WHY'N'HOW

Arterial-Spin Labeling

Jean Chen

Postdoctoral Fellow
A. A. Martinos Center for Biomedical Imaging
Massachusetts General Hospital, Harvard Medical School

02/17/2011

Why? How?

- Why is it called "arterial-spin labeling"?
- Why are there PASL, CASL and pCASL?
- How to choose which ASL to use?
- How to know what parameters to use?
- How can ASL go wrong?
- How to get cerebral blood flow maps?
- How long is this talk going to be?
- …

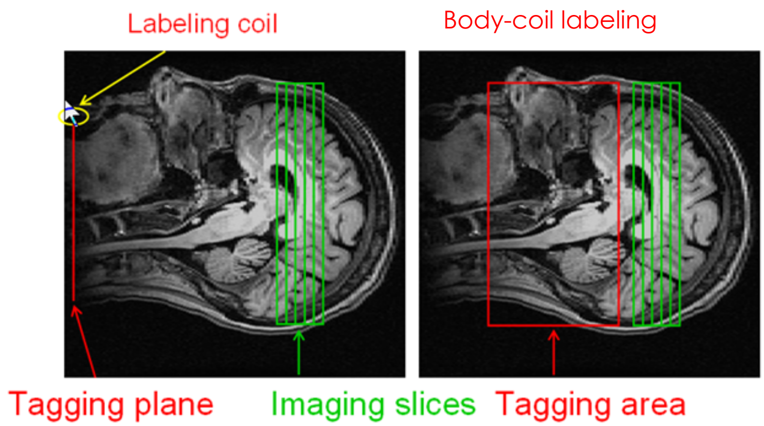
Arterial-Spin Labeling (ASL)

- "Labeled" spins in arterial blood **water** act as an endogenous **tracer**
- At the time of imaging, tagged spins have arrived in the regions of interest
- Water is **exchanged** between blood and tissue --- resulting tissue longitudinal relaxation ($\boldsymbol{T_1}$) is proportional to flow
- **CASL**: continuous ASL
- **PASL**: pulsed ASL

How do you "label"?

- CASL: flow-driven **adiabatic** fast-passage
  - Continuous and constant **RF** wave (1-2 sec)
  - Applied in a plane, no off-resonance behaviour
  - Relies on blood flow to achieve adiabaticity
- PASL: **adiabatic** RF pulses
  - Pulsed RF (a few msec)
  - Applied to a slab, ampl and freq-modulated
  - Using gradients to enhance spatial selectivity while reducing power deposition

CASL PASL

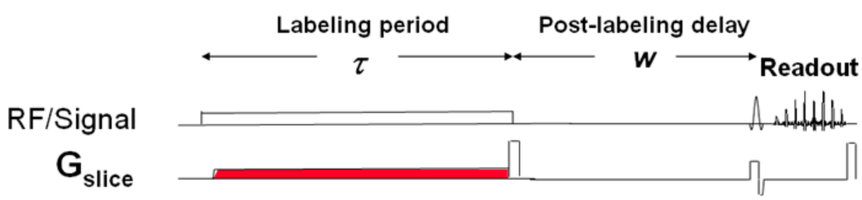


Amplitude-modulated control
Separate labeling coil
Pseudo-continuous

QUIPSS II

Courtesy: WM Luh

CASL (tag)



TR = τ + w + Acq

CASL

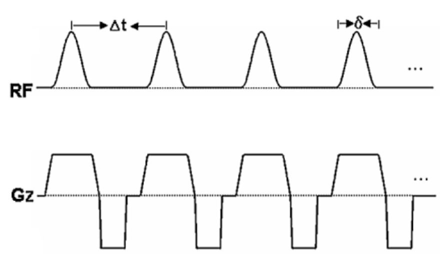
- Lower labeling efficiency
- Continuous RF not supported on most clinical scanners
- Requires separate coil to minimize MT (magnetization transfer) effects
- Higher SNR
- Minimally sensitive to tag dispersion

PASL

- Higher labeling efficiency
- Easily implemented on clinical systems
- Does not require additional hardware
- Lower SNR
- Sensitive to dispersion
- Most commonly used

Pseudo-Continuous ASL (pCASL)

