Medical Biophysics
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Cerebral Blood Flow Dynamics and Physiology

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Course objectives

1. What is cerebral blood flow (CBF), why does it matter
2. How does CBF change (in space and time)
3. Review basics of brain vascular anatomy
4. Review basics of brain vascular physiology
5. How did measurements of CBF changes get started - a century and a half ago!

Cardiovascular System

4. the oxygenated blood moves from heart (LV) into arteries

5. that deliver blood to organs and tissues

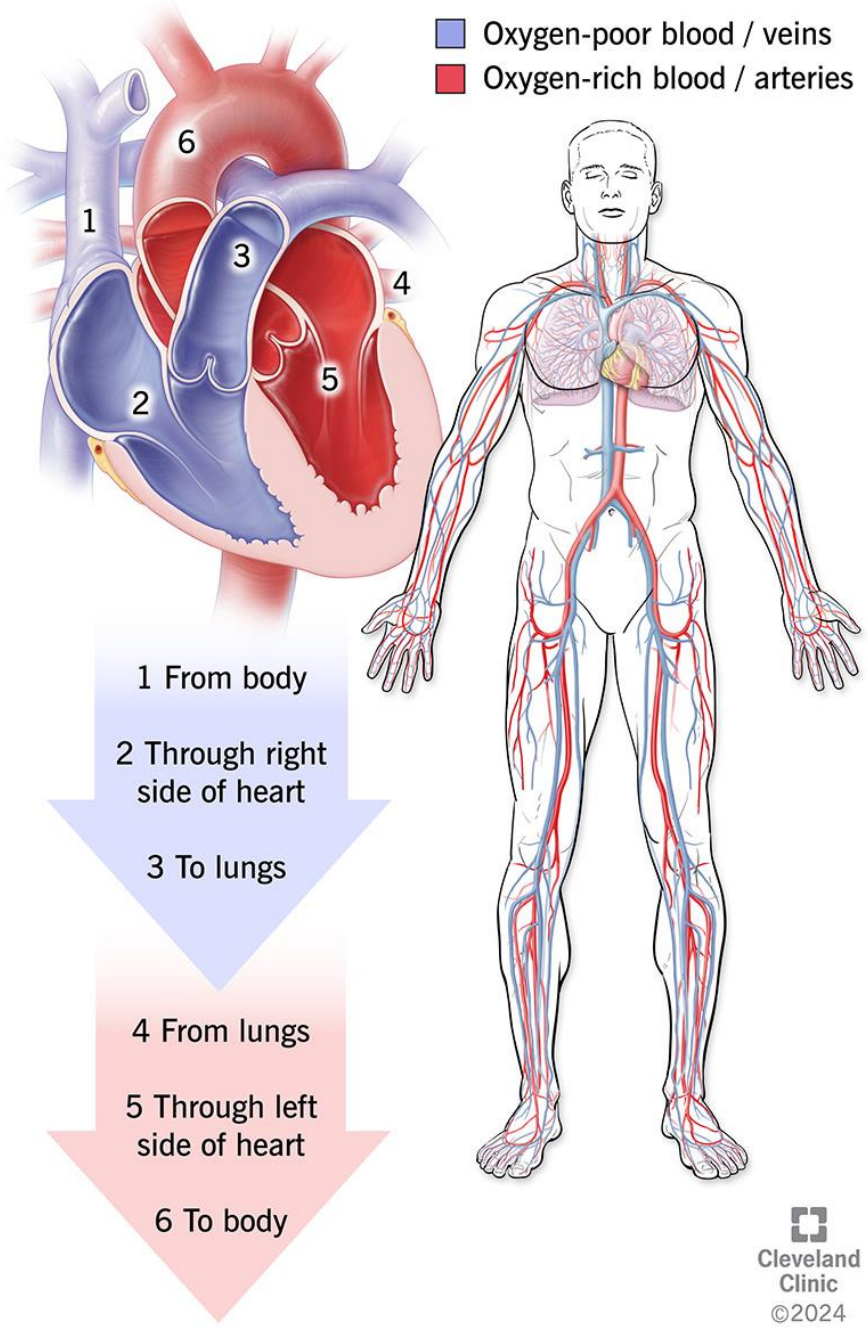
6. in tissues, blood oxygen and glucose are extracted and waste and carbon dioxide are picked up through network of capillaries

