Arterial Spin Labelling: Non-invasive measurement of perfusion

Michael A. Chappell
michael.chappell@eng.ox.ac.uk
www.ibme.ox.ac.uk/QuBIc

Institute of Biomedical Engineering & Oxford Centre for Functional MRI of the Brain
University of Oxford.

FSL for Arterial Spin Labelling

- BASIL: a toolset for resting ASL quantification:
  - ➡ CBF quantification.
  - ➡ Calibration / M0 estimation
  - ➡ Registration.
  - ➡ Partial volume correction.

  - ➡ Command line tools

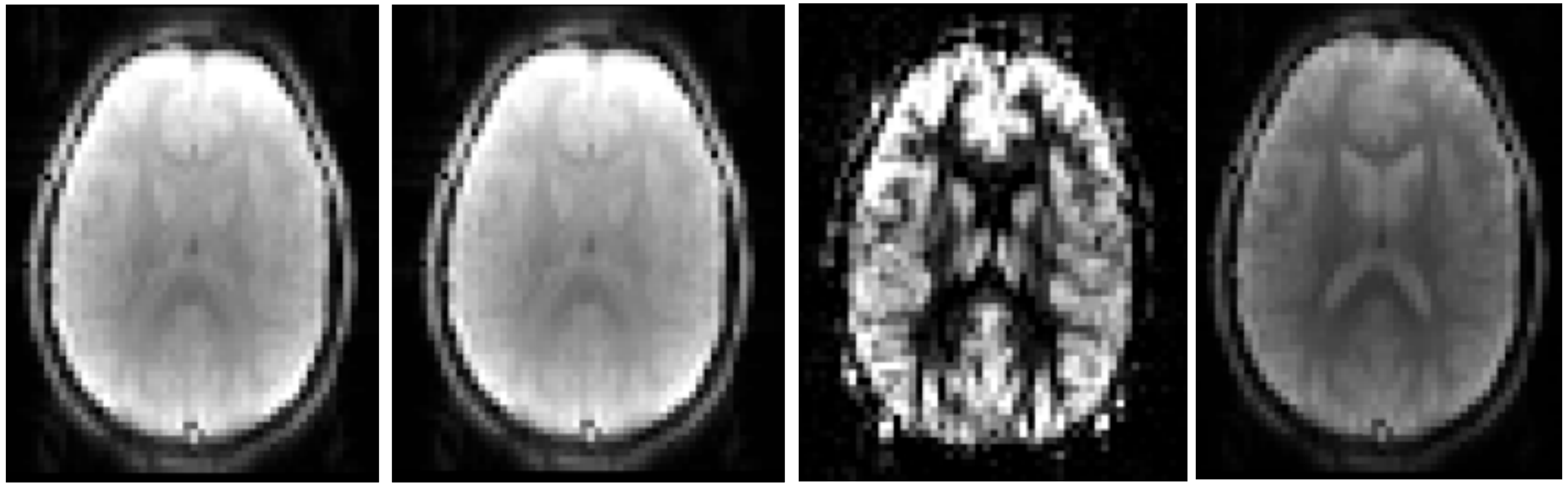
    ```
    oxford_asl, basil, asl_reg, asl_calib
    ```

  - ➡ Graphical User Interface (beta)

    ```
    Asl / Asl_gui
    ```

What Have I Got Here!?

- What I have...
- What I want...
- What should I do?



I just want to do something simple/easy!

I must have absolute perfusion (ml/100g/min)