Tag



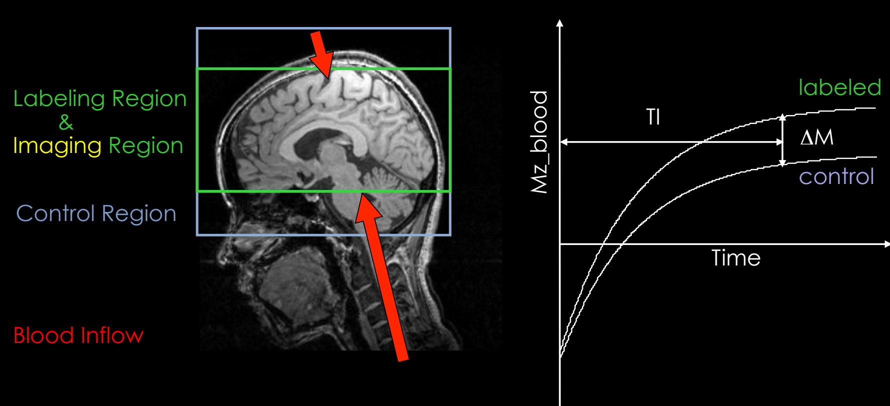
- A series of Hanning RF pulses, shaped to avoid aliased labeling planes
- Can be implemented on clinical scanners

Dai, W et al. Magn Reson Med 2008

Pseudo-Continuous ASL (pCASL)

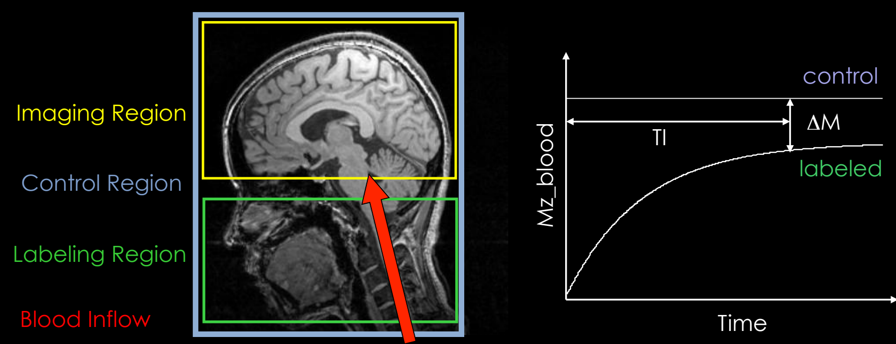
- Analogous to flow-driven adiabatic fast-passage, but using pulsed instead of continuous wave
  - Builds up pseudo steady-state to imitate CASL labeling
- Higher SNR than PASL
- Higher labeling efficiency than CASL
- **Not adiabatic** inversion
- Sensitive to flow velocity, gradient strength, RF timing and duty cycle
- Best performance in conjunction with angiography and flow phase mapping

FAIR PASL (fBIRN)



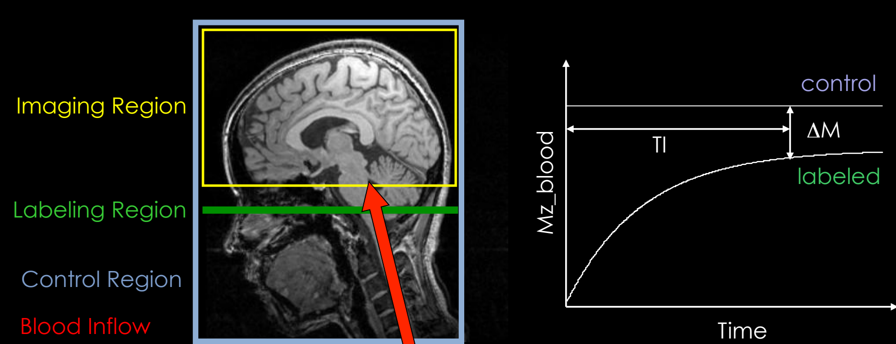
-image-slab tag, global control
-ascending & descending flow
-potential radiation damping

PICORE PASL (Siemens)



- Proximal tag, global control
- Magnetization transfer cancellation
- Background signal attenuation
- Sensitive to ascending flow only

pCASL (UPenn)



- Proximal tag, global control
- Magnetization transfer cancellation
- Sensitive to ascending flow only

