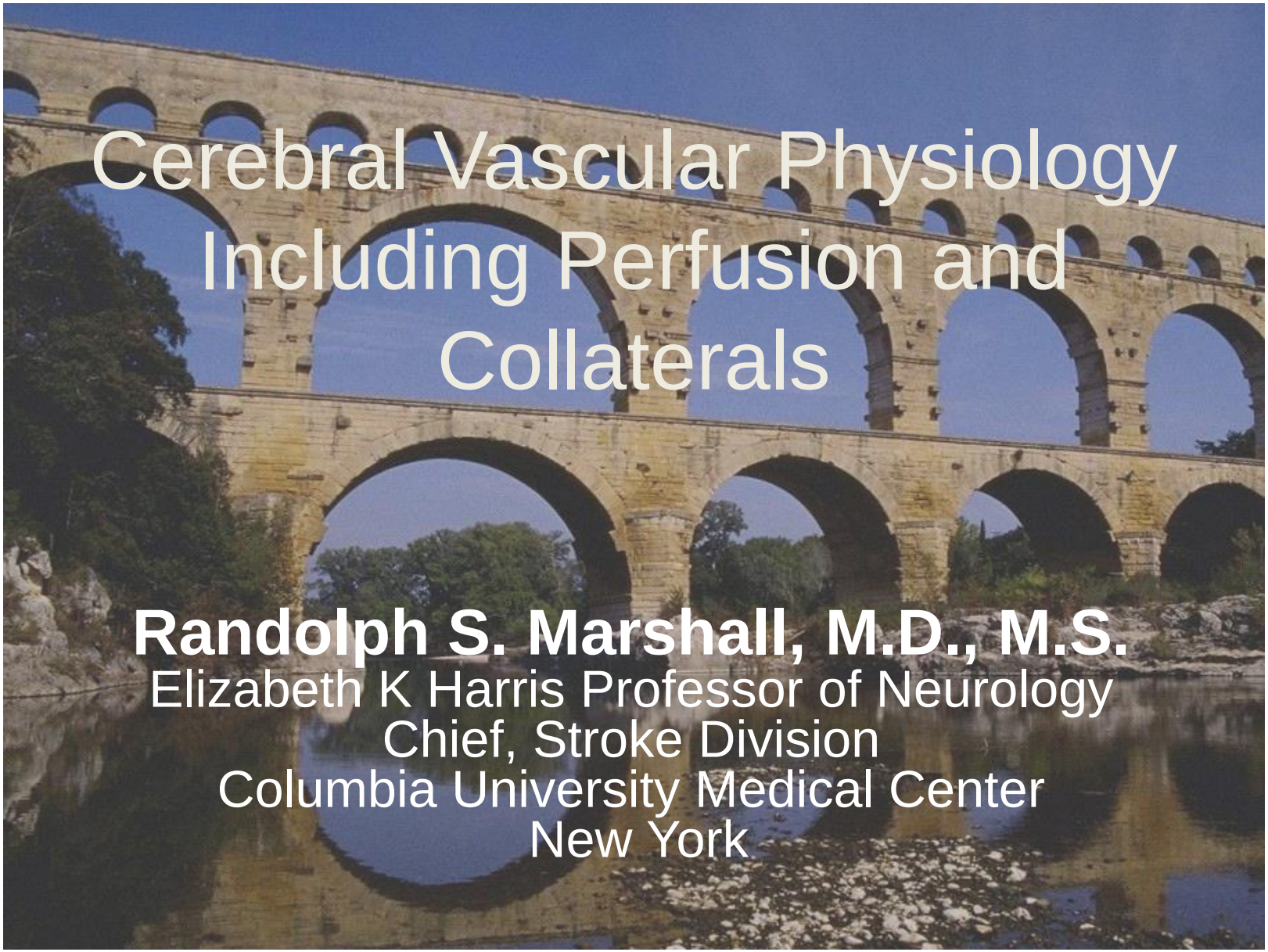

Cerebral Vascular Physiology Including Perfusion and Collaterals

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

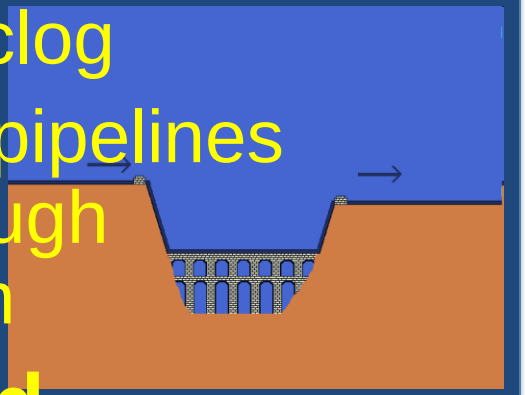
Affiliation/Financial Relationship	Company
• 1R01NS076277-01A1	• NIH/NINDS
• 5P50NS049060	• NIH/NINDS
• 1U10 NS086728	• NIH/NINDS
• Royalty Income	• Elsevier

Disclosure Statement of Financial Interest

I, Randolph Marshall, MD, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

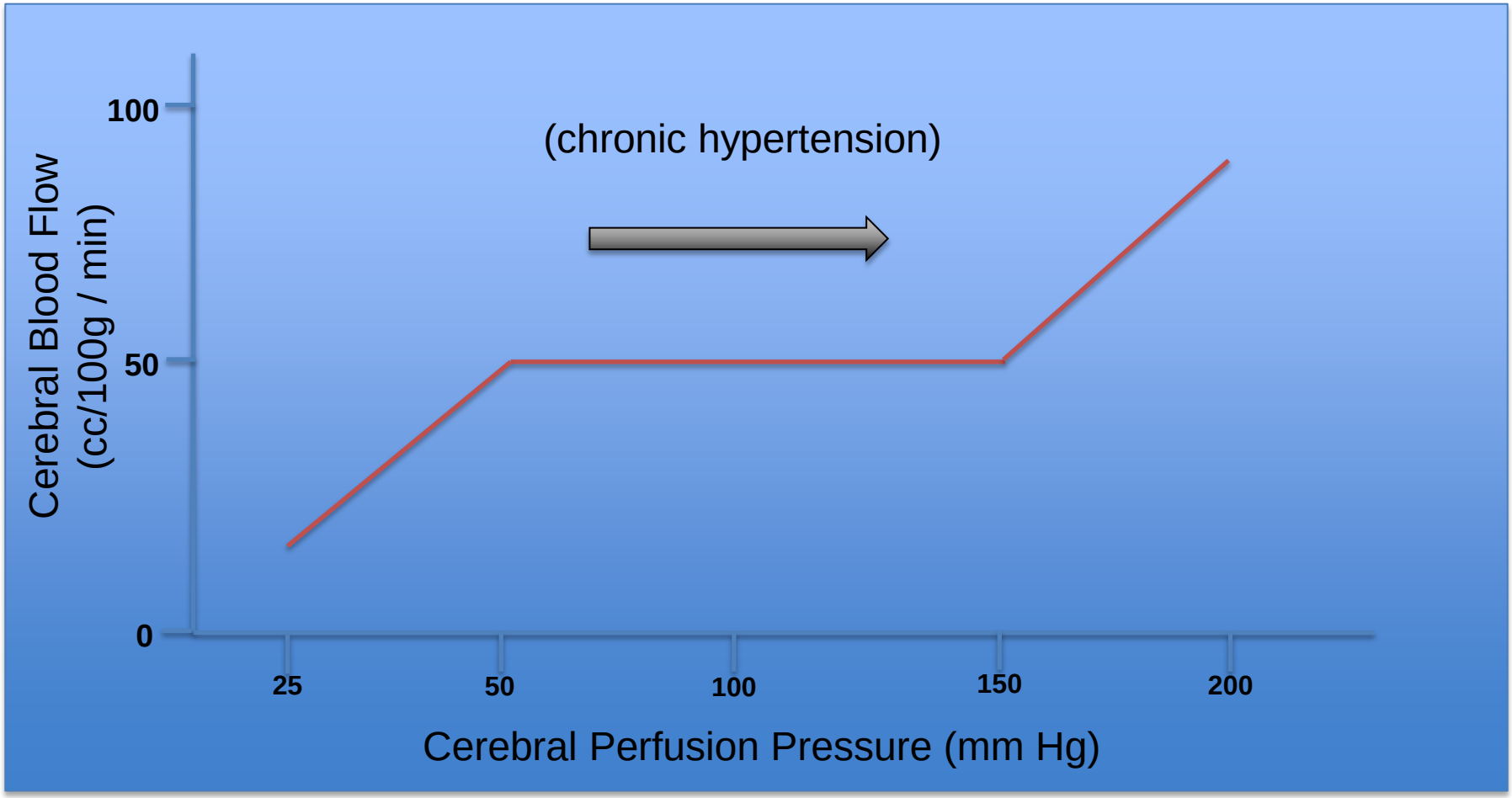
Hydrodynamics of Roman Aqueducts

- **Sophisticated construction**
  - gradient of 34cm per Km (descent of 17m over 50Km) – too steep → overflow; too flat → clog
  - Gravity-pressurized pipelines (siphons) to get through depressions of >50m

