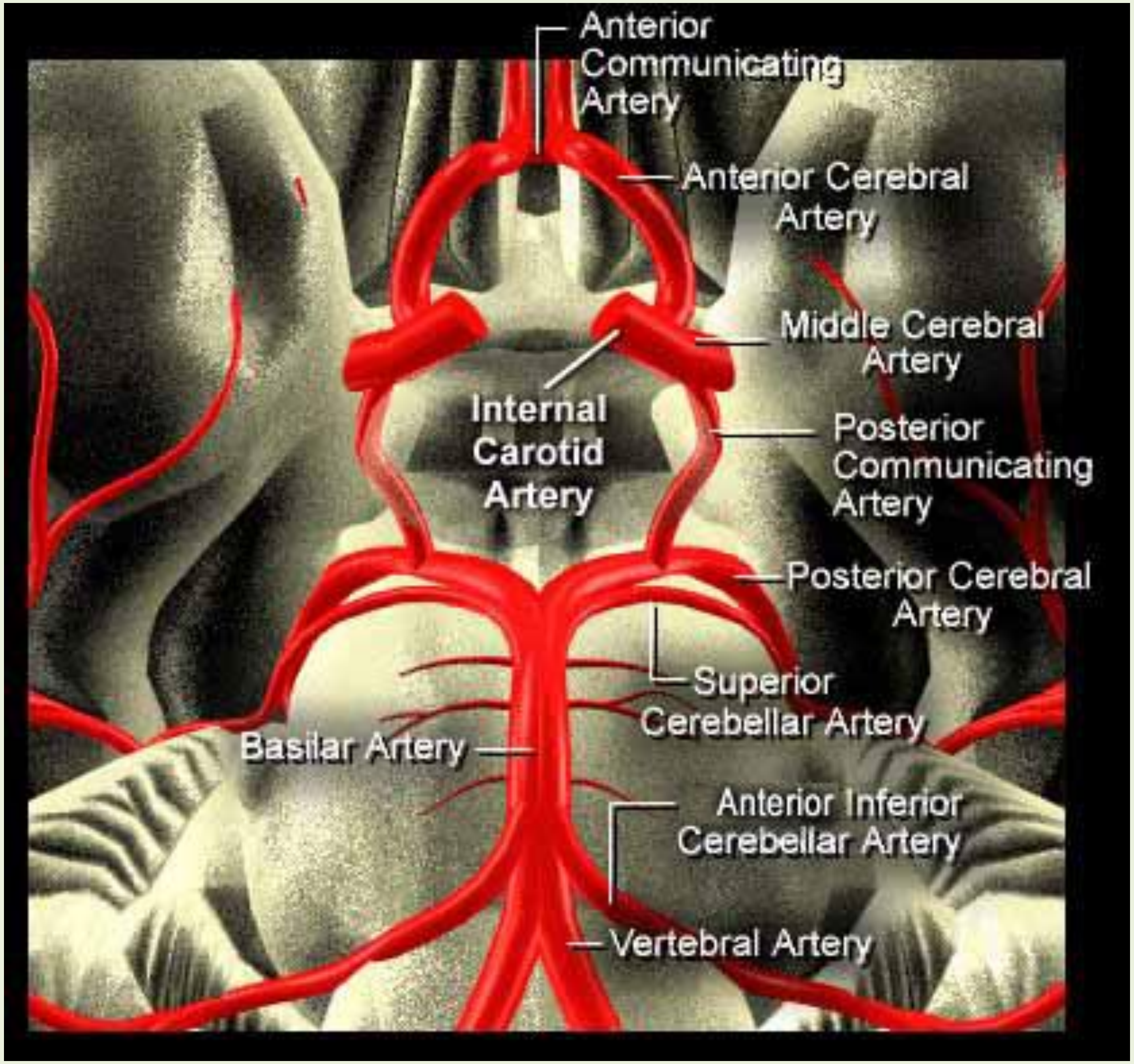
Cerebral blood flow = 55 to 60 ml/100 g brain tissue/min
Cerebral blood flow (gray matter) = 75 ml/100 g brain tissue/min
Cerebral blood flow (white matter) = 45 ml/100 g brain tissue/min (Rengachary, S.S. and Ellenbogen, R.G., editors, Principles of Neurosurgery, Edinburgh: Elsevier Mosby, 2005)

Oxygen consumption whole brain = 46 ml/min
Oxygen consumption whole brain = 3.3 ml/100 g/min

Blood flow rate through each carotid artery = 350 ml/min (Kandel et al., Principles of Neural Science, New York: McGraw Hill, 2000)
Blood flow rate through basilar artery = 100-200 ml/min (Kandel et al., 2000)
Diameter of vertebral artery = 2-3 mm
Diameter of common carotid artery (adult) = 6 mm
Diameter of common carotid artery (newborn) = 2.5 mm

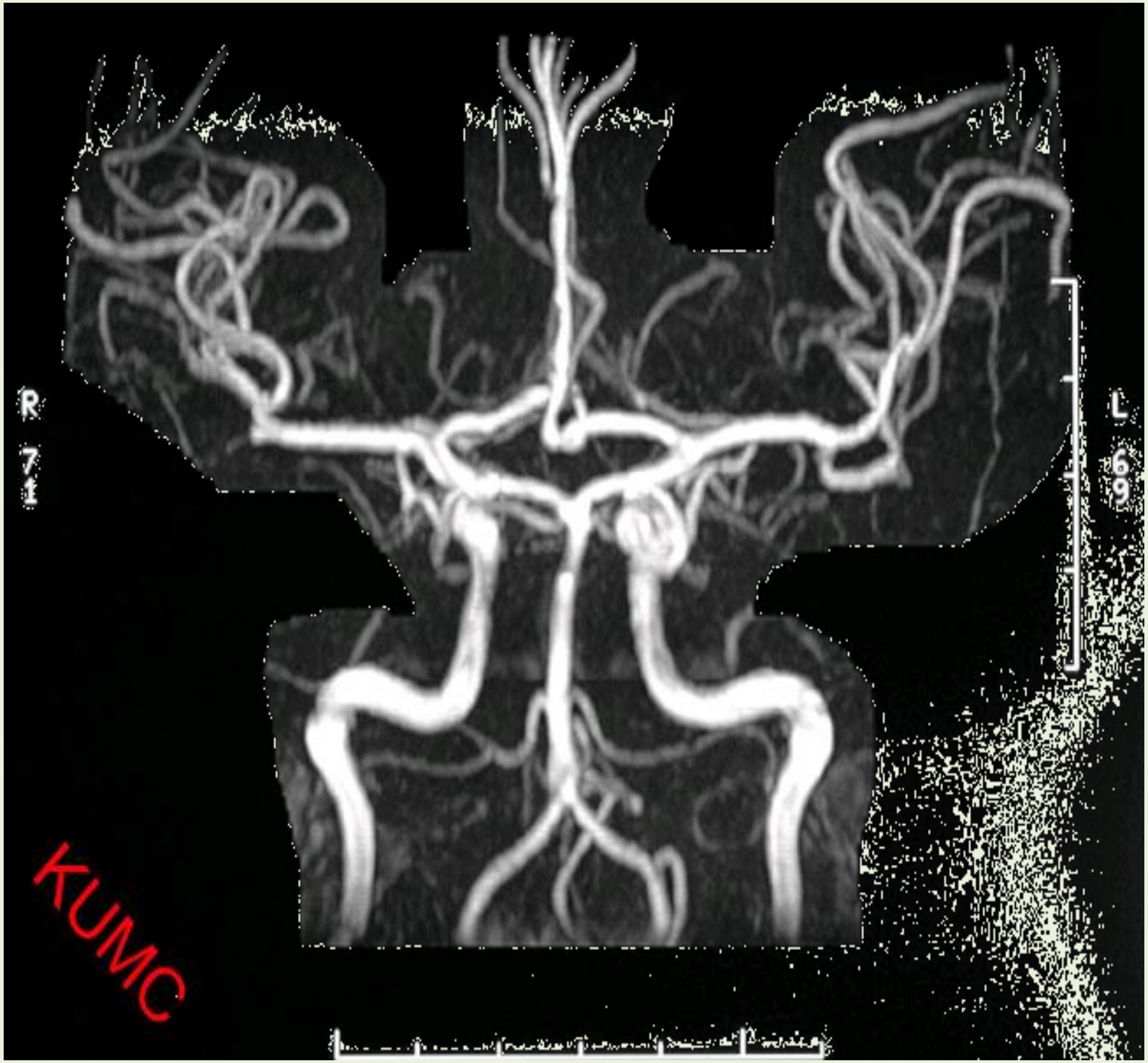
Diameter of MCA (M1 section)= 3 mm


Internal
Carotid
External
Carotid
Common Carotid
Arteries
Vertebral
Arteries

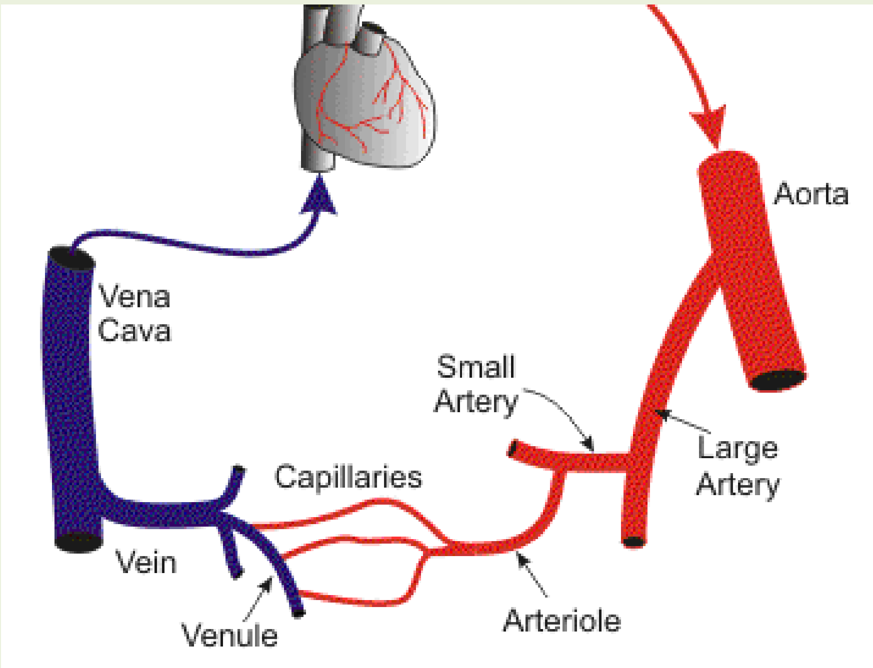


Anterior Communicating Artery
Anterior Cerebral Artery
Middle Cerebral Artery
Internal Carotid Artery
Posterior Communicating Artery
Posterior Cerebral Artery
Superior Cerebellar Artery
Basilar Artery
Anterior Inferior Cerebellar Artery
Vertebral Artery

