Perfusion fMRI

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Outline

- Cerebral Blood Flow (CBF)
- Arterial Spin Labeling (ASL) Techniques
- Data Processing
- Applications of ASL

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Cerebral Blood Flow (CBF)

CBF = Perfusion

= Rate of delivery of arterial blood to a capillary bed in tissue.

Units: $\dfrac{\text{(ml of Blood)}}{\text{(100 grams of tissue)(minute)}}$

Typical value is 60 ml/(100g-min) or 60 ml/(100 ml-min) = 0.01 s^{-1}, assuming average density of brain equals 1 gm/ml

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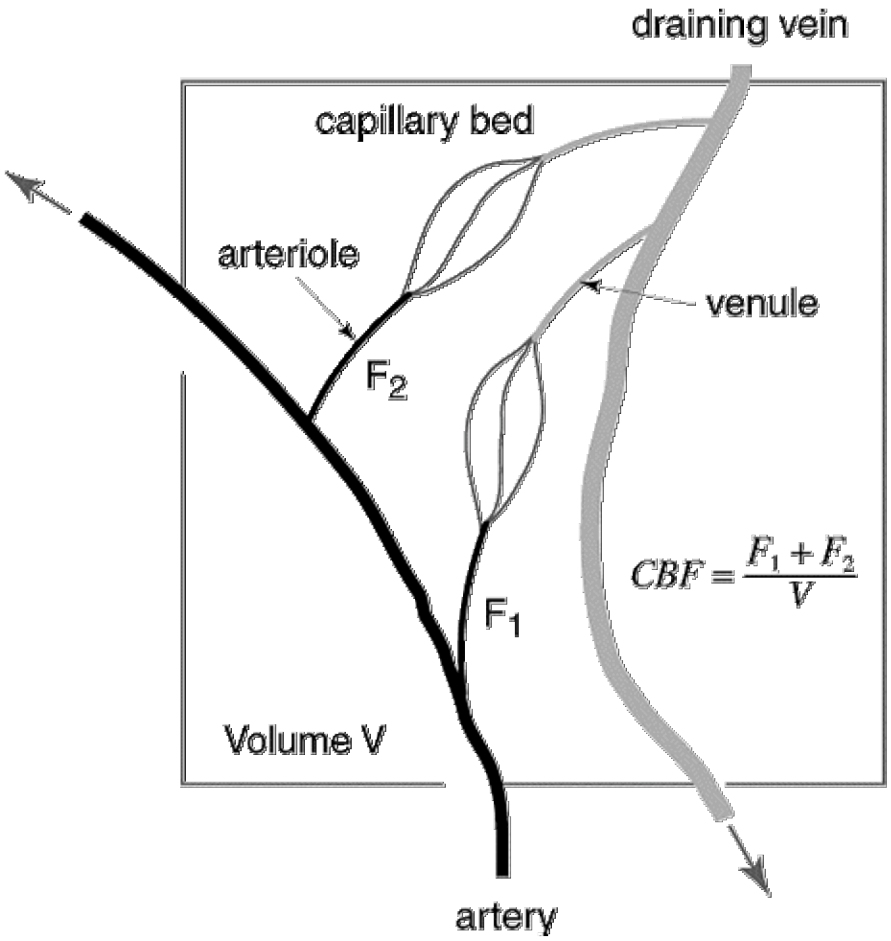


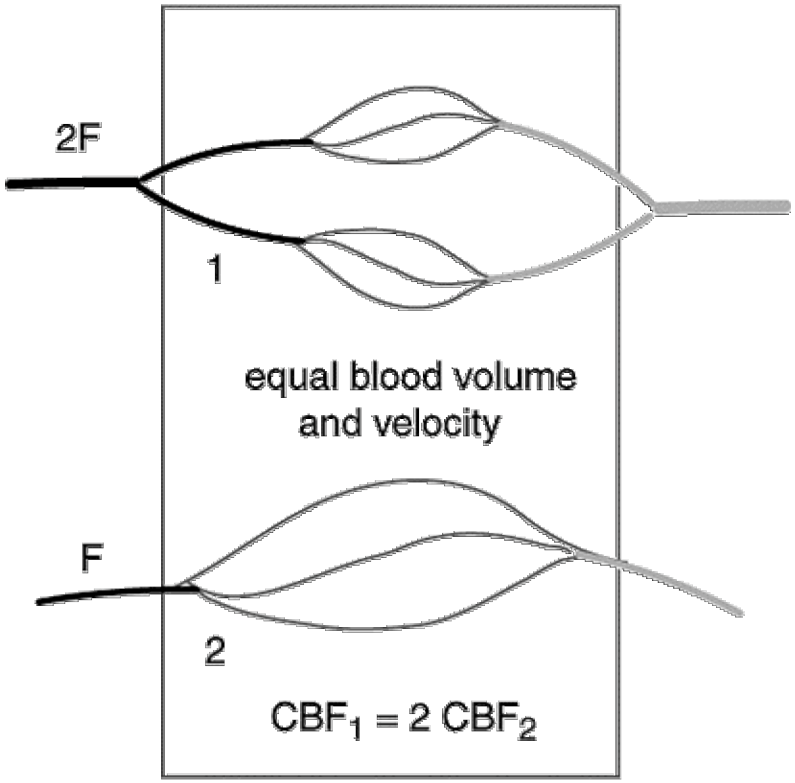
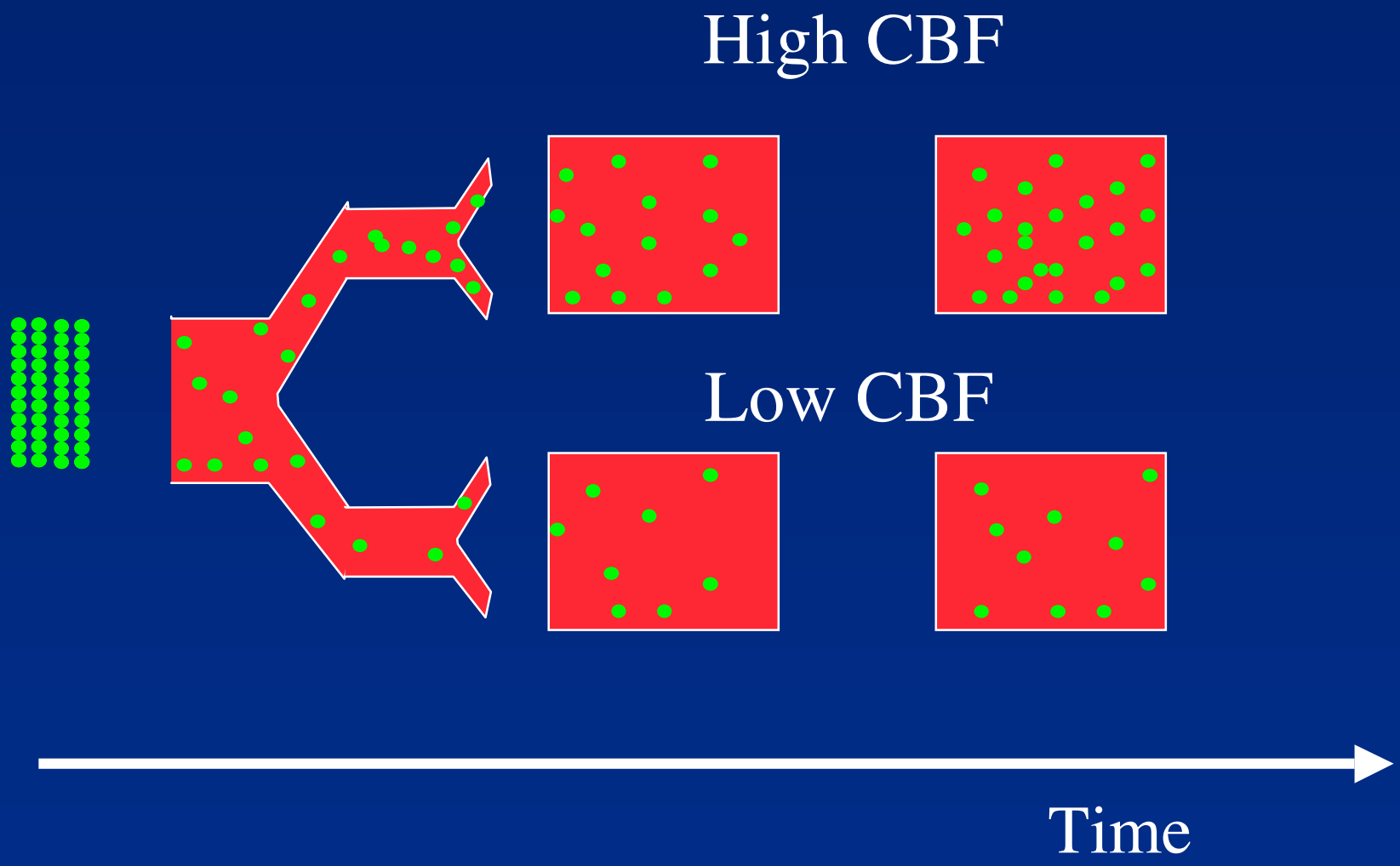


Fig. 2.2

Courtesy of Rick Buxton



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Arterial Spin Labeling

- Magnetically tag inflowing arterial blood
- Wait for tagged blood to flow into imaging slice
- Acquire image of tissue+tagged blood
- Apply control pulse that doesn't tag blood
- Acquire control image of tissue
- Control image-tag image = blood image

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Methods for Tagging Arterial Blood

- Spatially Selective ASL (SS-ASL) methods tag arterial blood in a region that is proximal to the imaging region of interest.
  - Continuous ASL (CASL) -- continuously tags blood as it passes through a thin tagging plane
  - Pulsed ASL (PASL) -- tags blood in a large slab proximal to imaging slice.
- Velocity Selective ASL (VS-ASL) tags arterial blood based on its velocity, and takes advantage of the fact that blood decelerates as it enters the capillaries and accelerates as it enters the veins.

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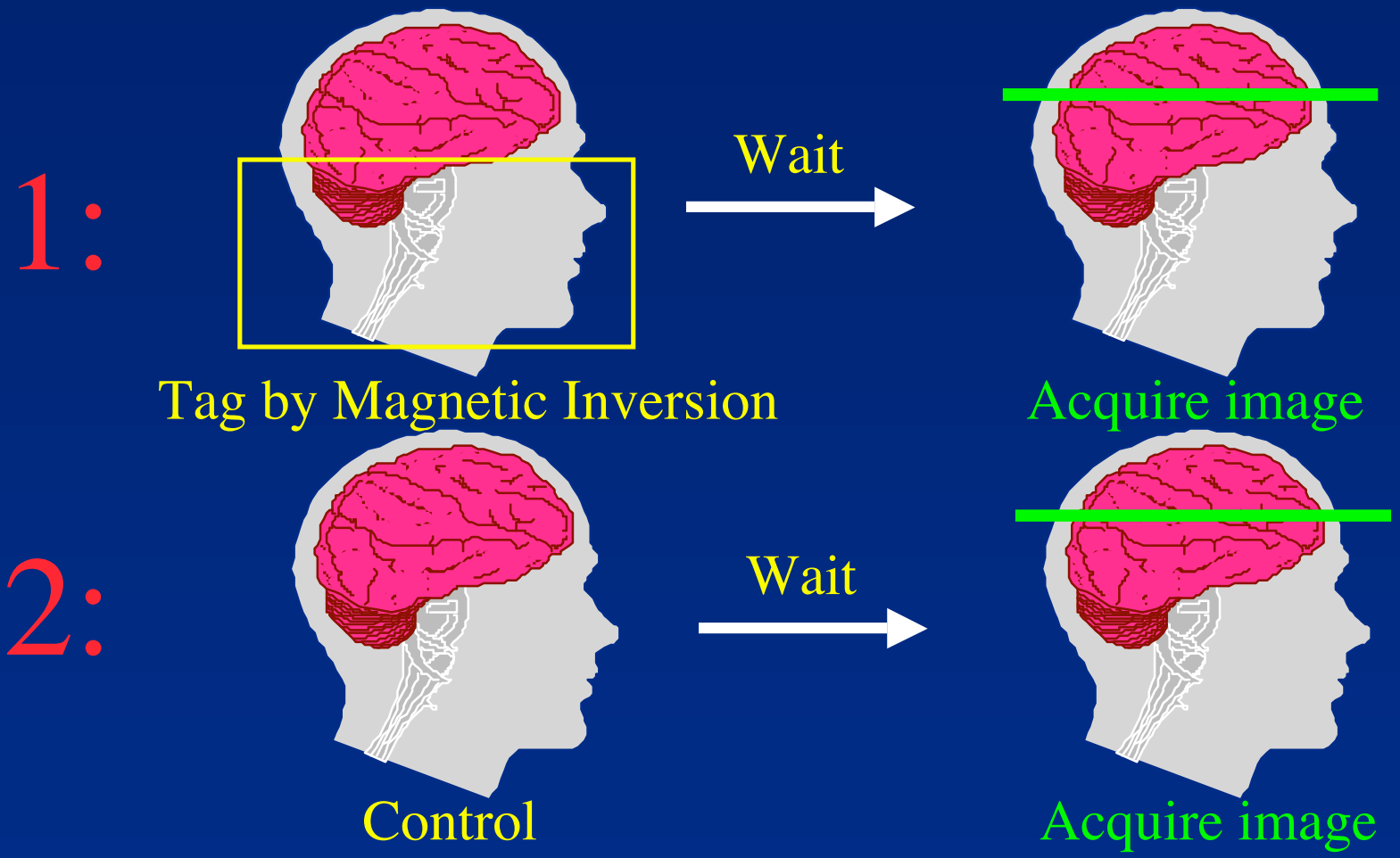
Arterial Spin Labeling (ASL)



Control - Tag CBF

Courtesy of Wen-Ming Luh

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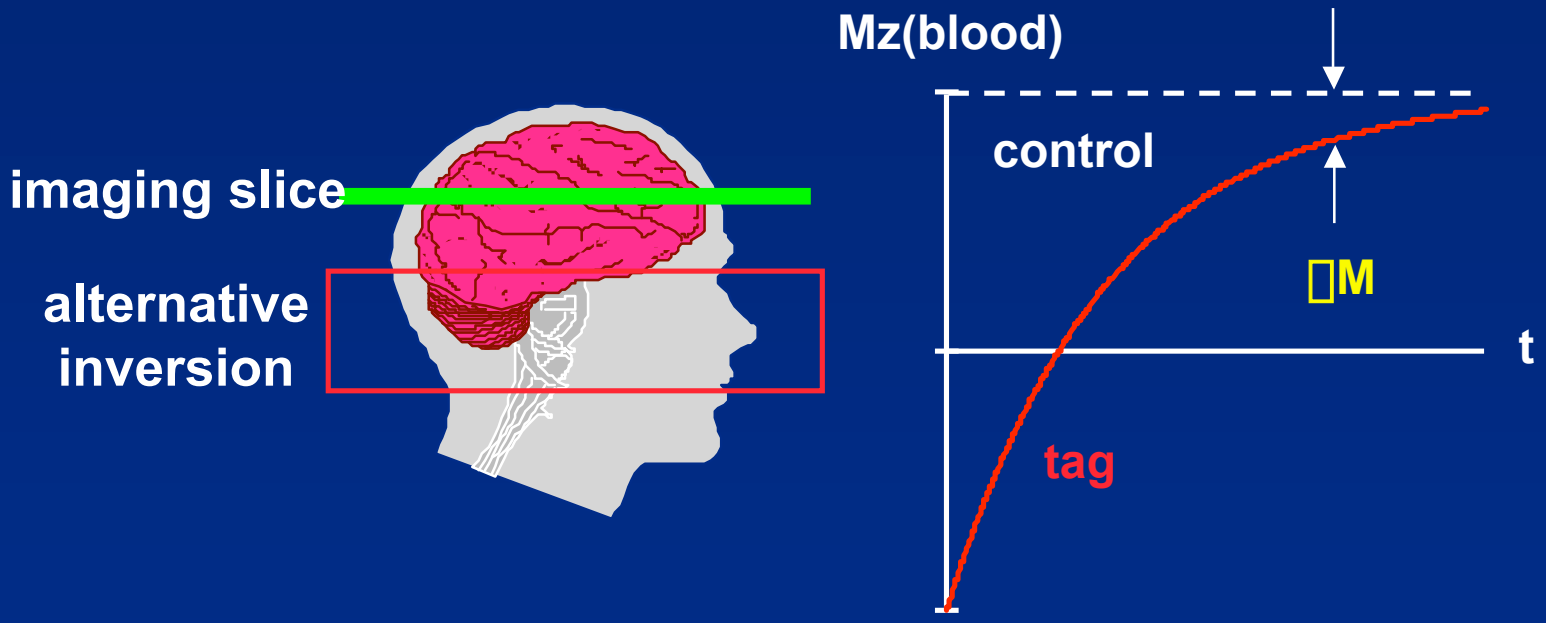
Arterial Spin Labeling (ASL)