ASL Assumptions

- Tag is fully delivered to imaging region
- Rapid water exchange between blood and tissue
- Intact blood-brain barrier
- Negligible tag washout at time of imaging
- Negligible partial-volume effects in voxel
- Tagged blood has completely washed out before the subsequent measurement

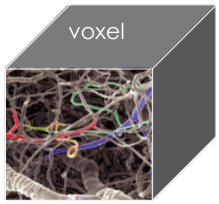
Arterial-Spin Labeling: the Math

- Modified Bloch's equation

$$\frac{dM_t(t)}{dt} = \frac{M_{0,t} - M_t(t)}{T1_t} + CBF \cdot \left(M_a(t) - \frac{M_t(t)}{\lambda} \right)$$

  - ***M*$_{0,t}$**: Tissue equilibrium magnetization
  - ***T*$_{1,t}$**: Tissue T_1
  - In plain terms:
    - the change of tissue magnetization (***M*$_t$**) due to the tagged arterial blood (***M*$_a$**) is proportional to CBF

Cerebral Blood Flow (CBF)



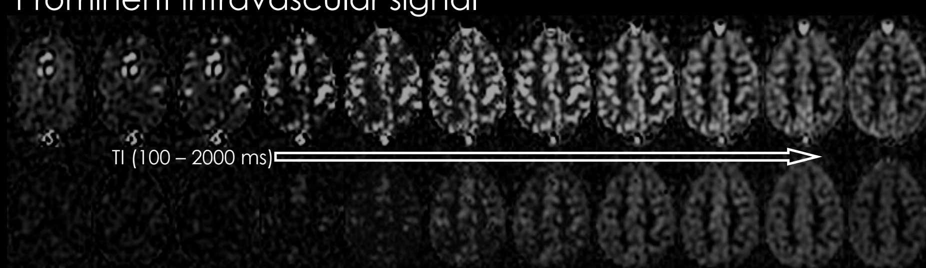
Quantitative CBF in humans:

GM CBF ≅ 60 ml/100 g/min
WM CBF ≅ 20 ml/100 g/min

$$\text{CBF} = \frac{\text{Net blood flow through voxel [ml/min]}}{\text{Mass of voxel [100g]}}$$

ASL Confounds: Intravascular Signal

Prominent intravascular signal

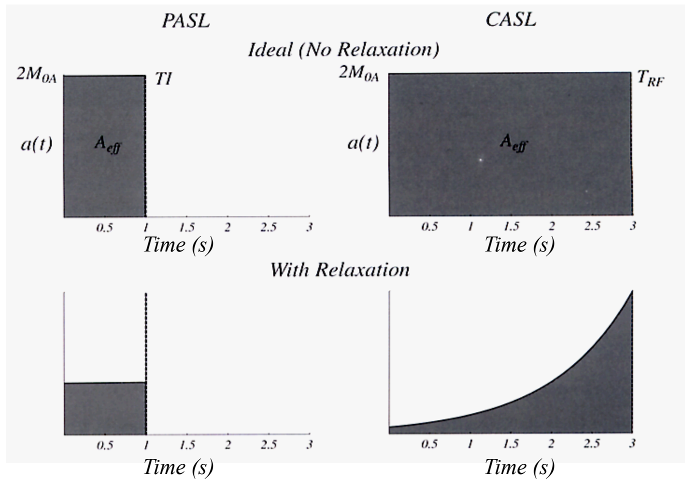


With crushers (Typically at 100cm/s, fBIRN & Siemens)

Intravascular signal contributes to CBF overestimation
Add crusher gradients to attenuate macrovascular contribution
OR, adjust TI to permit macrovascular flow to wash out