More realistic view: MRI angiography

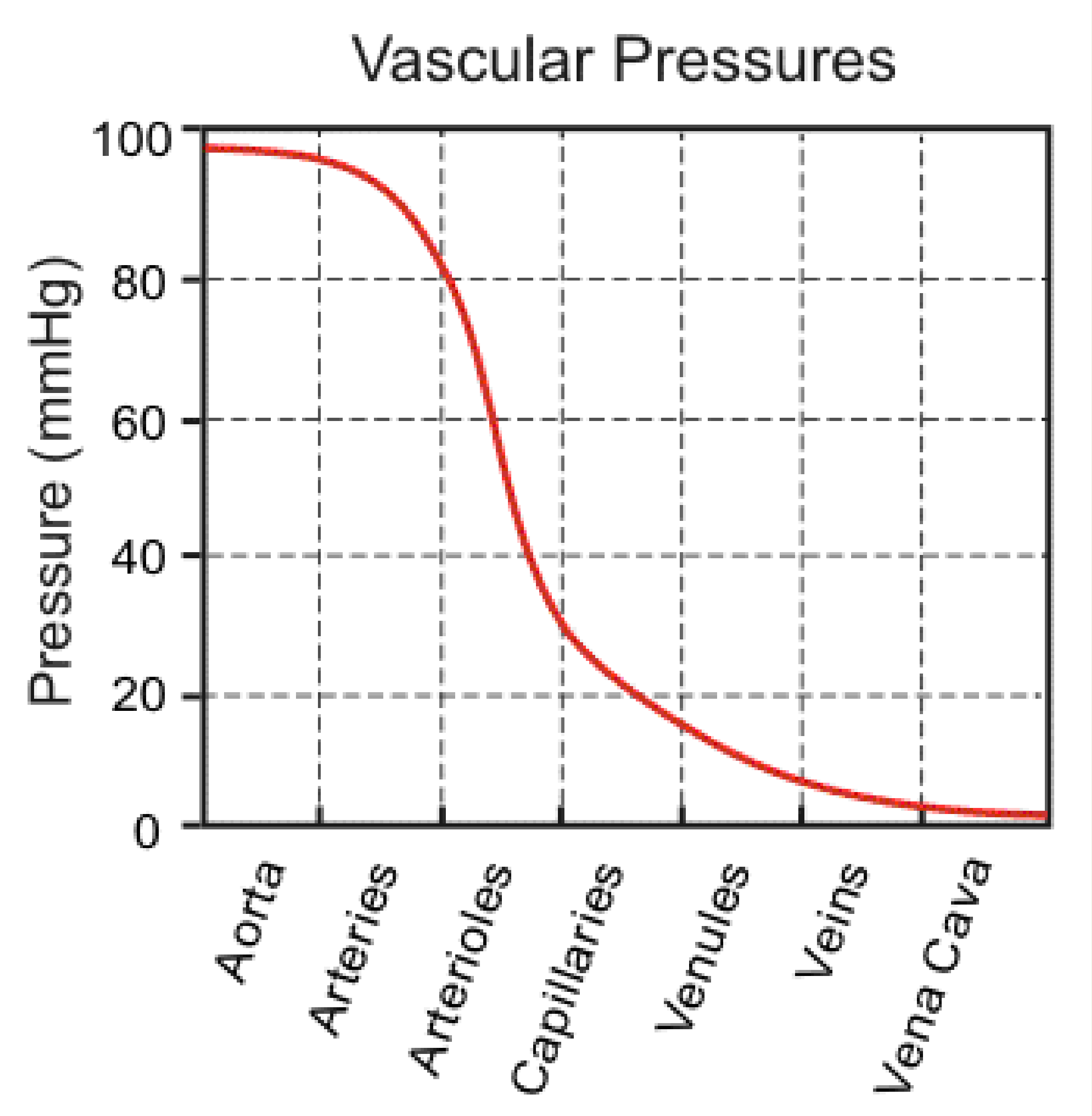


Pressure drop in the systemic arterial system



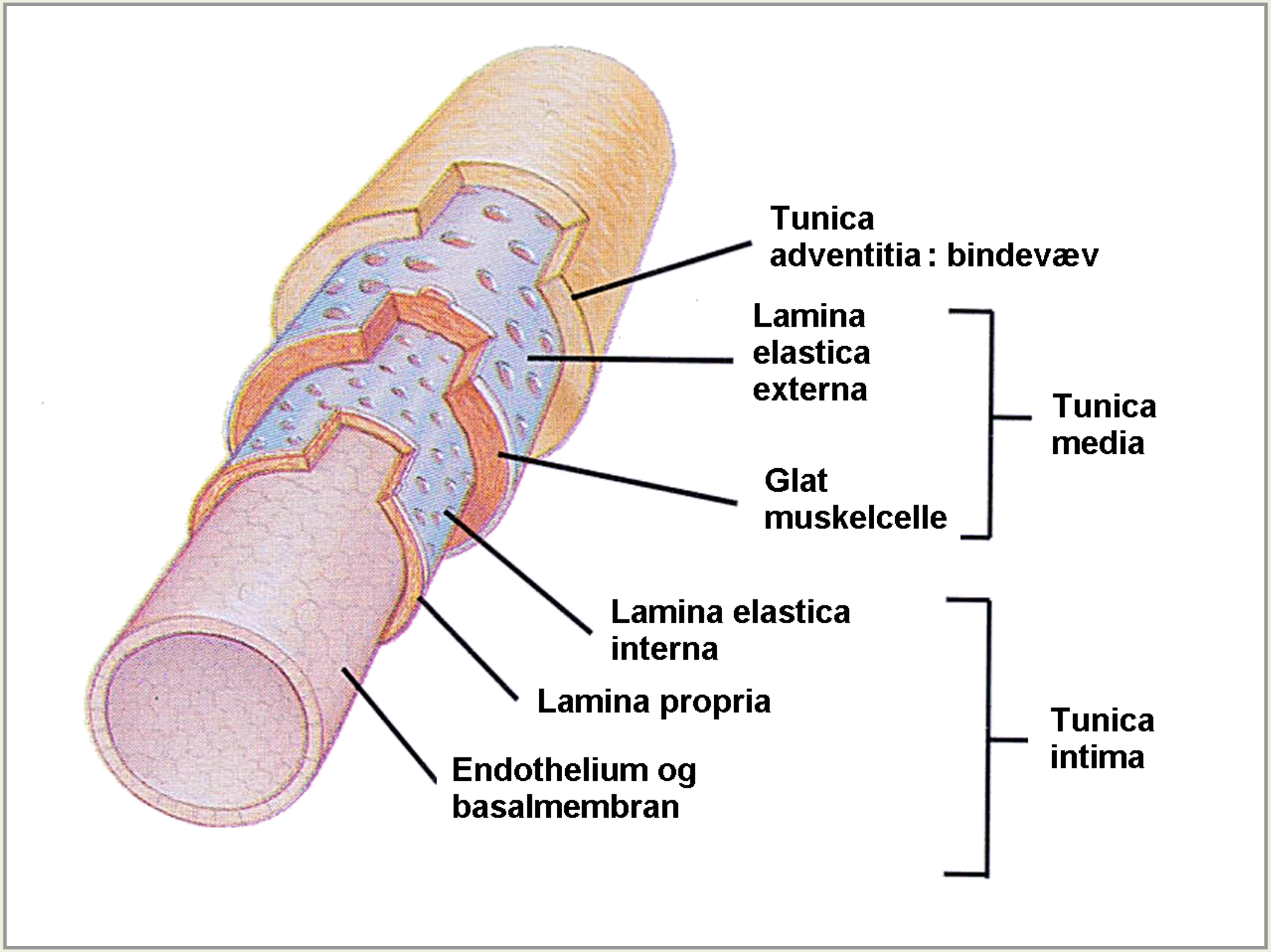
VESSEL TYPE	DIAMETER (mm)	FUNCTION
Aorta	25	Pulse dampening and distribution
Large Arteries	1.0 - 4.0	Distribution of arterial blood
Small Arteries	0.2 - 1.0	Distribution and resistance
Arterioles	0.01 - 0.20	Resistance (pressure & flow regulation)
Capillaries	0.006 - 0.010	Exchange
Venules	0.01 - 0.20	Exchange, collection, and capacitance
Veins	0.2 - 5.0	Capacitance function (blood volume)
Vena Cava	35	Collection of venous blood

Thanks to Dr.S.Troutner, Copenhagen



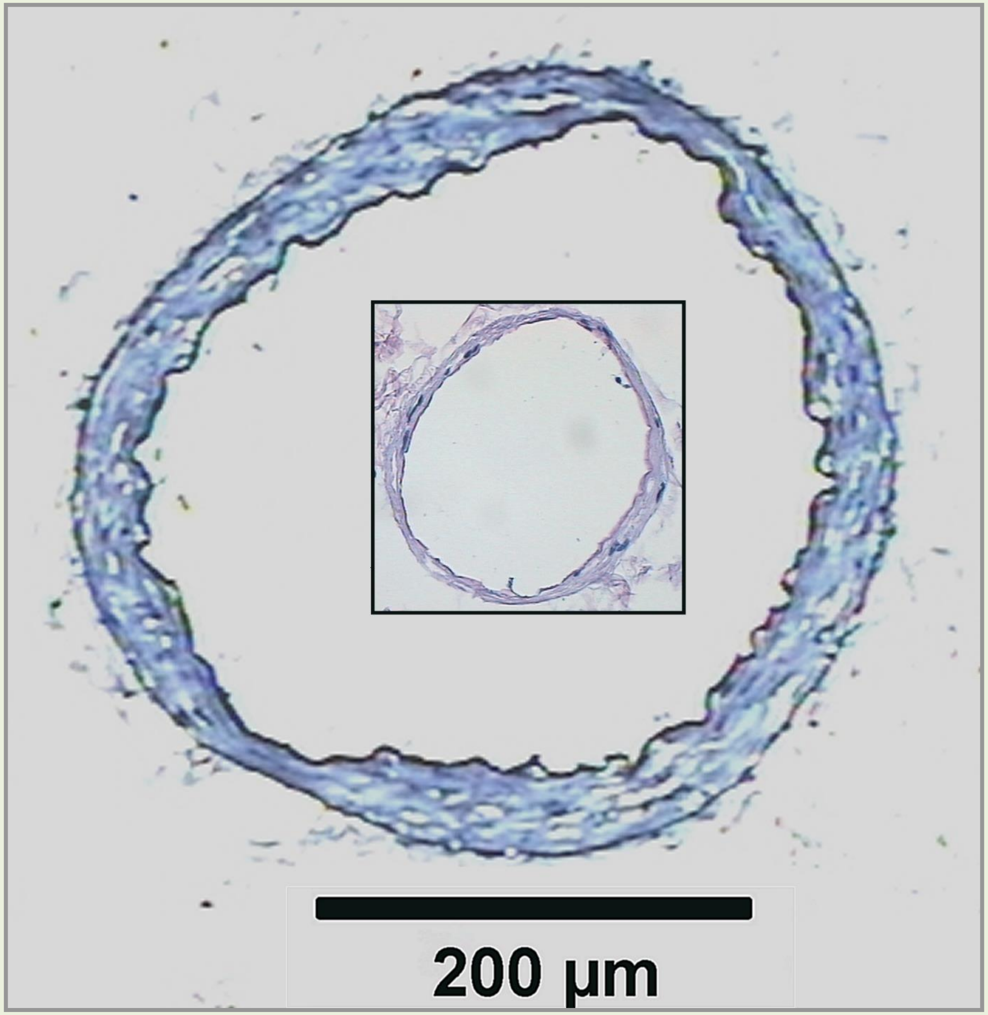
Thanks to Dr.S.Troutner, Copenhagen

Arterial histology



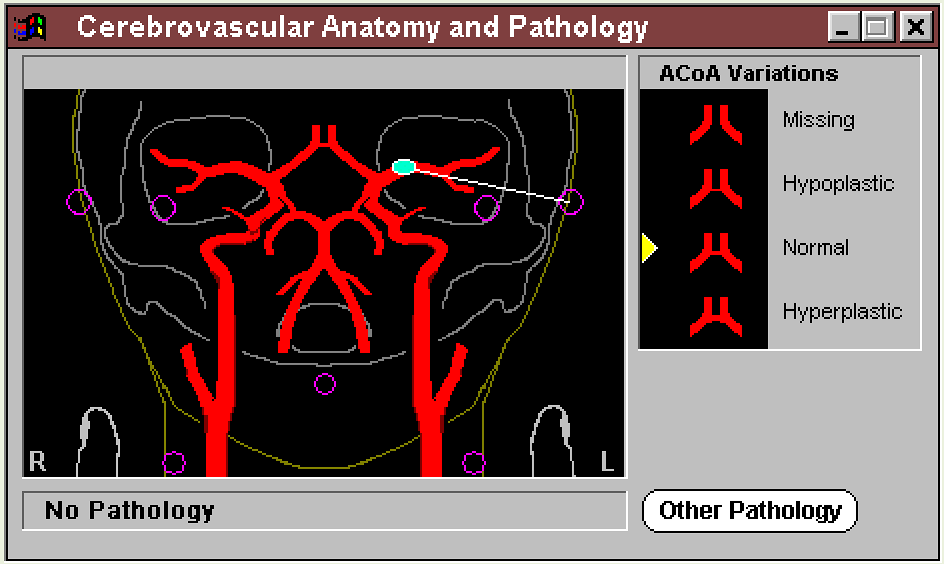
Thanks to Dr.S.Troutner, Copenhagen

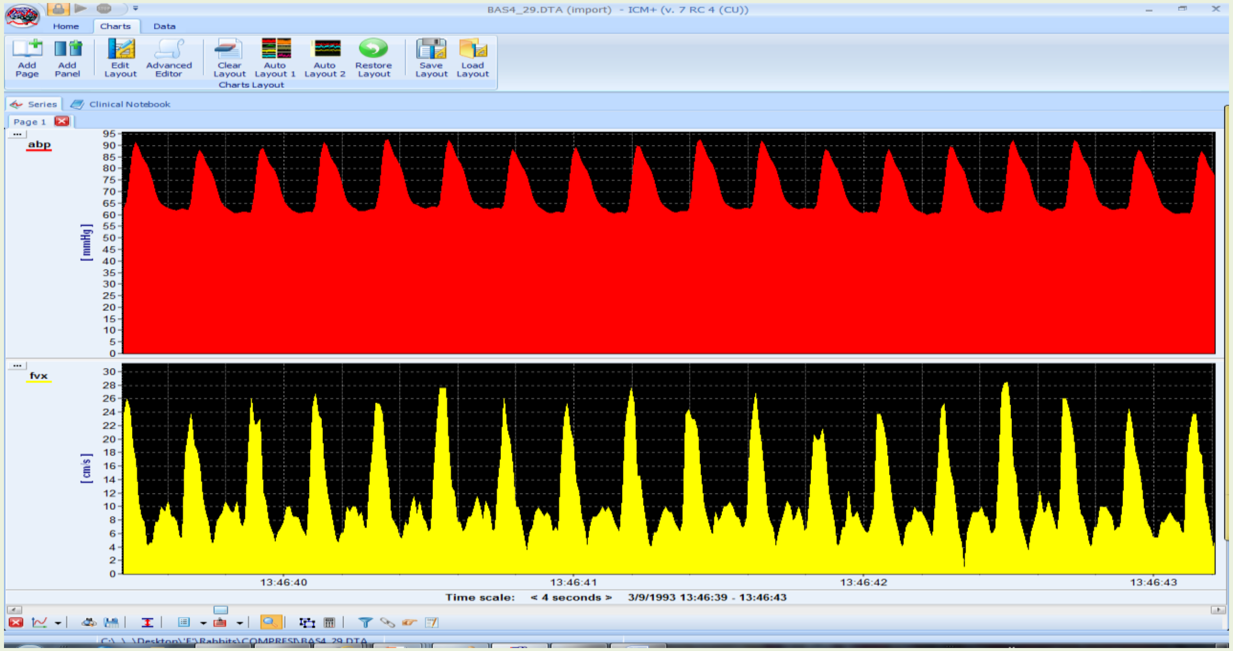
Vessel morphology; resistance vs. conductance arteries



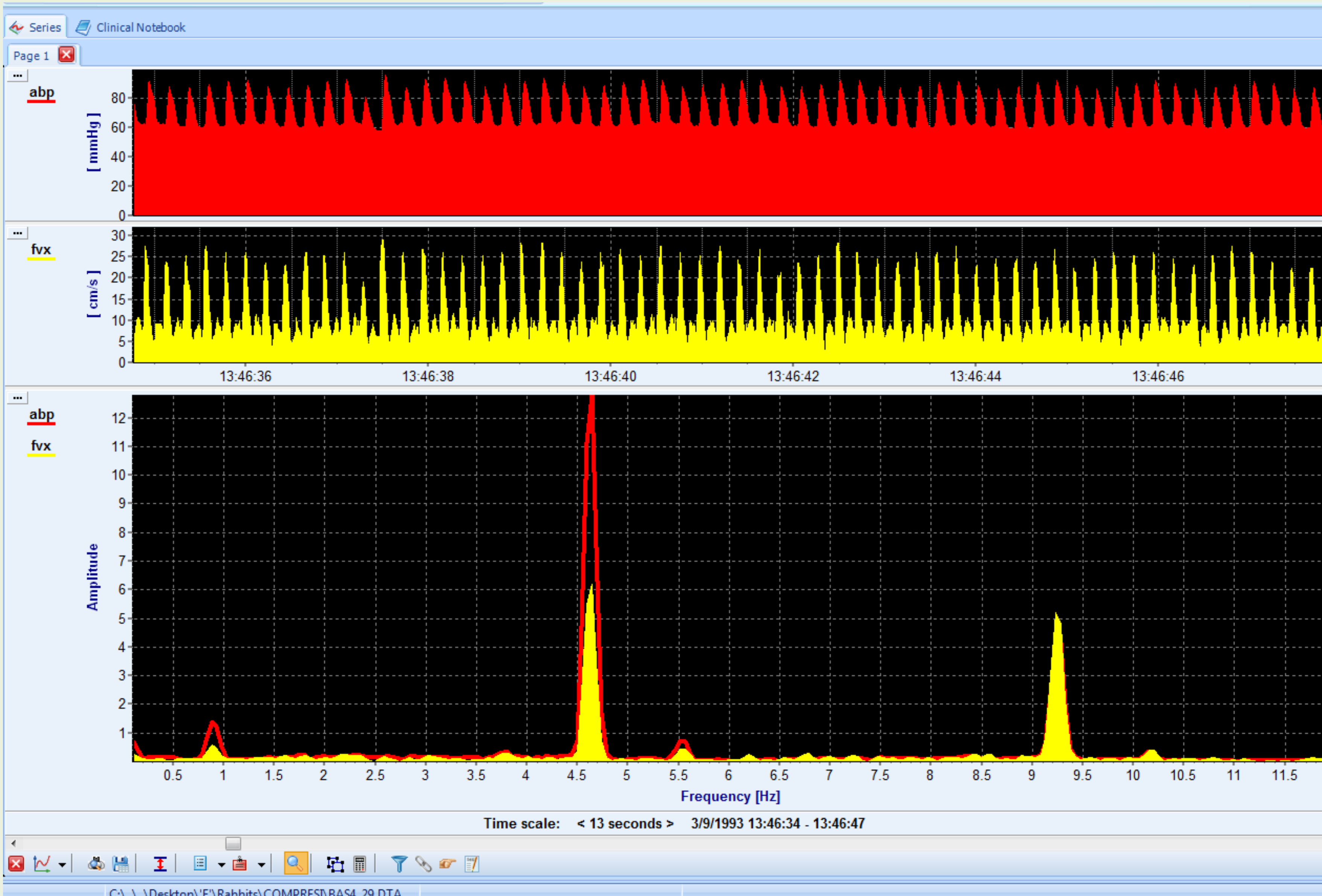
Thanks to Dr.S.Troutner, Copenhagen

Circle of Willis – Pulsatile MCA pressure and blood flow





Blood flow has usually stronger higher harmonics distortion than blood pressure



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NeuroImage 39 (2008) 107 – 118