- water protons as freely diffusible tracers



Courtesy of Wen-Ming Luh

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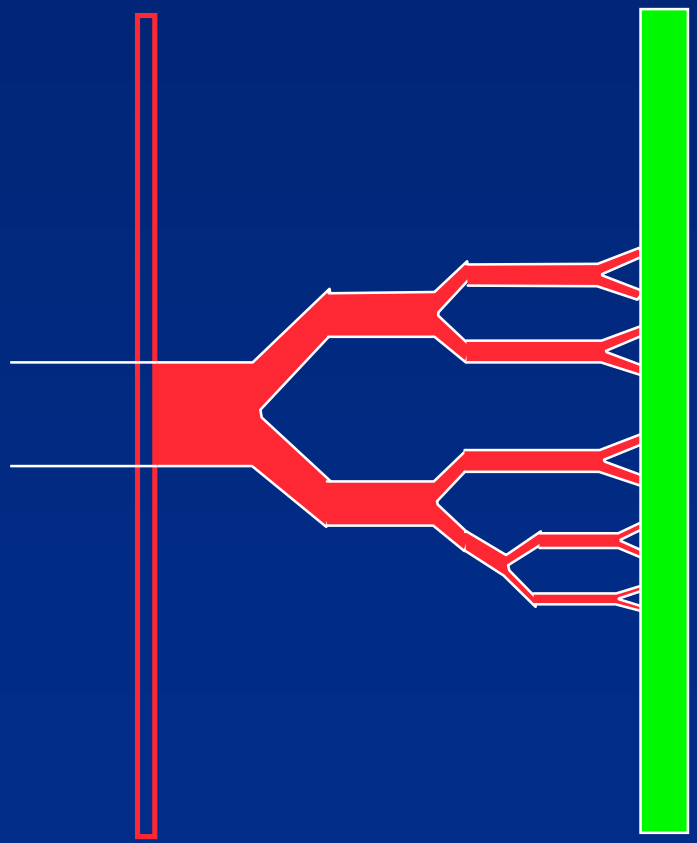
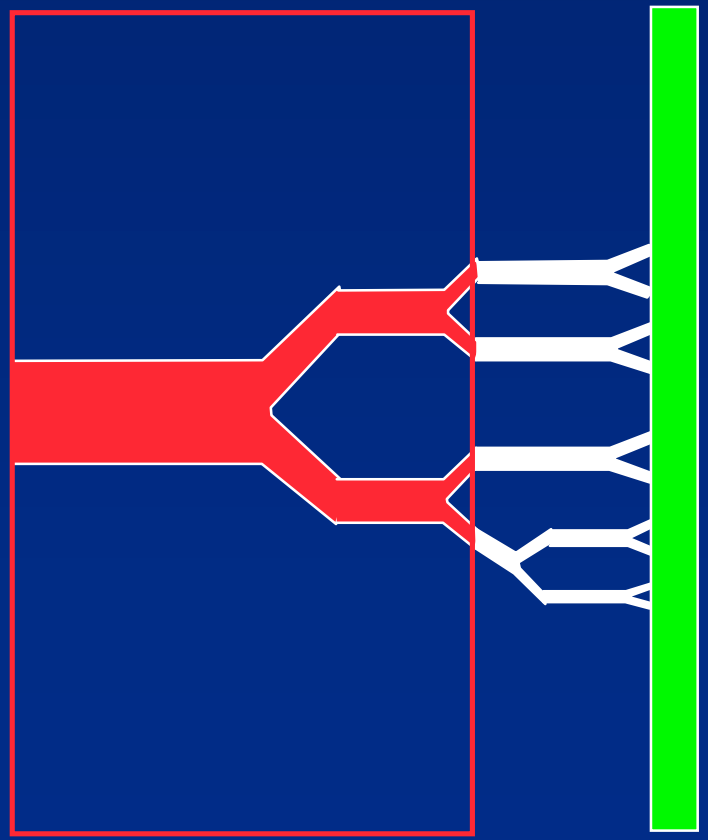
Continuous ASL

tagging plane
Tag duration ~ 2000 ms



Pulsed ASL

tagging region ~ 10 cm
Tag duration ~ 15 ms



Adapted from Wen-Ming Luh

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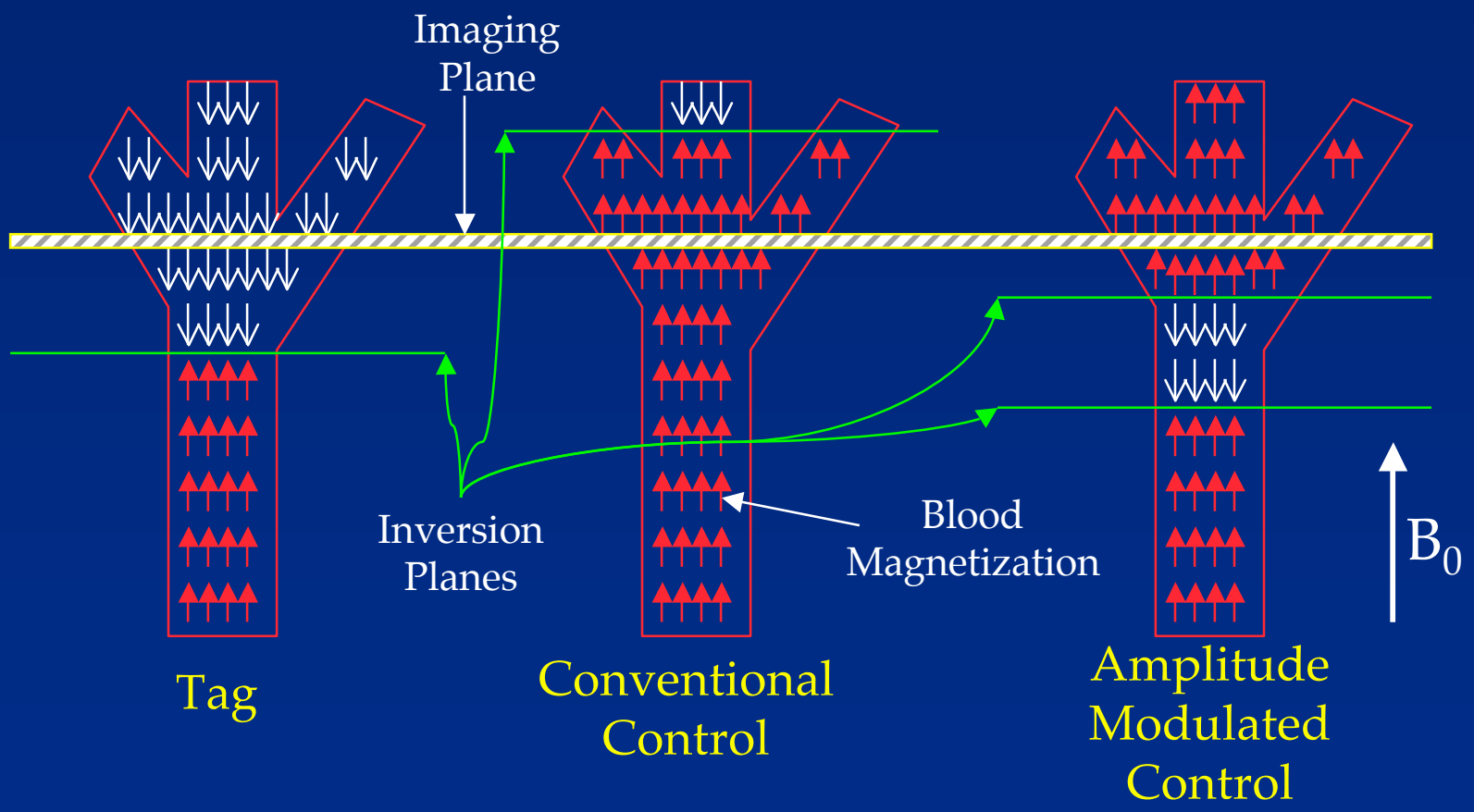
Continuous ASL



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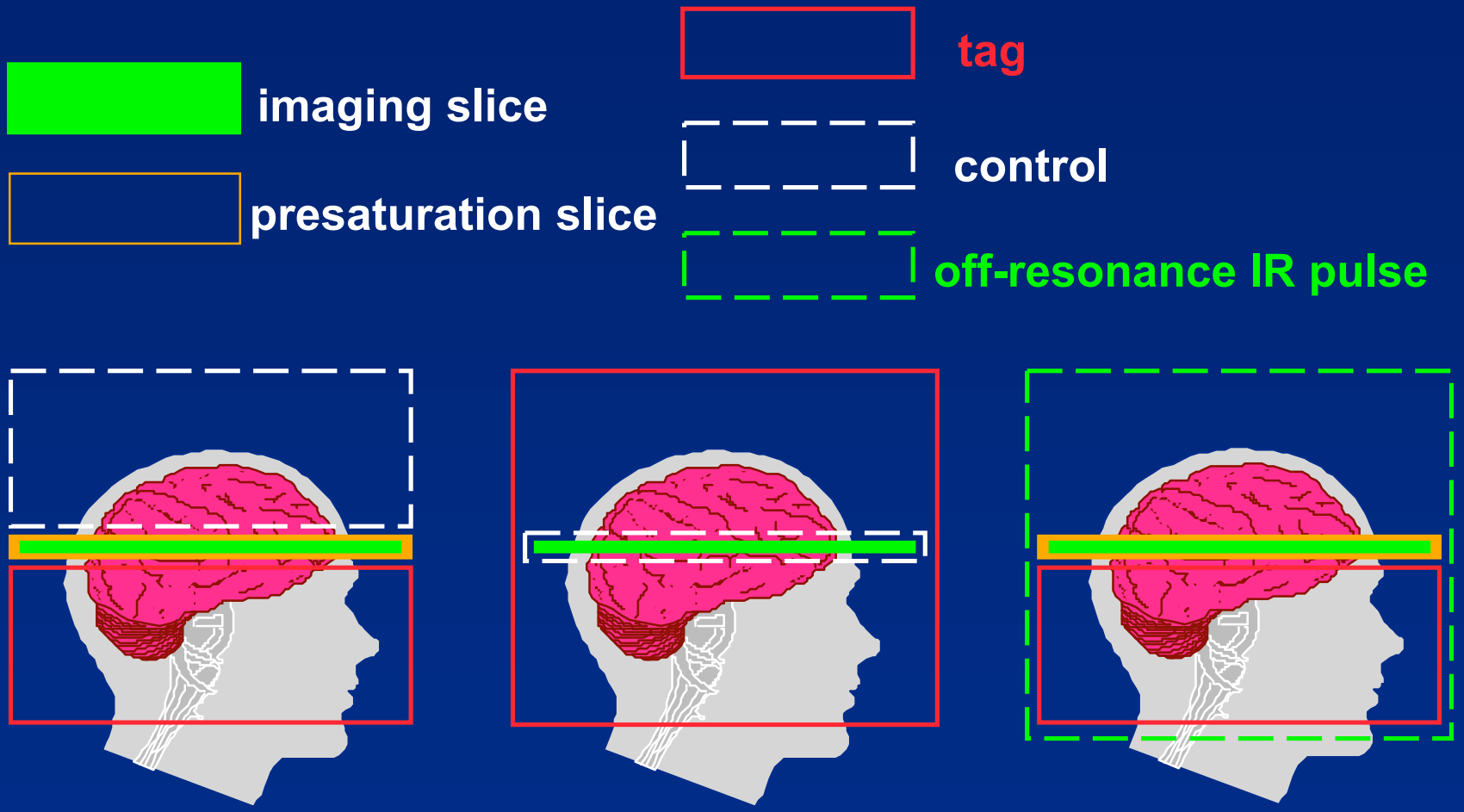
Conventional Pulsed ASL



Courtesy of Wen-Ming Luh

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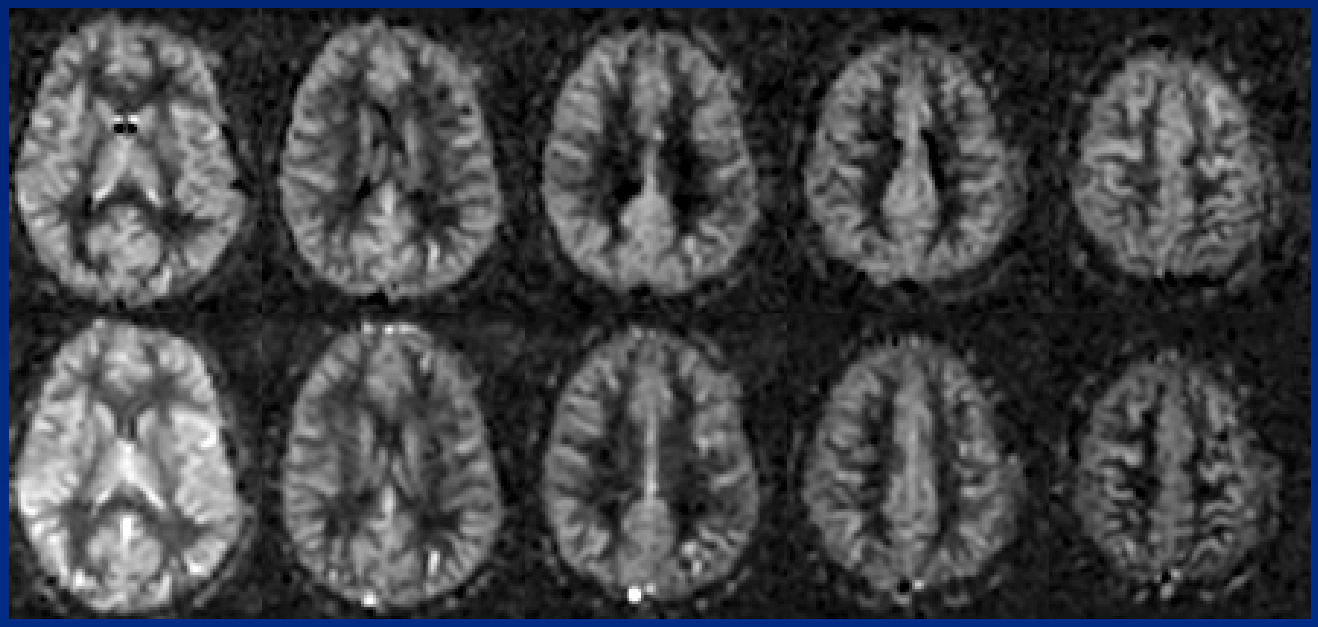
Multislice CASL and PICORE

CASL

PICORE
QUIPSS II



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CASL vs. PASL

- Inherent SNR for CASL is higher, but SNR/time is roughly the same.
- Temporal resolution for PASL slightly better (2 s TR vs. 3 s TR).
- PASL amenable to use of a presaturation pulse for simultaneous CBF/BOLD.
- CASL may be better for lower slices when using a head coil for transmit.
- Both have non-quantitative variants that are useful for mapping.
- CASL has higher SAR requirements.

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ASL Signal Equation

$$\Delta M = CBF \cdot A_{eff}$$

A_{eff} is the effective area of the arterial bolus. It depends on both physiology and pulse sequence parameters.

Goal: Make A_{eff} a well-controlled parameter that is robust to assumptions about physiological parameters.

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Major Sources of Error for ASL

- Transit Delays
- Bolus Width in PASL
- Relaxation Effects - different relaxation rates for blood and tissue, time of exchange.
- Intravascular signal -- blood destined to perfuse more distal slices.

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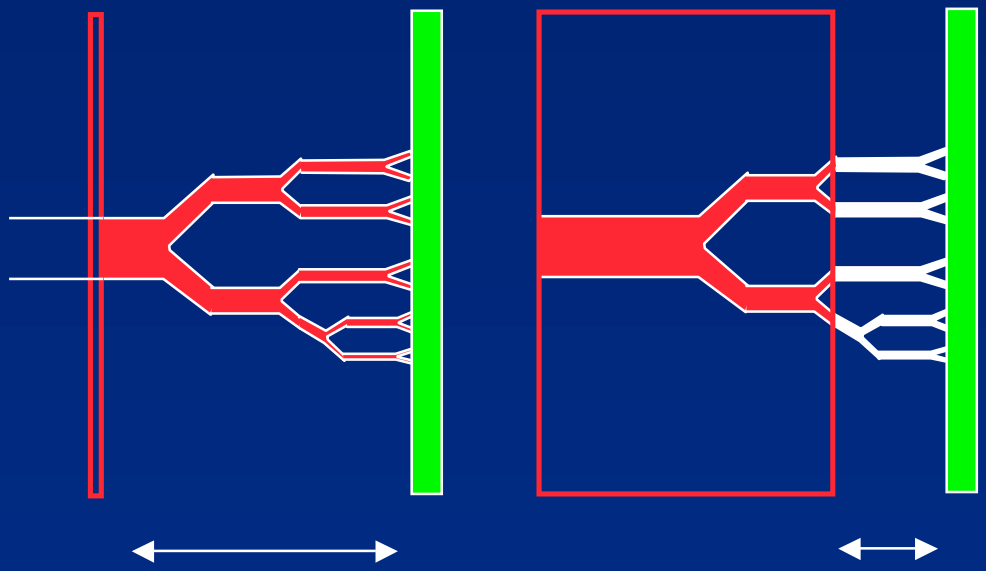
Transit Delays