Yang Y et al, Magn Reson Med 1998

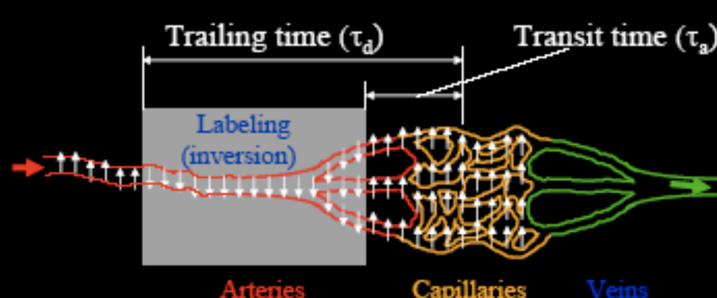
ASL Confounds: Relaxation



T_1 relaxation reduces signal from the tag

Compensate for decay incurred during acquisition delay

ASL Confounds: Transit Delay



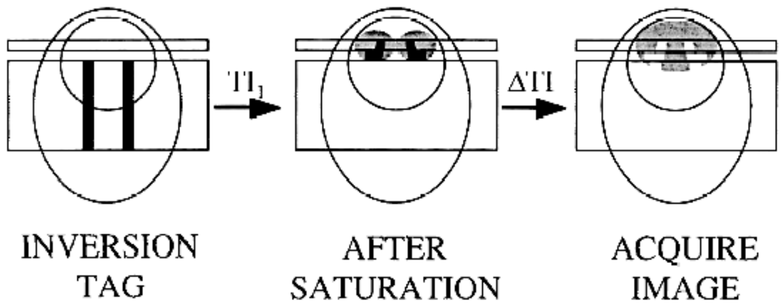
For a given TI, slower spins will not be able to reach imaging region, resulting in lower measured CBF

Worse in white matter, and may be exacerbated in aging and disease

Courtesy: H-L A. Liu

ASL Confounds: Transit Delay

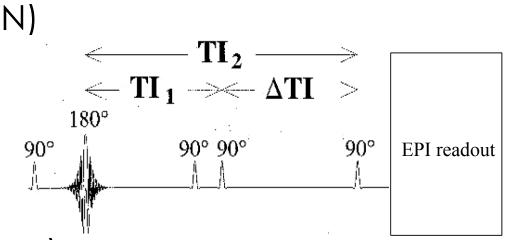
- Solution: Insert saturation pulse to cut off slower tail of tag, creating a well-defined tag width



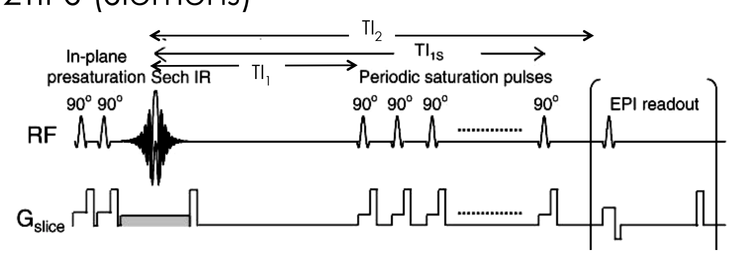
Wong EC et al, Magn Reson Med 1998

ASL Confounds: Transit Delay
Saturation Schemes

- QUIPSS II (fBIRN)



- Q2TIPS (Siemens)



ASL Acquisition Considerations

- Inversion time **TI_1**
  - Long enough to permit tag to leave tagging region
  - Short enough to ensure "QUIPSS II" effectiveness
  - More slices, longer TI_1
- Inversion time **TI_2**
  - Long enough to avoid intravascular signal and ensure tag exchange with tissue water
  - Short enough to reduce loss of tag
  - Slower flow, longer TI_2
- Tailor parameters for the aims of your study

ASL Acquisition Considerations

- **TR** must allow tag washout and refreshing (2 – 4 s)
- **TE** should be short to minimize T_2 contamination
- **Tag width** should be large, especially for multislice
- **Labeling gap** should be as small as possible
- Signal **drop-out** (if using gradient-echo EPI)
  - Increase bandwith, reduce slice thickness, use non-EPI
- T_2 "shine-through" (**static tissue & CSF**)?
  - Use background suppression (not in fBIRN or Siemens)
- Do not **angulate** > 45° relative to main feeding arteries
  - To maintain control of tag width and tagging efficiency

Typical ASL Protocols at 3 T

- FAIR QUIPSS II (fBIRN)

TR	4 s	#slices	24 (whole brain)
TE	12 ms	voxel	3.5x3.5x4 mm^3
TI1	600 ms	gap	10 mm
TI2	1600 ms	#frames	100

- Calibration Scan
  - Same readout as ASL scan (i.e. 2D gradient-echo EPI)
  - TR > 5 $T_{1,a}$ (i.e. TR = 10 s)
  - All other parameters = same as used for ASL scan

Typical ASL Protocols at 3 T

- PICORE Q2TIPS (Siemens)