Modelling vascular reactivity to investigate the basis of the relationship between cerebral blood volume and flow under CO_2 manipulation

Stefan K. Piechnik,* Peter A. Chiarelli, and Peter Jezzard

Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, University of Oxford, John Radcliffe Hospital, Oxford, OX3 9DU, UK

Received 17 May 2007; revised 8 August 2007; accepted 21 August 2007
Available online 25 August 2007

Stefan K. Piechnik

University of Cambridge

Trinity Hall

A Mathematical and Biophysical Modelling of Cerebral Blood Flow and Cerebrospinal Fluid Dynamics

Submitted for Ph.D. degree

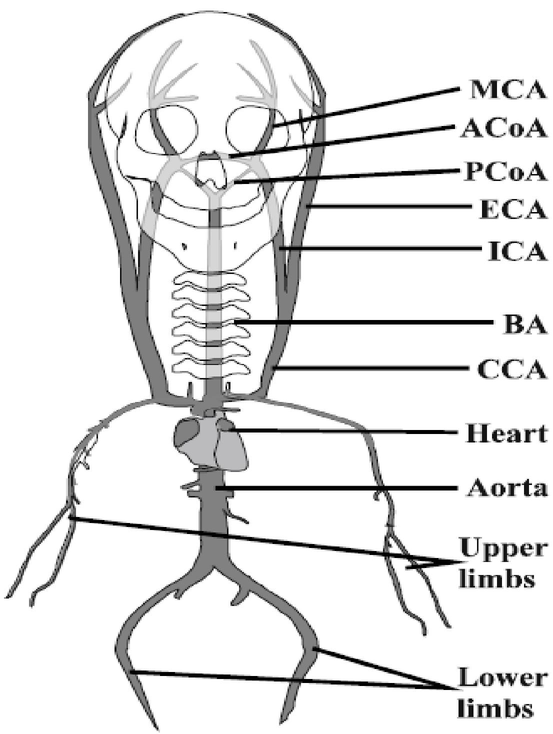


Fig. 4.1. *The schematic representation of the bilateral model of cerebral circulation.*

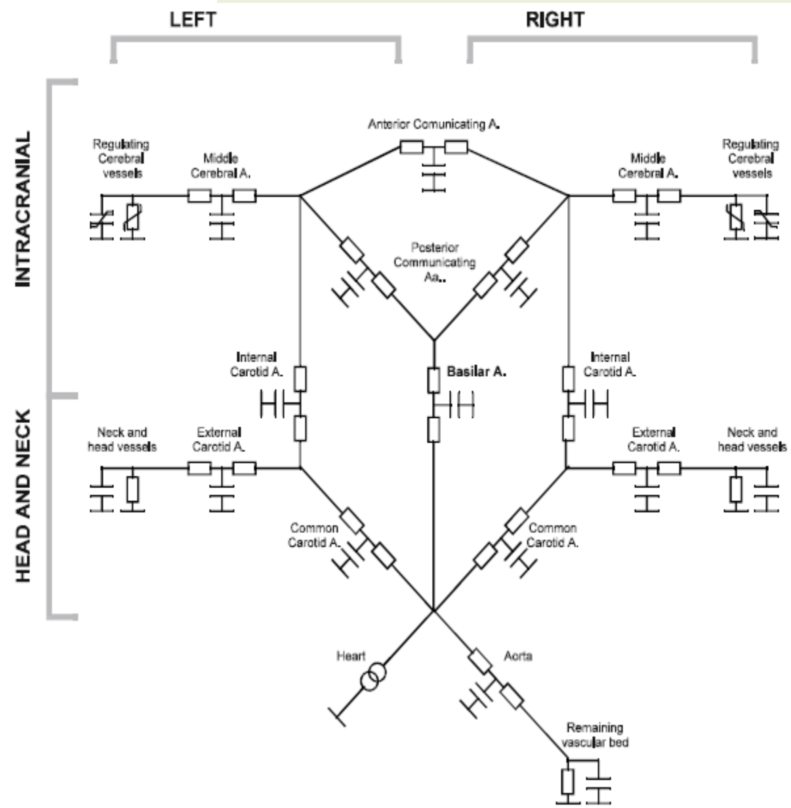
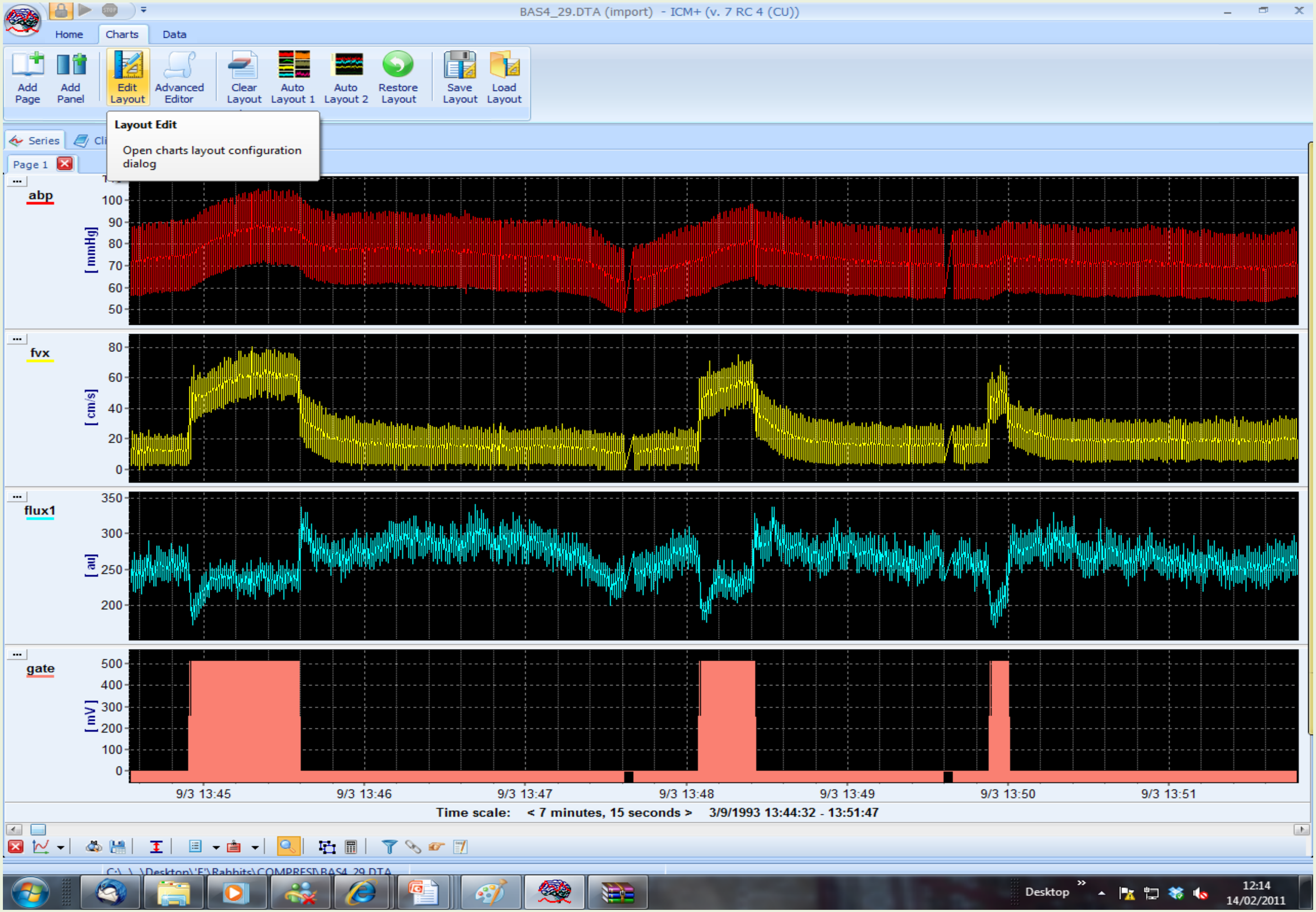
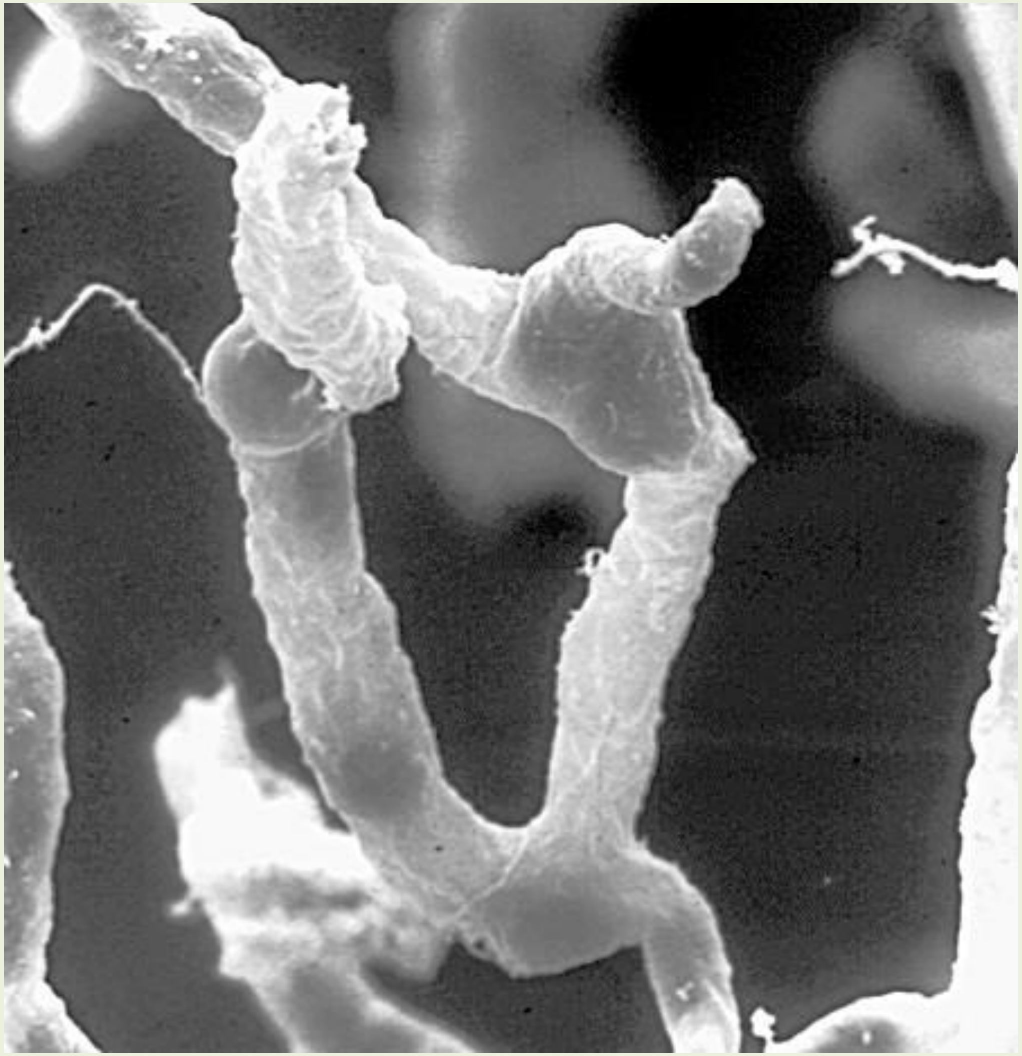


Figure 4.5. ***Electric equivalent of the model of hemispheric blood supply.***

Compression of Common Carotid Artery with TCD at Basilar Artery and Cortical flow in MCA area



Capillaries



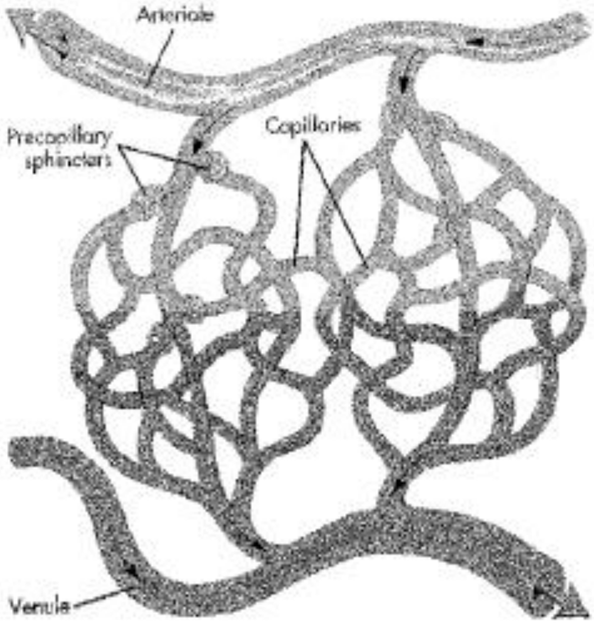


Fig. 2.6. The interconnected microvascular network. In contrast to larger vessels the anastomoses are very common. The flow pattern is established according to local demand by smooth muscle precapillary sphincters. Adapted from Seeley, Stephens & Tate, 1996.