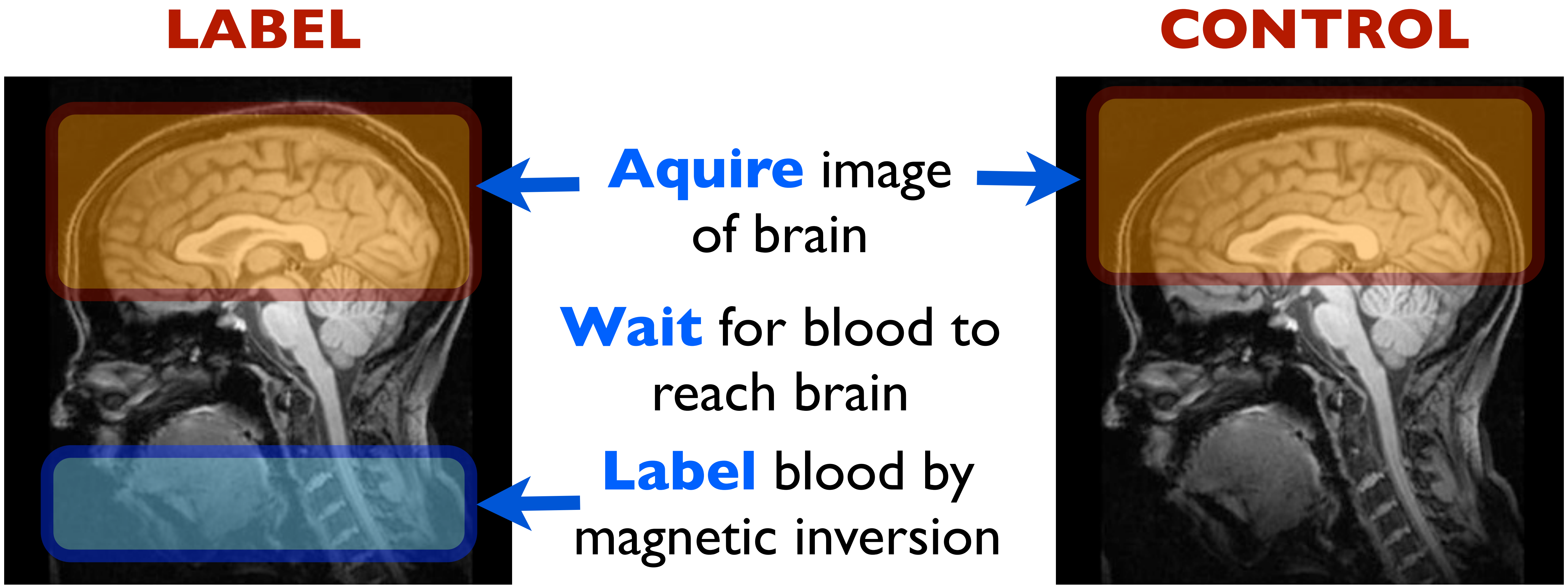
```
Command line instructions here for future reference...
```

OUTLINE

- Acquisition
- Keep it simple!
  - Perfusion weighted images.
  - Perfusion fMRI.
- Quantitative perfusion:
  - A short course in tracer kinetics.
  - Measuring arterial blood magnetization.
- Preparing for group analysis.
- Advanced quantification:
  - Macro vascular contamination
  - Partial Volume Correction

ASL ACQUISITION

- A tracer experiment with an endogenous tracer - **blood water**.