TR	4 s	TI_{1s}	1400 ms
TE	12 ms	#slices	24 (whole brain)
TI1	600 ms	gap	20 mm
TI2	1600 ms	#frames	100

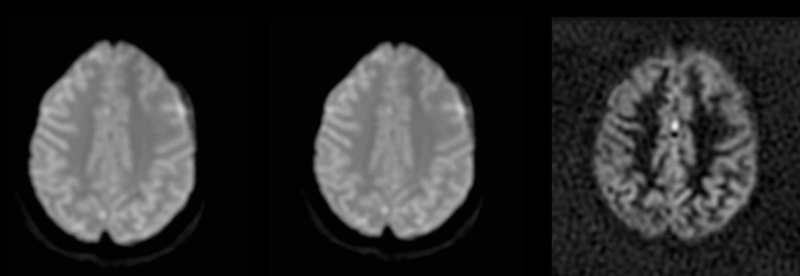
- pCASL (Upenn)

TR	5 s	#RF blocks	82
TE	22 ms	Label offset	80 mm
delay (TI)	1000 ms	mean Gz	1 mT/m
RF gap	360 us	#frames	40

CBF Quantification

1. Difference image (**ΔM**) calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)

ΔM Calculation

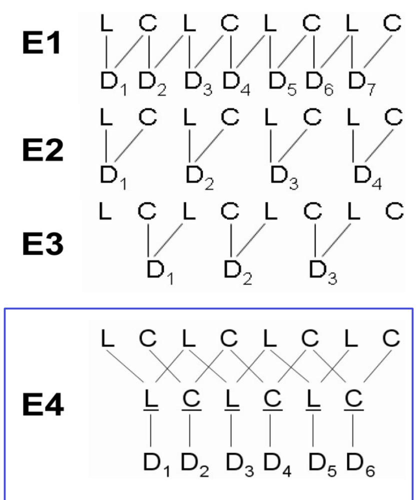


Control – Label = ΔM

ΔM is typically ~1% of the control signal

"CBF α diff(control, label)"

- E1: running subtraction
- E2&E3: pairwise subtraction
  - Timing mismatch = incomplete cancellation of BOLD effects
- E4: surround subtraction
- E5: Sinc-interpolated subtraction
  - Matched BOLD effect

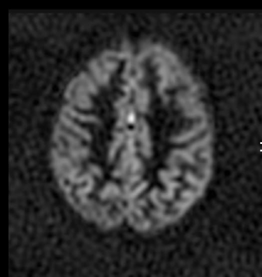


[Lu, H et al, MRM 2006]

"BOLD α mean(control, label)"

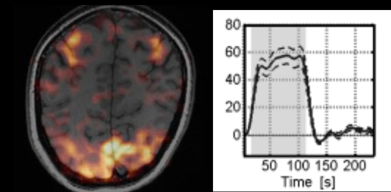
- Pros
  - Time savings
  - Increased temporal resolution
  - No need for ASL-BOLD cross-registration
- Cons
  - Lower SNR
  - Long echo-time needed for optimal BOLD contrast (causing ASL-BOLD cross contamination)
  - T_1-weighting

ΔM Calculation

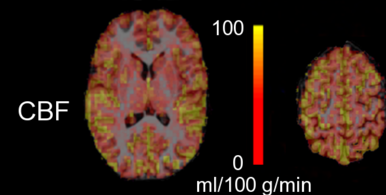


ΔM

CBF Changes



Resting CBF

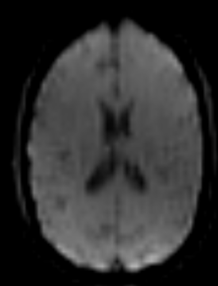


CBF Quantification

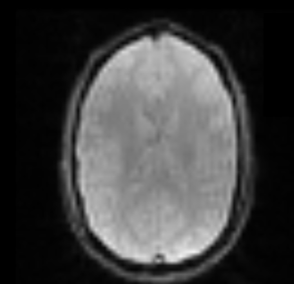
1. Difference image calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)
2. Arterial magnetization (***$M_{0,a}$***) estimation
   - Intensity non-uniformity compensation
   - Blood-tissue partition coefficient, T_1, T_2*

$M_{0,a}$ Estimation

ASL



Calibration Scan



Did not acquire a separate calibration scan?