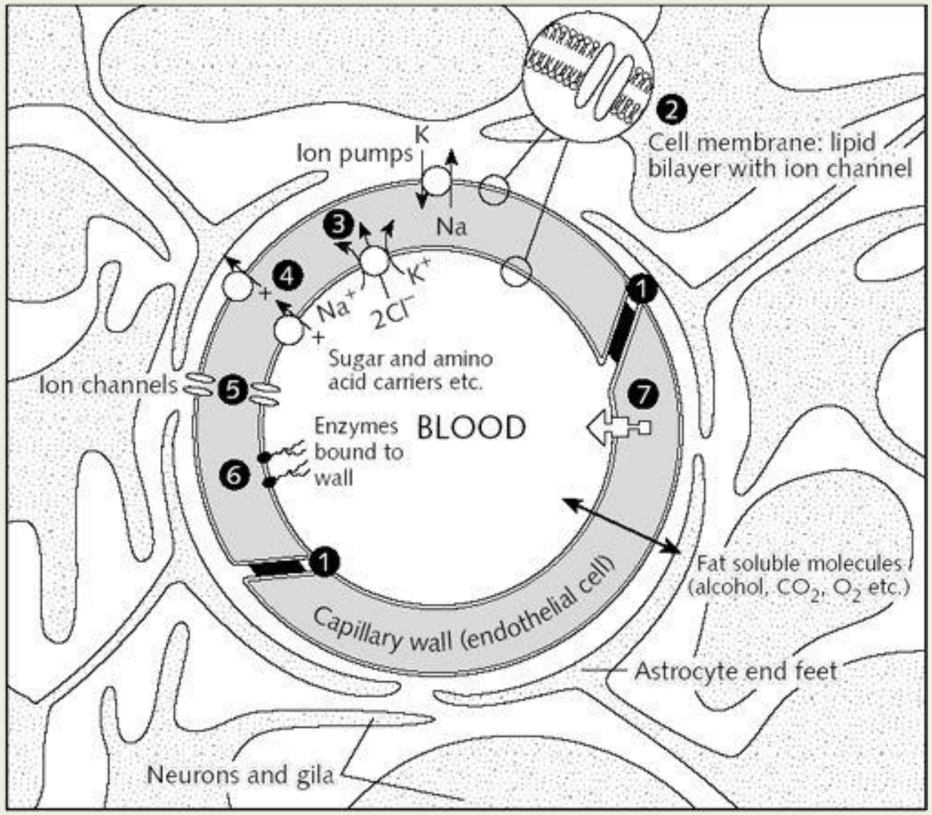


Diagram of a cerebral capillary enclosed in astrocyte end-feet. Characteristics of the blood-brain barrier are indicated: (1) tight junctions that seal the pathway between the capillary (endothelial) cells; (2) the lipid nature of the cell membranes of the capillary wall which makes it a barrier to water-soluble molecules; (3), (4), and (5) represent some of the carriers and ion channels; (6) the 'enzymatic barrier'that removes molecules from the blood; (7) the efflux pumps which extrude fat-soluble molecules that have crossed into the cells

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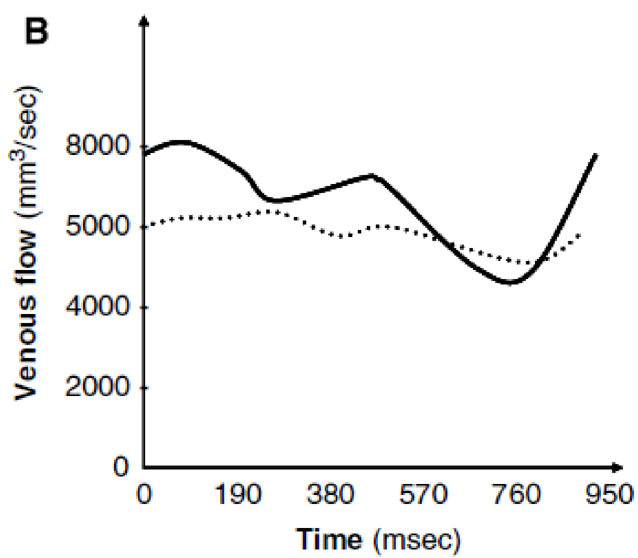
A phase-contrast MRI study of physiologic cerebral venous flow

Souraya Stoquart-ElSankari[1,2], Pierre Lehmann[3], Agnès Villette[3], Marek Czosnyka[4], Marc-Etienne Meyer[1], Hervé Deramond[3] and Olivier Balédent[1]

[1]*Department of Imaging and Biophysics, Amiens University Hospital, Amiens Cedex, France;* [2]*Department of Neurology, Amiens University Hospital, Amiens Cedex, France;* [3]*Department of Radiology, Amiens University Hospital, Amiens Cedex, France;* [4]*Academic Neurosurgical Unit, Department of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK*



Pulsatility of flow in IJV (solid) and in SSS (dotted)

Thanks to Dr. O.Baledent

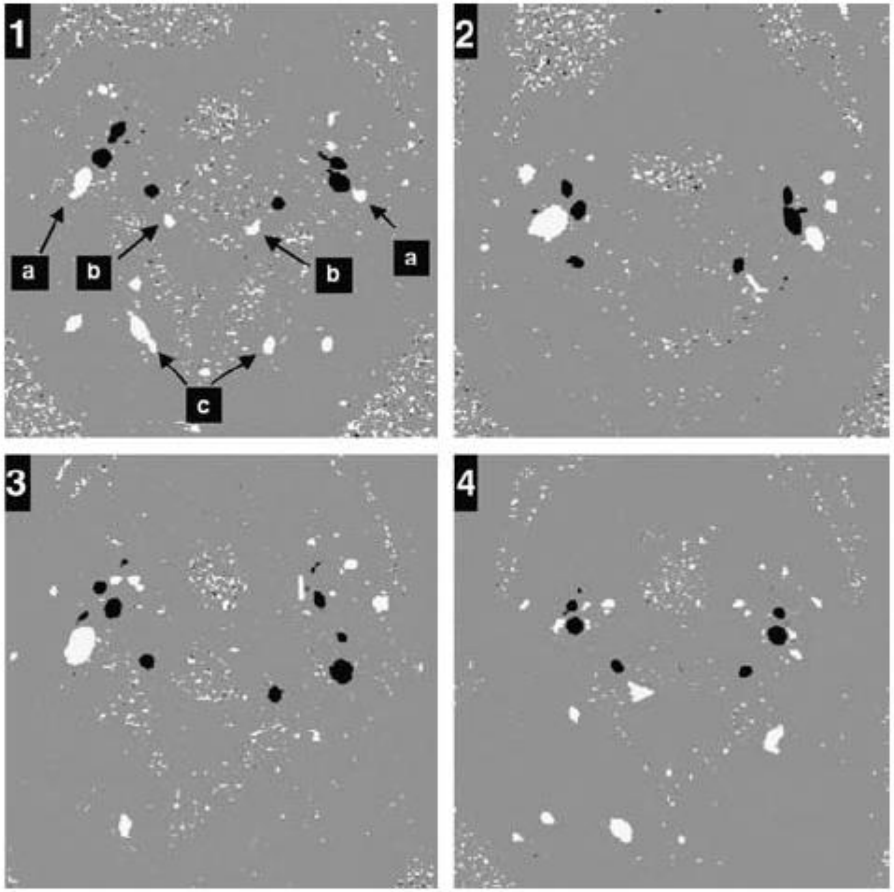


Figure 3 Physiologic variation of venous drainage pathways. Axial views at the cervical level show the vascular, arterial, and venous vessels in four healthy volunteers. In the first participant (1), we can observe a habitual venous pattern, with predominant jugular drainage, right dominant (arrow a). Accessory venous drainage is also obvious in epidural veins (arrow b) and in the vertebral plexus (arrow c). In the second (2), this jugular drainage is exclusive, and strictly unilateral (unique right jugular vein) in the third (3). On the contrary, the fourth participant (4) has venous drainage completely shunted from the jugular veins to the epidural and vertebral pathways.

Venous blood outflow: extremely heterogeneous even in healthy volunteers

Thanks to Dr. O.Baledent

CONCEPT

Cerebral Venous Blood Outflow: A Theoretical Model Based on Laboratory Simulation

Stefan K. Piechnik, Ph.D., Marek Czosnyka, D.Sc., Hugh K. Richards, Ph.D., Peter C. Whitfield, Ph.D., John D. Pickard, F.Med.Sci.

Wolfson Brain Imaging Centre (SKP, MC, HKR, PCW, JDP), Cambridge Medical Research Council Centre for Brain Repair and Academic Neurosurgery Unit, Addenbrooke's Hospital, Cambridge, England, and Institute of Electronic Systems (SKP, MC), Warsaw University of Technology, Warsaw, Poland

OBJECTIVE: The cerebrovascular bed and cerebrospinal fluid circulation have been modeled extensively except for the cerebral venous outflow, which is the object of this study.

METHODS: A hydraulic experiment was designed for perfusion of a collapsible tube in a pressurized chamber to simulate the venous outflow from the cranial cavity.

CONCEPT: The laboratory measurements demonstrate that the majority of change in venous flow can be attributed to either inflow pressure when the outflow is open, or the upstream transmural pressure when outflow is collapsed. On this basis, we propose a mathematical model for pressure distribution along the venous outflow pathway depending on cerebral blood flow and intracranial pressure. The model explains the physiological strong coupling between intracranial pressure and venous pressure in the bridging veins, and we discuss the limits of applicability of the Starling resistor formula to the venous flow rates. The model provides a complementary explanation for ventricular collapse and origin of subdural hematomas resulting from overshunting in hydrocephalus. The noncontinuous pressure flow characteristic of the venous outflow is pinpointed as a possible source of the spontaneous generation of intracranial slow waves.

CONCLUSION: A new conceptual mathematical model can be used to explain the relationship between pressures and flow at the venous outflow from the cranium. (Neurosurgery 49:1214–1223, 2001)

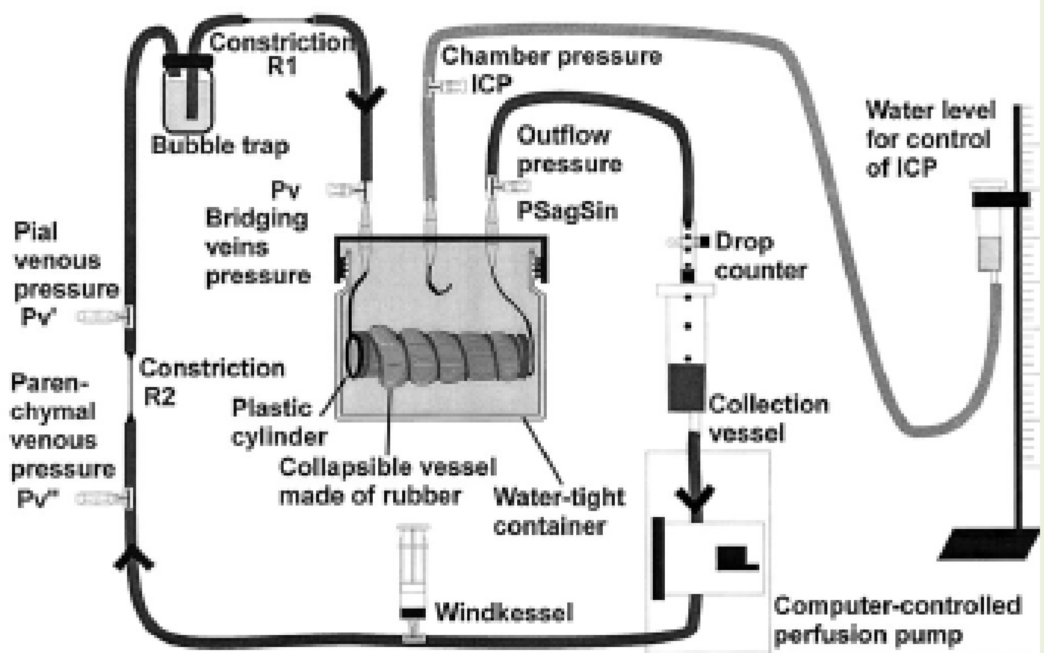


FIGURE 1. Simplified laboratory setup. The *dark-shaded* tubing represents the blood circulation motioned by the perfusion pump. The *light-shaded* areas represent the cerebrospinal fluid space within the container and the tubing connecting it to the water level. The inflow pressures are noted as *Pv*, *Pv'*, and *Pv''* according to the increasing distanc from the collapsible vessel.

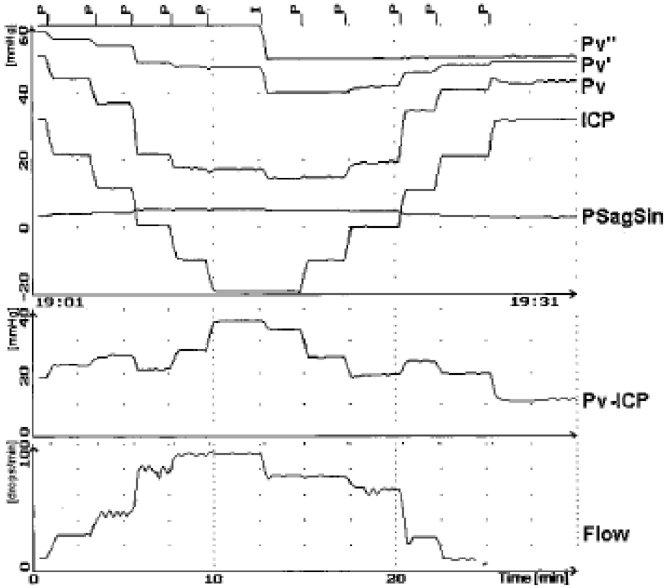


FIGURE 2. An example of the pressure and flow trends displayed during the experiment. The sequence of quick changes in ICP (*P* markers) performed at two levels of inflow pressure P_v'' (change is denoted by marker *I*). Note unstable oscillations on flow when ICP approaches P_{SagSin}. *Pv″*, *Pv'*, *Pv*, simulated inflow venous pressures from distal to proximal to the collapse; ICP, pressure inside the container simulating ICP; *PSagSin*, outflow pressure equivalent to sagittal sinus; *Flow*, rate of simulated venous flow in of drop counts per minute.