1. after leaving the tissues and organs, deoxygenated blood returns to heart (RA ->RV) through veins

2. the blood travels from heart (RV) to lungs to release carbon dioxide and pick up oxygen again

3. from lungs the blood travels to heart (LA -> LV)

- 100,800 beats per day (70bpm) corresponding to 7,000 L of blood being circulated per day



https://my.clevelandclinic.org/health/body/circulatory-and-cardiovascular-system

Blood Flow Drainage from the Brain

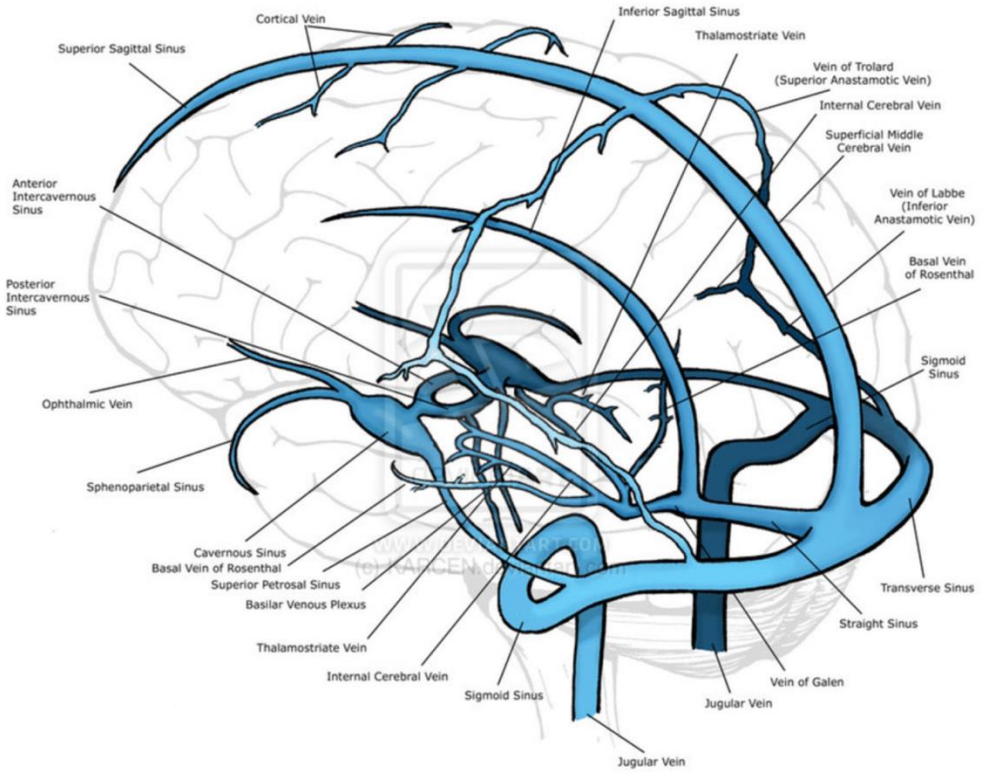
- Superficial Veins drain the cortex and outer white matter and empty into dural venous sinuses:
  - Superior cerebral veins
  - Superficial middle cerebral vein
  - Vein of Trolard (superior anastomotic vein)
  - Vein of Labbé (inferior anastomotic vein)

- Deep Veins drain the deep structures (e.g., basal ganglia, thalamus, deep white matter):
  - Internal cerebral veins
  - Basal vein of Rosenthal
  - Great cerebral vein (Vein of Galen) → joins with inferior sagittal sinus

- Dural Venous Sinuses (endothelial-lined channels between layers of dura mater) collect all cerebral venous blood

- From sigmoid sinuses, blood drains into the internal jugular veins

- **Only 3-5% of brain volume is in the vasculature** (2-4% in capillaries, 0.5-1% in arteries and 1% in veins)