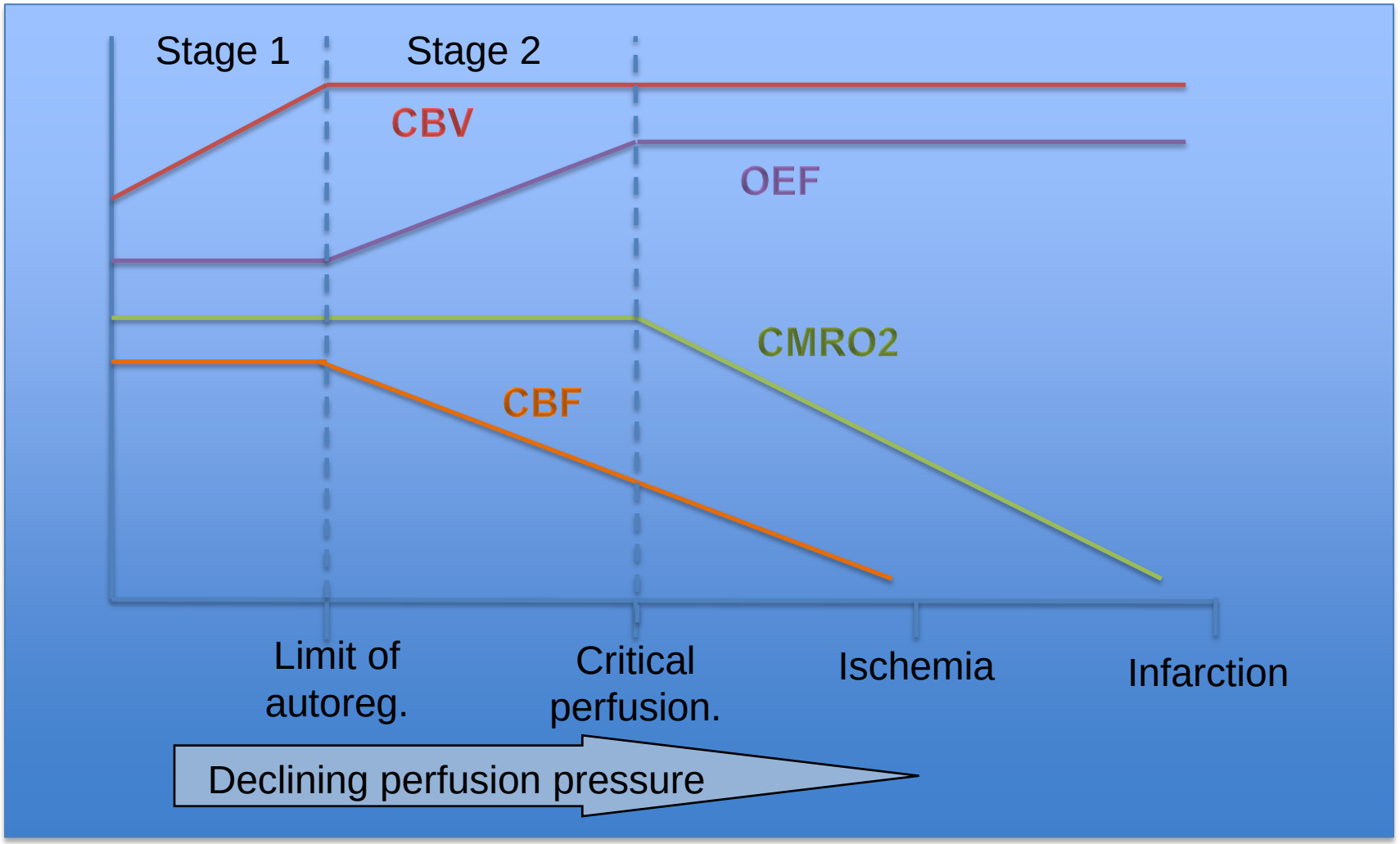


- **Supply and demand**
  - Eleven combined aqueducts brought >50 million gallons to Rome