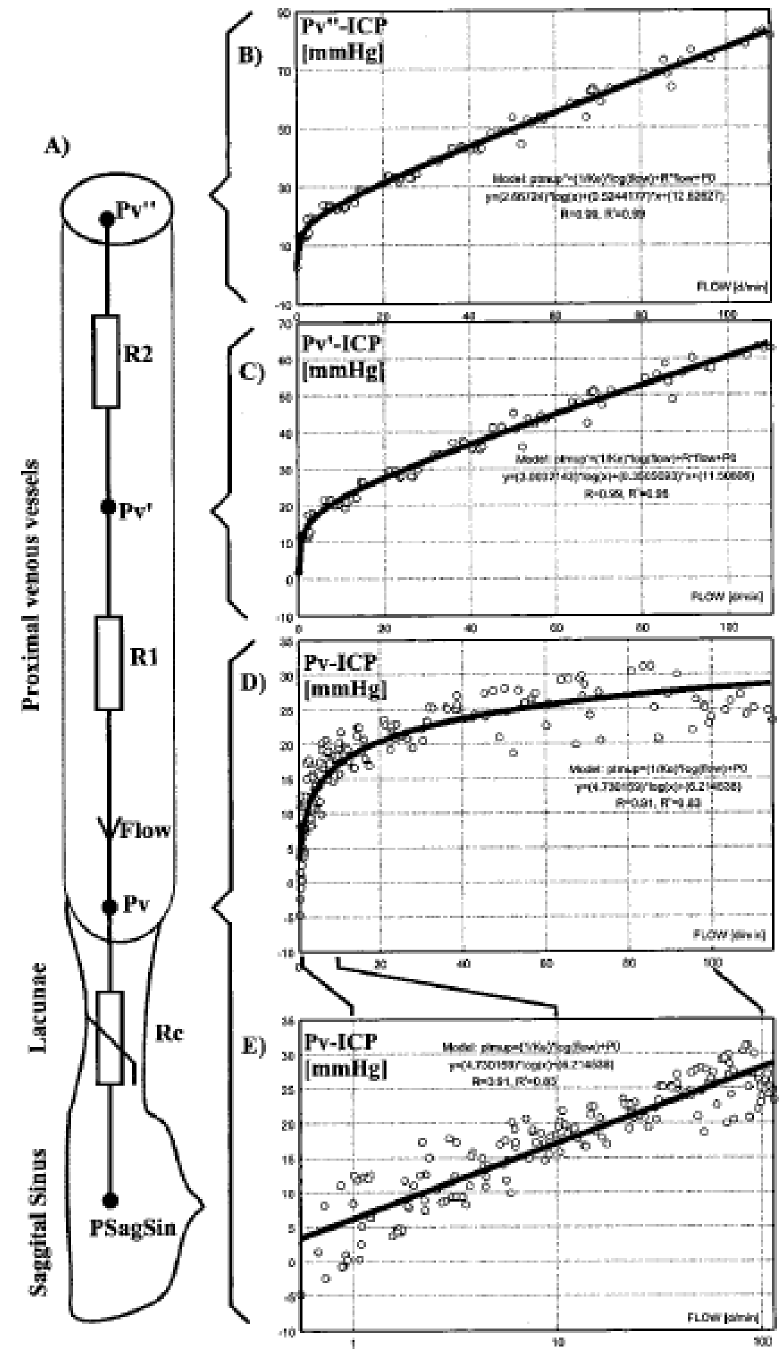


FIGURE 4. Divergent behavior of flow when ICP is positive. Flow is determined by the appropriate upstream transmural pressures at levels Pv, Pv', and Pv″ (*A*). At distal levels, Pv″ − ICP and Pv' − ICP change linearly with flow greater than the critical threshold of approximately 15 mm Hg (*B*, *C*). In contrast, the proximal Pv − ICP saturates below 30 mm Hg (*C*). The best-fit, logarithmic-linear models are marked with a *heavy line*. At the Pv level, the linear component is not necessary to provide accurate fit. When displayed in logarithmic-linear scale, the model is represented by a *straight line* (*E*). The magnification of the scale at low flow range is denoted by *connecting lines* between corresponding flow values on (*D*) and (*E*).

$$P_v(x) = \begin{cases} ICP + K_{10}\log(CBF) + R_{prox}(x) \cdot CBF + P_0 \ldots\ldots ICP \geq P_{SagSin} \\ (R_{prox}(x) + R_{dist}) \cdot CBF + P_{SagSin} \ldots\ldots ICP < P_{SagSin} \end{cases}$$

Variables:

$P_v(x)$, venous pressure at increasing distance "x" from the cerebral lacunae;

ICP, intracranial pressure;

P_{SagSin}, venous pressure in sagittal sinus; and

CBF, total cerebral blood flow.

Model parameters:

K_{10}, logarithmic model coefficient describing the steepness of the pressure-flow relationship of the idealized lumped "collapsible" outflow located in the lacunae;

$R_{prox}(x)$, proximal resistance of the vascular bed upstream;

P_0, minimum transmural pressure needed to open the collapsible end; and

R_{dist}, distal, downstream resistance to flow characterizing "fully" open lacunae.

Estimated value of pressure in bridging and cortical veins:

$$P_{bv}[\text{mm Hg}] = 1.8 \cdot \log(CBF[\text{ml/min}]) + ICP[\text{mm Hg}]$$

Thanks to Dr. SK.Piechnik

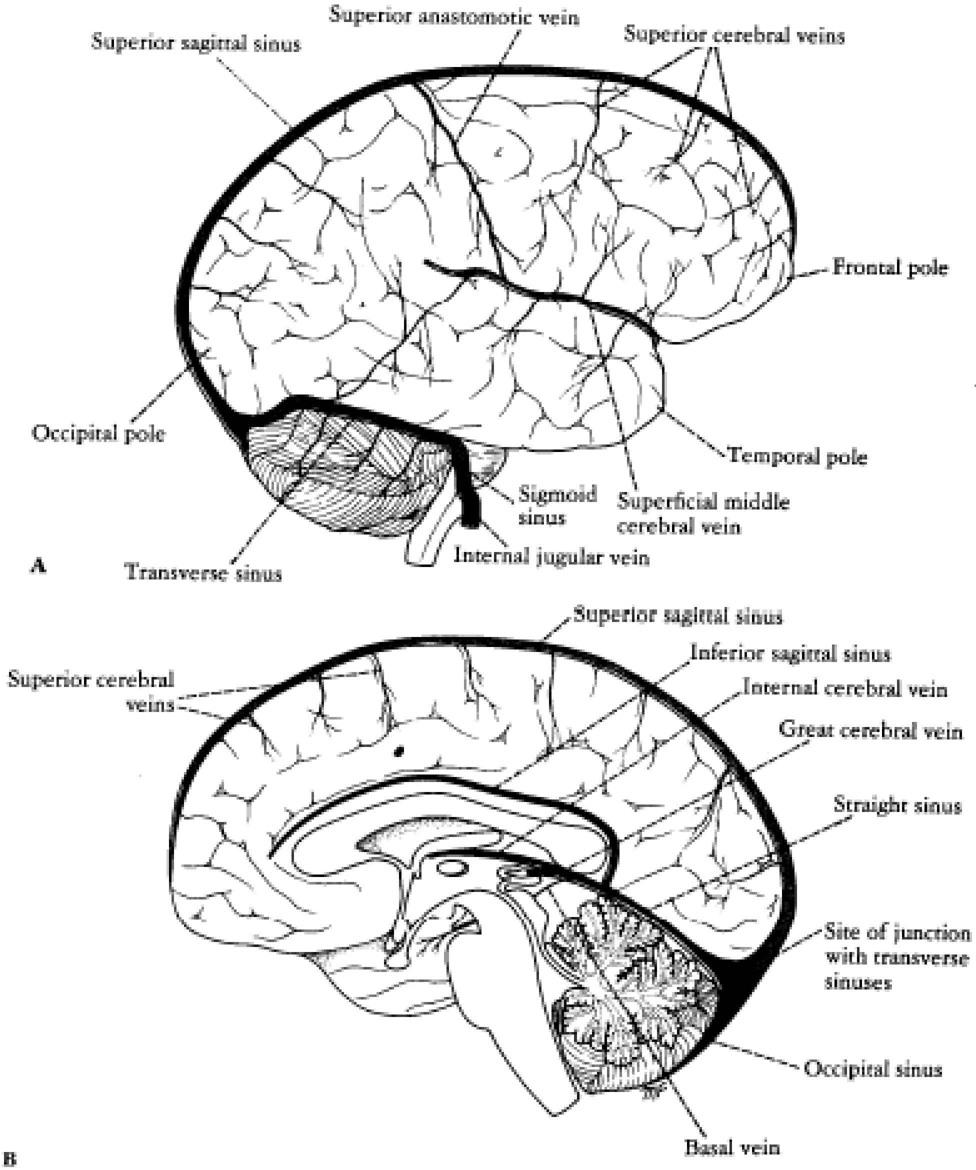
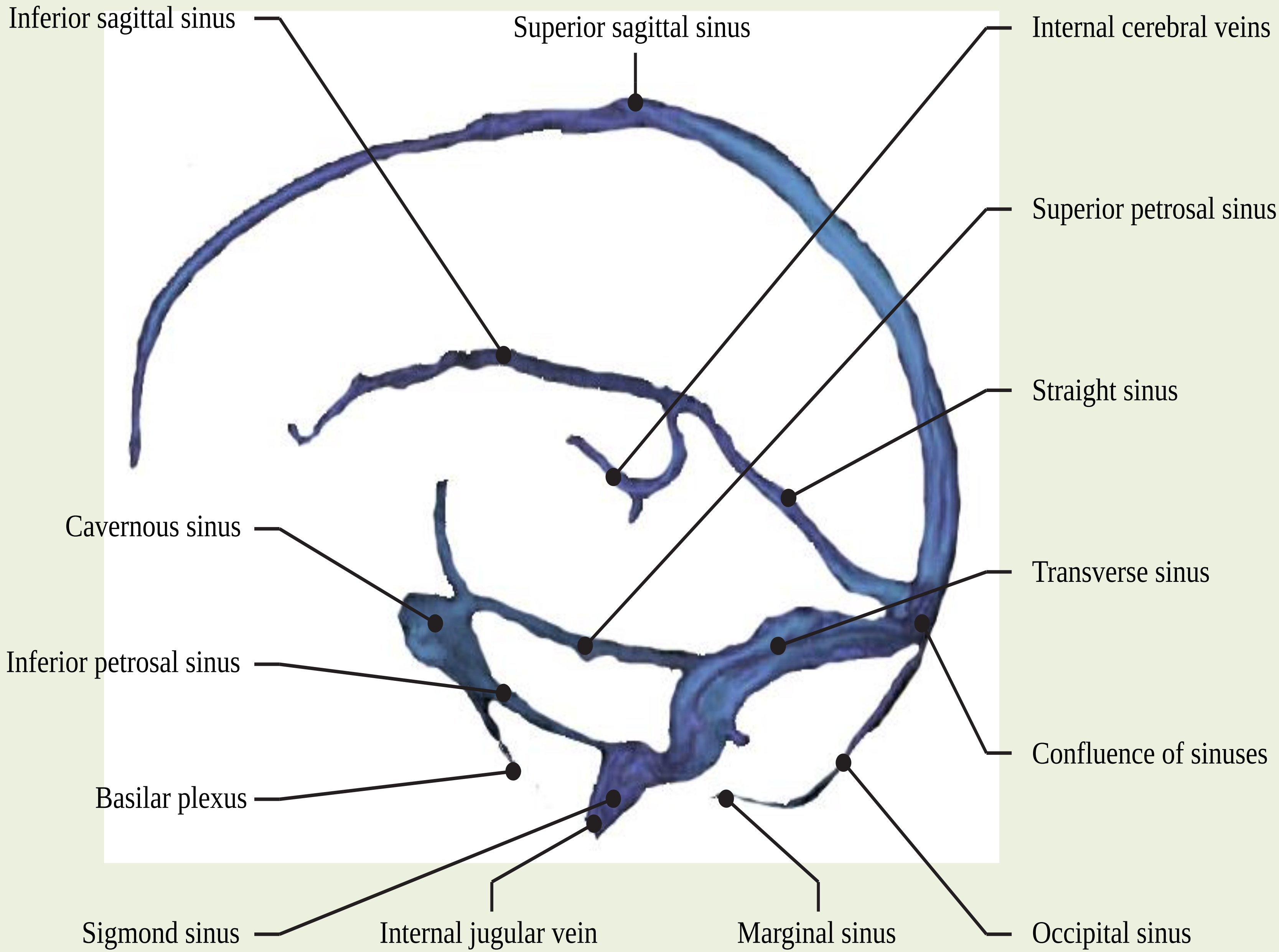


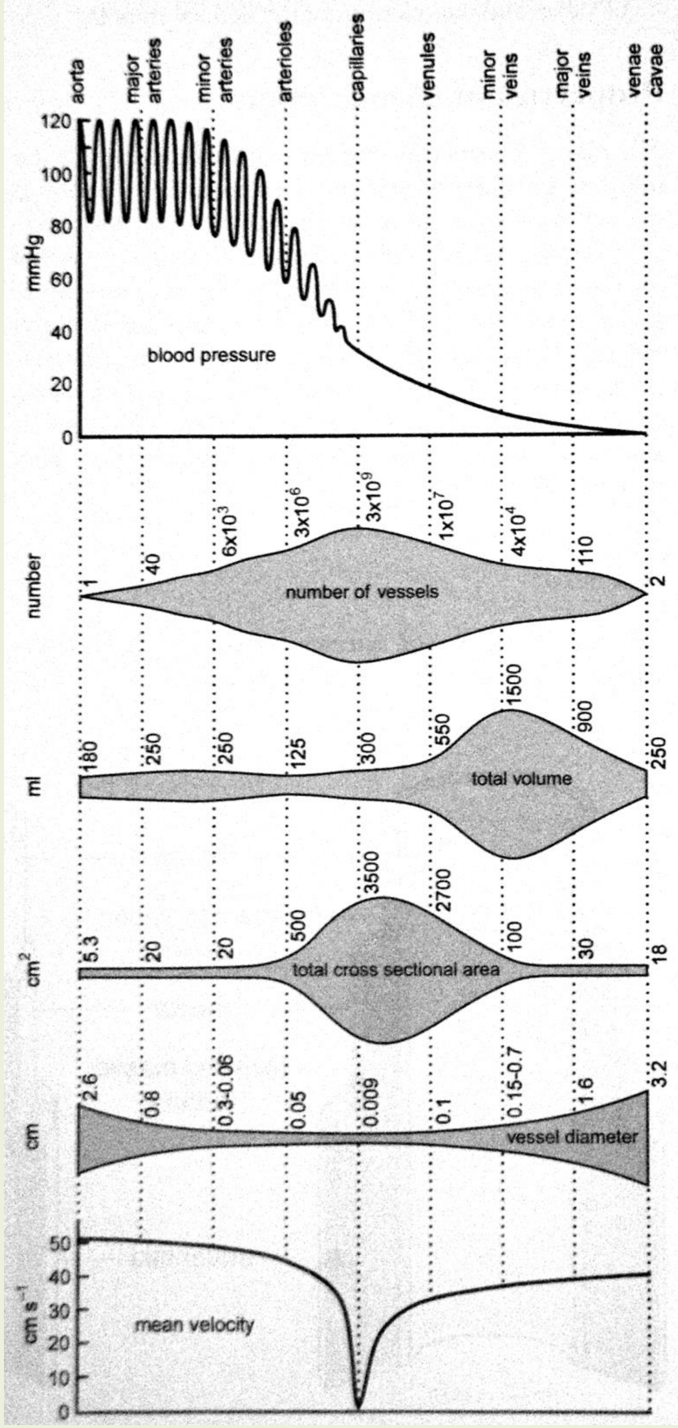
Fig. 2.9. Venous outflow pathways: A) lateral, B) medial views. Adapted from R.S. Snell 1992.