CASL PASL



~ 3 cm
$\Delta t < 1000ms$

~ 1 cm
$\Delta t < 700ms$

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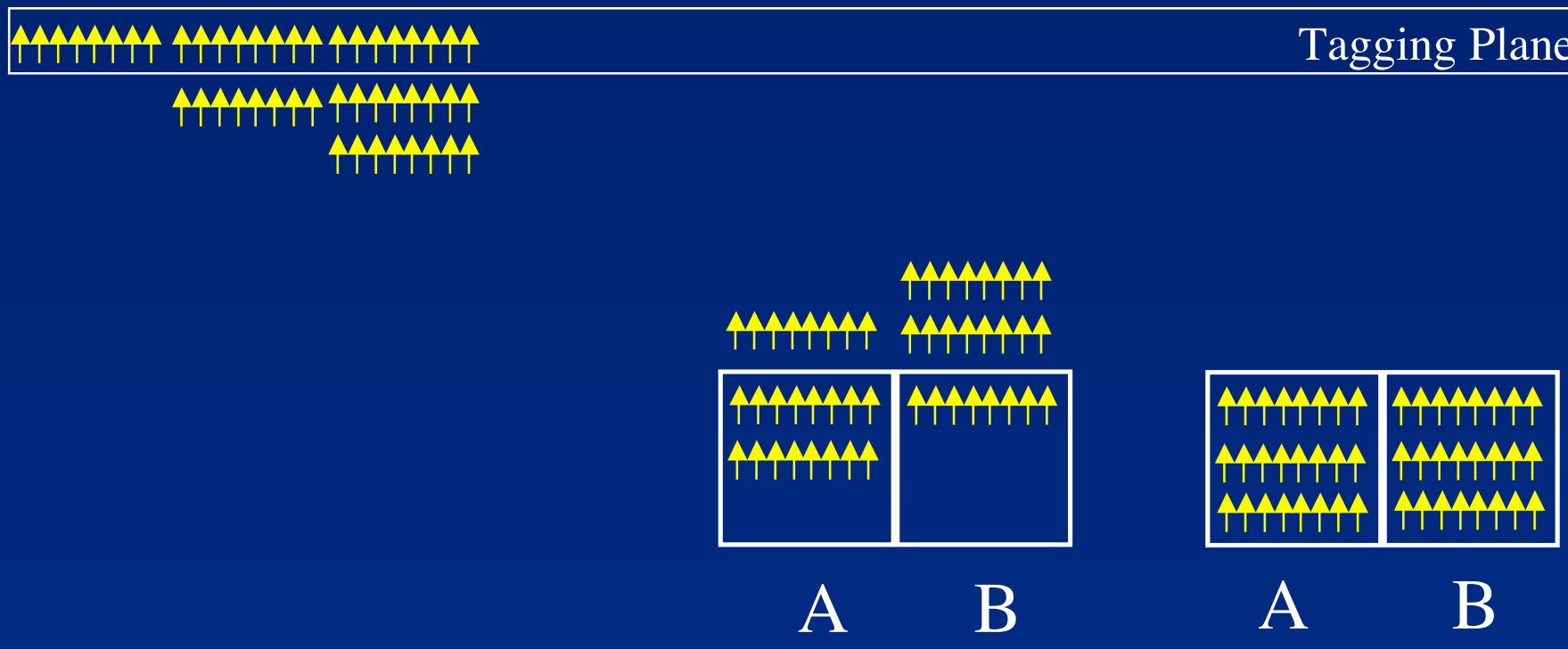
Controlling for Transit Delays in CASL



Voxels A and B have the same CBF, but voxel B will appear to have lower CBF if the measurement is made too early.

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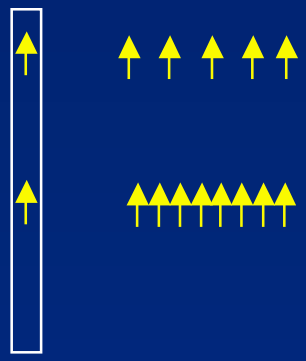
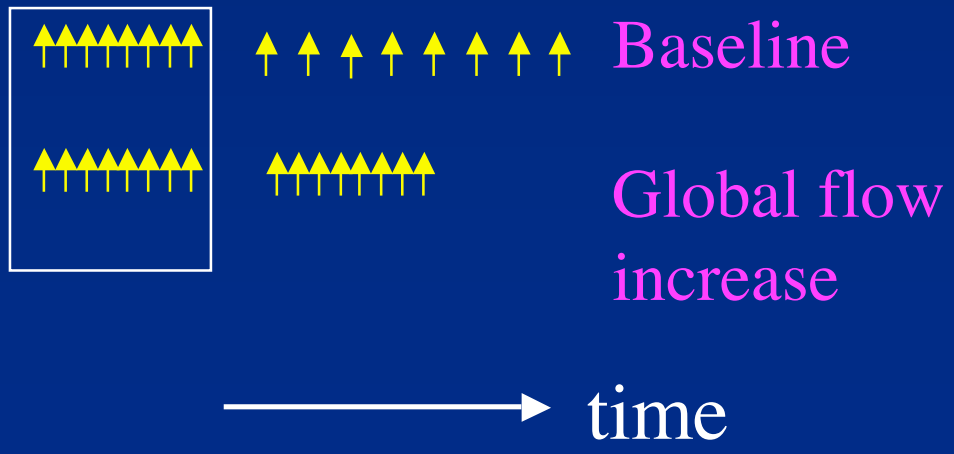
Arterial Bolus Width

CASL



Temporal Width of bolus determined by the pulse sequence

PASL



Temporal Width of bolus determined by arterial velocity and size of tagging slab. Underestimates global flow changes.

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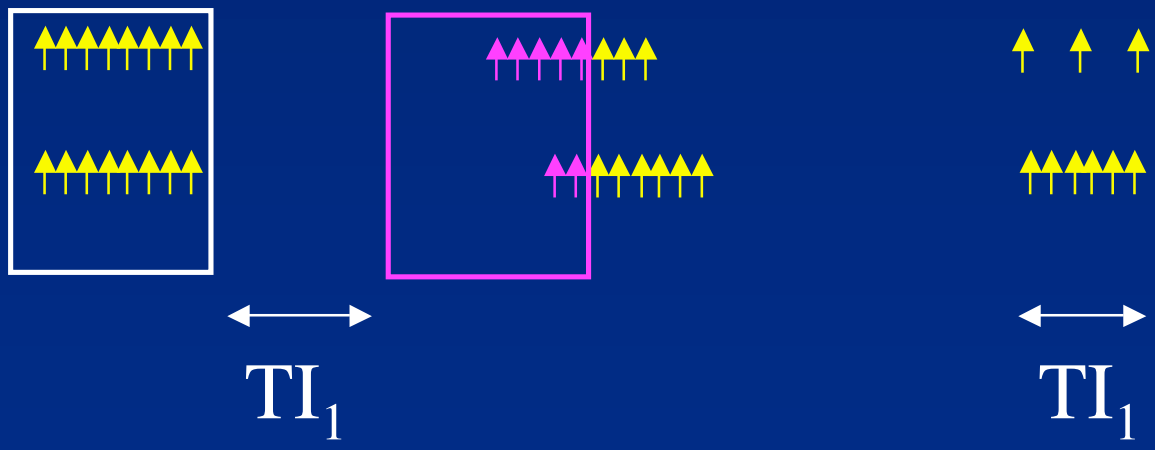
Defining Bolus Width in PASL (QUIPSS II)

Tag the spins

Saturate spins still in the slab

Bolus temporal width = TI_1



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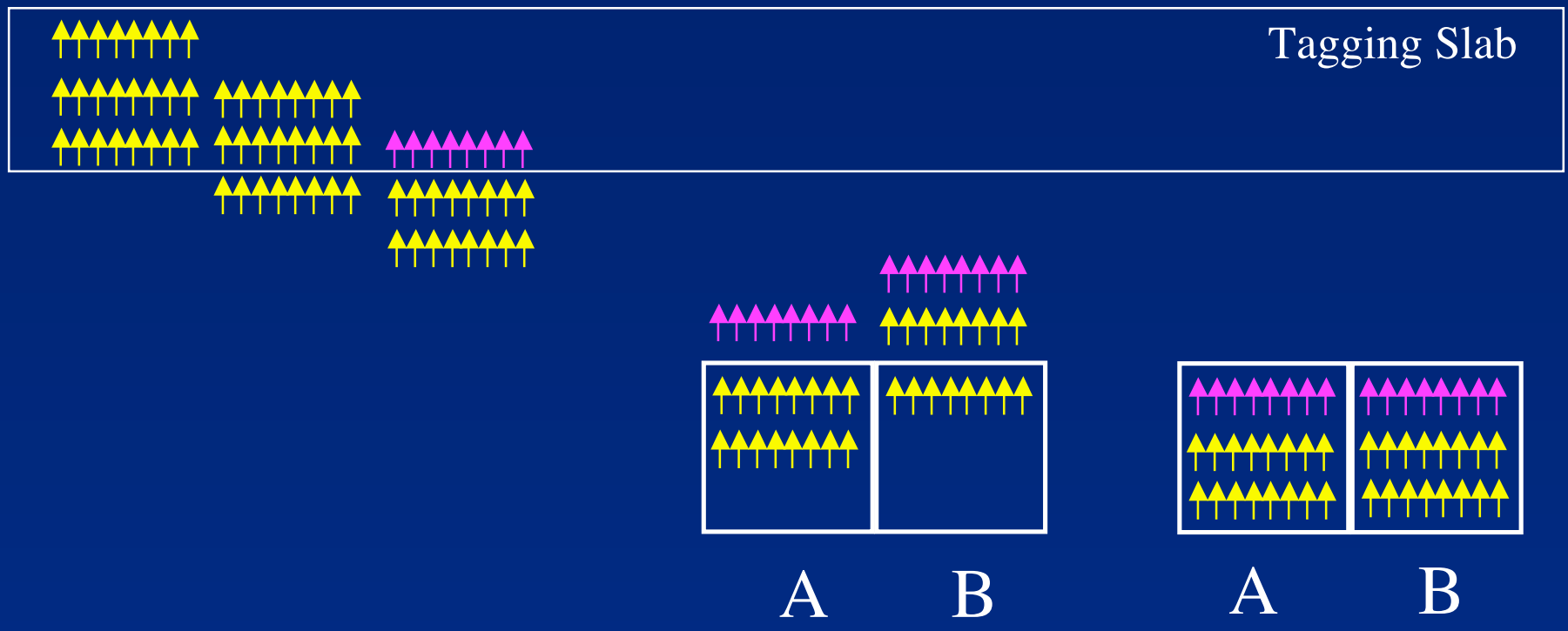
Controlling for Transit Delays in PASL



TI_1

$TI_2 > \Delta t + TI_1$

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Velocity Selective ASL

- Velocity selective radio-frequency pulse trains were introduced by Norris and Schwarzbauer in 1999.
- Velocity Selective ASL (VS-ASL) uses a velocity selective pulse train to tag blood that is flowing faster than a desired cut-off velocity (Wong et al. 2002).
- A typical cut-off velocity is 1 cm/s which corresponds to arterioles of about 50 μm.
- Essentially eliminates the problem of transit delays.

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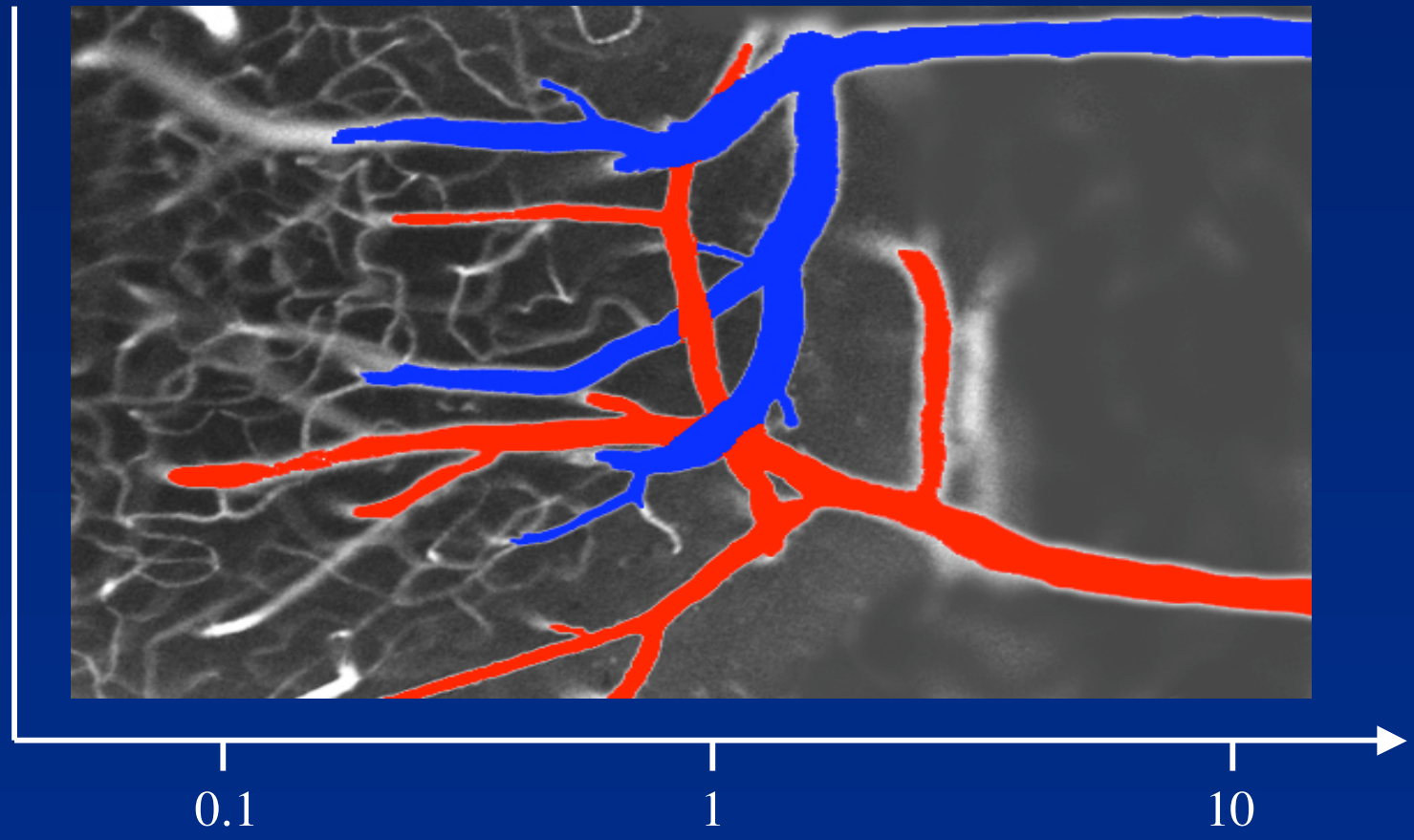
Velocity Distribution



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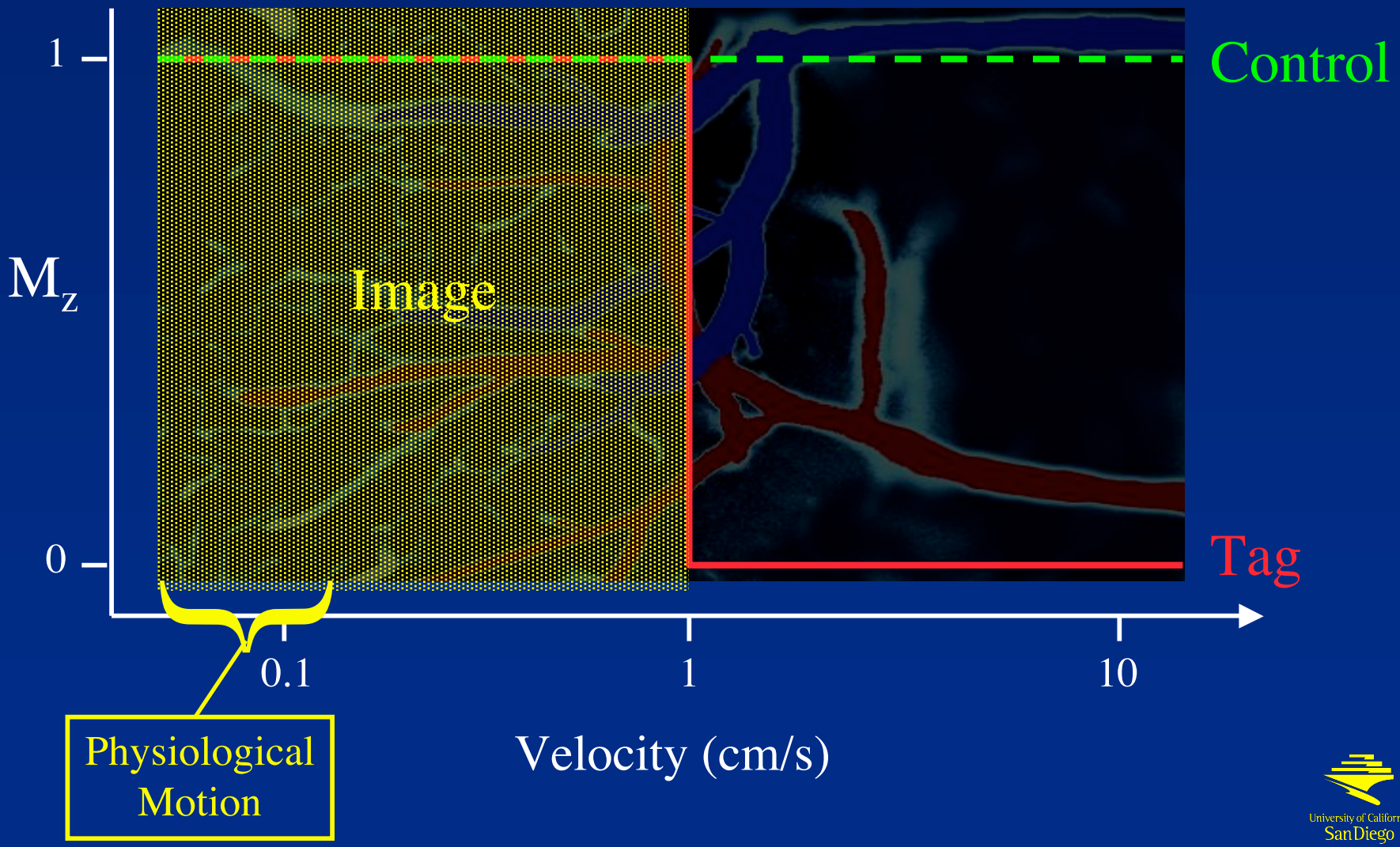
Ideal Velocity Selective ASL