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Brain Blood Flow

- total volume of blood flowing through the brain per unit time [ml/min]
- under physiological conditions adult human brain gets ca. 750 ml of blood per min; 10-20% higher in females than in males
- increases in development, peaks in the third decade of life then declines ~0.5% per yr to 80-85% of its peak level by the eighth decade of life (steeper decline in M than in pre-menopausal F)
- decline is region-specific: most of the decline happens in the prefrontal cortex (cognitive slowing, executive dysfunction) and least in occipital love (vision)
- slow decline due to e.g. progressive arterial wall stiffening, neurodegeneration, amyloid deposition on arterial walls
- rapid decline due to e.g. blood clot obstructing an arterial vessel, when sustained, leads to neuronal death and organism death

Brain Blood Flow

- brain has limited reserve of metabolites (little glycogen or fat stores) yet is very metabolically active (maintenance of ionic gradients and firing is expensive)
- ~20% of the body's oxygen and ~25% of glucose are used by the brain "at rest"
- continuous blood flow delivers glucose and oxygen, removes excess heat (no good ways to dissipate it), and removes metabolic wastes
- large buffer is key for long term resilience i.e. successful adaptation to changing internal and external environmental conditions

Brain Blood Flow

- even ”at rest,” CBF varies regionally: metabolically more active regions have higher regional CBF: eg cortical GM, posterior cingulate & precuneus (key DMN hubs), basal ganglia & thalamus (continuous relay & processing), hypothalamus (homeostatic regulation, hormone secretion/transport)

- even though CBF is already high at rest (50-65 ml/100 g with a CPP of 70 to 90 mmHg i.e. 15-20% of cardiac output), **CBF increases** further during local increases in brain activity (aka neurovascular coupling)

- neurovascular coupling is a feed forward (not feedback system!): neuronal activity leads to generation of vasoactive signals ~~(*vs.* metabolic shortage leading to blood flow increase)~~

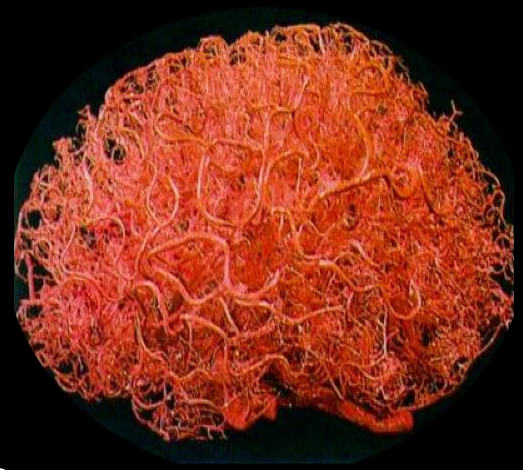
Neurovascular coupling (NVC)

Brain Tissue

increased neuronal activity

coordinated signaling

increased metabolism and E demand



Brain Vessels

rapid adjustments in local blood flow, volume

increased delivery of O_2 and glucose

clearance of wastes and cooling

NVC @ microscopic scale

Brain Tissue

Modest adjustment in activity of tens of thousands of heavily interconnected neurons of various types with high baseline levels of activity, supported/guided/modulated by glia

Brain Vessels

Redistribution of flow over tens/hundreds of seconds and hundreds of micrometres across a network of thousands of hierarchically organized vessels with significant resting tone & high resting flow

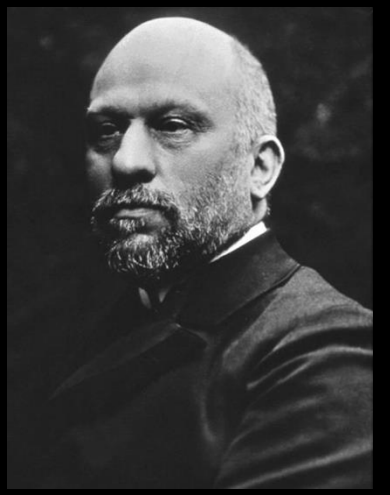
https://synapseweb.clm.utexas.edu/hippocampus-rat

Zheng et al, Sci Reports 2015

Brain Blood Flow Changes

- brain flow changes are (over)used as a **putative metric of brain activity** (fMRI, PET, NIRS, …)
- regulation of energy distribution is the raison d'étre not just of our brains (**allostasis**!) but of our minds (*cf.* **interpersonal neurobiology**)
- metabolic dysregulation and cerebrovascular impairment arise after **injury** and develop at the very **onset** of many brain diseases and often accelerate disease **progression**/hamper recovery from injury
- brain vessels may be an easier **treatment target** (e.g., no BBB in the way ☺ !)
- whereas cessation of blood flow to the brain is rapidly deadly, chronic disruption of neurovascular coupling leads to/exacerbates cognitive decline