Thanks to SK Piechnik

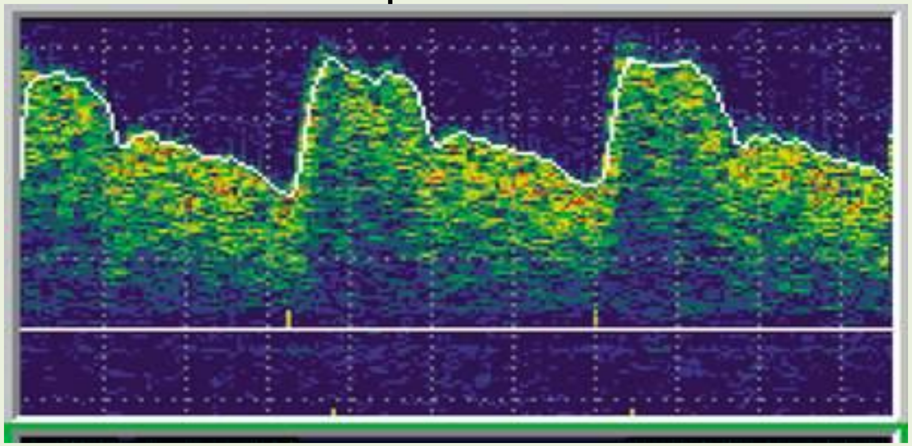
MRI venography



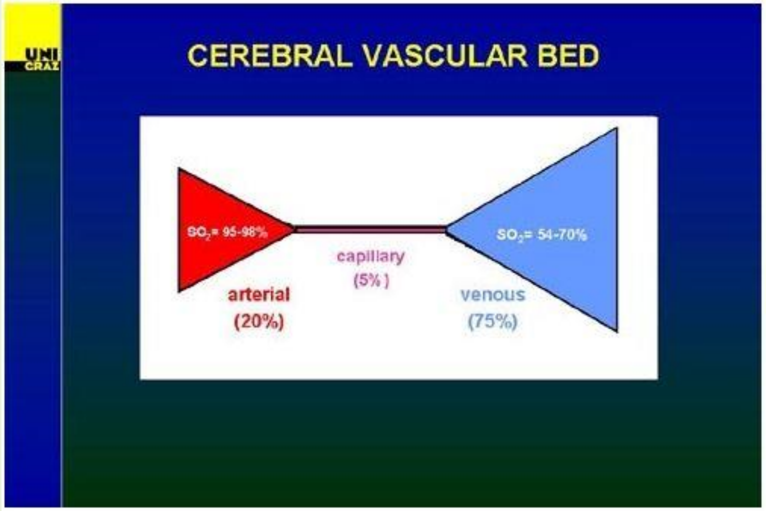
Compartmental vascular hemodynamics



Oates.C. Cardiovascular haemodynamics and Doppler waveforms explained



Pulsatile blood flow in MCA



Thanks to Dr. S.K.Piechnik

Flow in Tube: Hydrodynamic Resistance

The main assumptions underlying Hagen-Poiseuille formula

Hagen-Poiseuille formula (1840)

$$Q_0 = \frac{\pi \cdot D^4 \cdot \Delta P_0}{128 \mu L}$$

hydraulic resistance per tube length is constant and equal:

$$R_{H0} = \frac{\Delta P_0 / L}{Q_0} = \frac{128\mu}{\pi \cdot D^4}$$

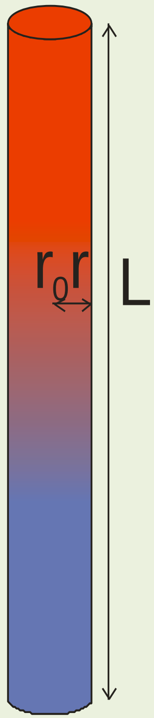
- flow is steady,
- the tube has constant and circular cross section
- fluid is Newtonian,
- the tube axis is straight,
- the tube is of infinite length (velocity profile is developed).

Thanks to Prof. K.Cieslicki

Methods: Tube, tubes, more tubes…

M1:

simple reactive tube



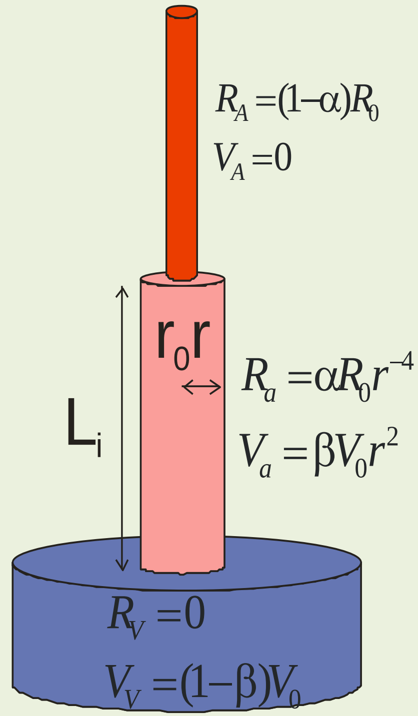
$$V = \pi L r_o^2 r^2 = V_0 r^2$$

$$R = \frac{\eta L}{8\pi r_o^4 r^4} = R_0 r^{-4}$$

$$F = P/R = F_0 r^4$$

M2:

Arteries+microcirculation+veins



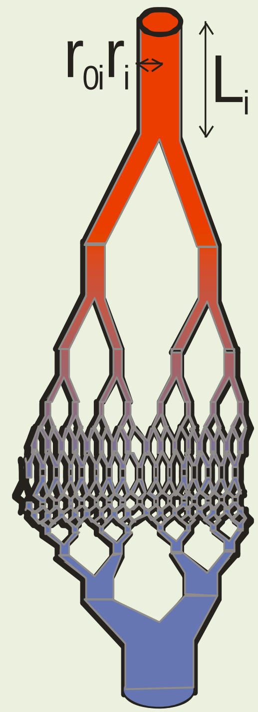
$$V = (1-\beta + \beta r^2)V_0$$

$$R = (1-\alpha + \alpha r^{-4})R_0$$

$$F = F_0 / (1-\alpha + \alpha r^{-4})$$

M3:

11 compartments Arteries-Veins



$$V = \sum_{i=2}^{12} N_i L_i \pi r_{oi}^2 r_i^2$$

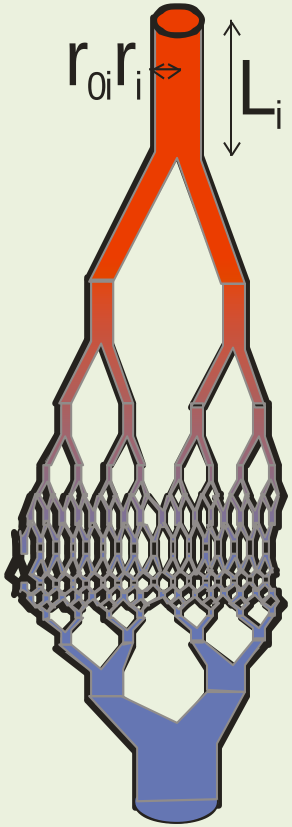
$$R = \sum_{i=2}^{12} \frac{1}{N_i} \frac{\eta_i L_i}{8\pi r_{oi}^4 r_i^4}$$

$$F = P / R(r_2, \dots, r_{12})$$

Thanks to Dr. S.K.Piechnik

M3:

hierarchical model of cerebrovascular circulation



Vessel	Level	Number	Length[mm]	D[mm]	Reactivity [%/mmHg]
ArteryL	2	2	150.	4.	0.68
ArteryM	3	25	45.	1.3	0.69
ArteryS	4	300	13.5	0.45	0.72
ArterioleL	5	5500	4.	0.15	0.83
ArterioleS	6	140000	1.2	0.05	1.18
Capillary	**7**	135000000	0.65	0.008	1.5
Venules	8	500000	1.6	0.1	0.18
VenulesL	9	33000	4.8	0.28	0.15
VeinsS	10	2000	13.5	0.7	0.14
VeinsM	11	105	45.	1.8	0.14
VeinsL	12	5.5	150.	4.5	0.14

$= \sum^{12} N_i L_i \pi r_i^2 r_i^2$

Milnor, W. R. (1982). Hemodynamics. Baltimore, Williams & Wilkins

Thanks to Dr. S.K.Piechnik

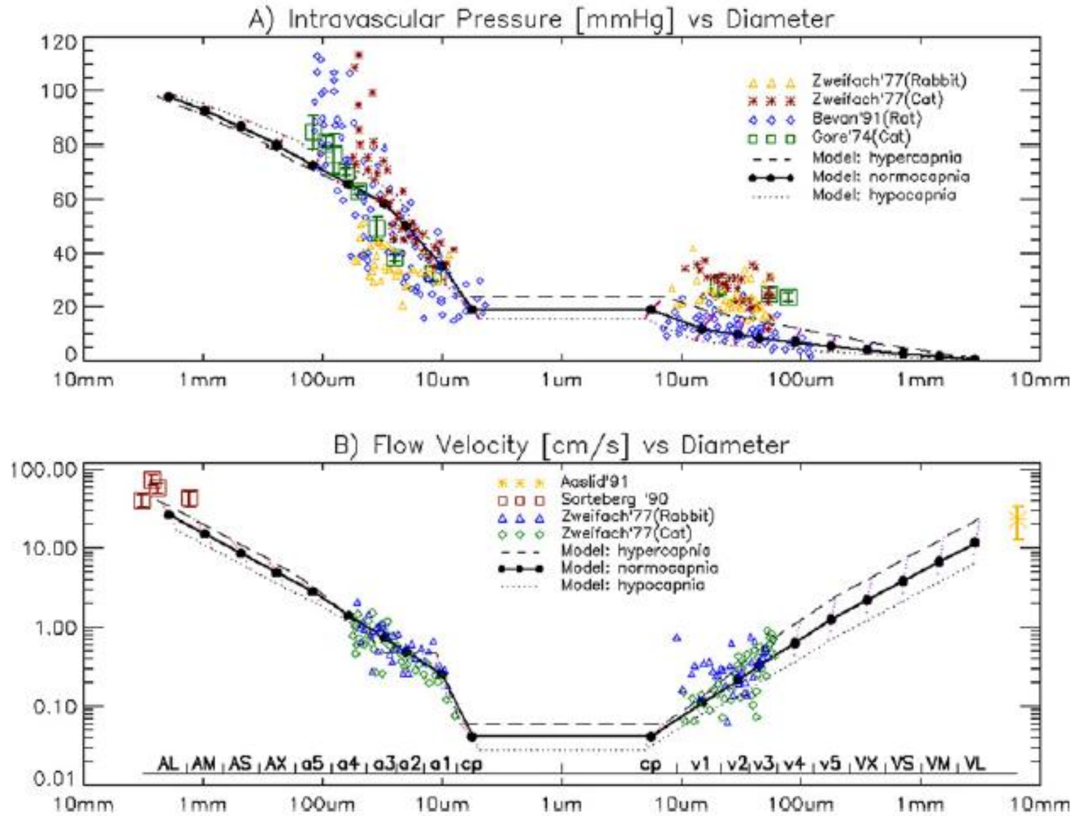


Fig. 5. Distribution of (A) pressure and (B) mean velocity of whole blood in the vascular tree under $PaCO_2$-manipulated perfusion (25−70 mmHg). Overlaid experimental data points indicate reference normal values (±S.D., where available) taken from literature reports of direct measurements in animal models (Bevan et al., 1991; Gore, 1974; Zweifach and Lipowsky, 1977) and human transcranial Doppler ultrasound studies (Aaslid et al., 1991; Sorteberg et al., 1990). Note: the transcranial Doppler measurements in large arteries and veins are based on the estimates of maximum spectral envelope and therefore are larger than the average flow velocity (two-fold in the case of laminar flow). For formulas used to calculate pressures and flow velocities see Supplementary Material.