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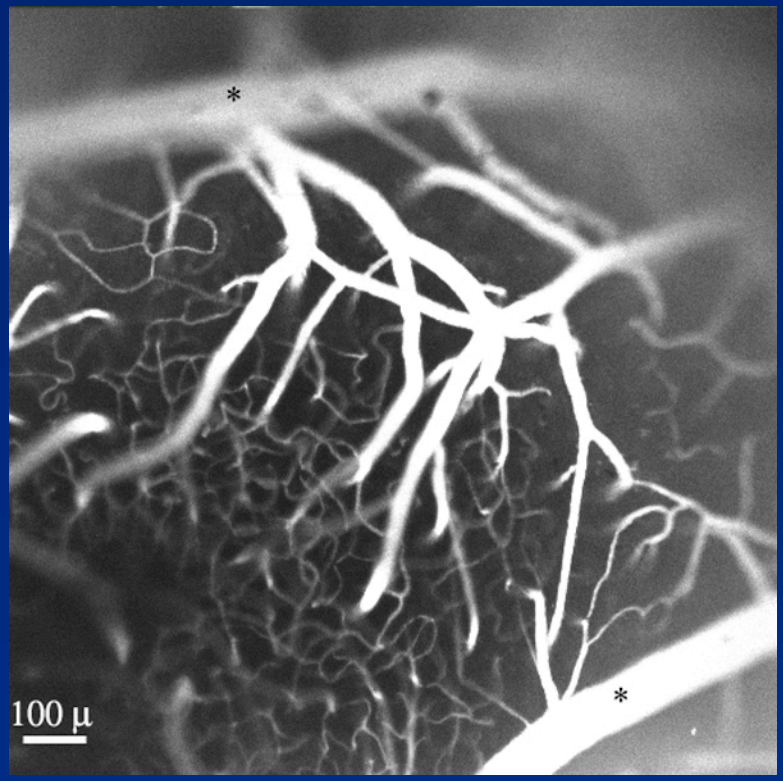
Spatial Localization



VENC of 0.5-2cm/s dephases spins
in 20-50um arterioles

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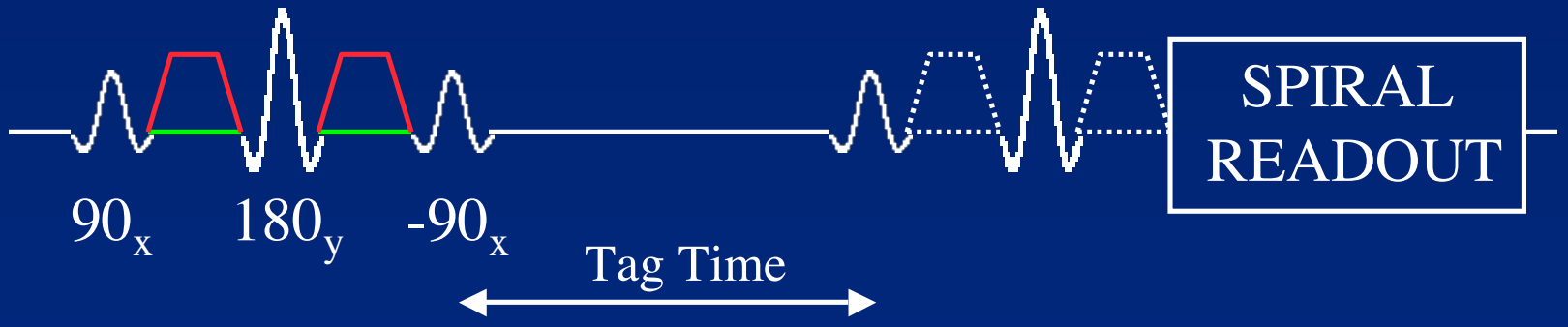
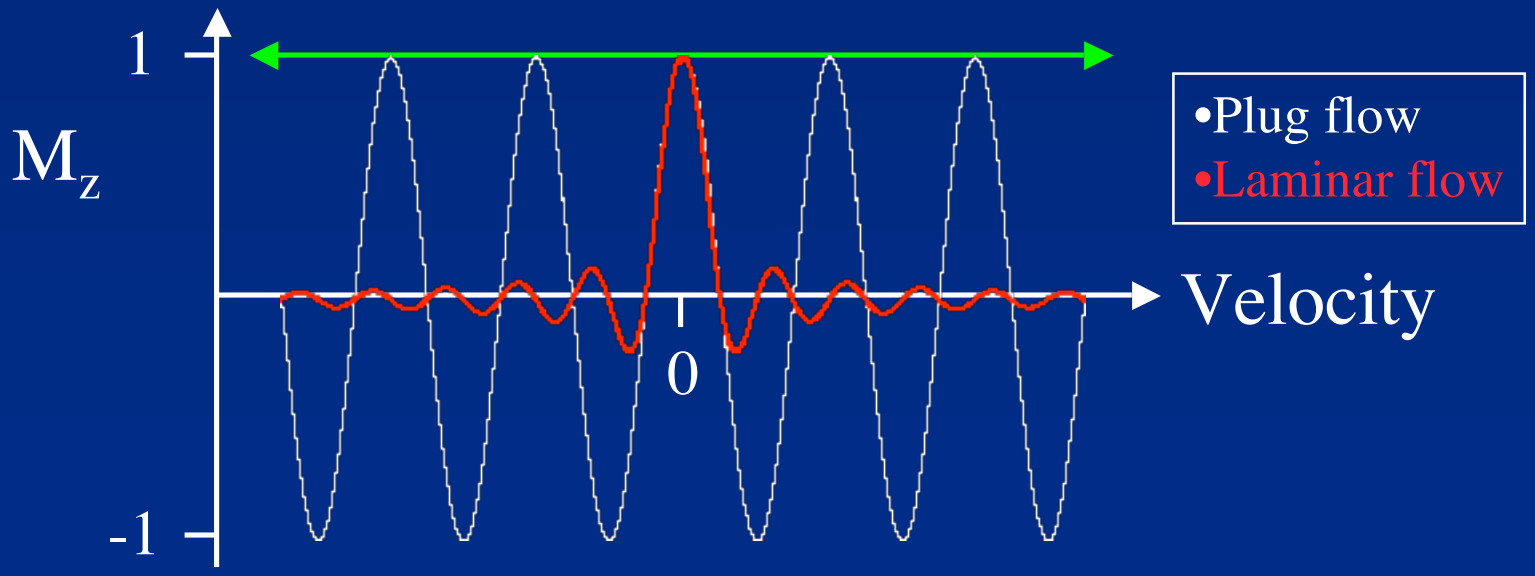
Initial Implementation (2002)





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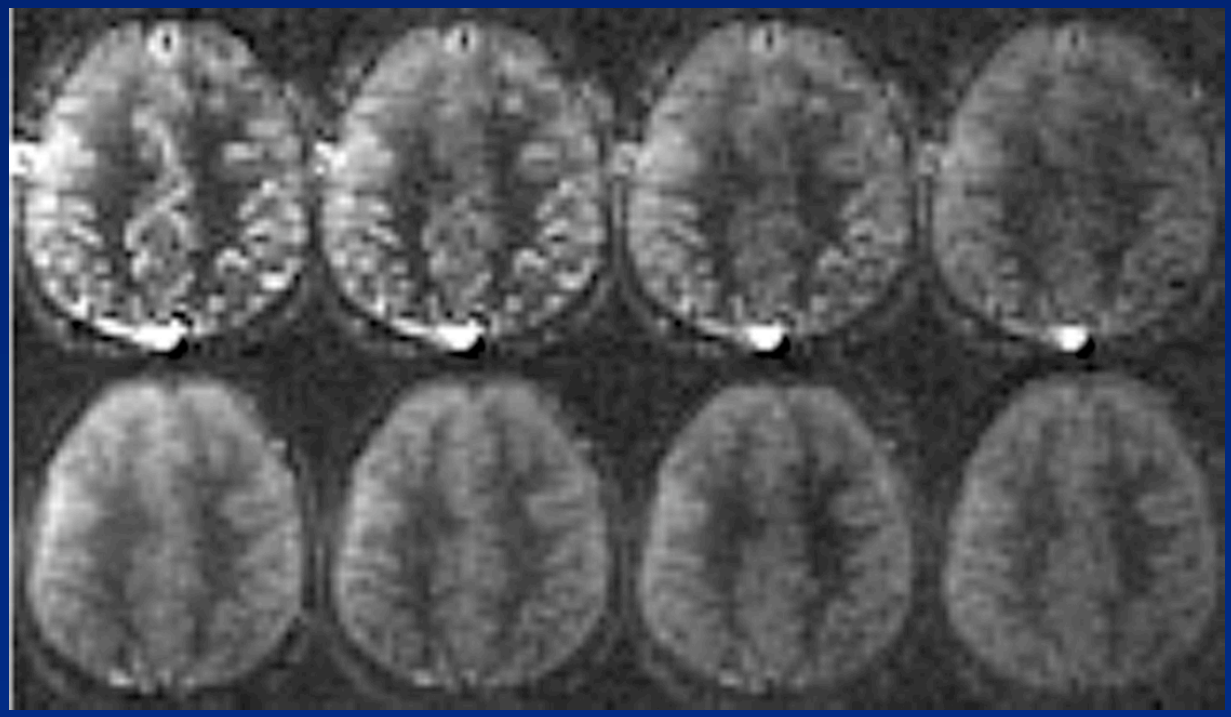
Results - Tag Time Dependence

Non Quantitative

Quantitative



Tag Time (ms): 700 800 1100 1300

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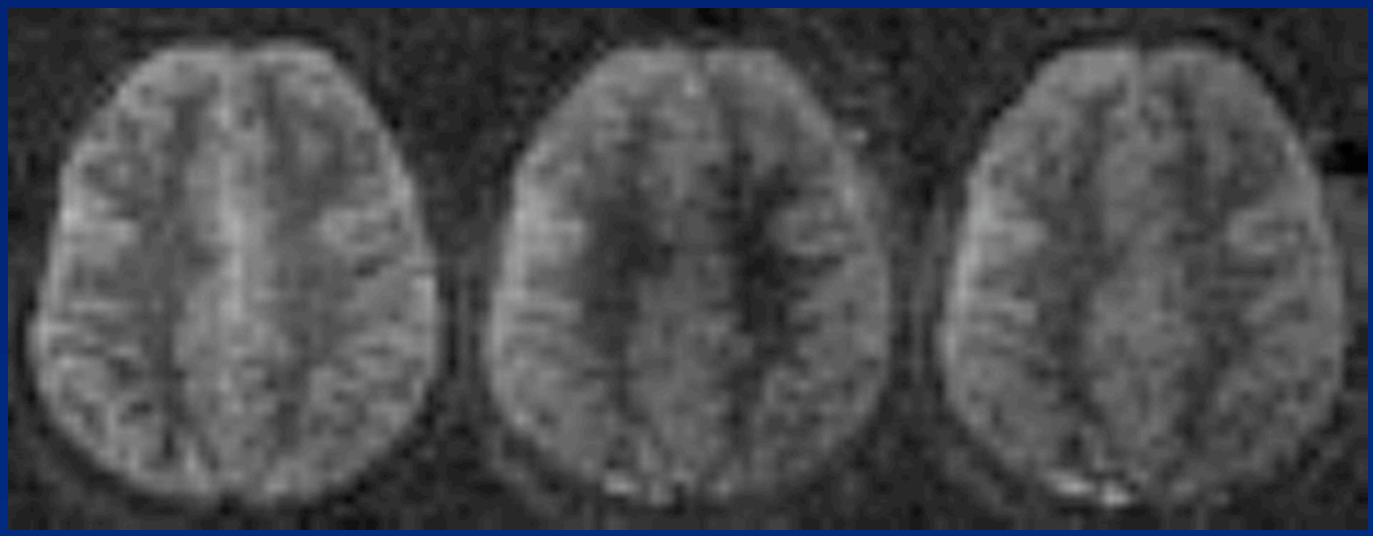
Results - VENC Dependence



VENC (cm/s):	0.5	1.0	2.0
Approximate Vessel Size (um):	20	30	50

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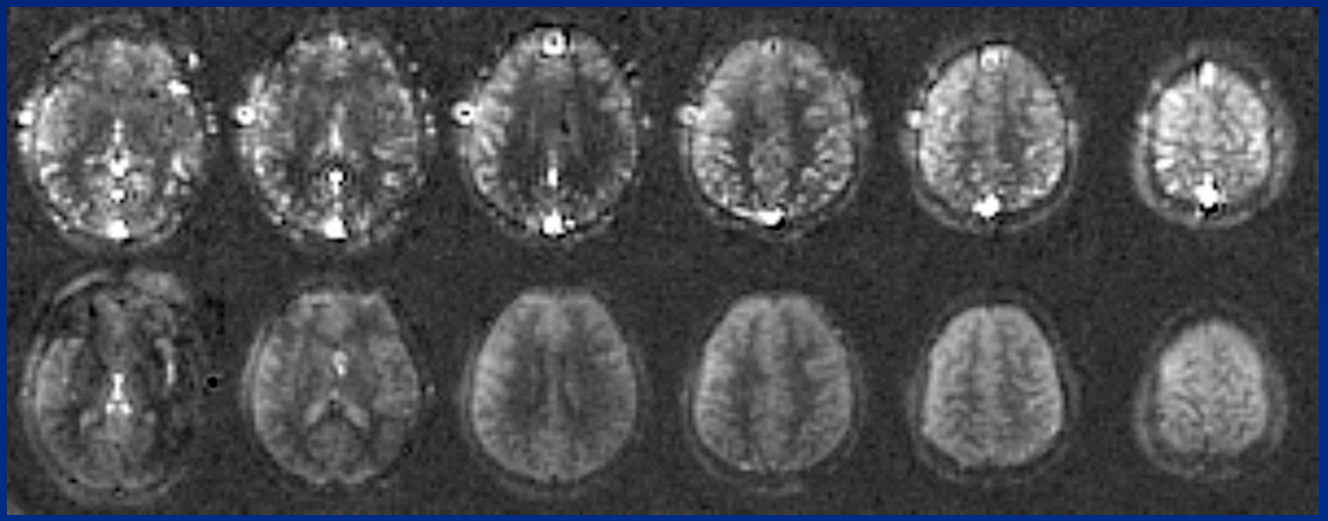
Results - Multislice VS-ASL

Non Quantitative

Quantitative



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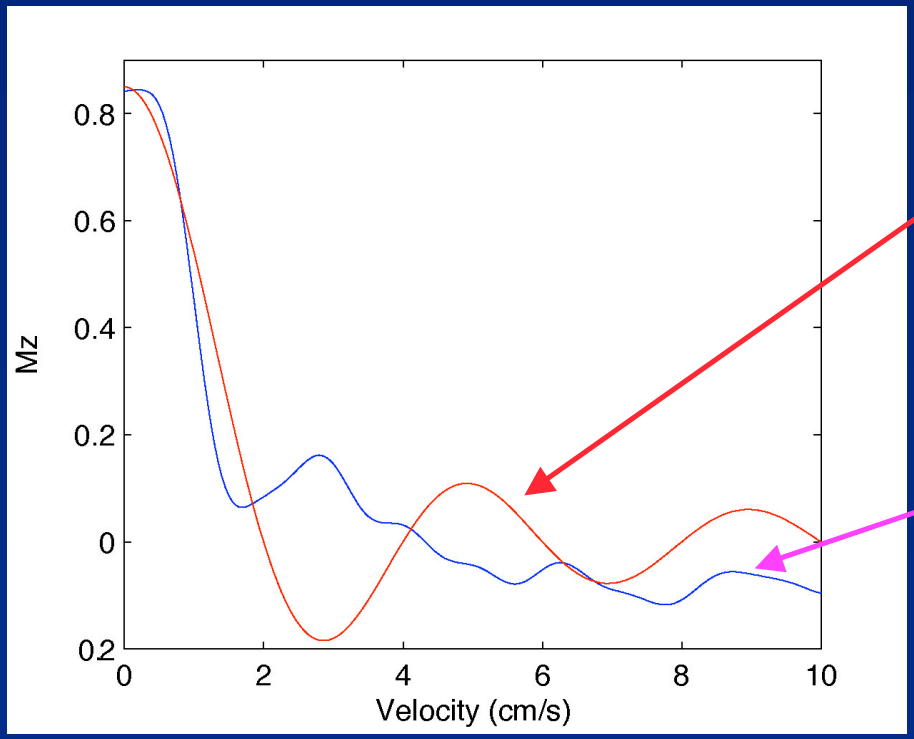
Future Development of VS-ASL

- Better velocity selective pulses should improve motion insensitivity and quantitation of CBF (Abstract #2181 at this meeting)



Velocity Profile of Initial Implementation

Velocity Profile of Hyperecho based sequencewith adiabatic pulses

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ASL Data Processing

- CBF = Control - Tag
- A CBF time series is formed from a running subtraction of Control and Tag images -- pairwise subtraction, etc. .
- BOLD weighting of CBF signal is small and can be minimized with short echo time acquisitions (e.g. spiral or partial Fourier) or spin-echo acquisitions.
- Use of subtraction makes CBF signal insensitive to low-frequency drifts.

