Principles and Potential of Perfusion Imaging: 
Realizing Cerebral Blood Flow 
from Hemodynamics to Permeability

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No potential conflicts to disclose

Objectives
- Introduce basic concepts in imaging cerebral blood flow
- Describe current and evolving perfusion modalities
- Explore mathematics of hemodynamic measures

Perspective
- Technical specifications of perfusion imaging require standardization (e.g., acquisition, processing, interpretation) spearheaded by ongoing work of STIR collaboration
- Limitations of oversimplified clinical impression (e.g., “MTT is best,” “is perfusion proven?”)
- Balanced perspective on current perfusion imaging tools, adapting use to ultimately improve clinical practice
- Understanding foundation of techniques & pathophysiology
- Using acute MCAO as a model
Practical

- Perfusion based on theoretical concepts, evident on routine imaging and not technique specific
- CT/MRI examples as most common modalities
- Relative advantage of multimodal imaging approaches
- Goal is not pretty pictures alone!
- Goal is not debate of CT versus MRI, CBV versus MTT, Tmax thresholds, mismatch size
- Tools to understand specific pathophysiology and hemodynamics apparent at the bedside

Vascular transit

- Artery
- Capillary

Parameters...

- CBF (cerebral blood flow) – volume of blood flowing through a given unit volume of brain per unit time
- CBV (cerebral blood volume) – total volume of blood in a given unit volume of brain
- MTT (mean transit time) – average transit time of blood through a given brain region
- ...many others
Gamma variate?

- BAT
- TTP
- Peak
- FWHM
- CBV
- CBF

Perfusion imaging modalities

- Ultrasound
- CTP
- XeCT – inhaled xenon and oxygen
- DSC MRI
- ASL MRI
- SPECT – intravenous radiopharmaceutical
- PET – intravenous H$_2$O
- DSA

“Perfusion” – CT and MRI

- Arteries, capillaries and veins
- Ischemic conditions – delay and dispersion as hallmark of collateral perfusion
Dynamic first-pass methodology

- Exogenous intravascular tracer (e.g., iodinated contrast or gadolinium)
- Assumptions – non-diffusible, neither metabolized nor absorbed
- BBB permeability derangements require modification

Nondeconvolution approach

- AIF – arterial input function
- VOF – venous output function
- CBV derived whole-brain perfused blood volume

Deconvolution

- AIF – arterial input function
- Signal intensity non-linear with gadolinium concentration
- SVD – singular value decomposition
- Delay and dispersion of contrast bolus
- Bolus delay correction
- Calculation of the residue function
  - CBF proportional to residue height
  - CBV proportional AUC
- Central volume principle
  - $\text{MTT} = \frac{\text{CBV}}{\text{CBF}}$
Pitfalls

- Poor cardiac output or low concentration
- Limited acquisitions that do not capture entire CBV
- Patient motion
- Permeability

CT perfusion

- Principles of spiral CT
- Path of rotating x-ray tube and detector
- Start of spiral scan
- Direction in which patient is moved

Location, location, location
CT hypodensity


CTP subtleties (ROI, large vessels)
DSC MRI (PWI)
- Gradient echo (GRE) or spin echo (SE) acquisition
- Measures $\Delta T^*_2$ or $\Delta T_2$
- Indicator dilution theory
- Assumes intact blood-brain barrier
- Preload contrast dose prior to bolus to saturate
- Time-intensity curves
Arterial spin labeling – detection of magnetically labeled water in arterial routes
- Pulsed or continuous
- Rapid relaxation of longitudinal magnetization
- Varying postlabeling delay times


Perfusion angiography
- Perfusion Angiography™ from film or digital copies of angiography performed at any site in a multicenter study, allowing for retrospective comparison of perfusion measures even when multimodal CT/MRI is unavailable.
- Advantages over CT/MRI perfusion methods include:
  - Identification of arterial inflow and venous outflow routes
  - Known signal intensity versus contrast concentration
  - Absence of recirculation effects
  - High resolution
  - Multiplanar projections
  - Contemporaneous with endovascular procedures
  - No additional contrast or radiation exposure
Novel perfusion parameters
Perfusion imaging – CT/MRI

Tissue concentration curves provide a wealth of data

Time-to-peak (TTP)

Relative perfusion measures
Low perfusion hyperemia
- 1968 – Waltz and Sundt
- 1980 – Tomita
- Temporal profiles in CBV during MCAO in cats
- Arteriolar vs venous

Hemodynamic stages
- CBV as critical parameter
- Bidirectional changes have defied mathematical models

Myth of autoregulation

- In acute MCAO, autoregulation is exhausted before collaterals are recruited

Autoregulation

- Vast majority of acute ischemic stroke cases involve thromboembolic occlusion, pure hypoperfusion exceedingly rare
- Distal arterial bed dilates instantaneously following proximal occlusion
- Autoregulatory changes exhausted before collateral recruitment, distal arterial bed pressure-passive zone
- Autoregulatory "failure" takes place before 911 called, likely never relevant in clinical practice

Low perfusion hyperemia

- Hyperemia, or increases in relative CBV values, were evident in regions of "oligemia" in all cases (p<0.001).
- CPP was decreased, exhibiting a gradient extending deep from the cortical surface in all cases (p<0.001).

Cerebral venous diversion

- CBV (predominantly venous) diversion to periphery from core/penumbra/"benign oligemia"
- Starling resistors in parallel, collapsible tubes
- Although incipient arterial insufficiency due to retrograde collateral flow, predominantly venous process

Venous pathophysiology

- Marginal arterial inflow causes venous collapse
- Venous blood is displaced (peripheral displacement of CBV)
- Downstream resistance increases due to venous collapse
- Resistance limits further arterial inflow (reduction in CPP)
- Progressive ischemia causes infarct evolution
- Infarct grows until CBV can maintain venous patency and preserve CPP (border of penumbra and benign hyperemia)

Benign oligemia revisited

- CBV underestimates final infarct
- CPP (1/MTT) overestimates final infarct
- CBV x CPP
Resistance

Pressure and resistance

\[ F = \frac{\Delta P}{R} \]

\[ R = \left( \frac{\nu L}{r^4} \right) \left( \frac{8}{\pi} \right) \]

FH MRI

Recanalization and reperfusion
No reflow

- Distal embolus?
- Complication of reperfusion therapies?
- Resistance due to venous collapse?
- Is complete reperfusion (TICI 3) impossible?

Permeability


CT permeability images
Conclusions

- Perfusion imaging techniques offer tremendous potential to probe hemodynamics, the critical variable in acute ischemic stroke.
- Ultimate goal to maximize use of perfusion imaging to exploit often subtle pathophysiology and optimize patient care.