LABEL

CONTROL

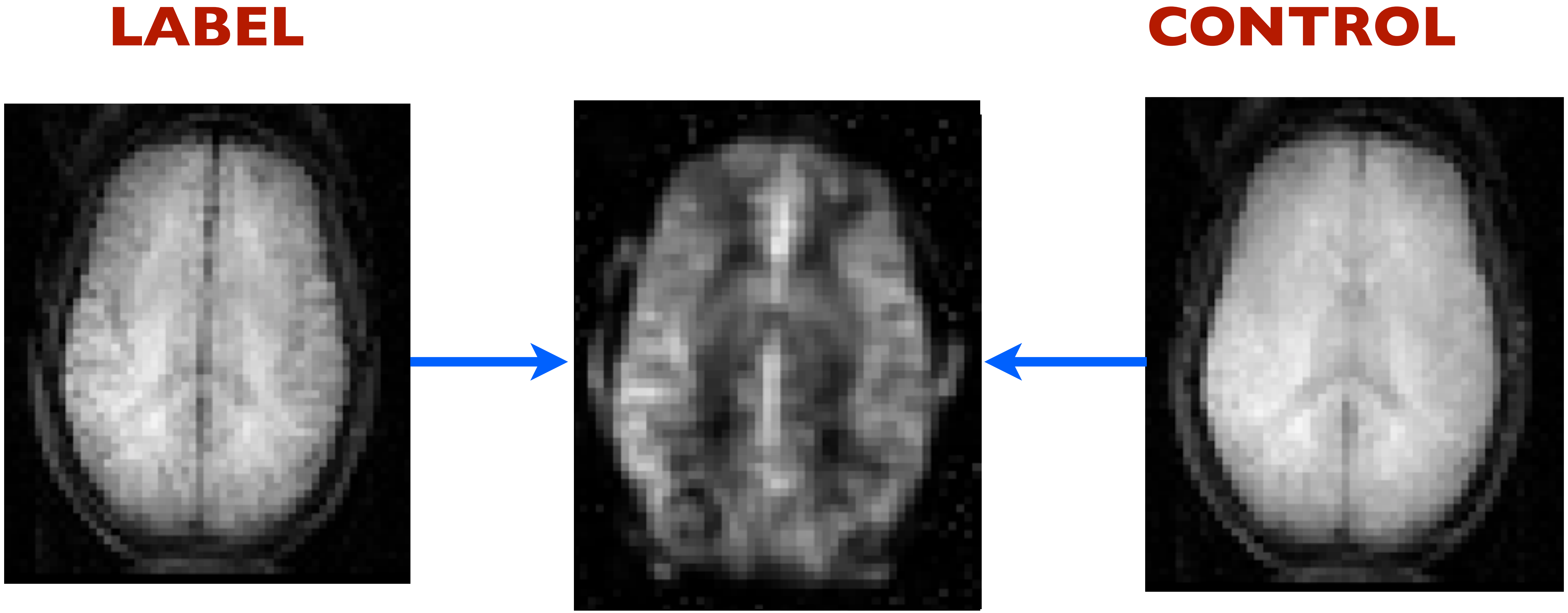
Aquire image of brain

Wait for blood to reach brain

Label blood by magnetic inversion

ASL ACQUISITION

- Spot the difference?