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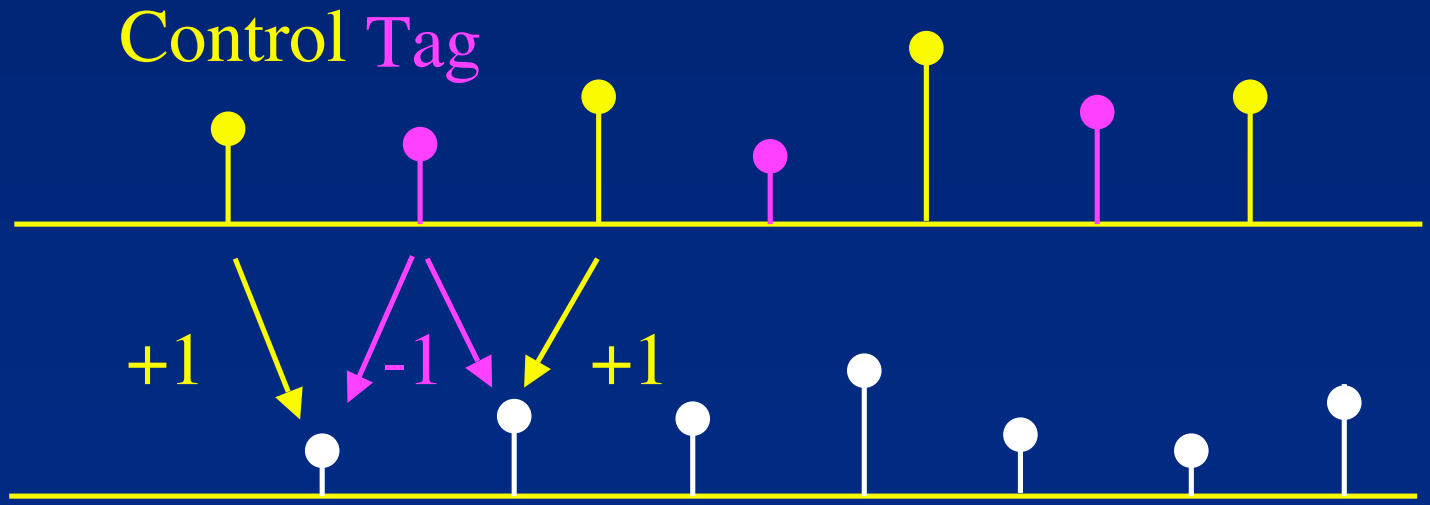
Pairwise subtraction example



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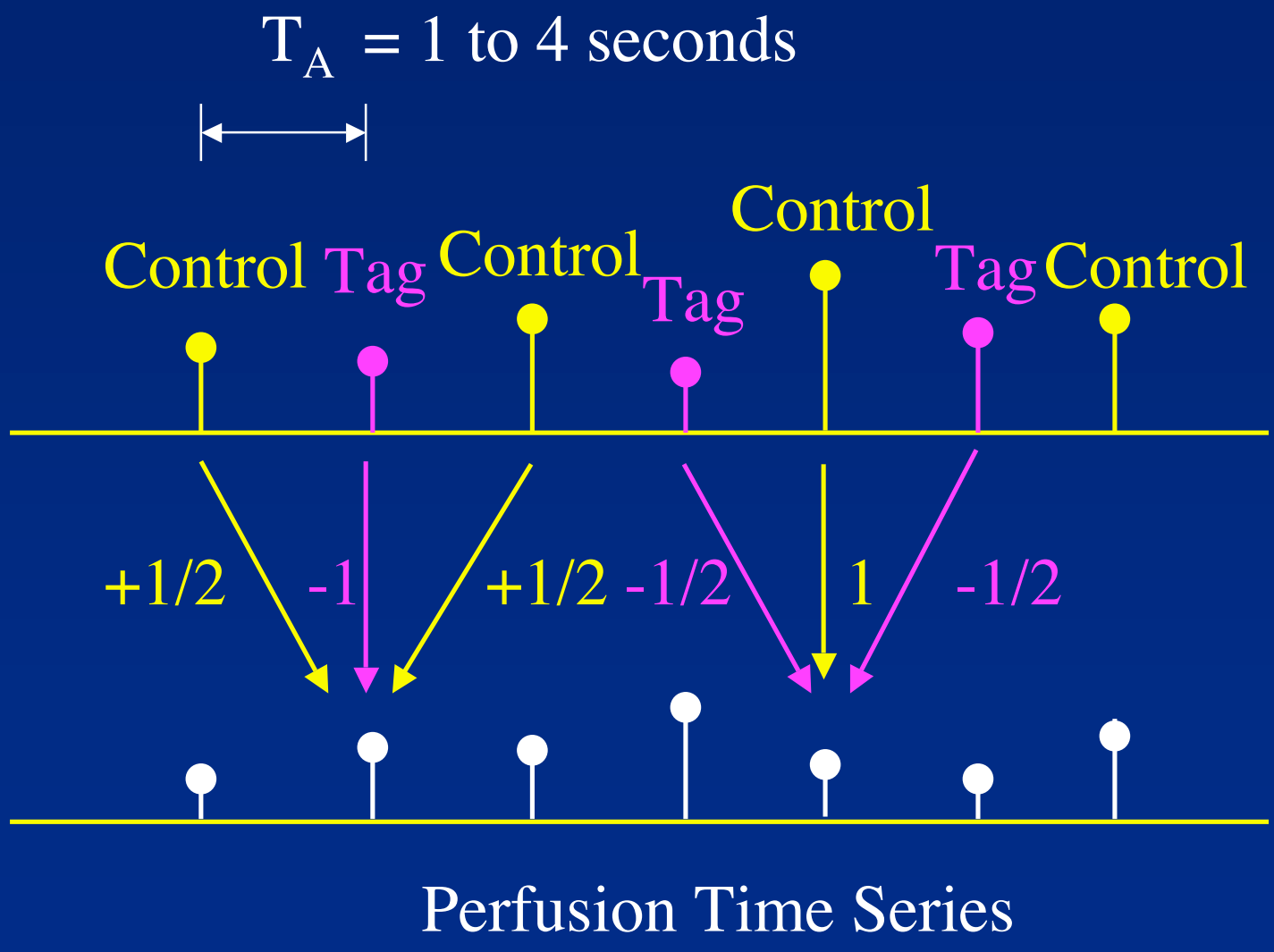
Running subtraction



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ASL Data Processing

- BOLD = average of Control + Tag images
- BOLD time series is formed from the running average of Control and Tag images.
- If a presaturation pulse is used, flow weighting of BOLD signal is minimized.

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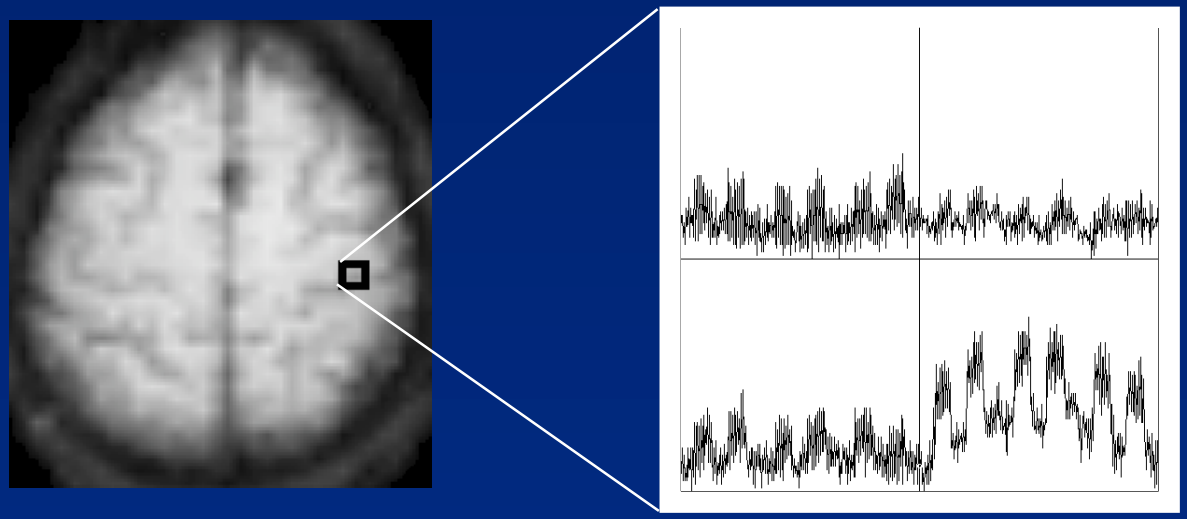
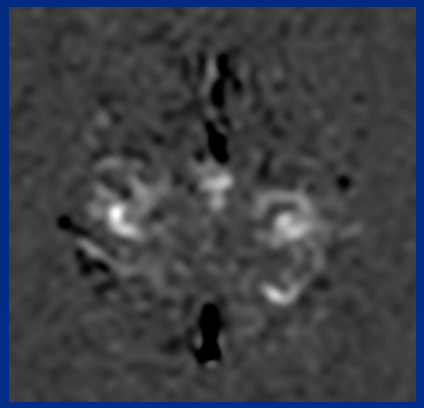
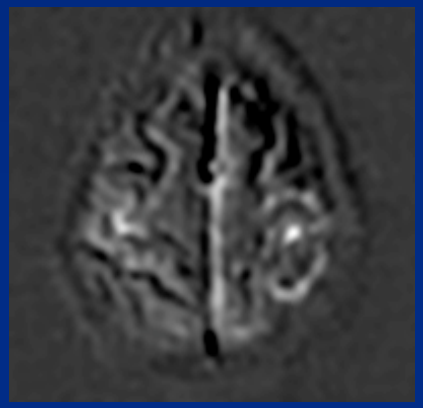
Simultaneous Flow and BOLD

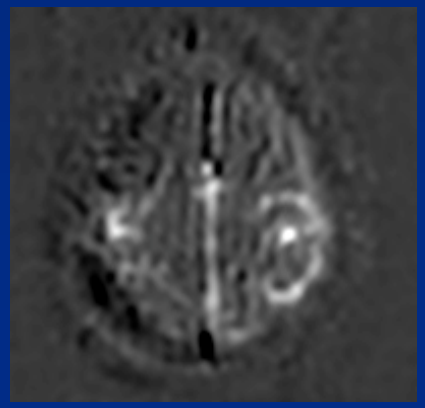




PERFUSION
UNREGISTERED



BOLD
UNREGISTERED



BOLD
REGISTERED

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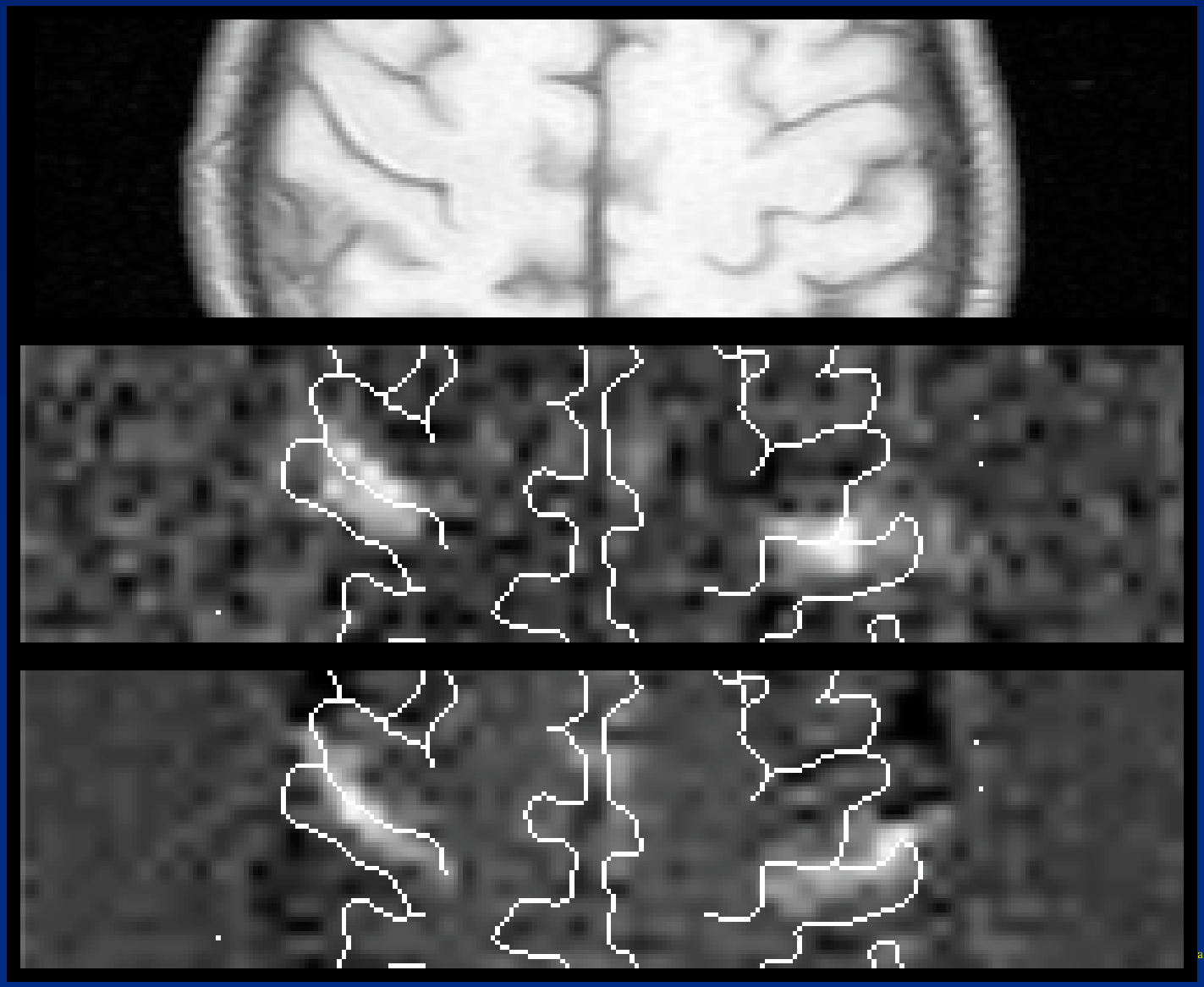
Simultaneous Flow and BOLD with PASL

Anatomy

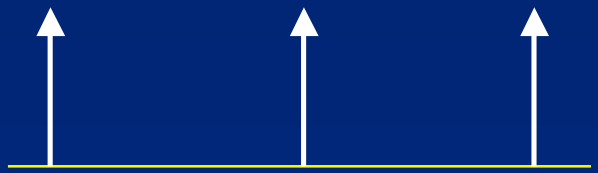
Flow change

BOLD change

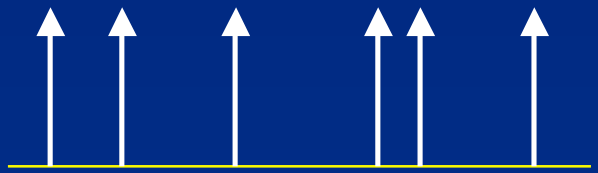


Event-related Perfusion fMRI

Stimulus

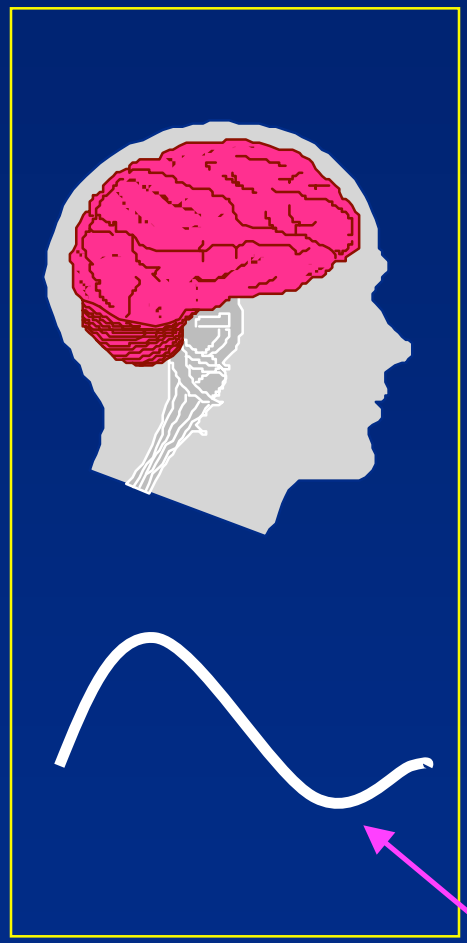


Periodic



Random

T_S = 1 second

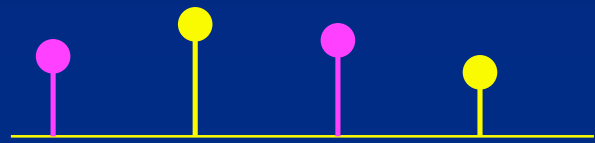


ASL Measurement

Control

Tag

T_A = 2 to 4 s



Goal: Estimate the Hemodynamic Response

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Event-related ASL

- ASL time series = tag time series interleaved with control time series
- Tag and control time series are analyzed separately.
- Tag and control time series are acquired at a reduced sampling rate, i.e. they are downsampled.
- Can analyze with a general linear model (GLM) with downsampling matrices to reflect the fact that tag and control are interleaved.

