Blood Oxygenation Level-dependent (BOLD) fMRI

fMRI Paradigm

No Stimulus

Stimulus

No Stimulus

Healthy volunteers
Signal Change: 2-4%
Blood Oxygenation Changes Influence MR Signal

\[ \text{HbO}_2: \text{ Diamagnetic} \quad \text{Hb: Paramagnetic} \]

Oxygenated RBC

De-Oxygenated RBC

Proton signal dephased by local fields: \( \downarrow T_2(*) \)
Many Possibilities Underlying BOLD Changes

Positive BOLD Effect
- CBF
- CBF
- CBF

Negative BOLD Effect
- CBF
- CBF
- CBF
Arterial Spin Labeling (ASL)

Measuring CBF with Arterial Spin Labeling (ASL)

Control – Label = CBF-weighted image

Quantify CBF (ml blood/100g tissue/min) from difference image
Arterial Spin Labeling (ASL)

- By varying TI:
  - CBF
  - Arterial transit time (ATT)
- Noninvasive

diffsig_invtime

ASL Sensitive to CBF and Transit Time
Arterial Spin Labeling (ASL)

Measuring CBF Changes with ASL fMRI

3.0T ASL fMRI
Right hand joystick movement (1 Hz)
Spatial resolution=3.8x3.8x3.8 mm³
CBF change =60-70%
TR/TI=2500/1600 ms
Arterial Spin Labeling (ASL)

ASL Manuscripts

- Total
- Neuroscience Applications

Year

Arterial Spin Labeling (ASL) Publications
Vascular space occupancy (VASO)

Measuring CBV with Vascular-space-occupancy (VASO) MRI

Vascular space occupancy (VASO)

Measuring CBV Changes with Vascular-space-occupancy (VASO)


Neuronal Activation: CBV increase

VASO: Null blood water signal

Observe: Signal (tissue + CSF) decrease

Voxel size=780µm x 780µm
Slice thickness 3 mm
SENSE factor 2.5
TR/TI/TE=3000/889/32 ms

fMRI:
Visual stimulus (6 Repetitions of 30s off/on flashing checkerboard)
Vascular space occupancy (VASO)

VASO Manuscripts

- Total
- Neuroscience Applications

Year:
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010

Manuscripts:
- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8

Vanderbilt University
Improving Interpretability: ASL and VASO

Whole-brain BOLD, CBF and CBV Activation Maps (Visual + Motor)

Flashing checkerboard (8 Hz) + 1 Hz RH joystick movement; 60s/30s off/on
Siemens 3.0T, Spatial resolution = 3.8 x 3.8 x 3.8 mm³, TE=40 ms
BOLD, CBFw (ASL) and CBVw (VASO) Time Courses (n=7)

**BOLD**

Motor ΔS/S%: 1.5 ± 0.3  
Visual ΔS/S%: 1.9 ± 0.3

**VASO**

Motor ΔCBV%: 8±3  
Visual ΔCBV%: 17±7

**ASL**

Motor ΔCBF%: 46±11  
Visual ΔCBF%: 63±12

Siemens 3.0T  
Mean (n=8) ± standard error  
Spatial resolution=3.8 mm isotropic

Sequence Improvements: ASL and VASO

2D Readouts and ASL / VASO Slice Timing

Problem: Excitation must be applied at blood null time

![Graph showing magnetization vs time for different brain regions (GM, Blood, CSF)]
Sequence Improvements: ASL and VASO

3D GRAdient And Spin Echo (GRASE)


1) 3D GRASE: Single 90 for whole-brain at blood null time

2) Series of refocusing pulses between EPI readouts
Sequence Improvements: ASL and VASO

Sequence Improvements: ASL and VASO

3D GRASE with VASO-FLAIR

Sequence Improvements: ASL and VASO

3D GRASE with ASL

Arterial Transit Time Reduces with Increased Neuronal Activation

Arterial Spin Labeling (ASL)

Pseudo-continuous ASL (pCASL)

Pulsed

Label

\[ \text{B}_0 \]

Flip = 180

3-15 ms

Pseudo-continuous

Label

\[ \text{B}_0 \]

Flip < 180

1000-2000 ms
Reduction of Transit Time Sensitivity with pCASL

Considerations: ASL

ASL: Spin Compartmentalization


Takes 1.5-2 sec following carotid labeling for blood water to reach tissue
Considerations: VASO

Effect of Inflow of Fresh Blood on VASO Contrast

Considerations: ASL and VASO

### Arterial spin labeling (ASL)
- Long TI $>1500$ ms to allow labeled blood water to reach tissue
- High SNR (pCASL, 3D GRASE)
- Reduce slice timing discrepancy (3D GRASE, pCASL)
- Mindful of transit time reductions (pCASL or multi-TI PASL)

### Vascular space occupancy (VASO)
- Long TR $>4000$ ms to reduce inflow
- High SNR (3D GRASE)
- Reduce CSF sensitivity (VASO-FLAIR, separate CSF measurement)
- Reduce slice timing discrepancy (3D GRASE)
Whole-brain VASO Application to Stroop Task

Estimating Metabolic Information from Multi-modal fMRI

Lu H, Golay X, Pekar JJ, Van Zijl PC.
Uncoupling of CBF/CBV and CMRO2?

BOLD undershoot disappears during breath-hold (unchanging CMRO$_2$)

Donahue et al. JCBFM. 2009 Jan;29(1);176-85
Possible ASL Undershoot?

Griffeth, V.E., Simon, A.B., Perthen, J.E., and Buxton, R.B. International Society for Magnetic Resonance in Medicine, 2009
**Conclusions**

**BOLD sensitive to many parameters, e.g.**
- Cerebral blood flow (CBF)
- Cerebral blood volume (CBV)
- Cerebral metabolic rate of oxygen (CMRO$_2$)

**BOLD contrast can be better understood by measuring these parameters:**
- CBF: Arterial spin labeling, ASL
- CBV: Vascular space occupancy, VASO

**BOLD, ASL and VASO can be performed with near whole-brain coverage**
- Temporal resolution: BOLD (2-3s), ASL (4-8s), VASO (1-5s)
- Spatial resolution: 3 - 4 mm isotropic (3.0T)

In many applications, ASL and VASO may be useful for complementing, or replacing, BOLD contrast. Knowledge of contrast mechanisms crucial to improving interpretability