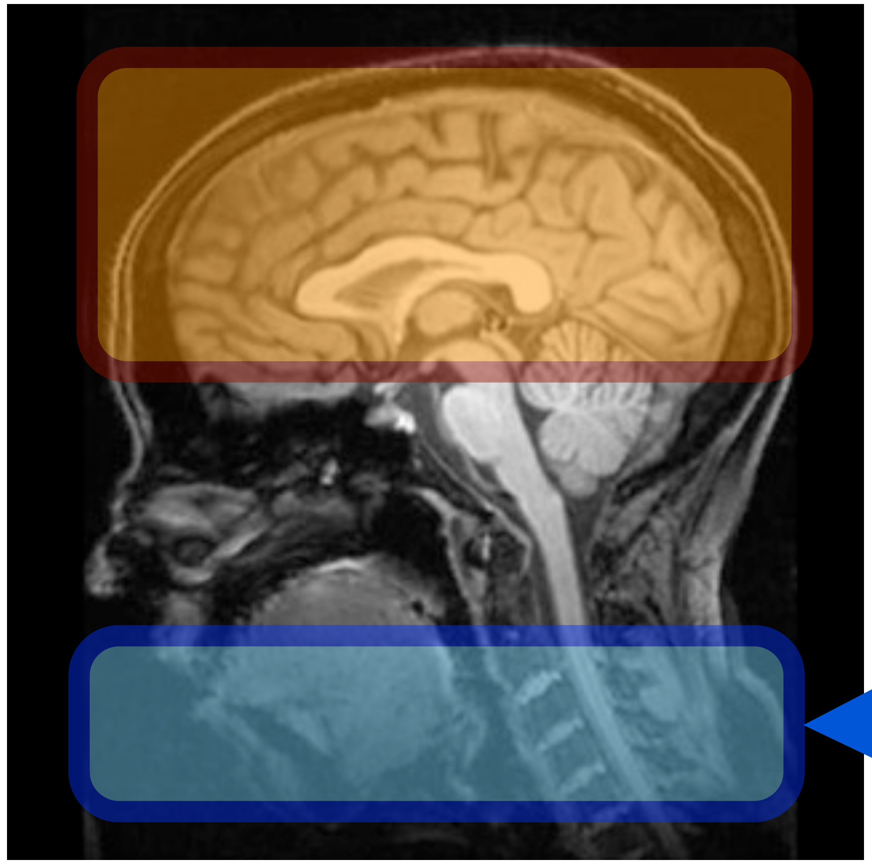


Perfusion is ~60 ml/100g/min = 0.01 s^{-1}
Signal is ~ 1-2%

ASL ACQUISITION

- Nuts & bolts: Labelling

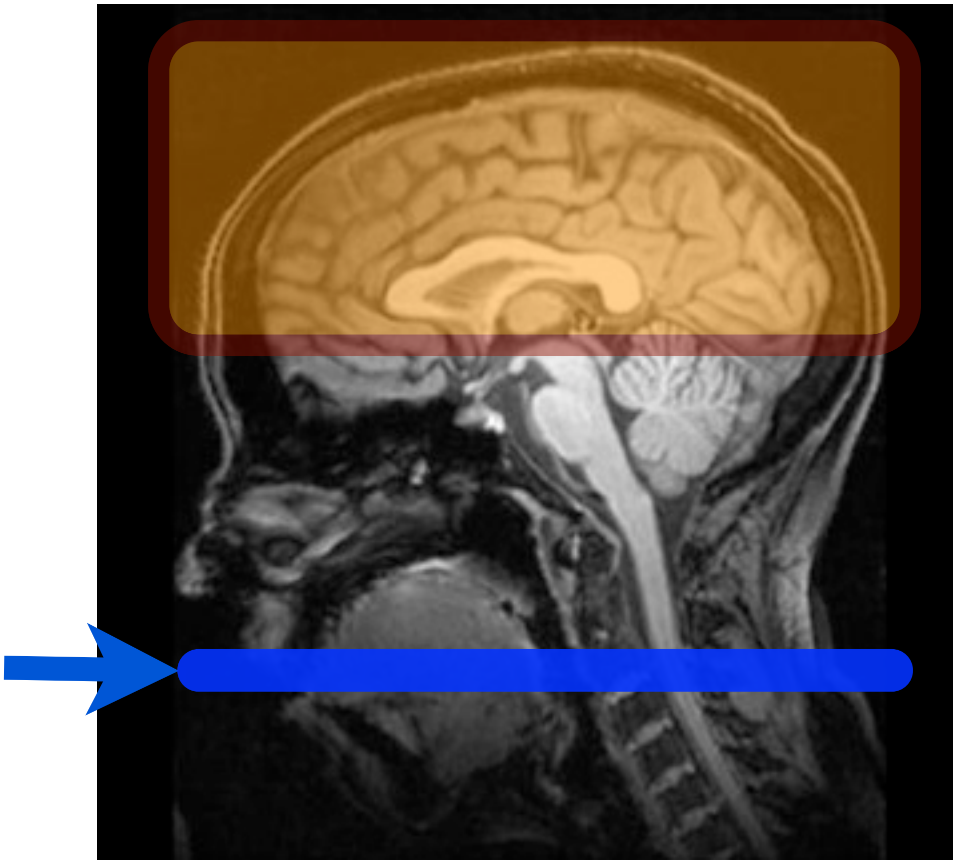
pASL: Pulsed ASL