Early CBF measurements

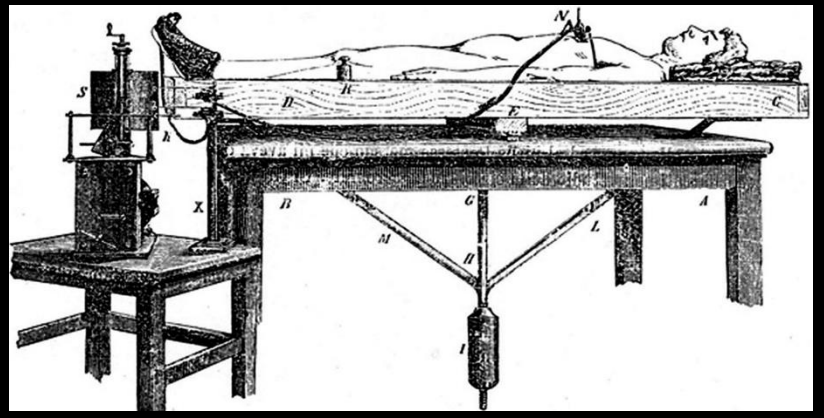


Angelo Mosso (1846-1910)

- first described by Angelo Mosso, a professor of pharmacology and physiology at the University of Turin

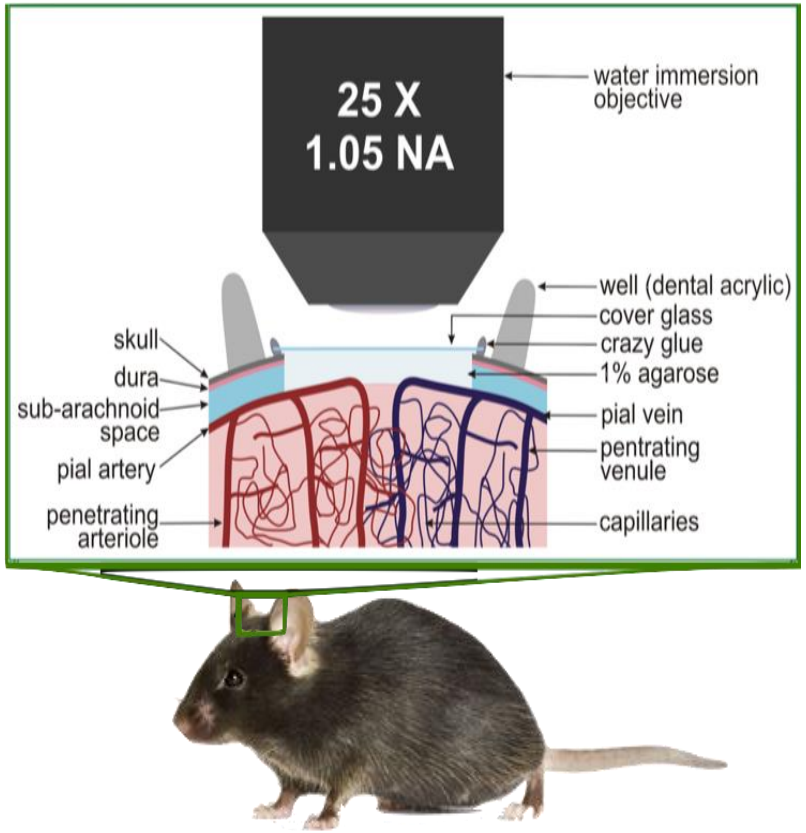
- recorded cortical pulsations following neurosurgery in patients with skull defects:
  - observed their changes during mental activity
  - inferred that CBF increases during mental activity (formulated in the late 1870s – a decade *before* Roy and Sherrington's work)
  - tested CBF changes during mathematical calculations in patients with frontal skull breach via plethysmograph

- invented the 1st neuroimaging technique: "human circulation balance" to measure the redistribution of blood flow during intellectual activity whilst carefully accounting for a host of artefacts