Cerebral Hemodynamics: Autoregulation



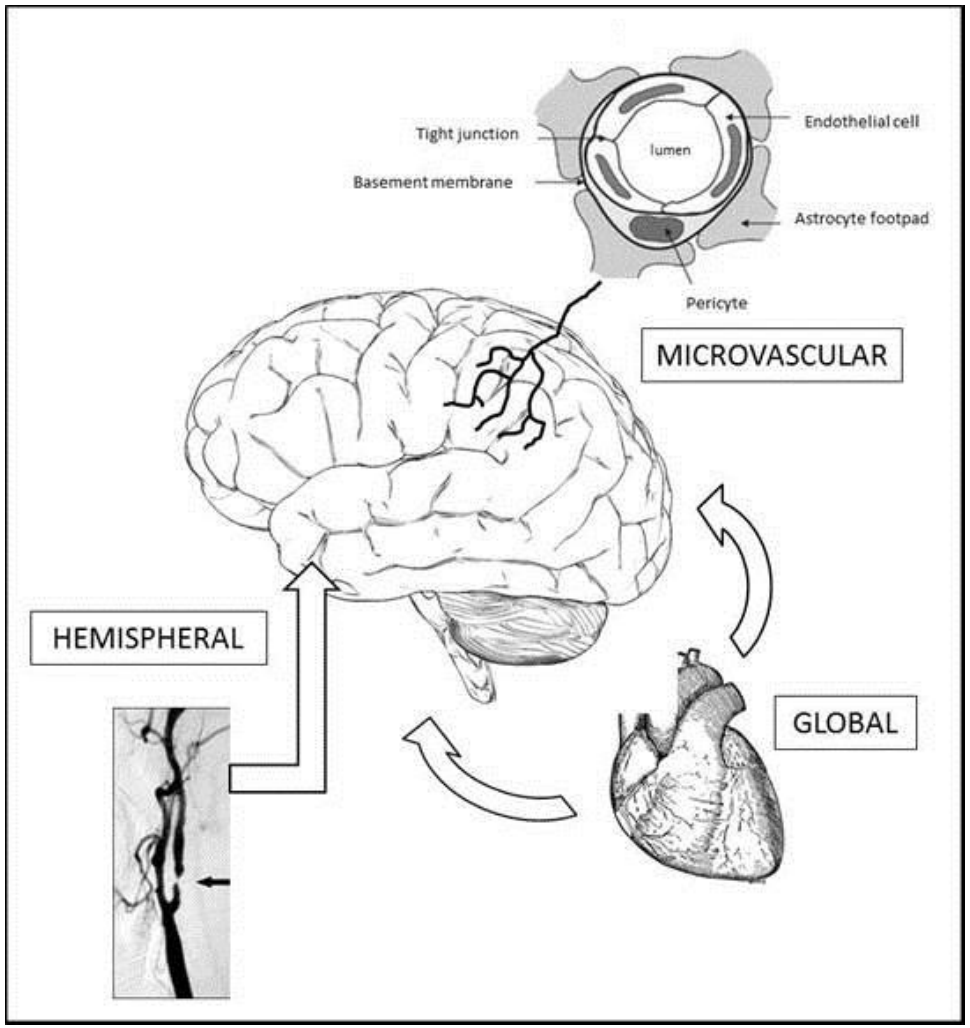
Cerebral Response to Hypoperfusion



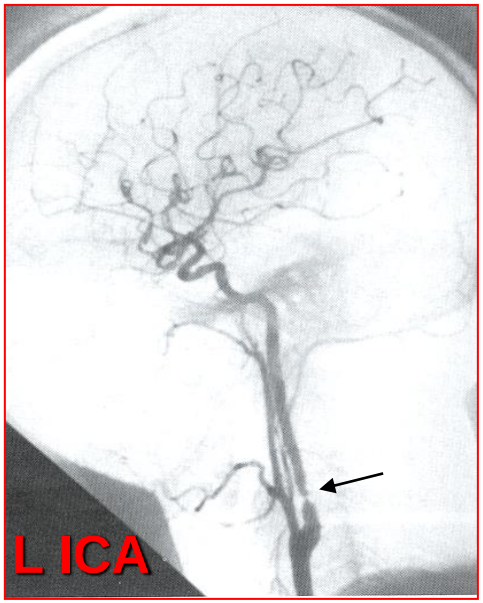
Reasons for autoregulation

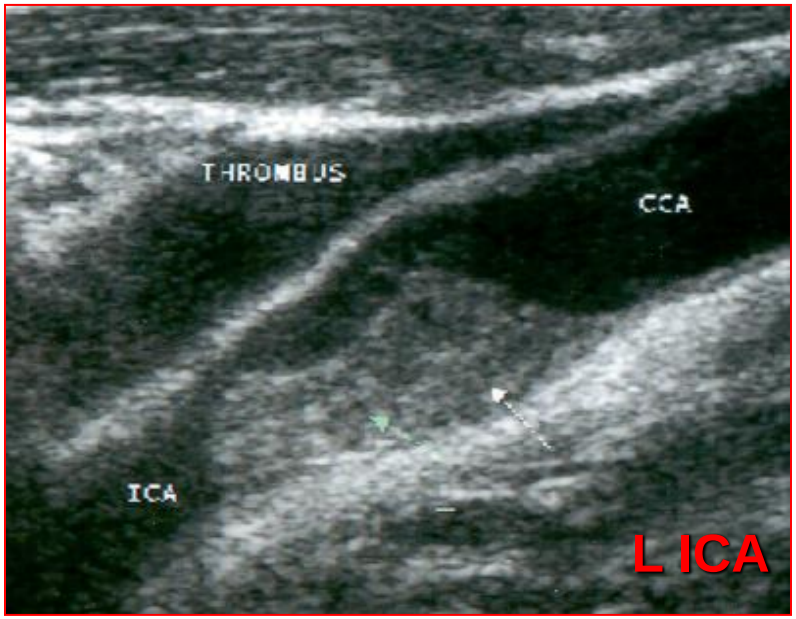
- **Protection of brain from extremes of hypoperfusion and hyperperfusion**
- **Maintain homeostasis: rapid CBF adjustments to fluctuating perfusion pressures within normal range**
- **Neurovascular coupling to ensure adequate blood flow for neural activity**