Label a region in a single pulse

Label blood by magnetic inversion

cASL: Continuous ASL
pcASL: psuedo-continous ASL

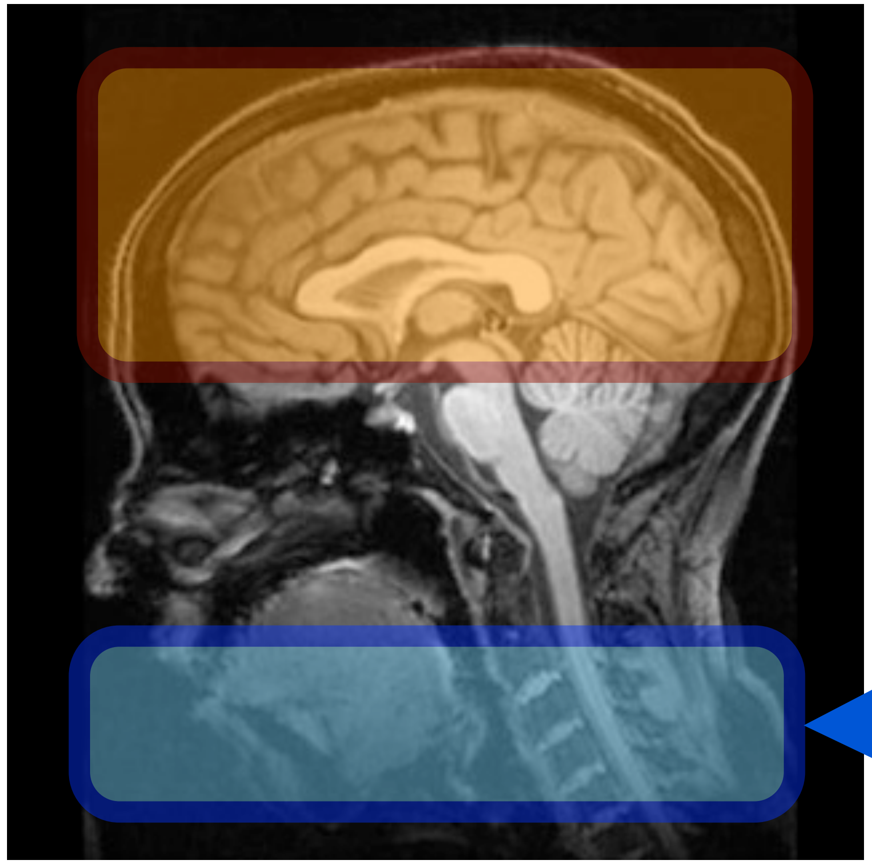


Label blood flowing through a plane for some time