Thanks to Dr. S.K.Piechnik

Reynolds number (From Wikipedia)

In fluid mechanics, the Reynolds number Re is a dimensionless number that gives a measure of the ratio of inertial forces ρV^2/L to viscous forces μV/L^2 and consequently quantifies the relative importance of these two types of forces for given flow conditions. The concept was introduced by George Gabriel Stokes in 1851,[1] but the Reynolds number is named after Osborne Reynolds (1842–1912), who popularized its use in 1883.[2][3]

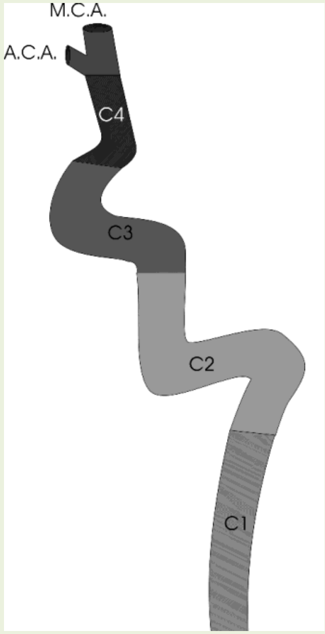
$$\mathrm{Re} = \frac{\rho \mathrm{V} L}{\mu} = \frac{\mathrm{V} L}{\nu}$$

where:

- V is the mean velocity of the object relative to the fluid (SI units: m/s)
- *L is a characteristic linear dimension, (travelled length of the fluid) (m)*
- μ is the dynamic viscosity of the fluid (Pa·s or N·s/m^2 or kg/(m·s))
- ν is the kinematic viscosity (ν = μ / *ρ) (m^2/s)*
- p is the density of the fluid (kg/m^3)

Re> 2300 flow may be turbulent

Centrifugal effects induced by successive bends



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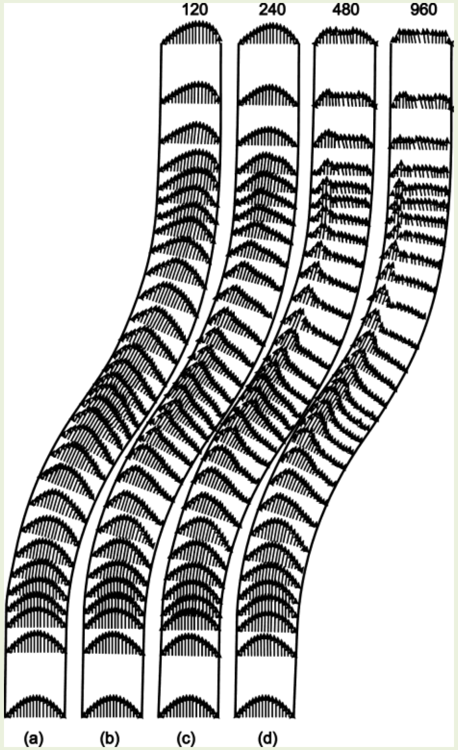
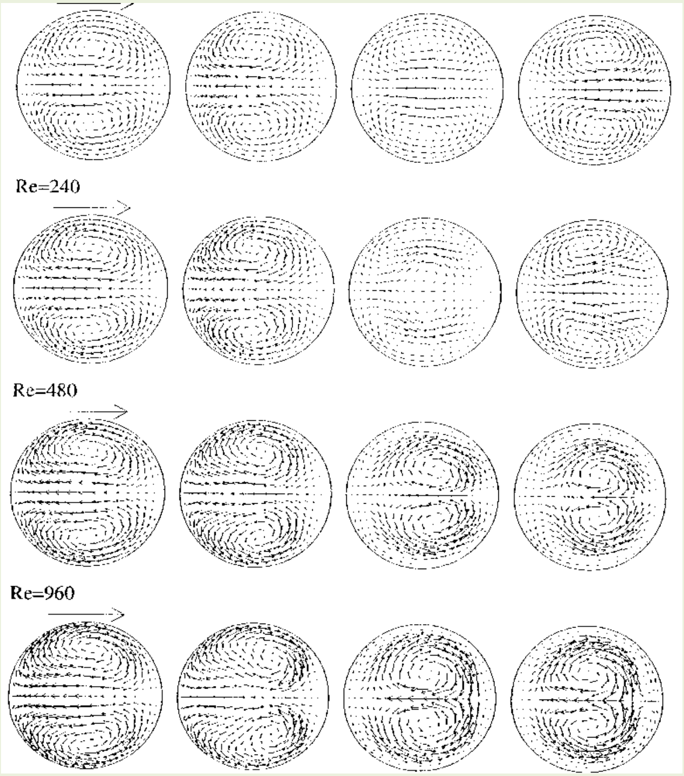
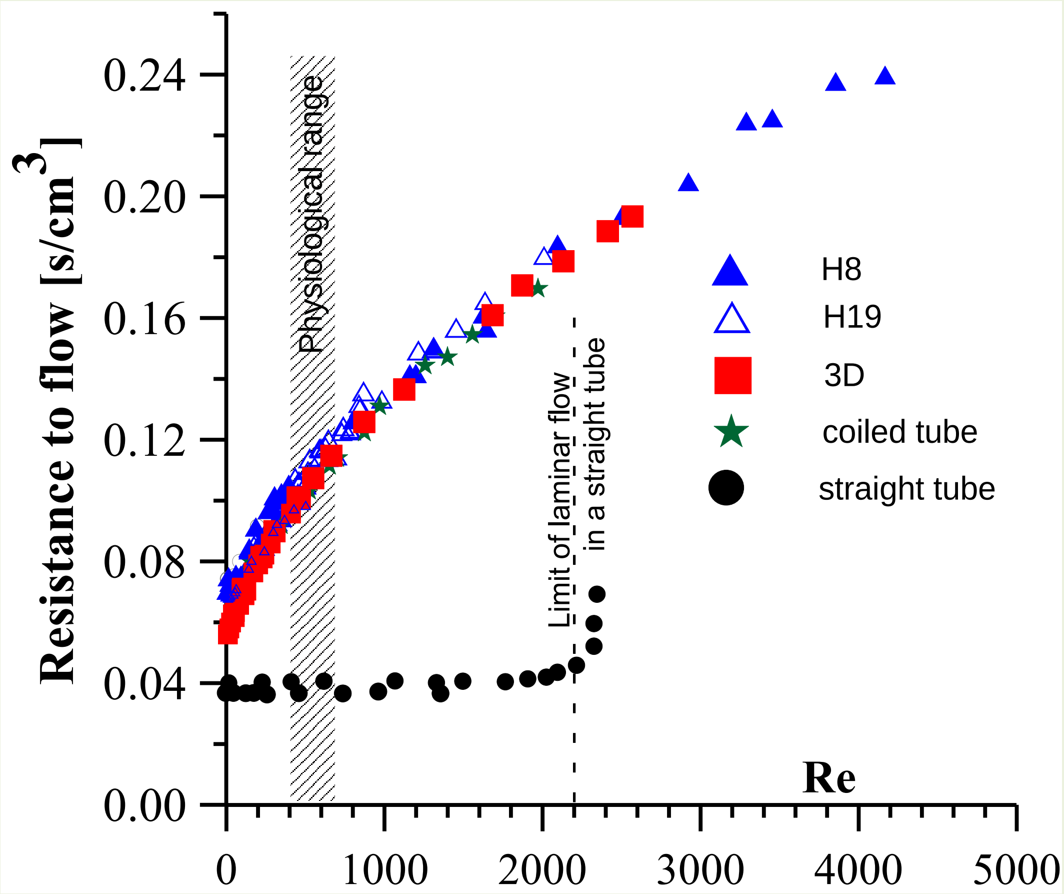




- Centrifugal effect deforms axial velocity profile and develops the secondary flow which has vortex pattern.
- The resultant flow is helical in both halves of the tube

Thanks to Prof.K.Cieslicki

Resistance to flow of tortuous tubes

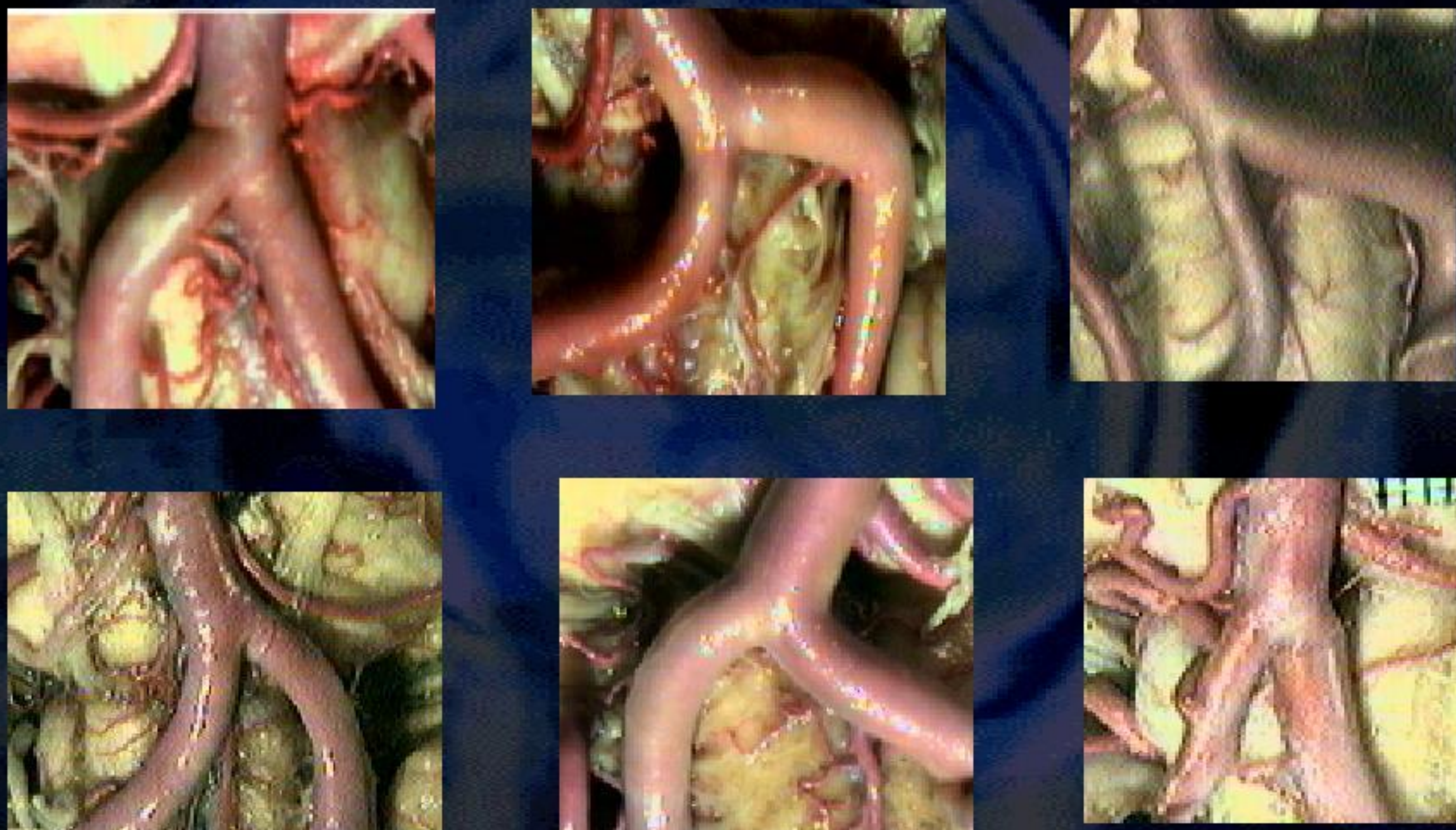


- All characteristics start from the value obtained for a straight tube (HP formula)
- Regardless the tube shape, the resistance to flow is well fitted by equation:
- $Z = J/Q = A + B\ Re^{0.5}$

- The resistance to flow of curved tube is velocity dependent
- In physiological range of flow the resistance to flow is about four times grater than the resistance to flow of a straight tube

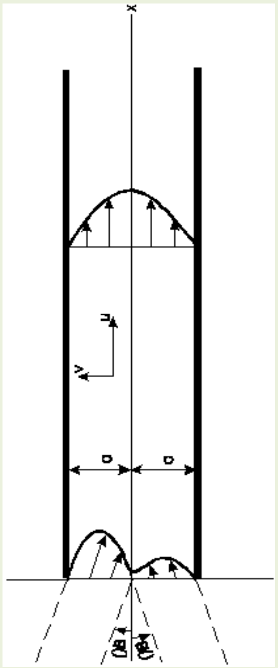
Thanks to Prof. K.Cieslicki

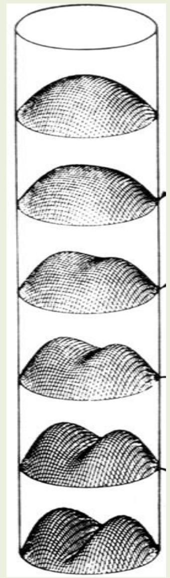
Vertebrobasilar junctions

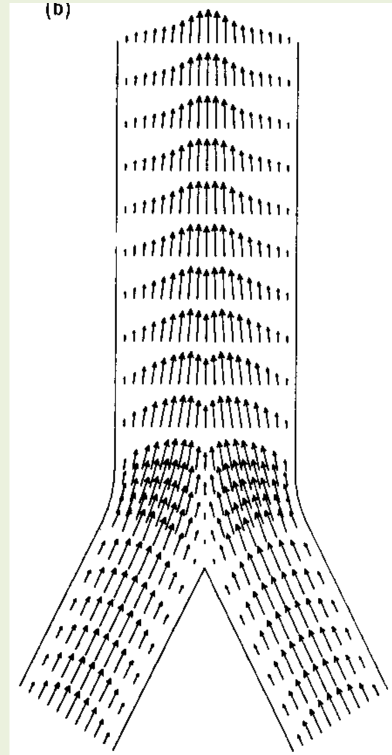


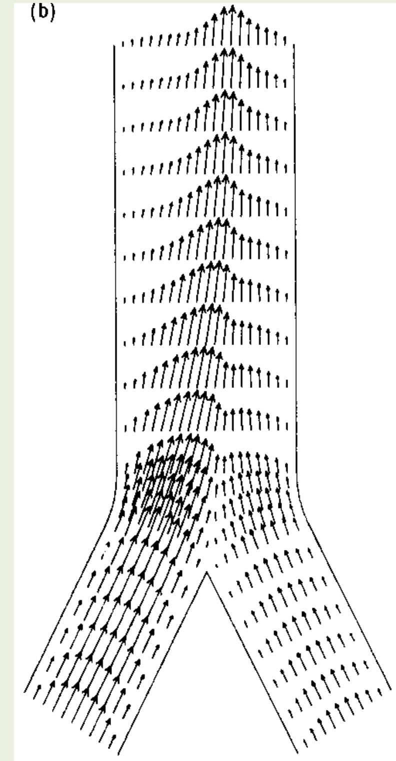
Thanks to Prof. K.Cieslicki

Velocity profile in BA in the light of numerical calculation









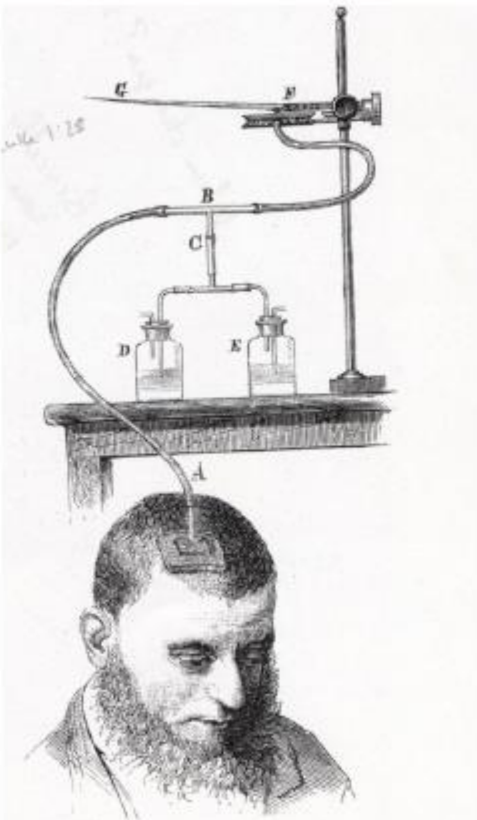
- Double hump velocity profile at the entrance of the BA gradually transforms into parabolic.