It's common to use the 1st control image of the ASL dataset, if magnetization fully relaxed.

$M_{0,a}$ Estimation

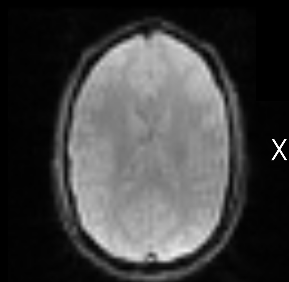
$M_{0,a}$ will vary depending on

- Static field (B_0) inhomogeneities
- RF field (B_1) inhomogeneities
- Receive coil sensitivity nonuniformity

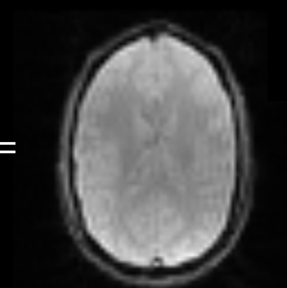
Calibration methods:

1. CSF (cerebrospinal fluid) based
2. White matter based
3. <u>Local tissue based</u>: intrinsic normalization for nonuniformities

$M_{0,a}$ Estimation



$\times \quad 1/\lambda \bullet e^{TE/T_{2t}} \quad =$



Calibration scan

$M_{0,t}$

$M_{0,a}$

Distinguish between grey matter and white matter when assuming values for $T_{2,t}$ and λ.

$M_{0,a}$: local-tissue calibration

- *Ideally*, one should
  - Measure T_1 and T_2 of tissue (grey matter and white matter separately)
- However, it's more common to assume:

(ms)	1.5T	3T	7T
T_{1t}	900	1300	1900
T_{1b}	1300	1600	2300
T_{ex}	$\{\tau+w;\mathrm{TI}_2\}$ + 200		

Courtesy: WM Luh

CBF Quantification

1. Difference image (ΔM) calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)
2. Arterial magnetization ($M_{0,a}$) estimation
   - Intensity non-uniformity compensation
   - Blood-tissue partition, T_1, T_2*
3. Decay correction

Decay Correction

- T_1 decay of tag incurred during transit must be compensated for acquisition delay

$$\exp(-TI/T_{1a})$$

- This delay is dependent on the order of slice acquisition

$$TI_{corrected} = TI_{\mathrm{nominal}} + slice\_order * slice\_time$$

CBF Quantification

1. Difference image (ΔM) calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)
2. Arterial magnetization ($M_{0,a}$) estimation
   - Intensity non-uniformity compensation
   - Blood-tissue partition, T_1, T_2*
3. Decay correction
4. Plug into ASL signal model

Standard Kinetic Model

- PASL

$$\boxed{CBF = \frac{\Delta M \times \lambda}{2\alpha \times M_{0,a} \times TI_1 e^{-TI_2/T_{1a}}}}$$

Ideally, $\Delta M = 2 \cdot M_{0,a} \cdot CBF \cdot TI$

- $M_{0,a}$: Arterial blood equilibrium magnetization
- λ: Tissue blood-water partition coefficient
- α: Labeling efficiency

Standard Kinetic Model

- CASL & pCASL

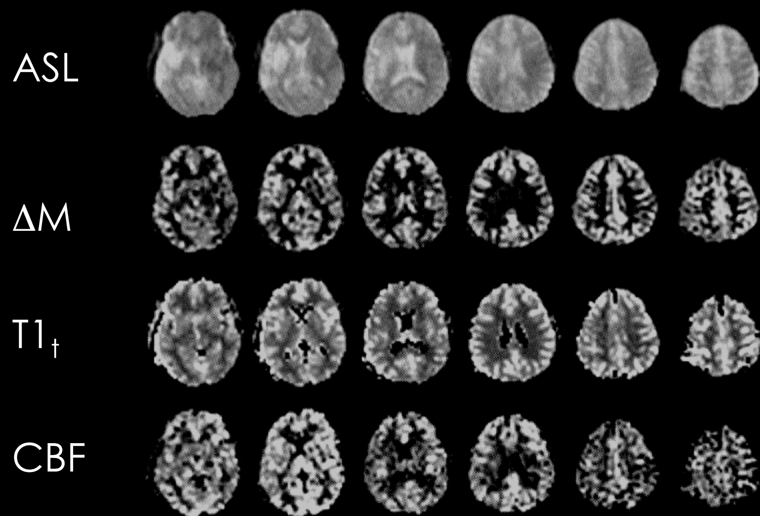
$$\boxed{CBF = \frac{-\Delta M \times \lambda}{4\alpha \times M_{0,a} \times T1_t \times (e^{-(\tau+w)/T_{1,a}} - e^{-w/T_{1,t}})}}$$