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GLM for ASL Experiments

$$y_{tag} = D_{tag}Xh_{tag} + Sb_{tag} + n$$

$$y_{con} = D_{con}Xh_{con} + Sb_{con} + n$$

Downsampling Matrices

Estimates →

$$\hat{h}_{perf} = \hat{h}_{con} - \hat{h}_{tag}$$

$$\hat{h}_{BOLD} = \hat{h}_{con} + \hat{h}_{tag}$$

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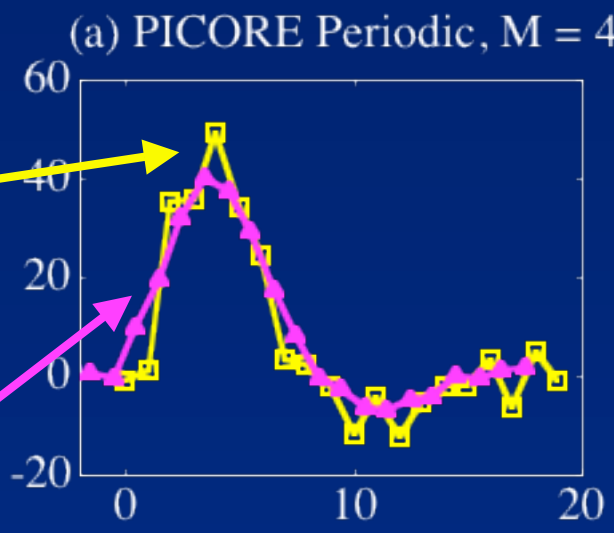
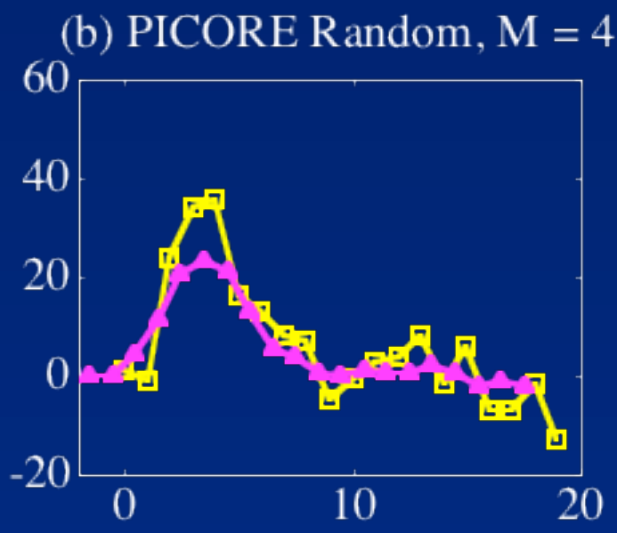
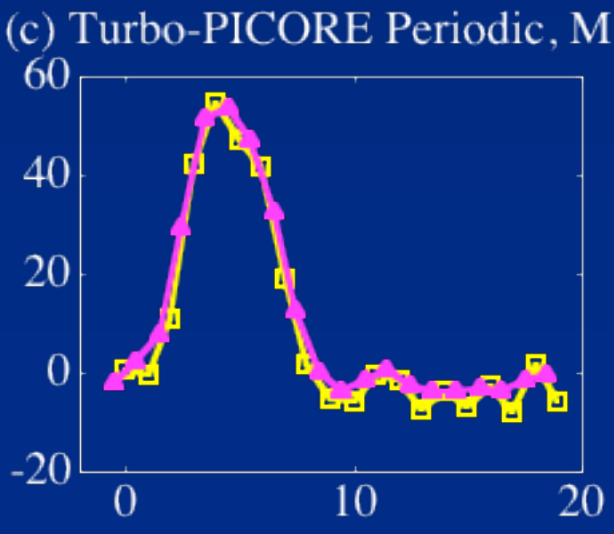
Results

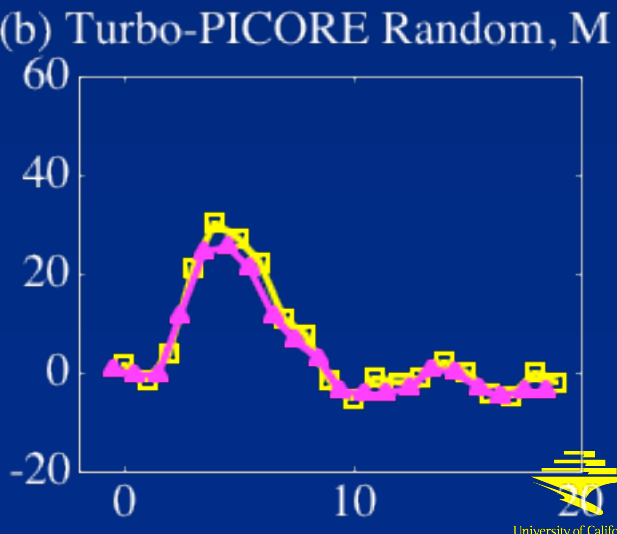
Direct

Running Subtraction









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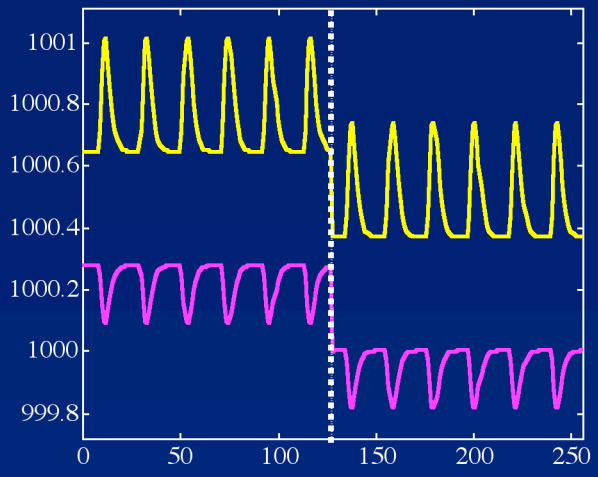
Motion Sensitivity

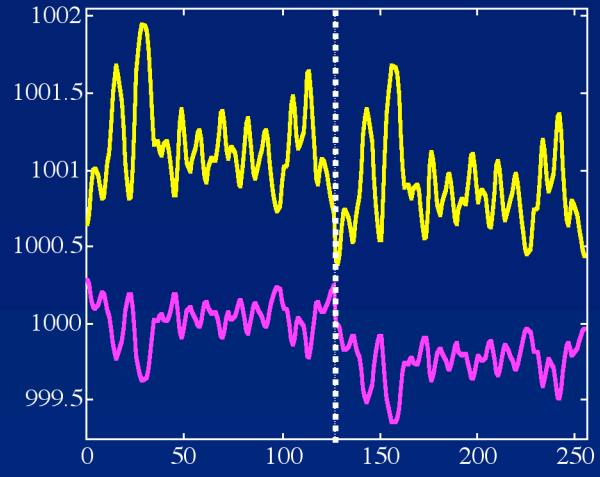
Periodic

Random

Control

Tag

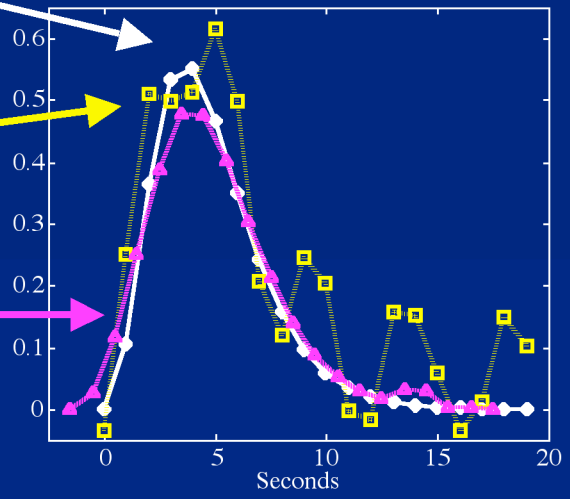


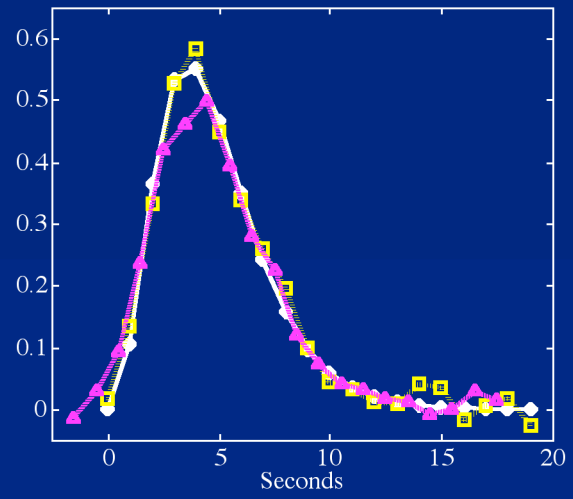


Ideal

Direct Estimate

Running Subtraction Estimate





Non-quantitative ASL

- ASL signal reflects delivery of blood to capillary beds, so it is more localized than BOLD.
- Quantitative ASL has lower temporal resolution and lower CNR when compared to BOLD.
- If quantitation of CBF is not necessary, then non-quantitative ASL can be used achieve better temporal resolution and higher CNR.
- Techniques:
  - Turbo-ASL
  - Close-tag CASL

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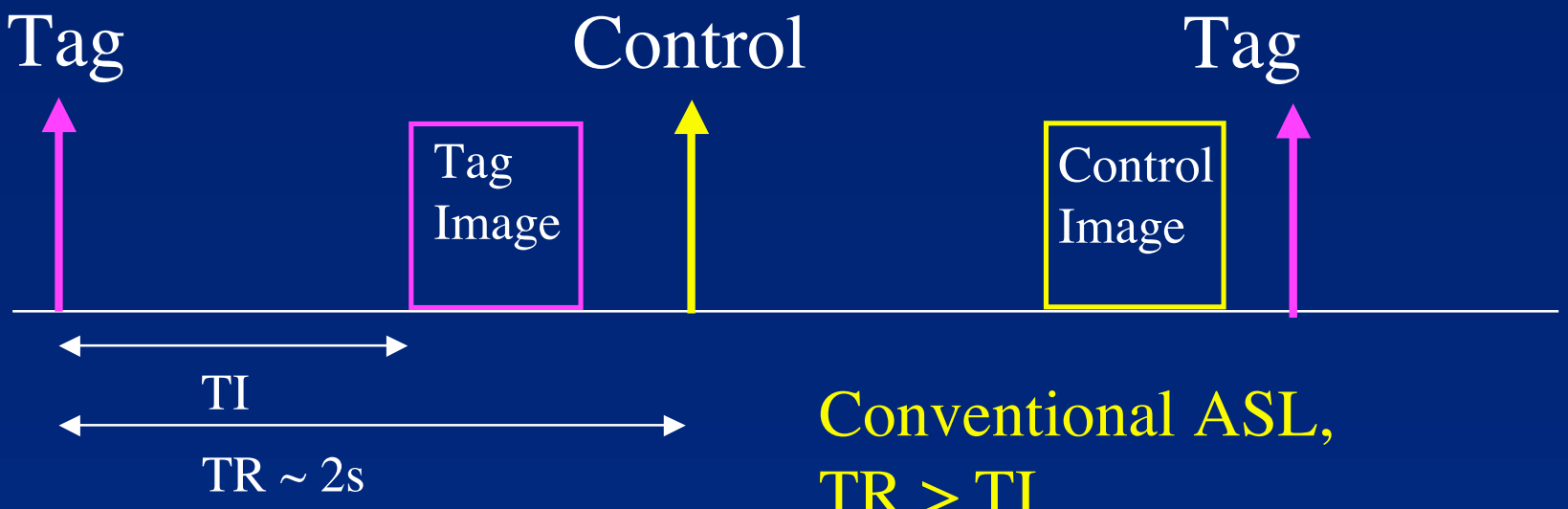
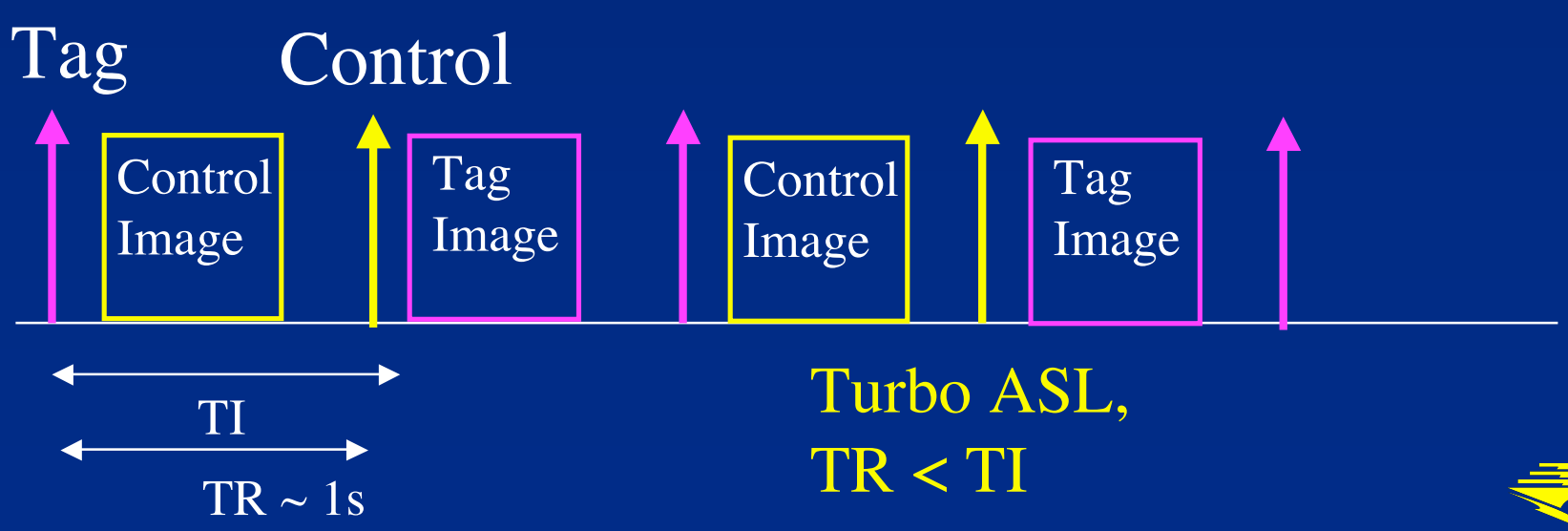
Turbo ASL



Conventional ASL,
TR > TI



Turbo ASL,
TR < TI

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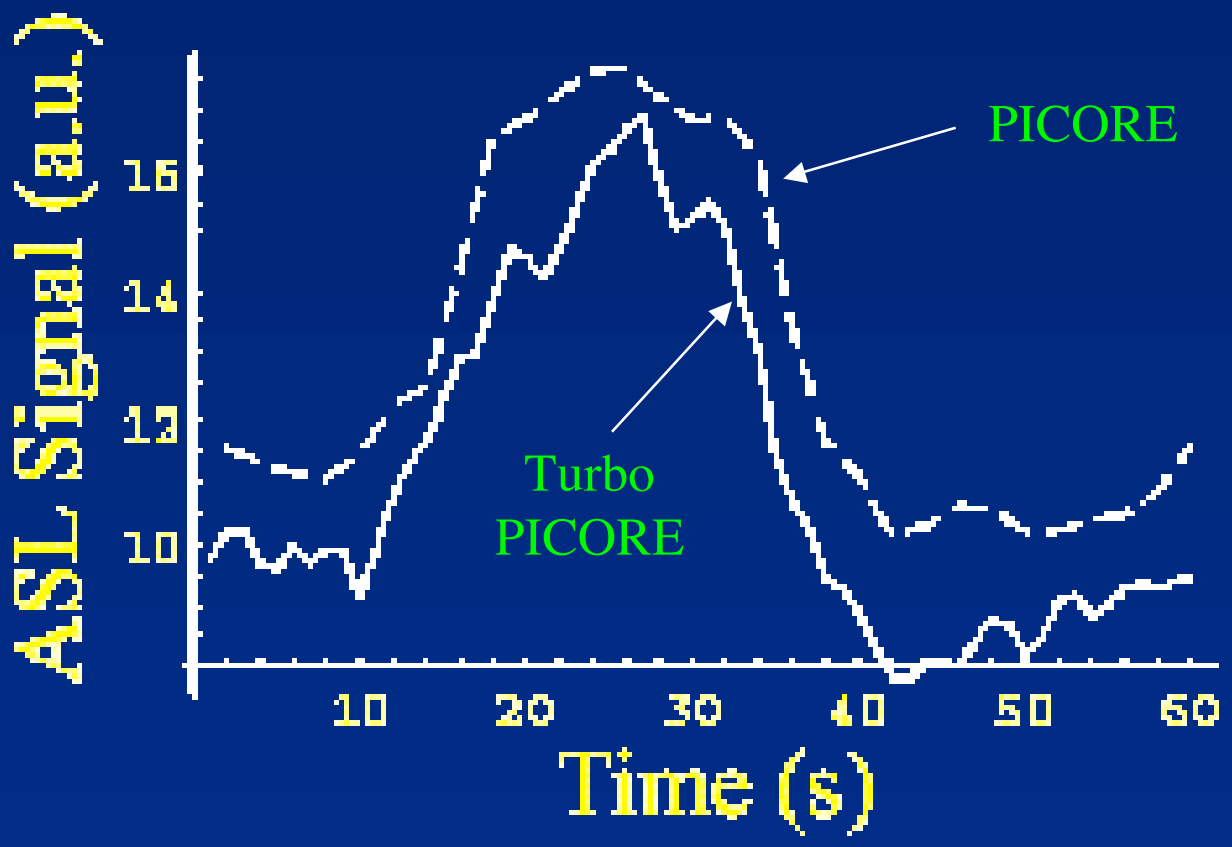
Finger Tapping