- Laminar velocity profile development at the entrance region of a channel leads to an overall change in the axial pressure drop

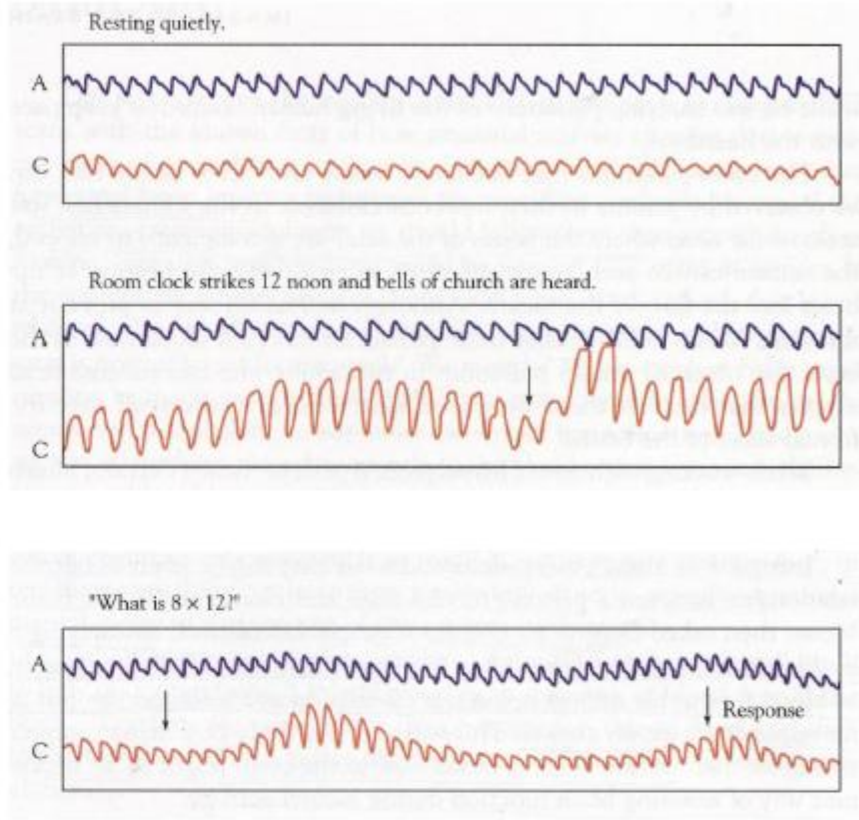
- Due to small BA length an asymmetric in-flow results in an asymmetric out-flow

Thanks to Prof. K.Cieslicki

Cerebral Blood Flow (CBF) vs. Brain Function



The apparatus used by Mosso to record brain pulsations.



(A) Forearm; (C) Brain

By Angelo Mosso, late 19 century

Cerebral metabolism

The brain, undertaking normal intellectual functioning, uses oxygen at a rate of approximately 35 mL/min/kg brain tissue; so, for a 70 kg man with 1.5 kg brain, basal whole body oxygen consumption is 280 mL/min with brain oxygen consumption of 50 mL/min.

CBF x AVDO2 = CMRO2

AVDO2- arterio venous difference of oxygen concentration

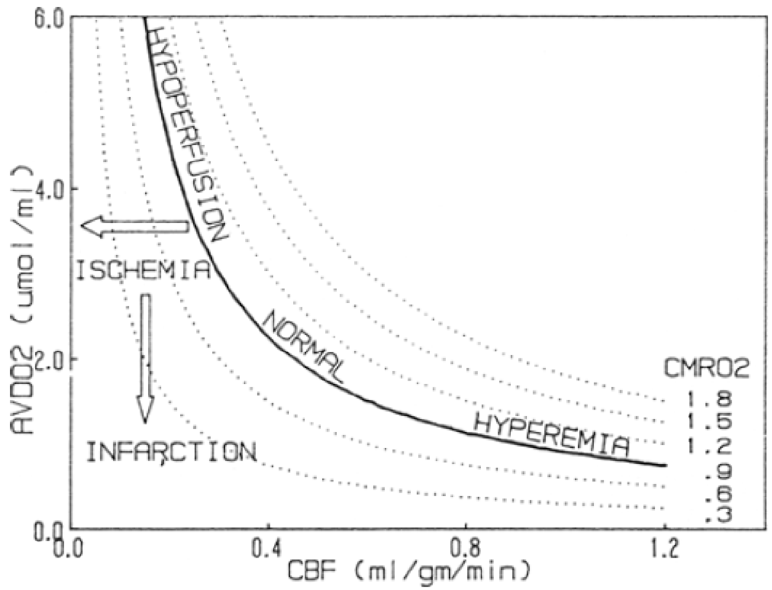
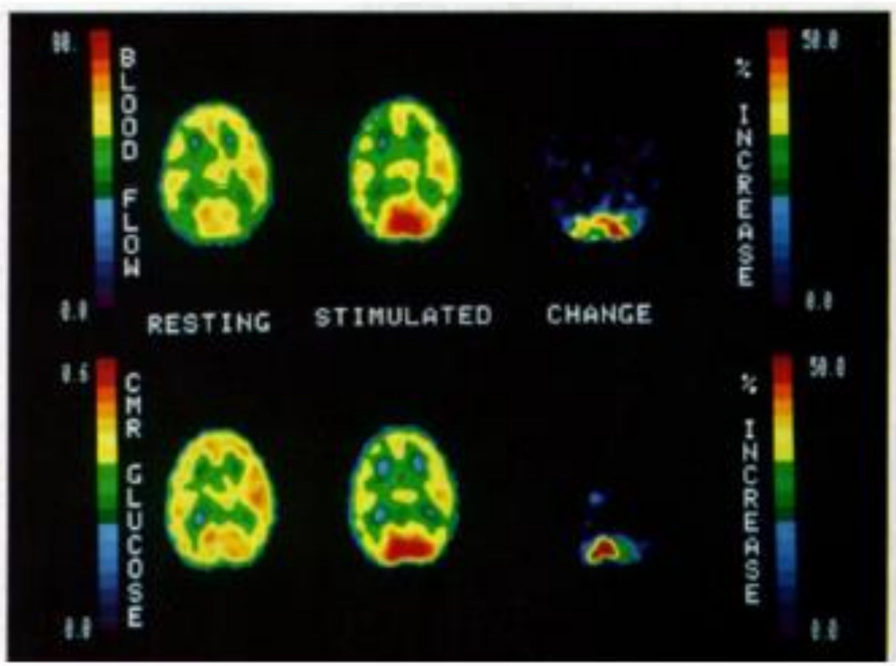


FIG. 8. Model diagramming the relationship between cerebral blood flow (CBF) and cerebral metabolism in comatose patients. In the absence of cerebral ischemia, the arteriovenous oxygen difference ($AVDO_2$) and CBF have the relationship illustrated by the solid curve, with cerebral metabolic rate of oxygen ($CMRO_2$) averaging 0.9 μmol/gm/min. In the presence of cerebral ischemia/infarction *(open arrows)*, $AVDO_2$ and CBF have an unpredictable relationship.

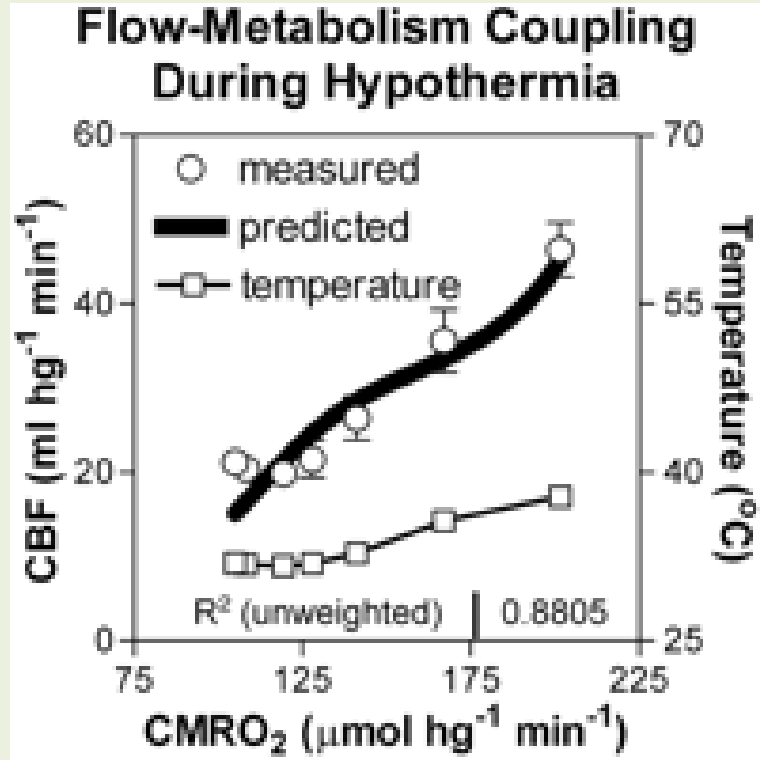
From CS.Robertson et al.n J.Neurosurg 1989:70

Flow- Metabolism coupling

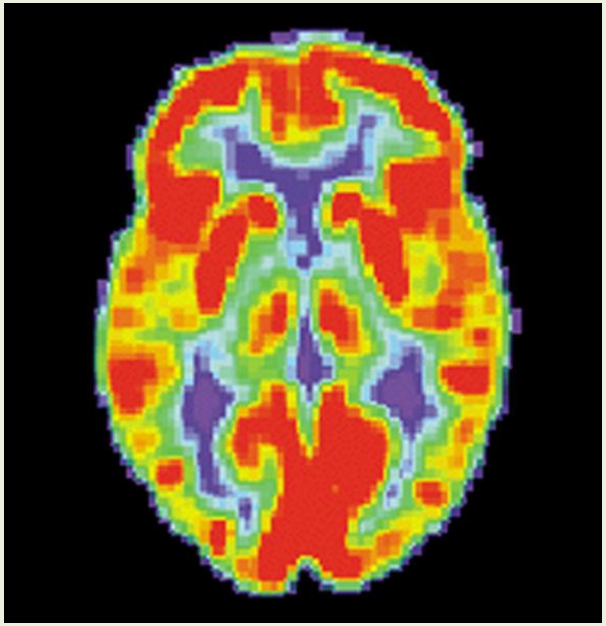


CBF: 50%

CMR_{Glc}: 51 %



Cerebral metabolism can be measured with PET



CMRO2

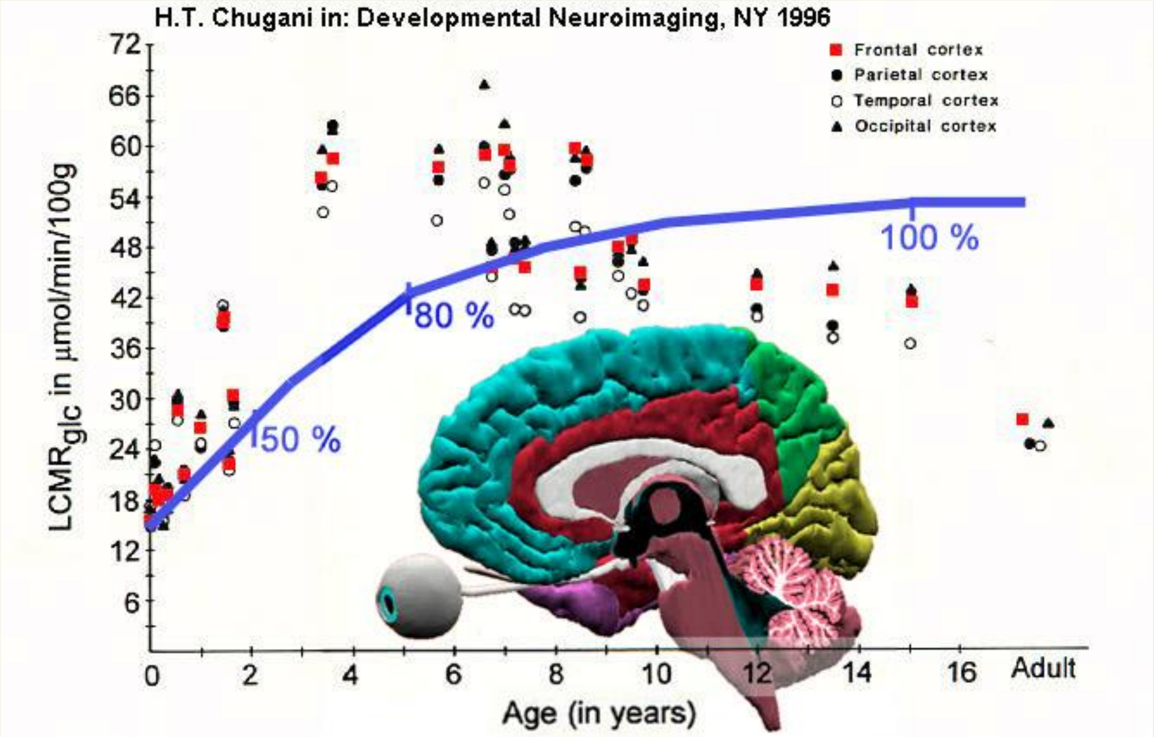


Figure 5 Absolute values of local cerebral metabolic rates for glucose (LCMRglc) for cortical brain regions, plotted as a function of age in normal infants and children, and corresponding adult values. In the infants and children, points represent individual values of LCMRglc; in adults, points are mean values from 7 subjects, in which the size of the symbols equals the standard error of the mean.

CMRGlu

Messages to take home:

- Cerebral blood flow about 2000 times greater than CSF flow
- four compartments: Arteries, arterioles, capillaries, veins
- Circle of Willis- ideal mixer?
- Venous outflow: highly individual
- Role of bridging veins- site of coupling ICP and cerebral venous pressure