Why’N’How

Arterial-Spin Labeling

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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 ($T_1$) 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

QUIFSS II

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)

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

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

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9/45

10/45
**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

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

- \( M_{0,t} \): Tissue equilibrium magnetization
- \( T1_t \): 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 \( \approx 60 \text{ ml/100 g/min} \)

**WM** CBF \( \approx 20 \text{ ml/100 g/min} \)

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

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

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


ASL Confounds: Transit Delay

Saturation Schemes

- QUIPSS II (fBIRN)
- Q2TIPS (Siemens)
ASL Acquisition Considerations

- Inversion time $T_{I1}$
  - Long enough to permit tag to leave tagging region
  - Short enough to ensure “QUIPSS II” effectiveness
  - More slices, longer $T_{I1}$
- Inversion time $T_{I2}$
  - Long enough to avoid intravascular signal and ensure tag exchange with tissue water
  - Short enough to reduce loss of tag
  - Slower flow, longer $T_{I2}$
- 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 bandwidth, 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)**
  
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR</td>
<td>4 s</td>
</tr>
<tr>
<td>TE</td>
<td>12 ms</td>
</tr>
<tr>
<td>TI1</td>
<td>600 ms</td>
</tr>
<tr>
<td>TI2</td>
<td>1600 ms</td>
</tr>
</tbody>
</table>

- **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

**PICORE Q2TIPS (Siemens)**

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<td>TI2</td>
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</tr>
</tbody>
</table>

**pCASL (Upenn)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR</td>
<td>5 s</td>
</tr>
<tr>
<td>TE</td>
<td>22 ms</td>
</tr>
<tr>
<td>Delay (TI)</td>
<td>1000 ms</td>
</tr>
<tr>
<td>RF gap</td>
<td>360 us</td>
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</table>

- Mean Gz = 1 mT/m
- Label offset = 80 mm
- #RF blocks = 82
- #frames = 40

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CBF Quantification

1. Difference image ($\Delta M$) calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)

$\Delta M$ Calculation

Control $- \ Delta M$ Label $= \Delta M$

$\Delta M$ is typically $\sim 1\%$ of the control signal
“CBF $\alpha$ 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 $\alpha$ 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

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, \( T_1, T_2^* \)
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. Local tissue based: intrinsic normalization for nonuniformities
Distinguish between grey matter and white matter when assuming values for $T_{2,t}$ and $\lambda$.

$M_{0,a}$: 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:

<table>
<thead>
<tr>
<th>(ms)</th>
<th>1.5T</th>
<th>3T</th>
<th>7T</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{1t}$</td>
<td>900</td>
<td>1300</td>
<td>1900</td>
</tr>
<tr>
<td>$T_{1b}$</td>
<td>1300</td>
<td>1600</td>
<td>2300</td>
</tr>
<tr>
<td>$T_{ex}$</td>
<td>${r + W ; T_2} + 200$</td>
<td></td>
<td></td>
</tr>
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</table>
CBF Quantification

1. Difference image (ΔM) calculation
   - Surround subtraction (minimize contamination)
   - Average across frames (maximize SNR)
2. Arterial magnetization (M₀,a) estimation
   - Intensity non-uniformity compensation
   - Blood-tissue partition, T₁, T₂*
3. Decay correction

Decay Correction

- T₁ decay of tag incurred during transit must be compensated for acquisition delay
  \[ \exp(-TI/T₁a) \]
- This delay is dependent on the order of slice acquisition
  \[ TI_{corrected} = TI_{nominal} + slice \_order \times slice \_time \]
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

\[
\text{CBF} = \frac{\Delta M \times \lambda}{2\alpha \times M_{0,a} \times T_1 e^{-T_2/T_1 a}}
\]

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

- \( M_{0,a} \): Arterial blood equilibrium magnetization
- \( \lambda \): Tissue blood-water partition coefficient
- \( \alpha \): Labeling efficiency
Standard Kinetic Model

- CASL & pCASL

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

- \(M_{0,a}\): Arterial blood equilibrium magnetization
- \(T_{1,a}\): Arterial blood \(T_1\)
- \(\lambda\): Tissue blood-water partition coefficient
- \(\alpha\): Labeling efficiency
- \(\tau\): 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] \(\cong\) CBF[1/s] \(\times\) 6,000
CBF Quantification

ASL

ΔM

T1\textsubscript{1}

CBF

Sample Quantitative CBF Map

Courtesy: H-L A. Liu
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 $\Delta B_0$ and $\Delta B_1$: 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