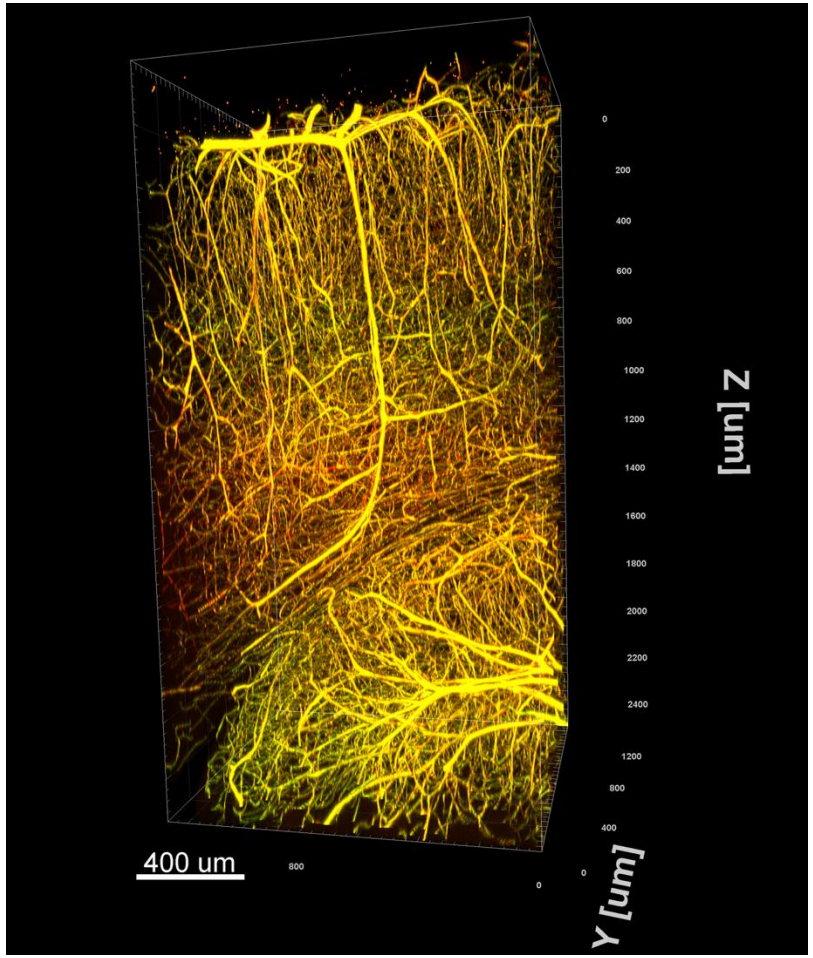
Mosso A. Applicazione della bilancia allo studio della circolazione sanguigna dell'uomo, *Atti R Accad Lincei Mem Cl Sci Fis Mat Nat*, 1884, vol. XIX (pg. 531-43)