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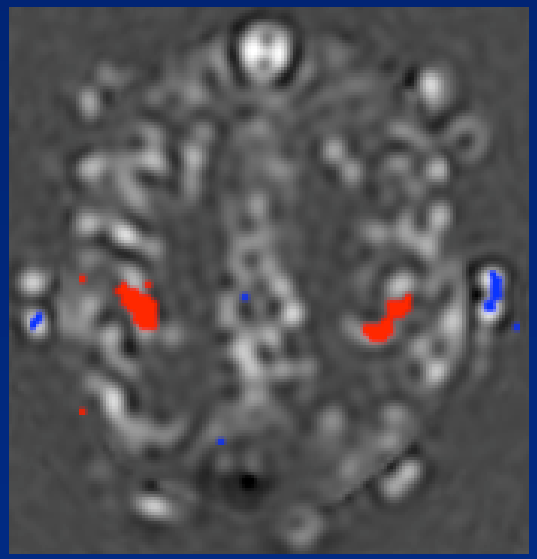
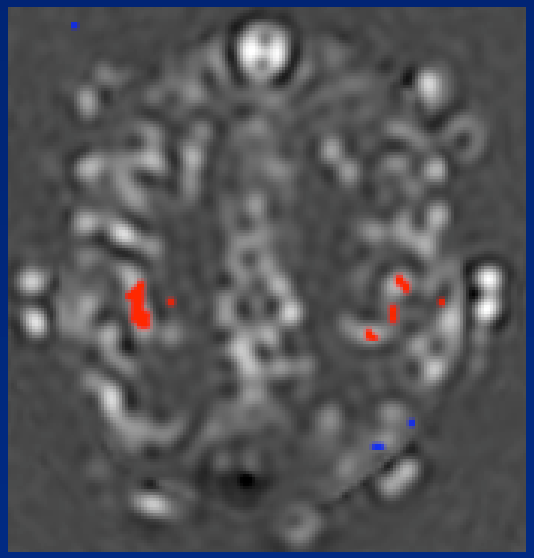
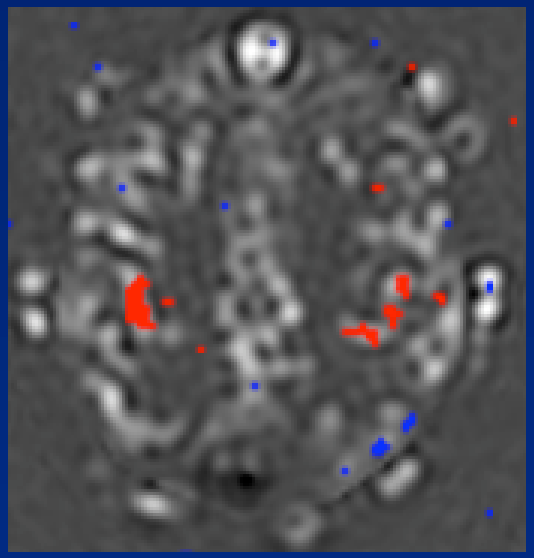
Finger Tapping



Turbo PICORE
|r|>0.3
(twice as many points)



PICORE
|r|>0.42
(same significance)



PICORE
|r|>0.36
(same # of pixels)

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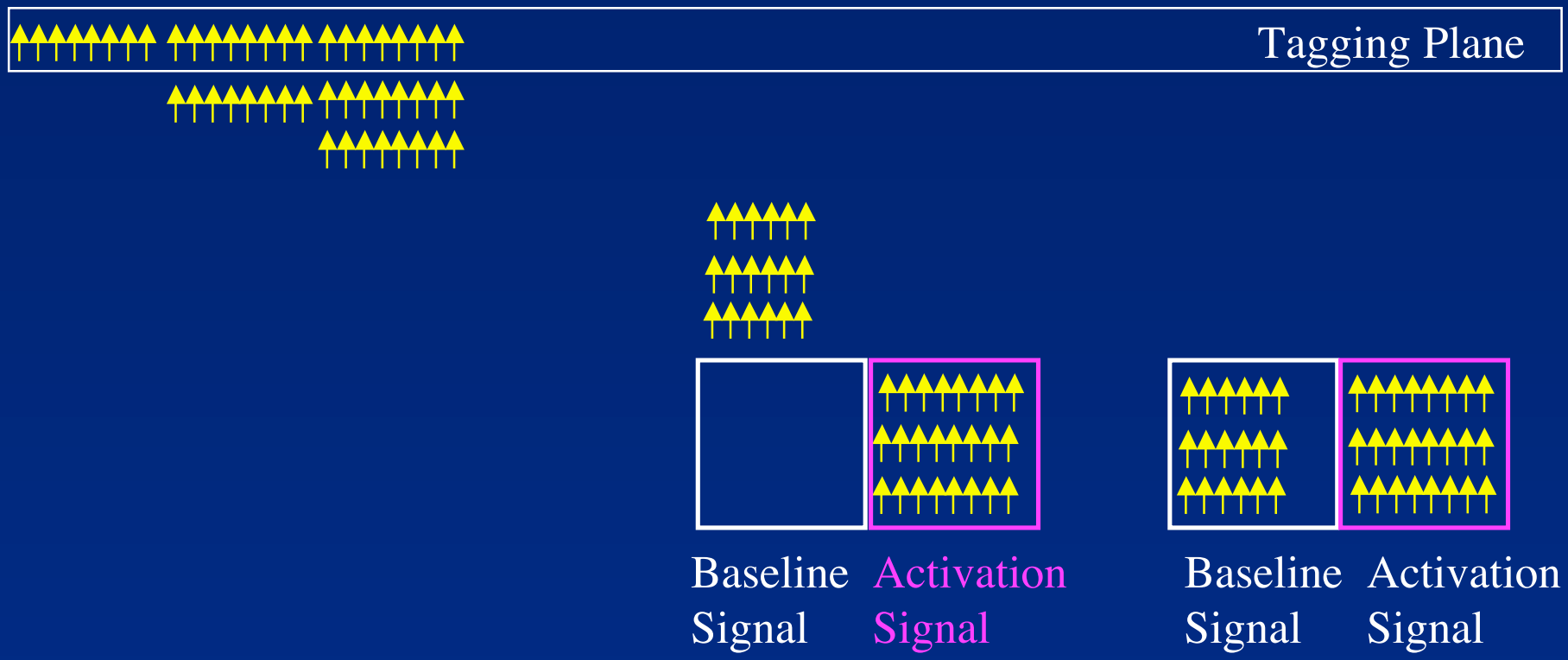
Amplifying Transit Delays Effects in CASL



Acquiring the signal at an earlier TI amplifies the difference between the activated state and the baseline state.

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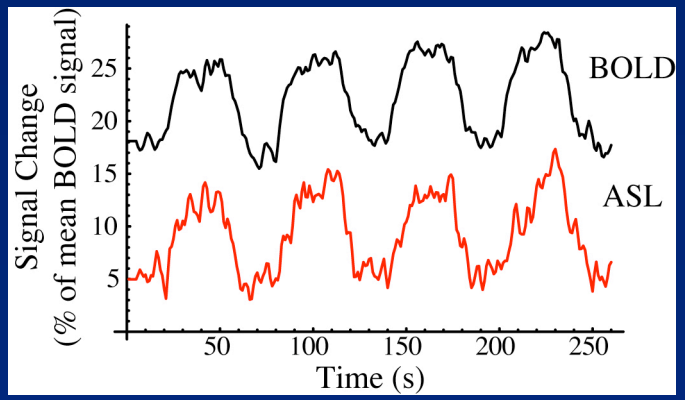
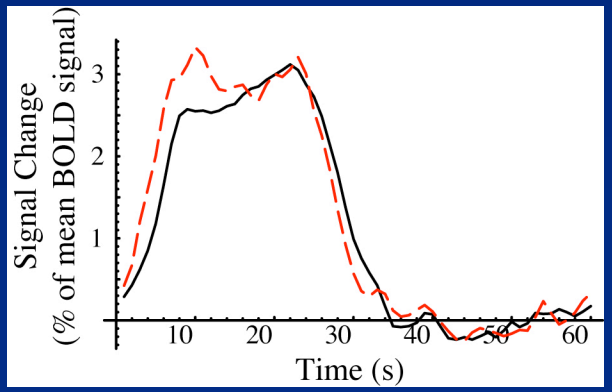
Close Tag CASL

- CASL with tagging plane 1cm from imaging slice
- Control is CASL tag on opposite side of slice
- Tag duration 700ms
- Delay to image 200ms
- TR 1000ms
- Single shot spiral acquisition
- 3.75mm in plane
- 8mm slice
- ROI chosen by cc>0.4 for ASL



Single pixel



ROI average

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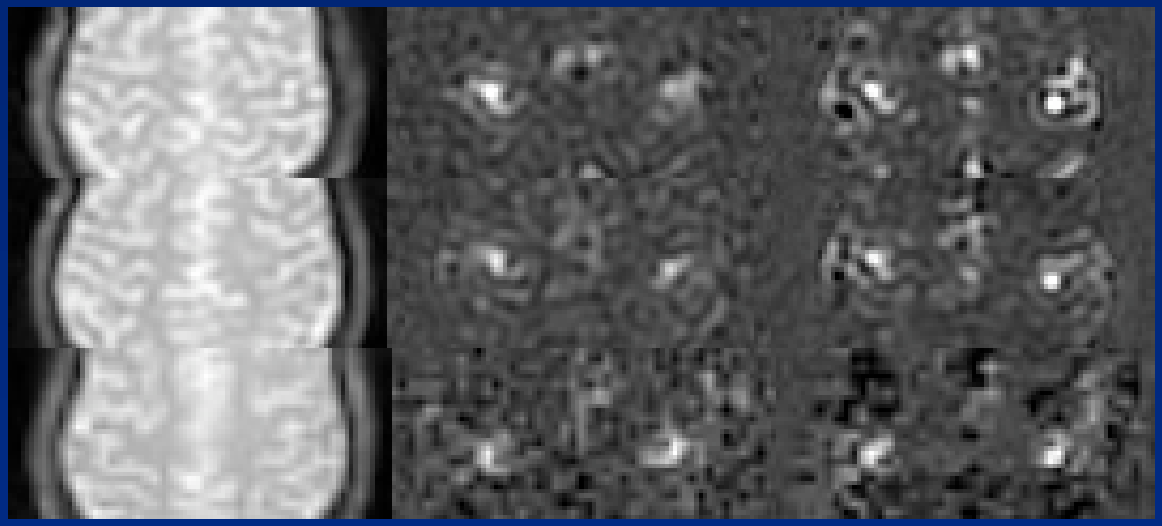
Close Tag CASL

Subject 1

Subject 2

Subject 3



Anatomy CASL BOLD

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ASL Applications

- Quantitative ASL
  - Reliable measurement of CBF across subjects, brain regions, experimental conditions, disease states, and time.
  - Simultaneous CBF/BOLD measurements to study the physiology of the fMRI response.

- Non-Quantitative ASL
  - Mapping regions of activation with better localization to the sites of neural activity.

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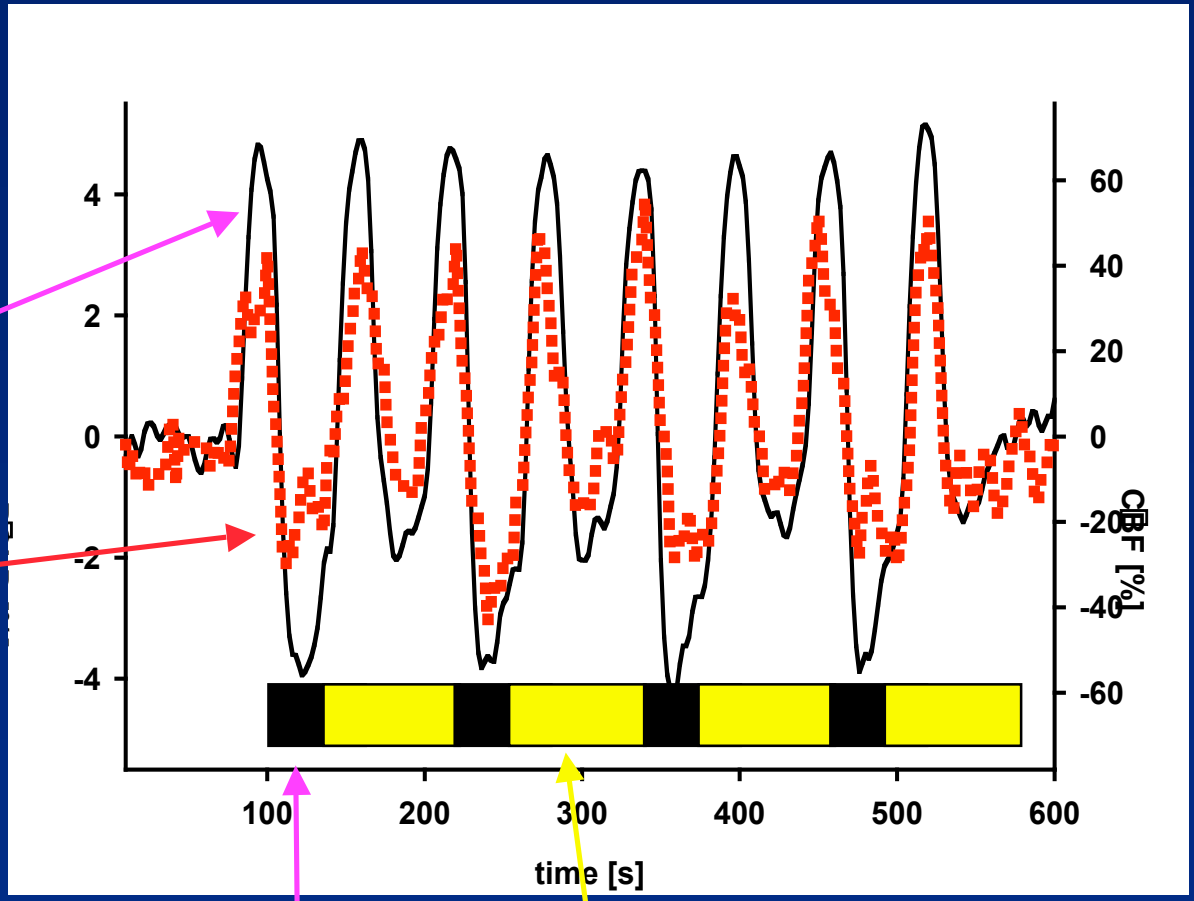
CBF and BOLD with Eyes Open/Closed

BOLD

CBF

PICORE

QUIPSS II



CLOSED OPEN

Courtesy of Kamil Uludag

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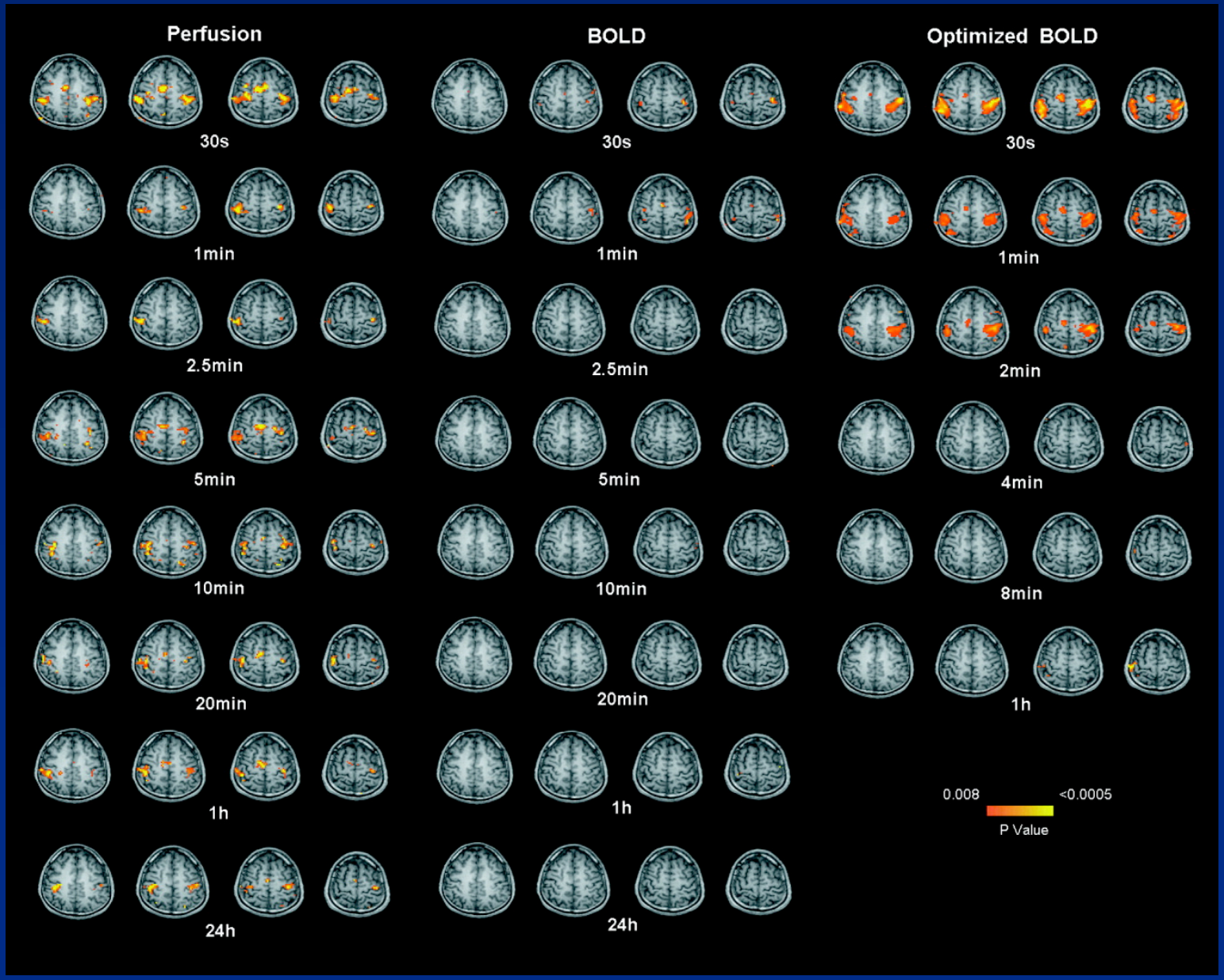
ASL with very low task frequencies - WANG et al., MRM 2003