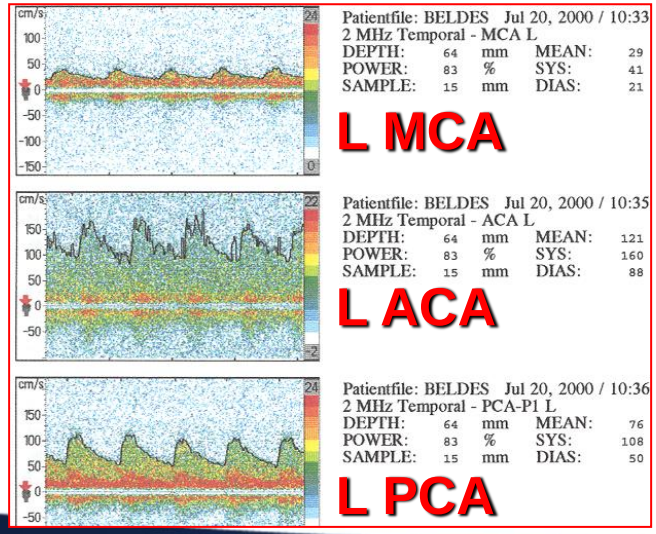
Causes of Cerebral Hypoperfusion

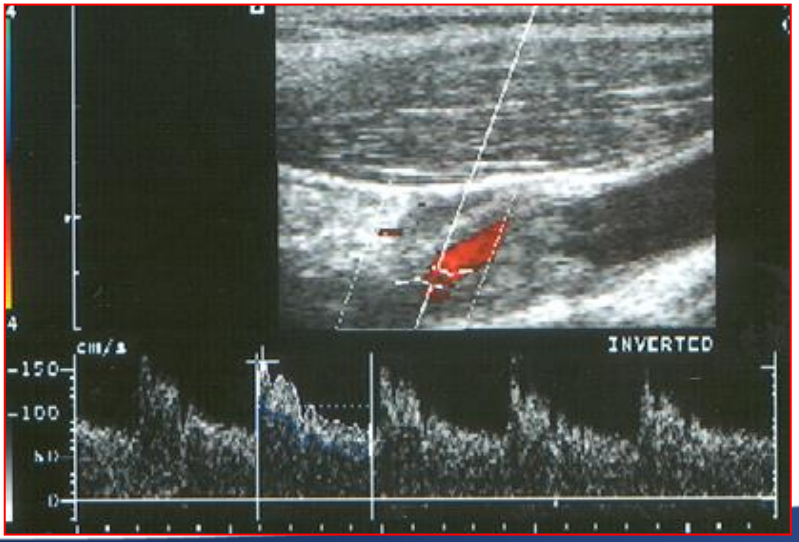


Extracranial 80-90% ICA stenosis



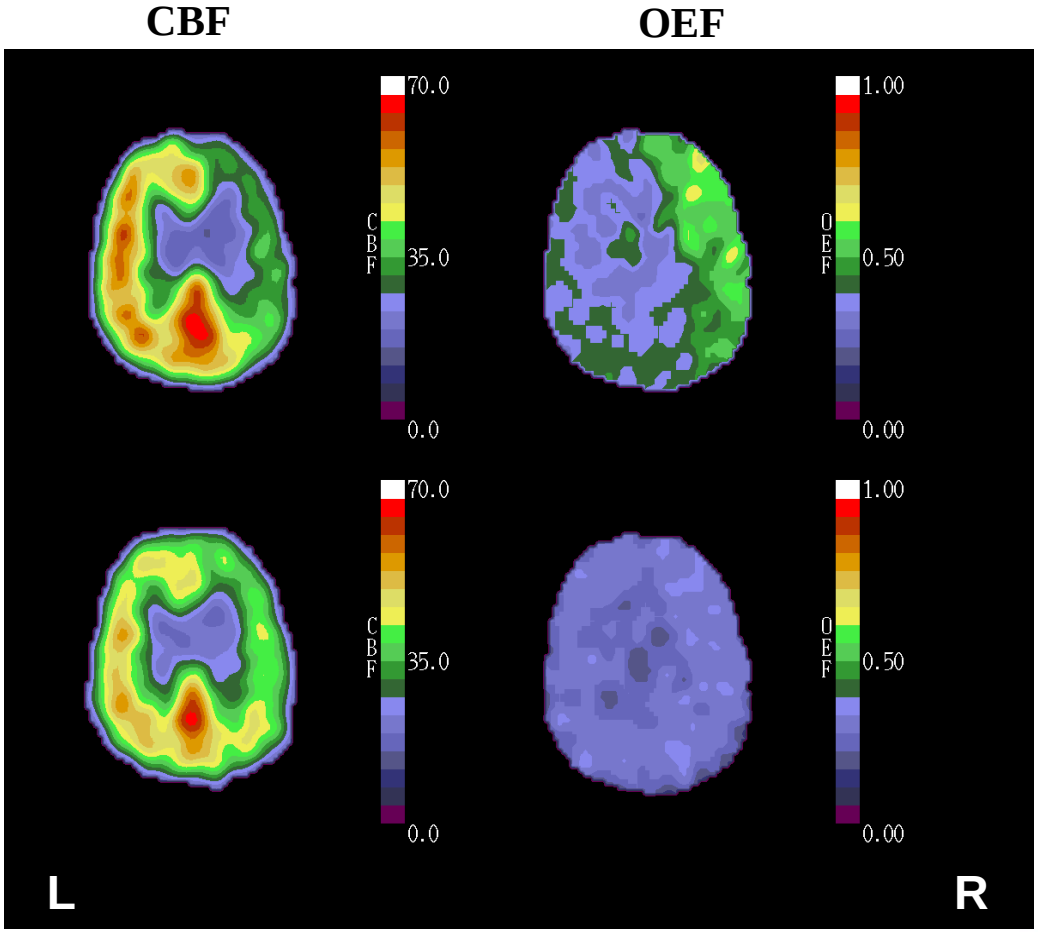






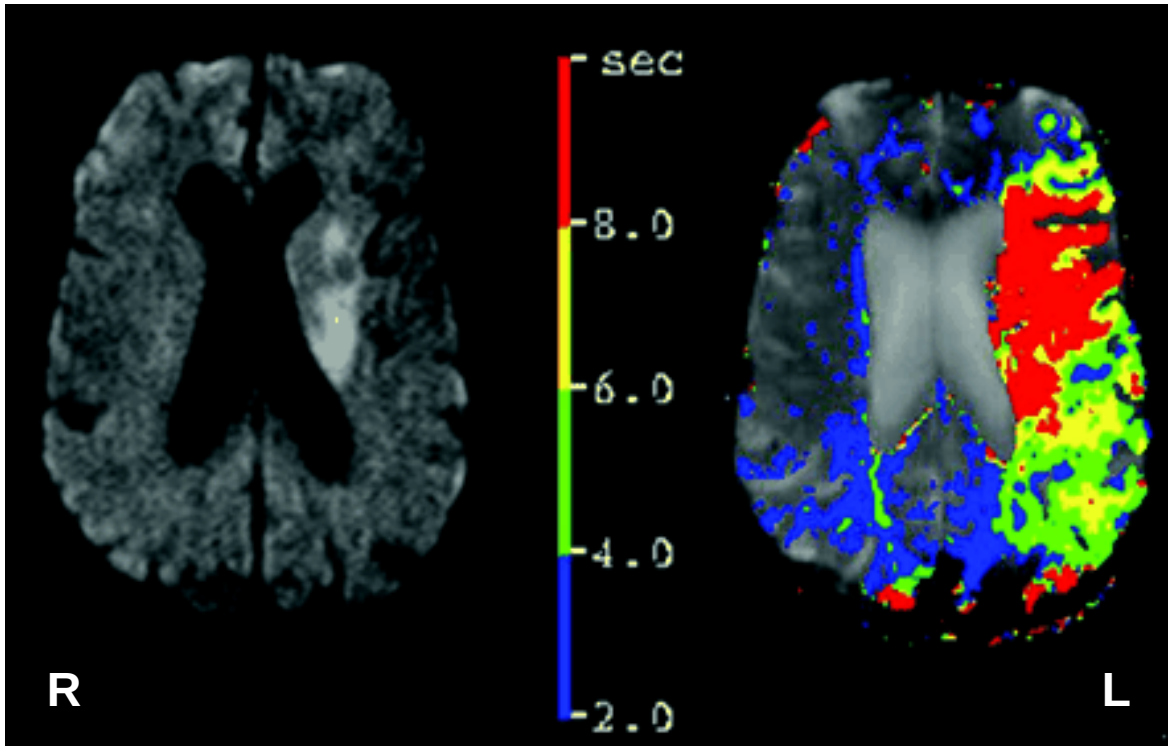
PET imaging of Stage 2 Hemodynamic Failure: Right Carotid Artery Occlusion

After EC/IC Bypass



MRI-guided Stroke Treatment Window

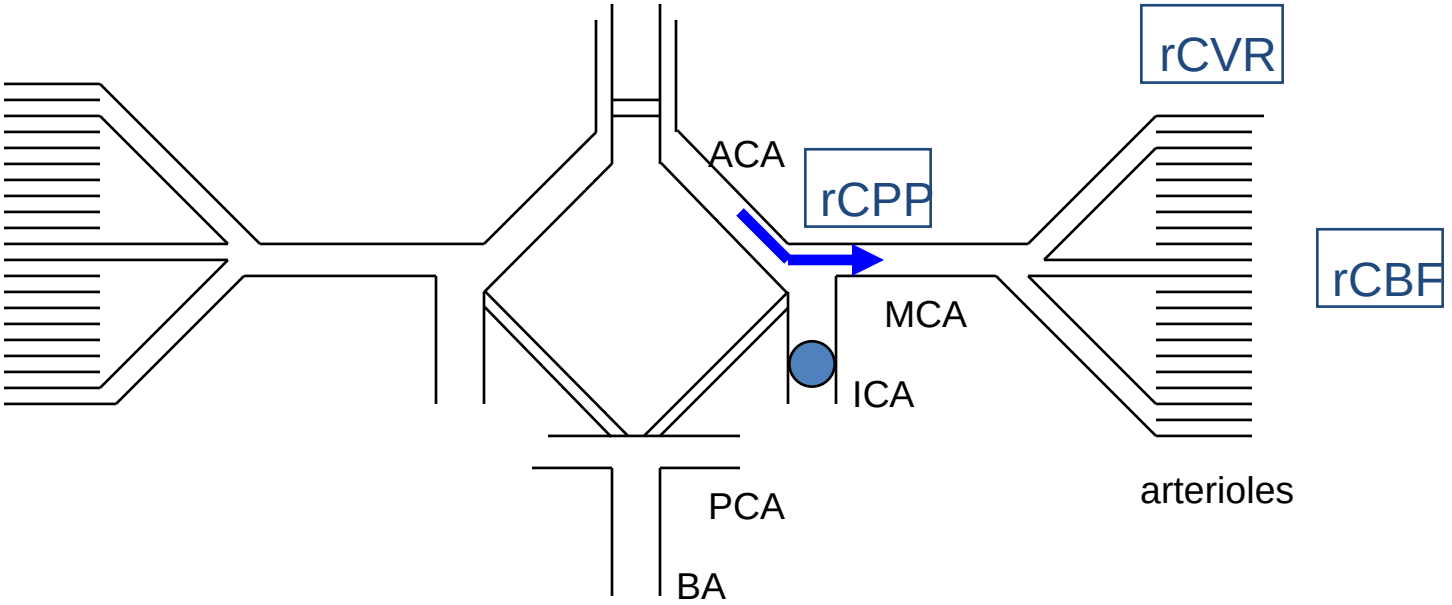
Diffusion-Perfusion Mismatch



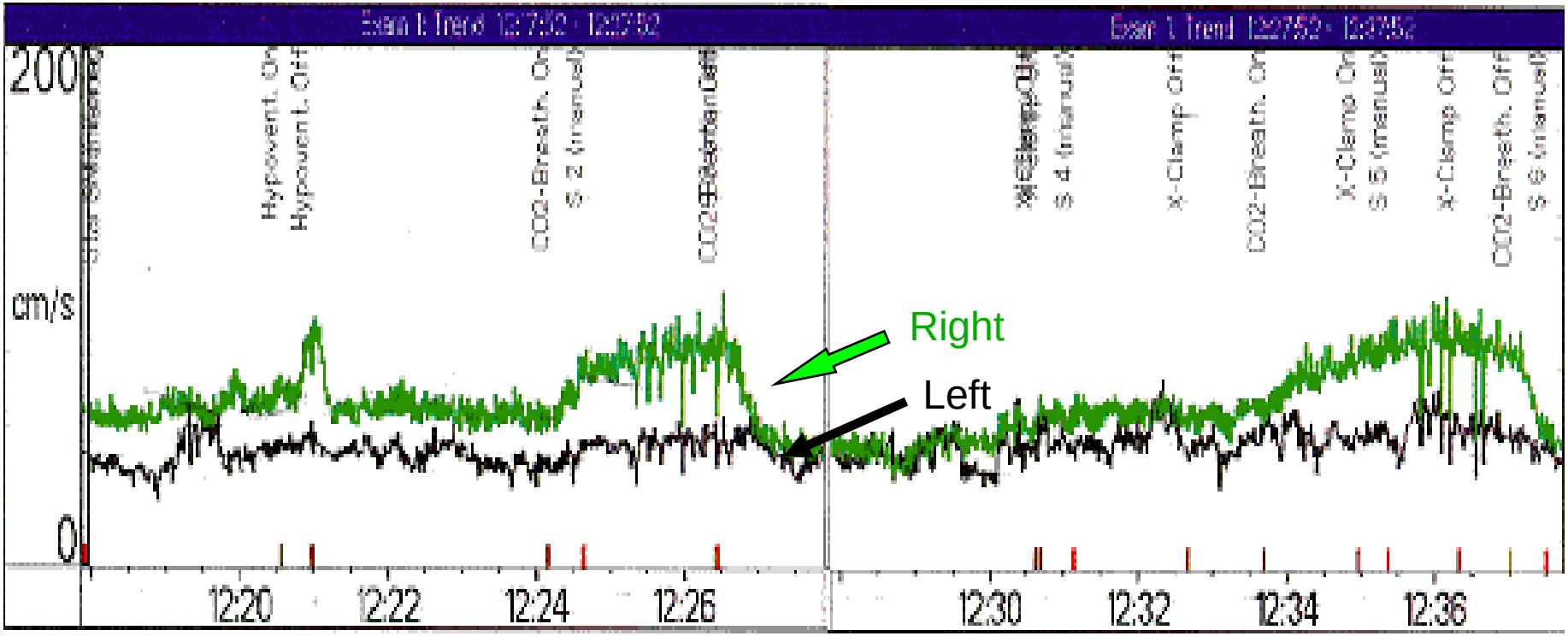
Suzuki S. Stroke 2005;36:e17

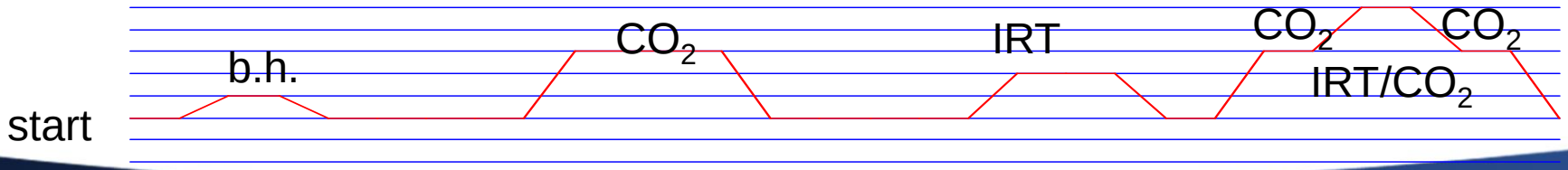
Hemodynamics of Circle of Willis

$$rCBF = rCPP / rCVR$$



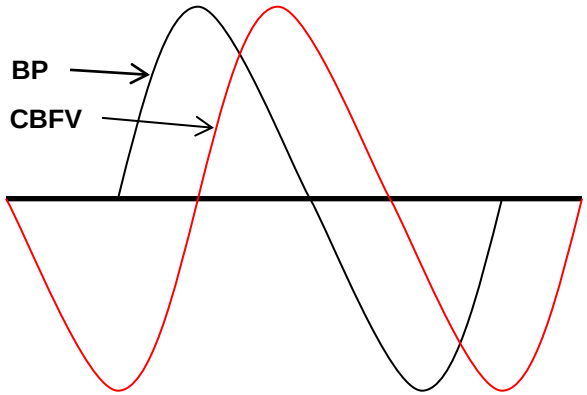
Cerebral Vasodilatory Capacity (CVC): Symptomatic LICA occlusion