- $M_{0,a}$: Arterial blood equilibrium magnetization
- $T_{1,a}$: Arterial blood T_1
- λ: Tissue blood-water partition coefficient
- α: Labeling efficiency
- τ: post-labeling delay
- w: label width

CBF Quantification

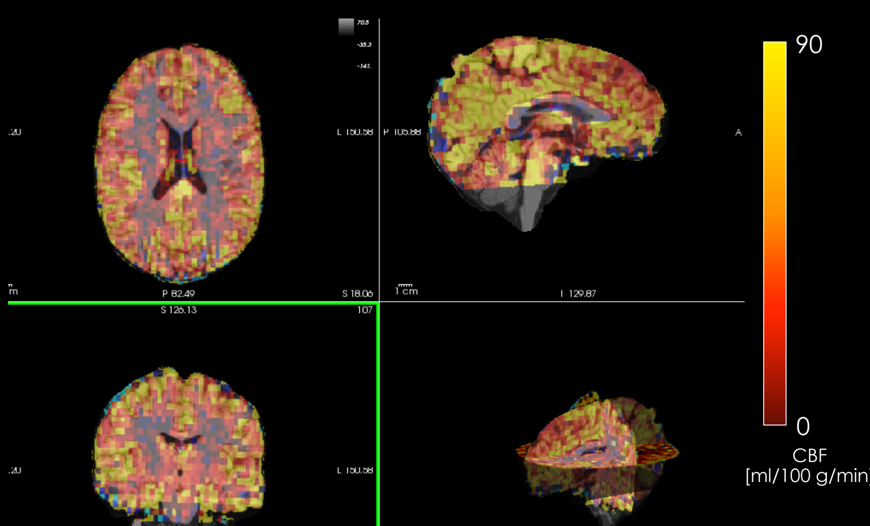
1. Difference image calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)
2. Arterial magnetization estimation
   - Intensity non-uniformity compensation
   - Blood-tissue partition, T_1, T_2*
3. Decay correction
4. Plug into ASL signal model
5. Scaling: CBF [ml/100g/min] ≅ CBF[1/s] x 6,000

CBF Quantification

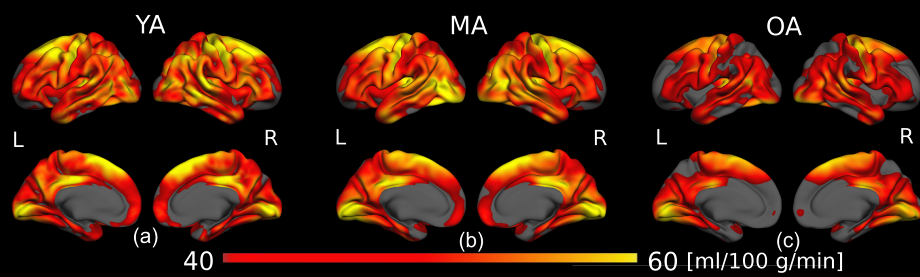


Courtesy: H-L A. Liu

Sample Quantitative CBF Map



Sample Quantitative CBF Maps



Effect of Normal Aging ⇨

Chen et al., NeuroImage 2011

ASL at Higher Field

- Pros
  - Greater M_0: higher available signal
  - Longer T_1: less tag decay
- Cons
  - Shorter T_2*: more BOLD contamination, signal drop-out and geometric distortion
  - Higher ΔB_0 and ΔB_1: harder to achieve adiabaticity
  - Shorter body coil: more limited tag width
  - Higher power deposition: do fewer slices per unit time

ASL Applications

- Cerebral blood flow
  - White matter CBF measurement still challenging
- Cardiac, pulmonary and renal perfusion
- ASL processing methods:
  - SPM-compatible Perfusion Toolbox:
    - http://www.cfn.upenn.edu/~zewang/ASLtbx.php
  - In-house method:
    - www.nmr.mgh.harvard.edu/~jjchen/ASL.html