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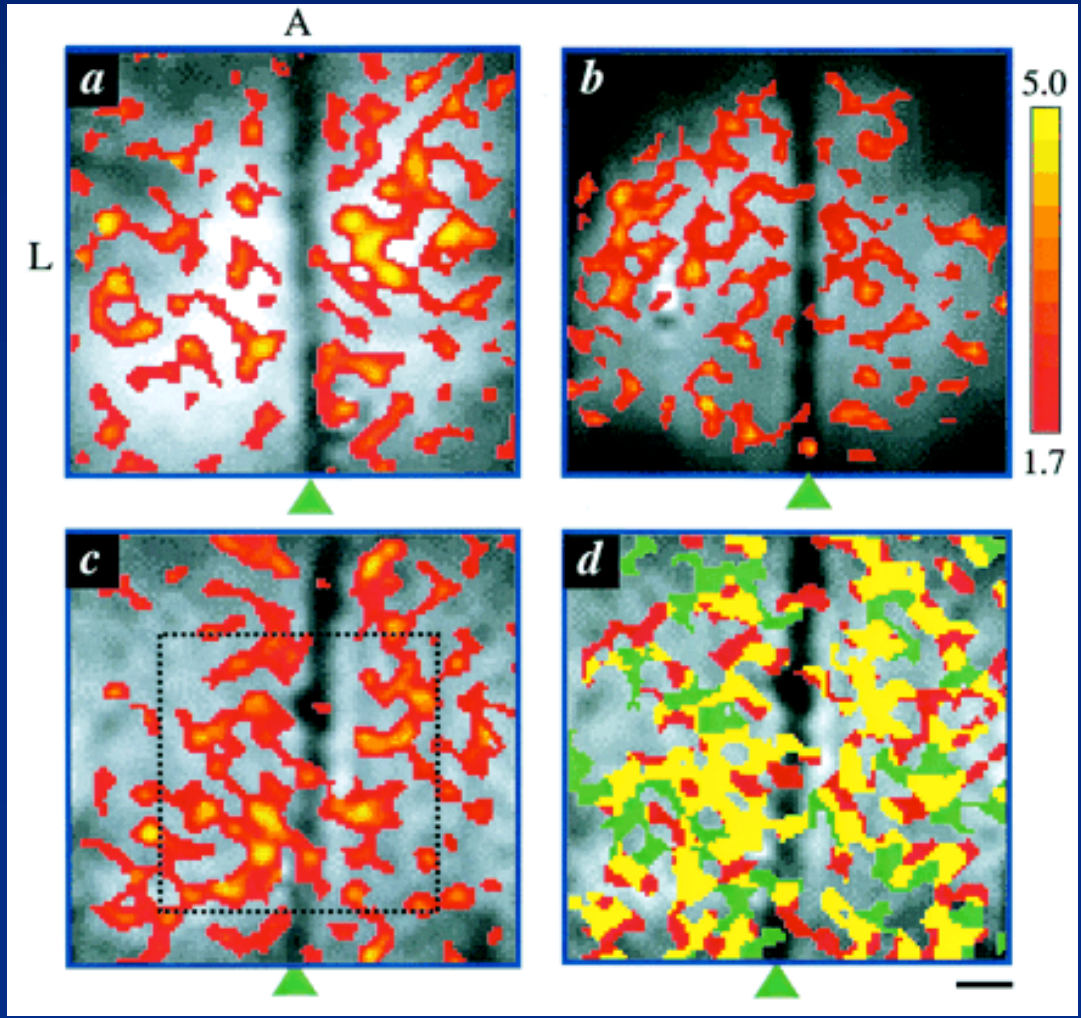
ASL Mapping of Cortical Columns in Cat Visual Cortex
Duong et al, PNAS, 2001.
FAIR sequence, TI = 1500 ms, TR 3000 ms



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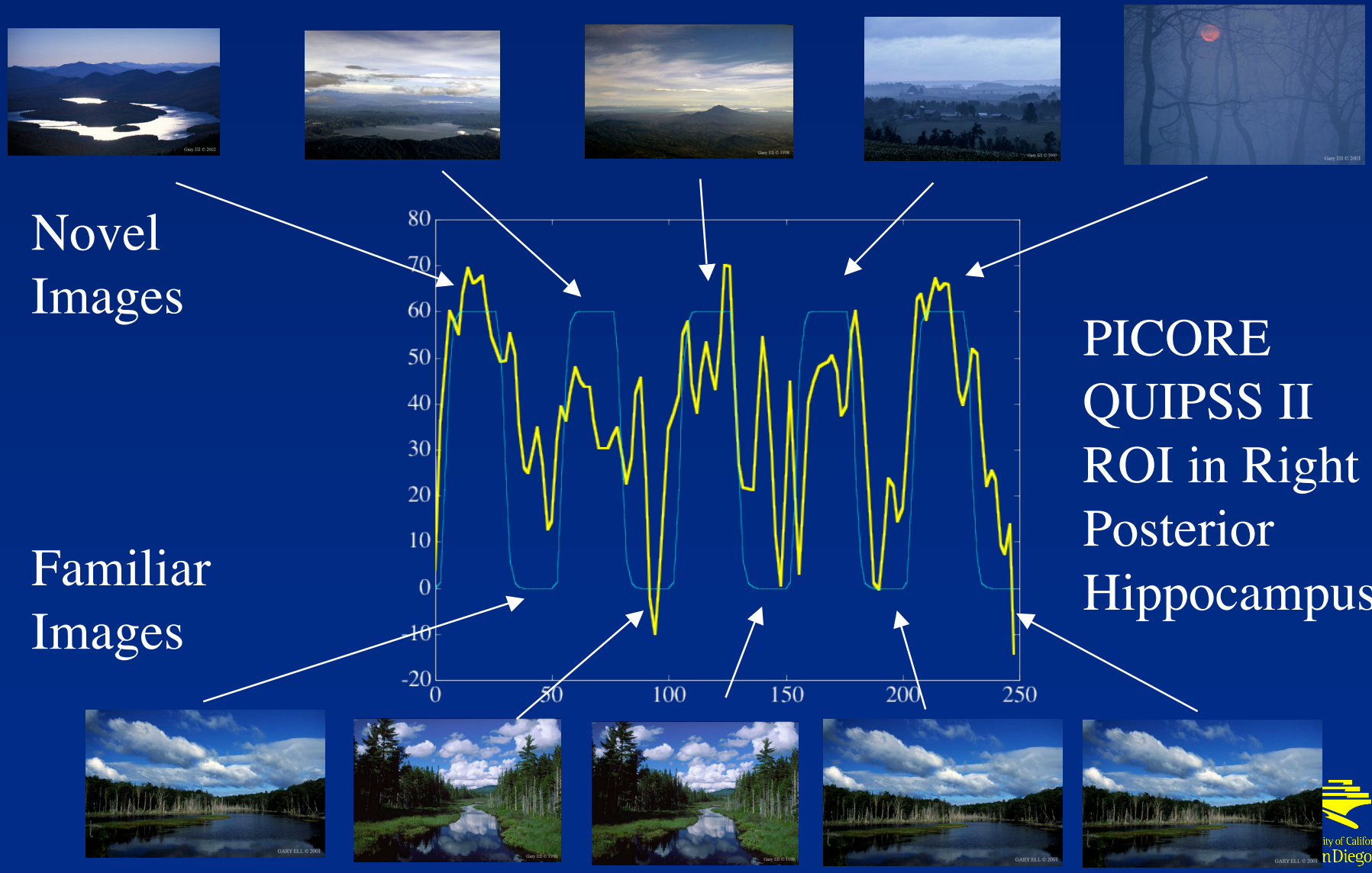
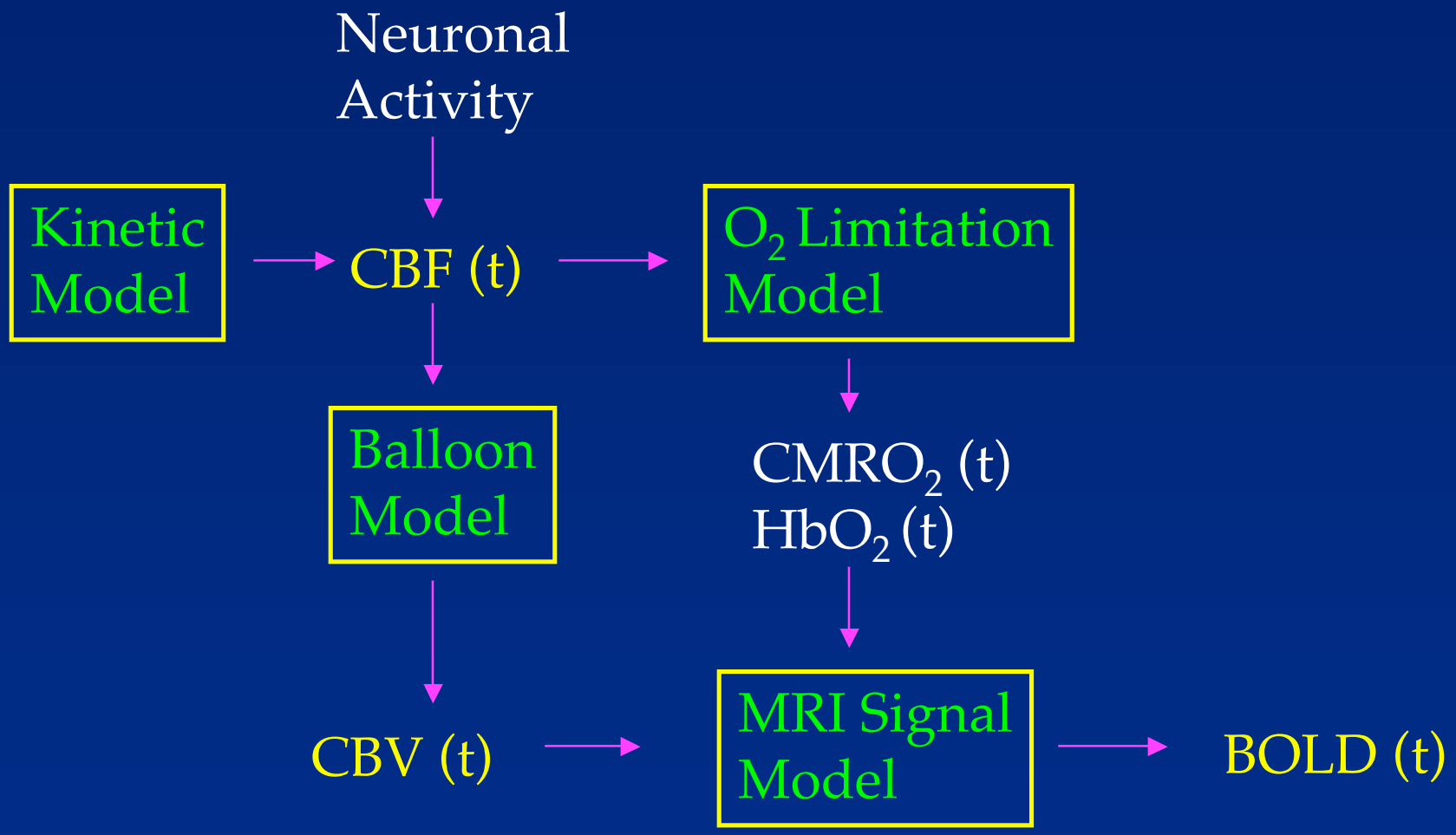
Memory Encoding Experiment w/ ASL



Overview of BOLD Mechanisms



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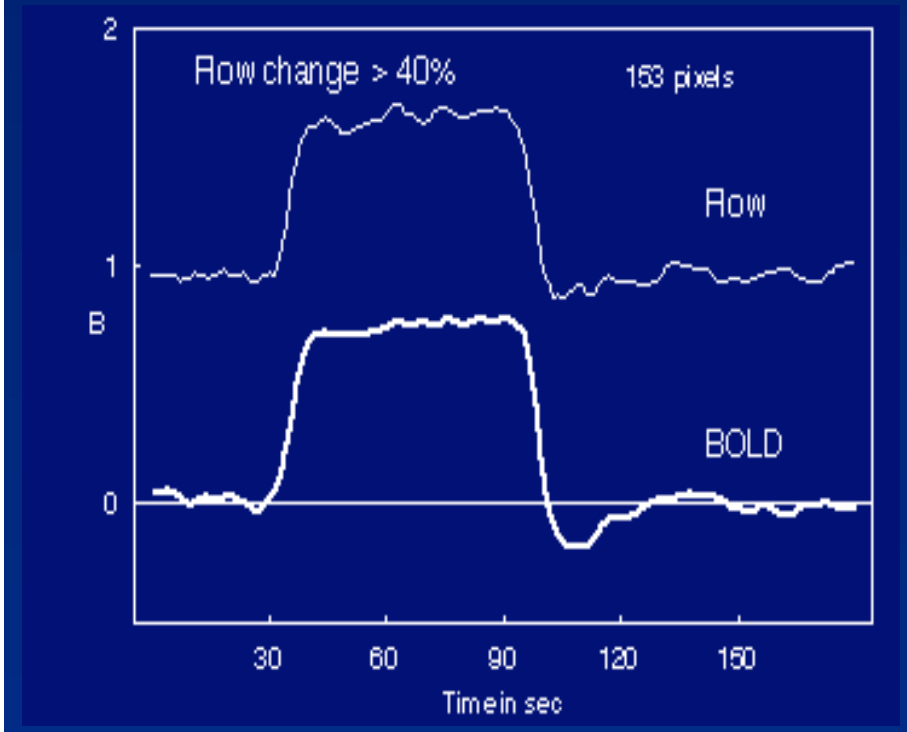
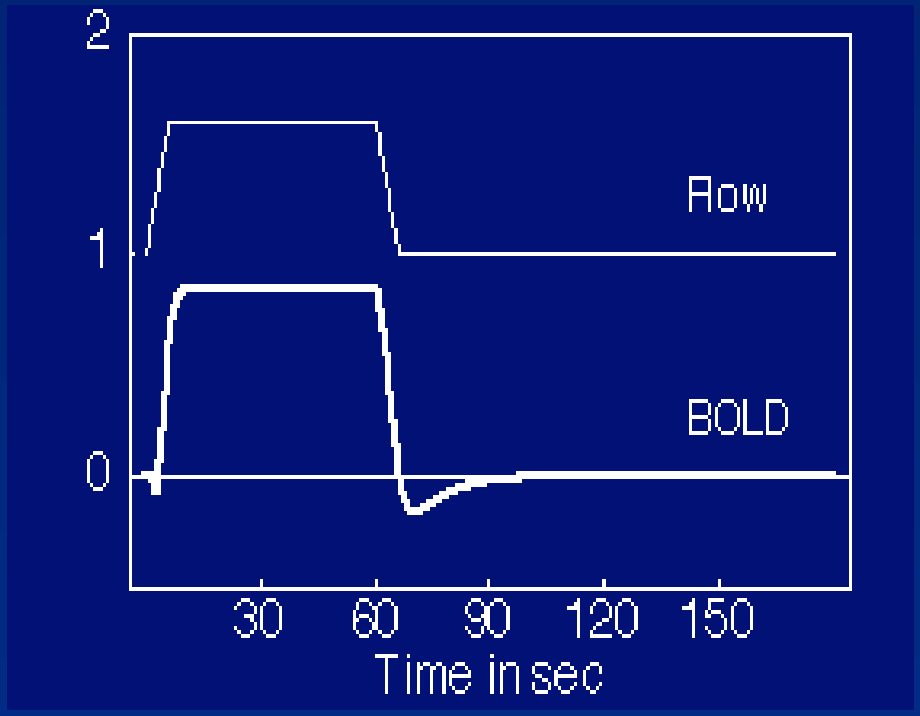
Post-Stimulus Undershoot



Finger tapping (6 subjects)



Balloon Model

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Conclusions

- ASL provides a non-invasive means of measuring CBF.
- Transit Delays must be addressed properly in order to obtain quantitative CBF with CASL and PASL.
- Velocity Selective ASL is a promising technique for dealing with long transit delays, e.g. in stroke.
- Non-quantitative ASL techniques such as Turbo-ASL and Close tag CASL have good temporal resolution and high CNR. They have the potential to provide better spatial mapping than BOLD.

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