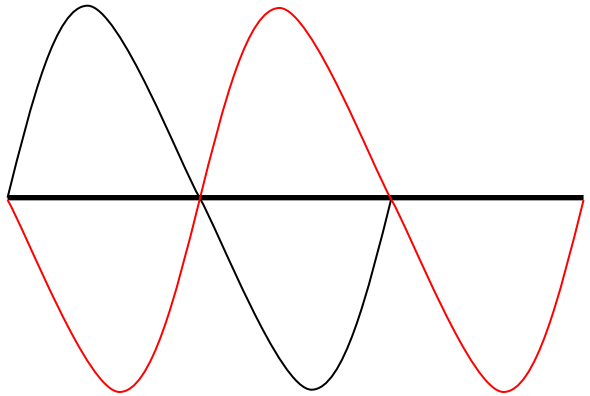


Dynamic Cerebral Autoregulation (DCA)

- Analogous to a ‘correlation’ statistic
  - But applied to two data streams
- Allows calculation of:
  - Coherence: the ‘frequency dependence’ in specific frequency domains (Fourier transform)
  - Phase shift: relative separation of signals



90 degrees out of phase



180 degrees out of phase

DCA Before and After Revascularization

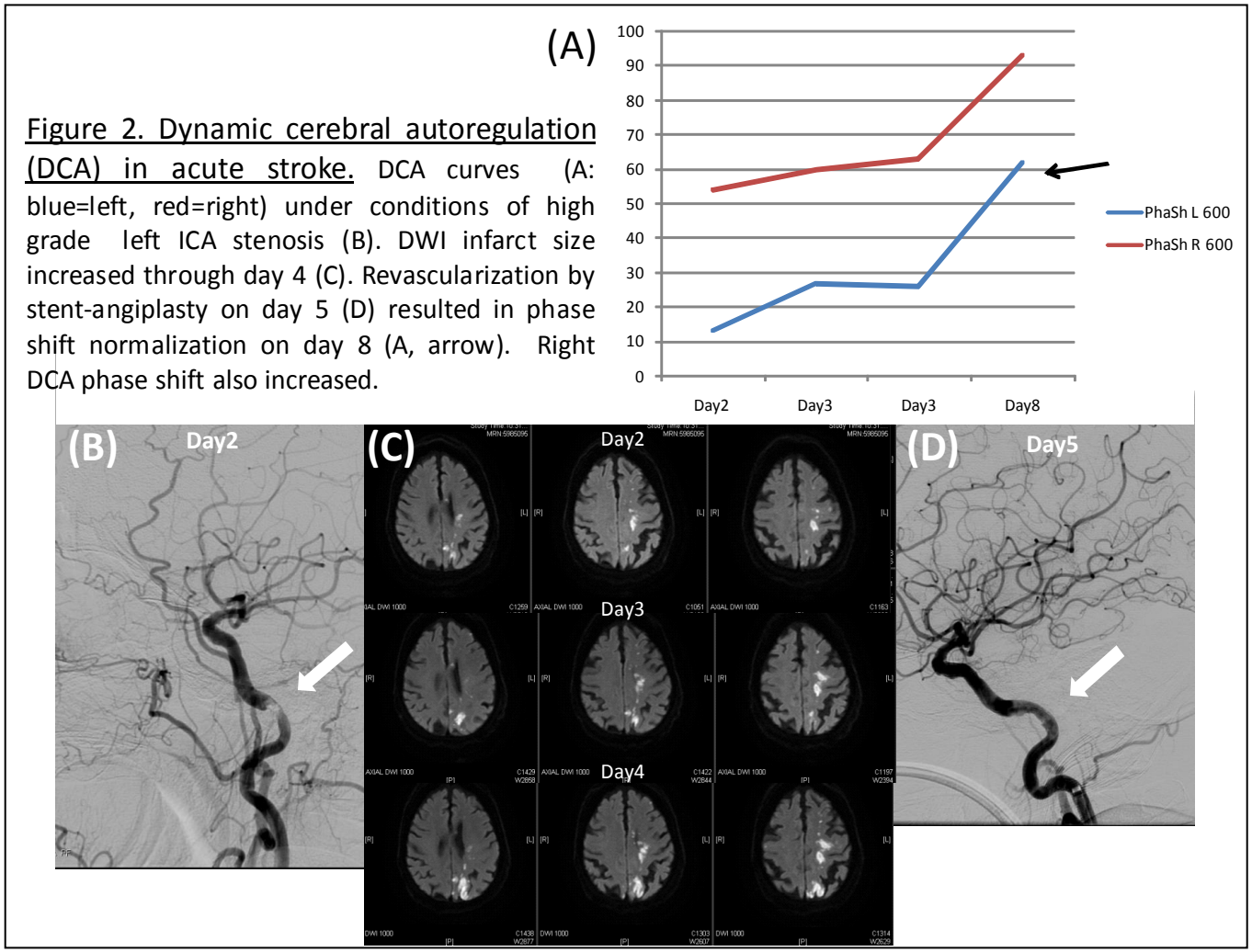
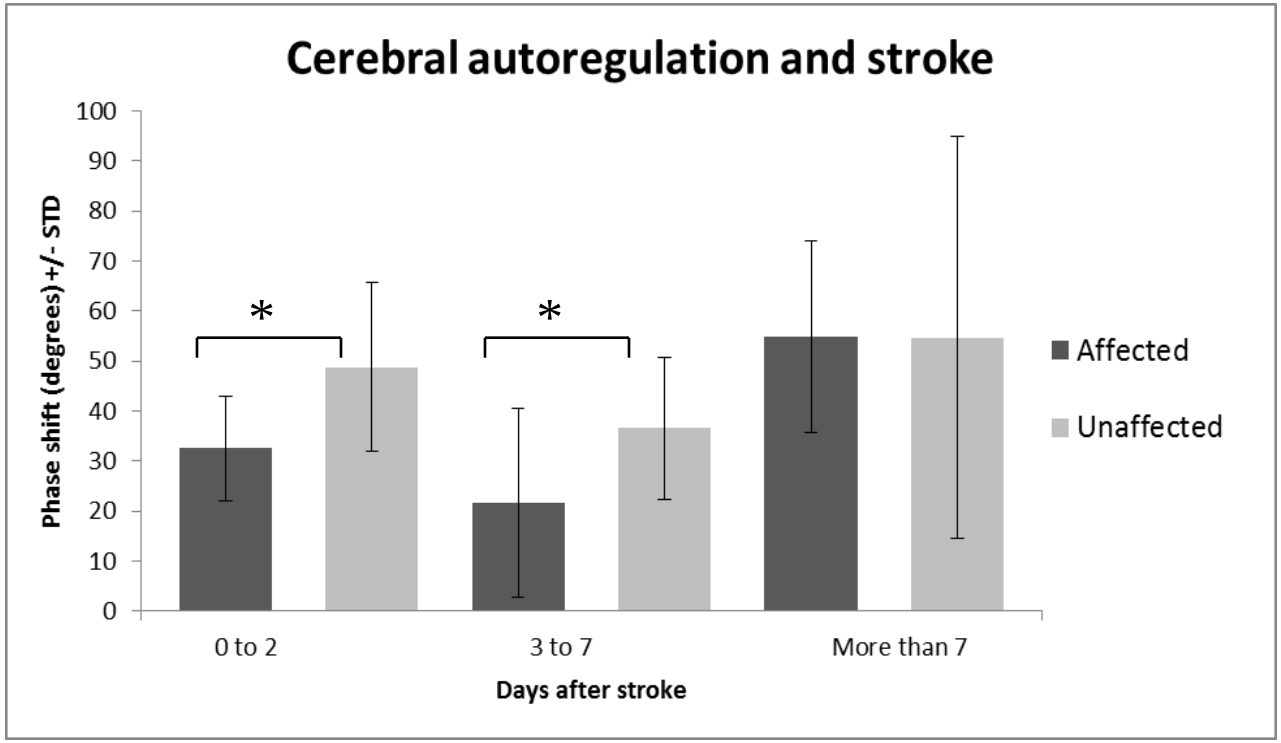