2PFM Imaging: Meta Protocol

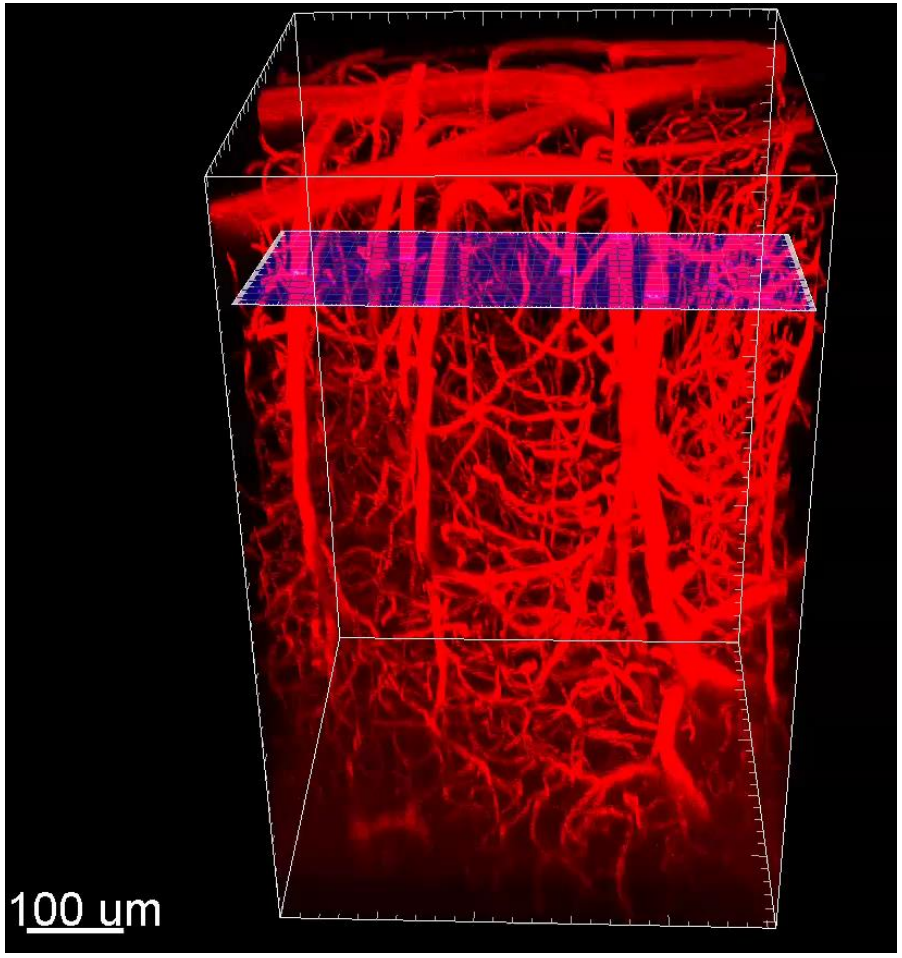


2PFM data on brain vasculature and flow

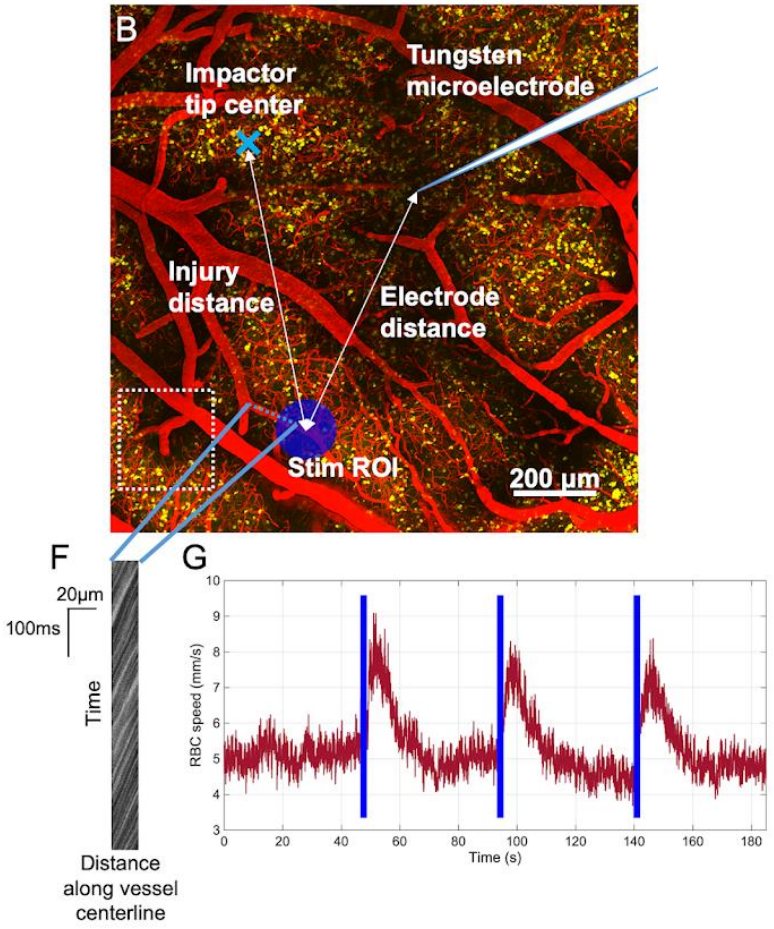
3D STACKS OVER TIME



2D SLICE OVER TIME



1D LINE OVER TIME



THANK YOU!