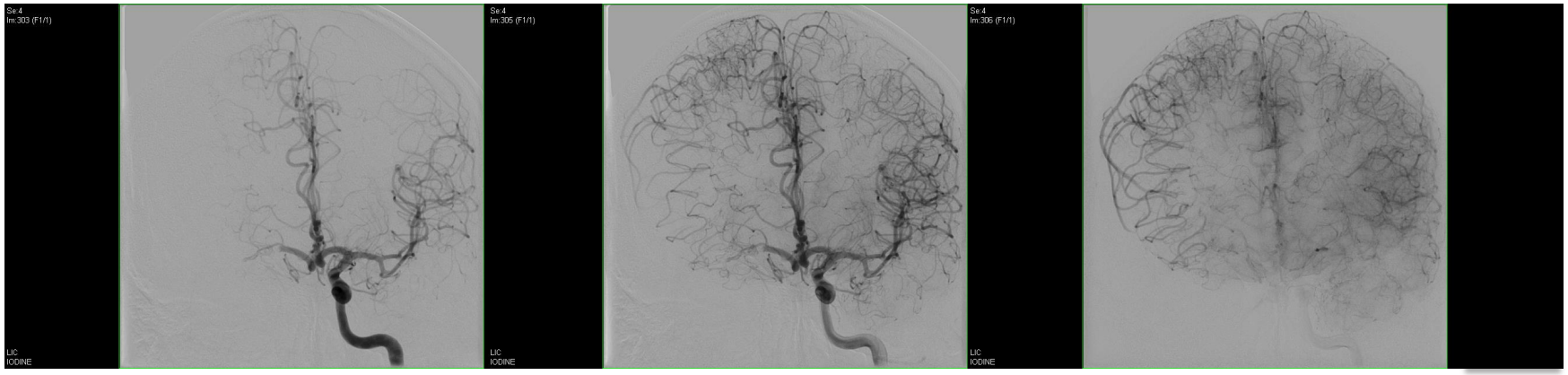
Figure 2. Dynamic cerebral autoregulation (DCA) in acute stroke. DCA curves (A: blue=left, red=right) under conditions of high grade left ICA stenosis (B). DWI infarct size increased through day 4 (C). Revascularization by stent-angiplasty on day 5 (D) resulted in phase shift normalization on day 8 (A, arrow). Right DCA phase shift also increased.

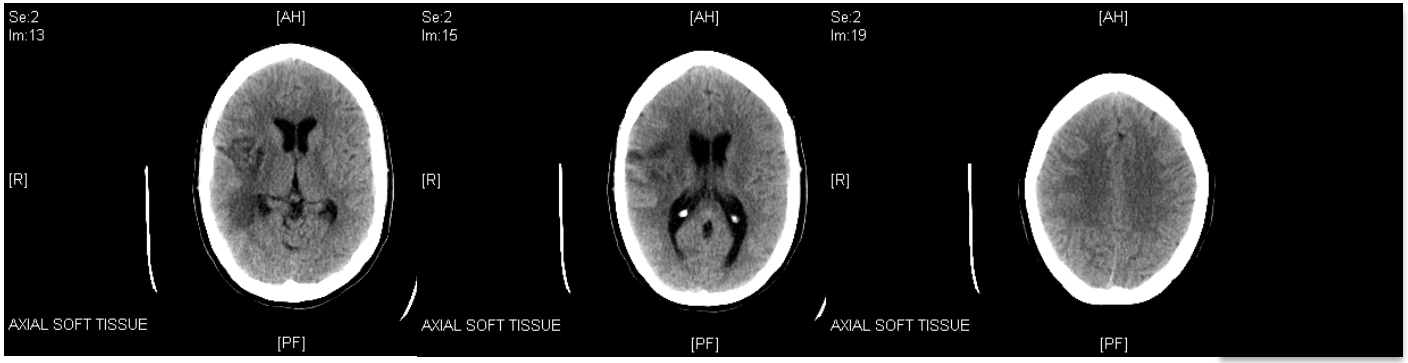
DCA normalization after Acute Stroke

32 patients (mean NIHSS=10±7.3; age=62.9±16.9; 17F) with acute, (embolic, large) ischemic stroke in the middle cerebral artery territory. DCA was assessed on days 0-2, 3-7 and >7 after stroke. Transfer function analysis was applied to calculate average phase shift (PS) in the low frequency range (0.06-0.12 Hz). At mean 1.1±0.6 days after stroke the average PS in the affected hemisphere was **32.5**±10.4 degrees versus **48.8**±16.9 degrees in the unaffected hemisphere (p=0.026). At 4.6±1.3 days, the PS in affected and unaffected hemisphere was **21.6**±18.9 vs. **36.5**±14.3 degrees, respectively (p=0.029). At mean 10.3±2.1 days stroke there was no difference between affected and unaffected hemisphere (**54.8**±19.1 versus **54.7**±40.28 degrees, p=0.99).

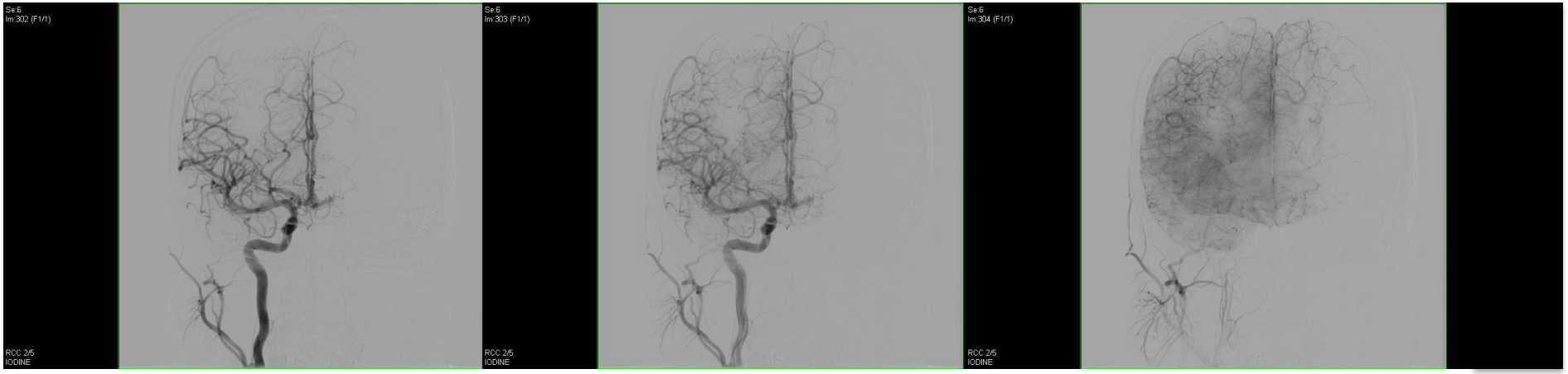


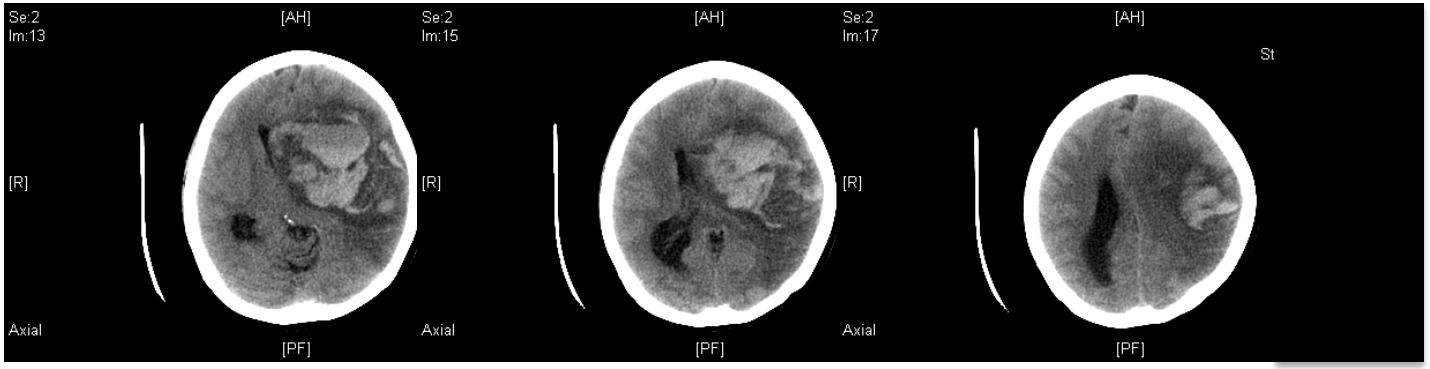
Good Collaterals in Acute Stroke



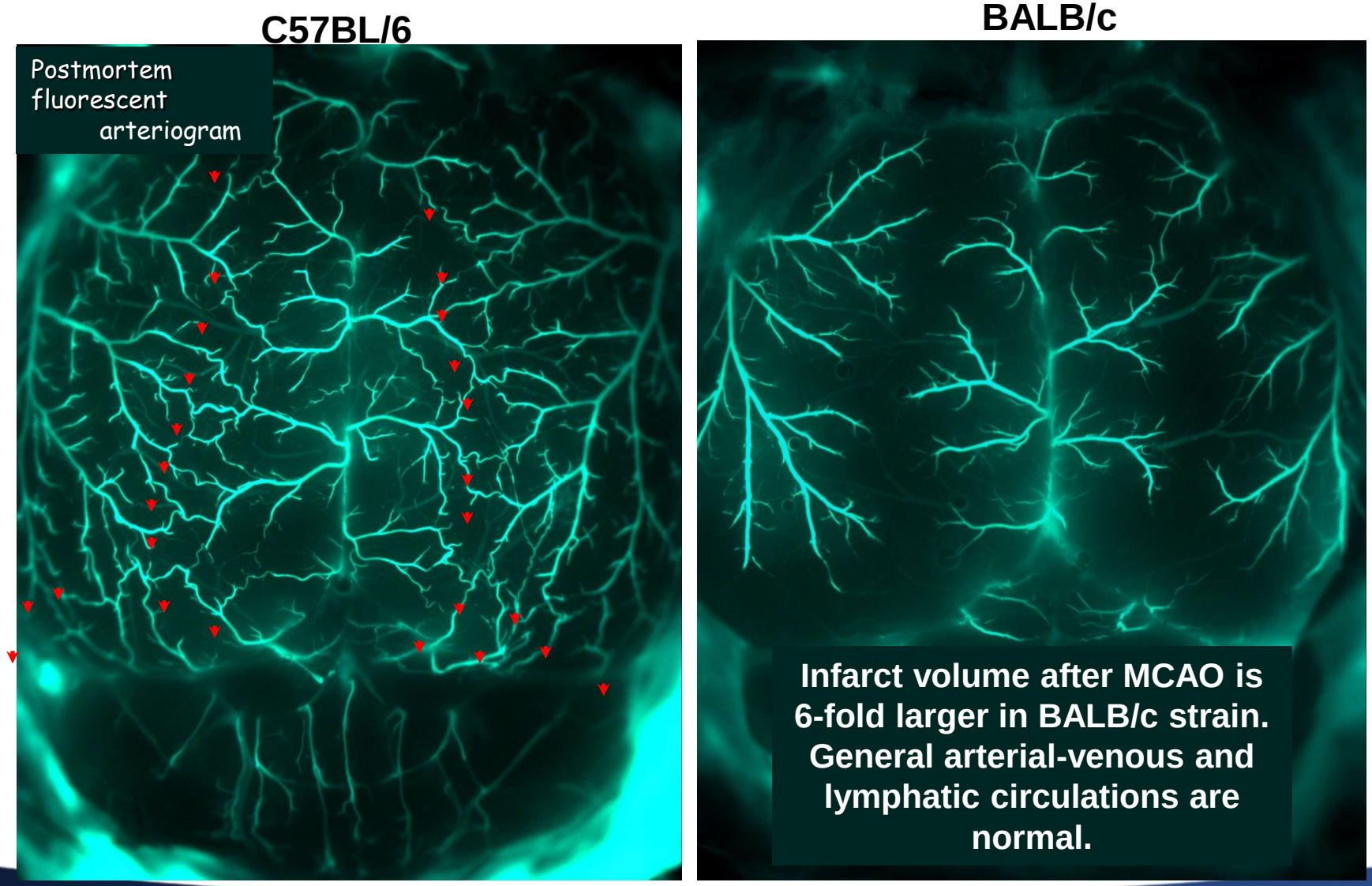


Poor Collaterals in Acute Stroke



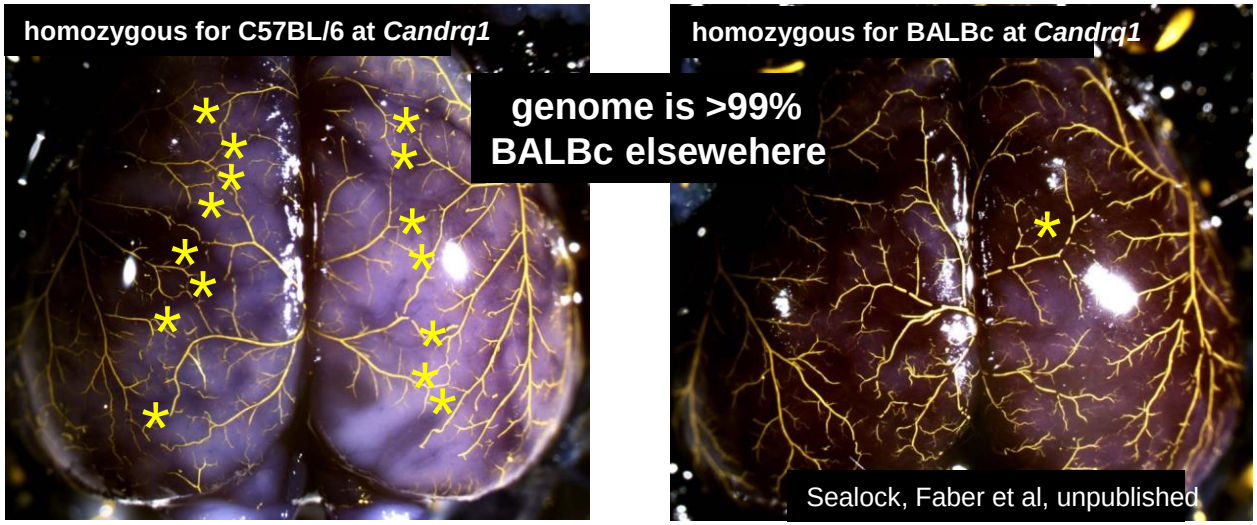


Wide variation in mouse cerebral collaterals



Chalothorn, Faber et al *Physiol Genomics* 2007

Substitution of the "high" collateral 744Kb *Candrq1* allele of the C57BL/6 strain into the BALB/c strain with poor collateral number and diameter largely corrects the defect:



- GENEDCSS study (James Faber, P.I. –UNC)
  - Looking for genetic polymorphisms for collaterals in humans in acute stroke
  - Buccal swab for Candrq1 equivalent
  - Imaging collateral status
  - Clinical outcomes

END

Quantitative CBF by ASL MRI

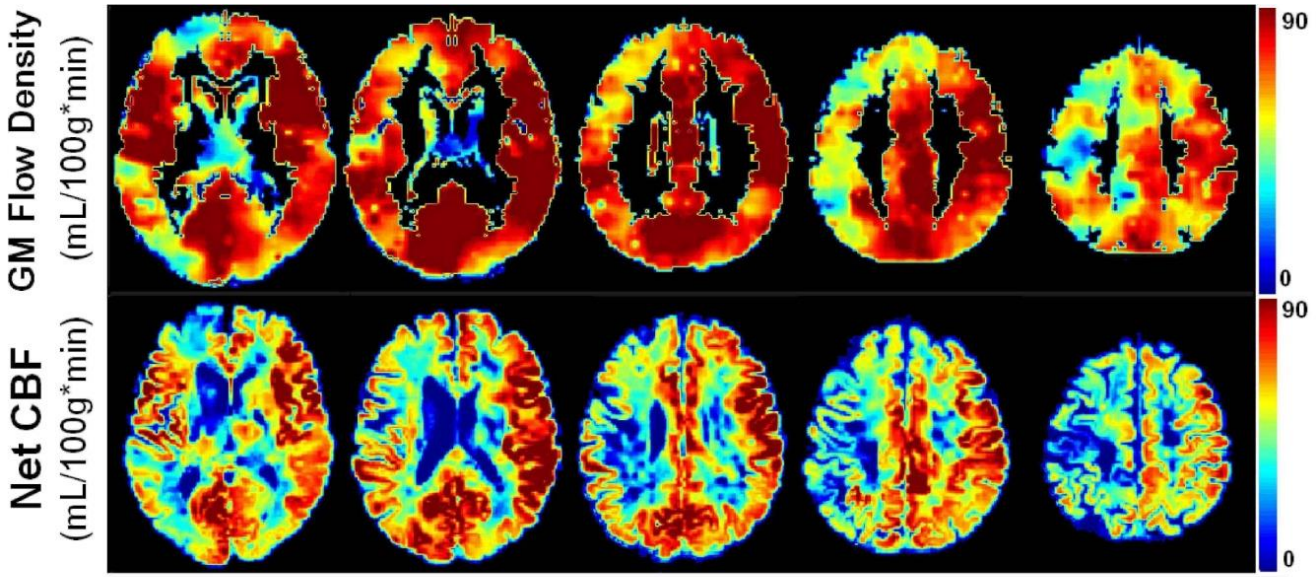
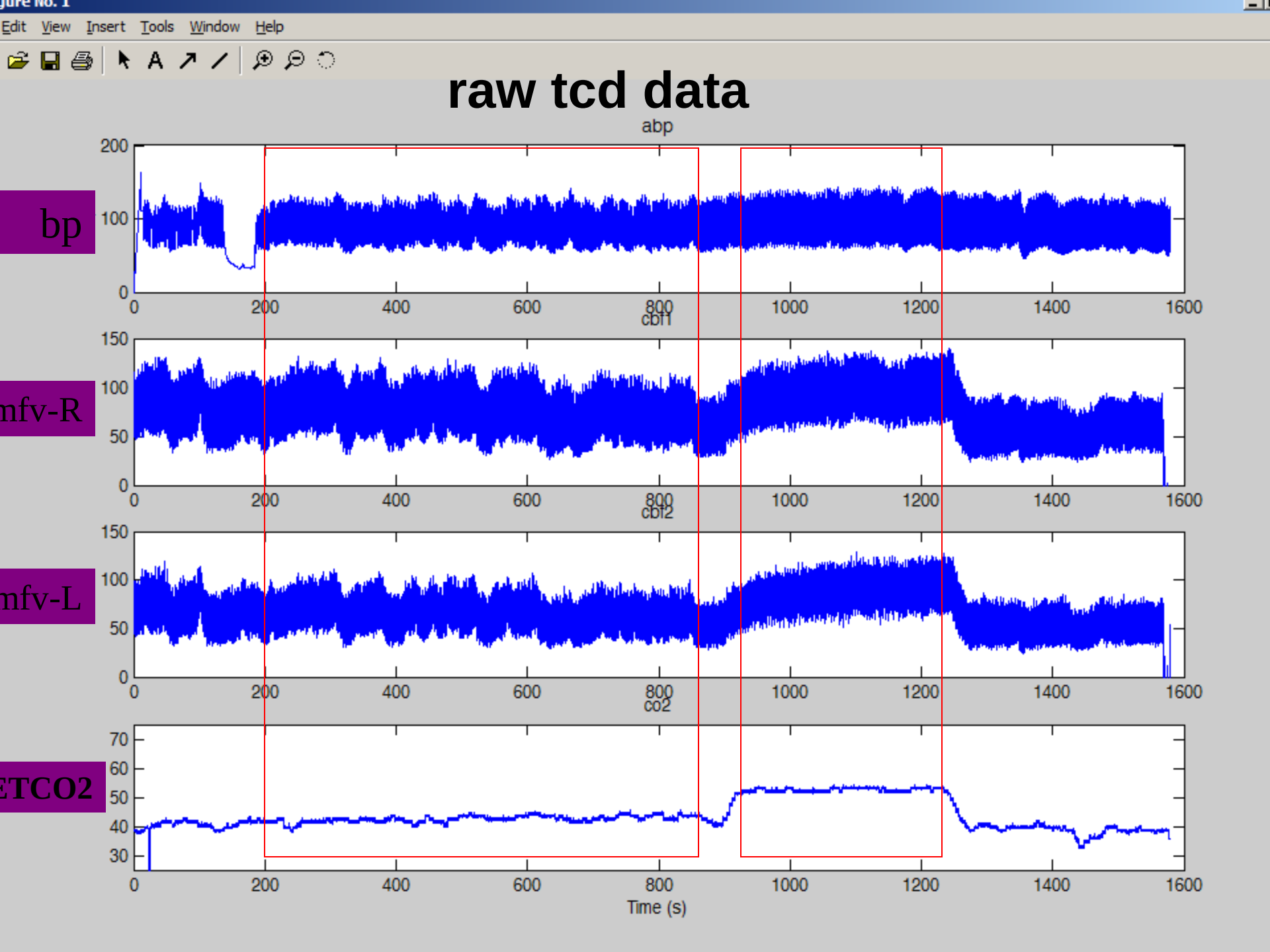


Fig.4: GM flow density (1st row, obtained as per Eq.[1], section 5.4) and net CBF images (2nd row, obtained as per Eq.[5], section 5.4) from the 84 year old patient with 100% left ICA occlusion. Note the assymetry between the affected and unaffected hemispheres. GM flow density does not include tissue content information and as such is expected to be fairly homogenous across the brain in healthy subjects.

Asllani 2009

raw tcd data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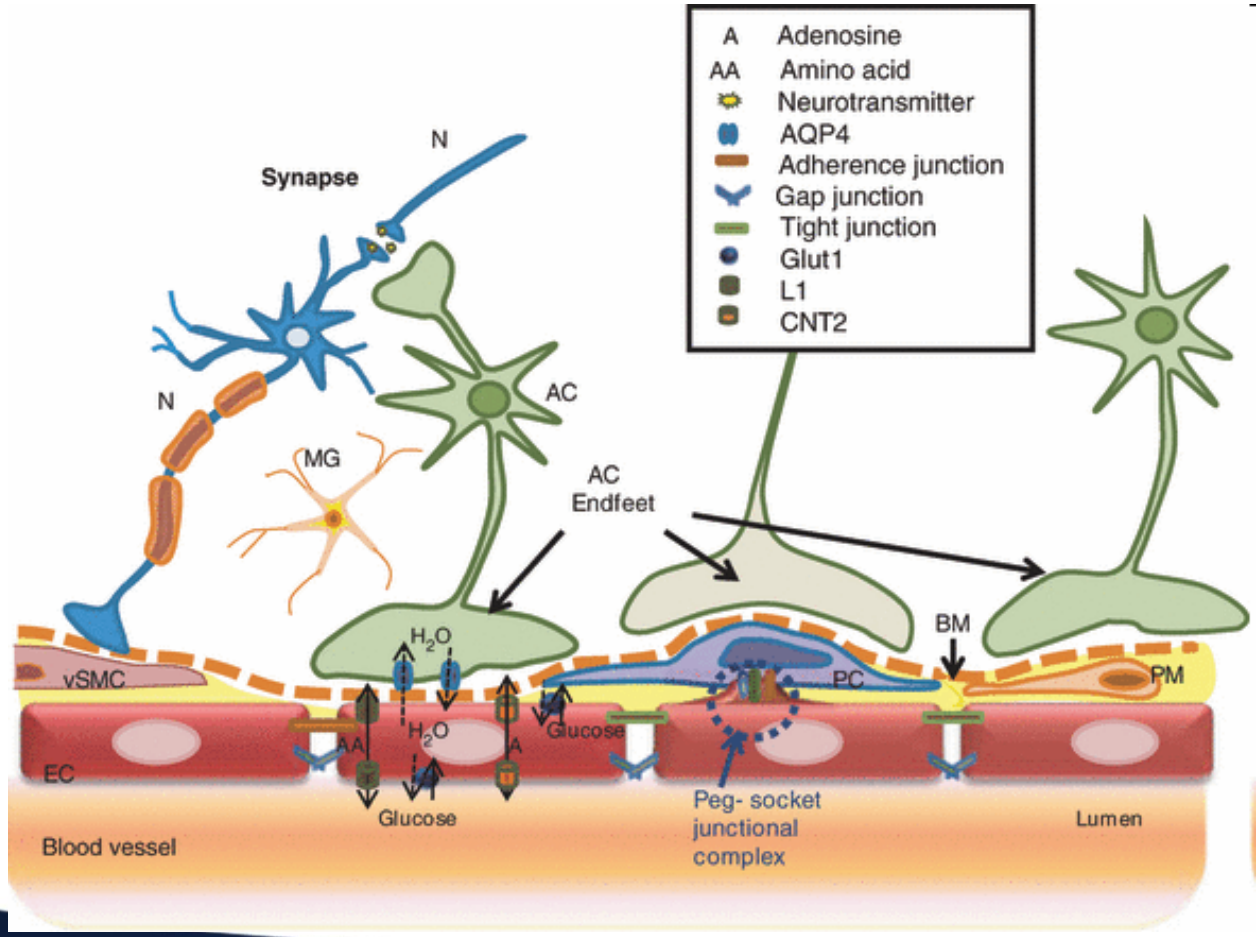
ETCO2

Cellular communication at the neurovascular interface



The neurovascular unit consists of neurons (N), endothelial cells (EC) astrocytes (AC), pericytes (PC), vascular smooth muscle cells (vSMC), microglia (MG) and perivascular macrophages (PM). Endothelial cells form a blood–brain barrier characterized by tight, adherence and gap junctions, as well as a specialized transporter system. Pericytes share basement membranes with blood vessels and directly contact endothelial cells via peg–socket junction complexes. Astrocytes stretch their endfeet toward blood vessels and neuronal synapses to integrate neuronal activity with the vascular response. A single astrocyte contacts >10^5 neurons.

Lee et al. FEBS J. 2009 Sep;276(17):4622-35