pcASL uses pulses and is more widely available

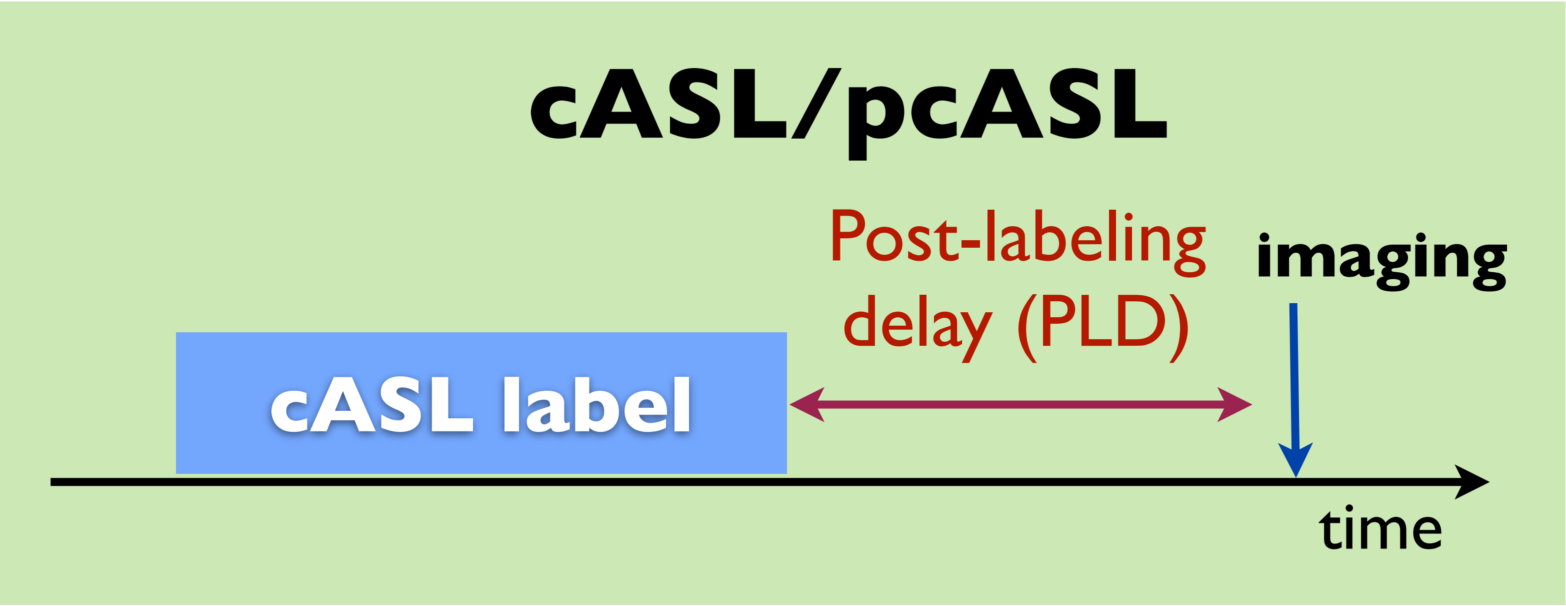
ASL ACQUISITION

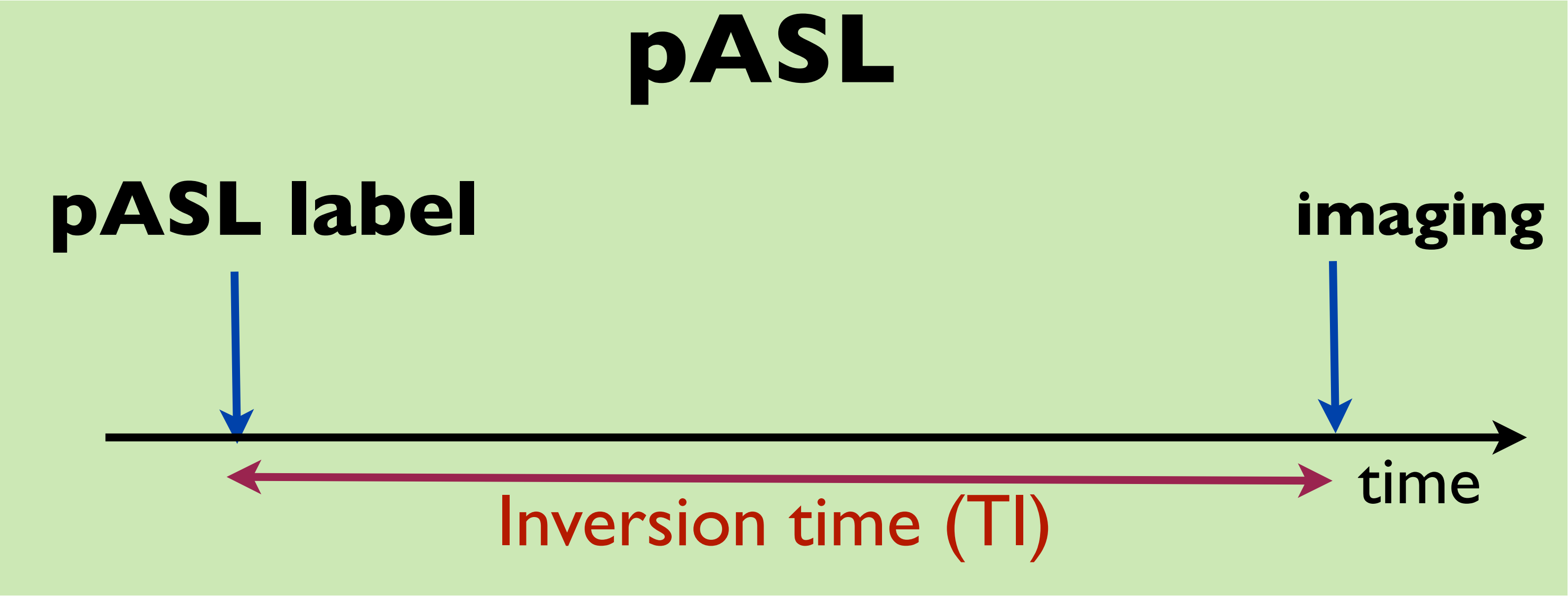
- Nuts & bolts: Inflow time



Wait for blood to reach brain

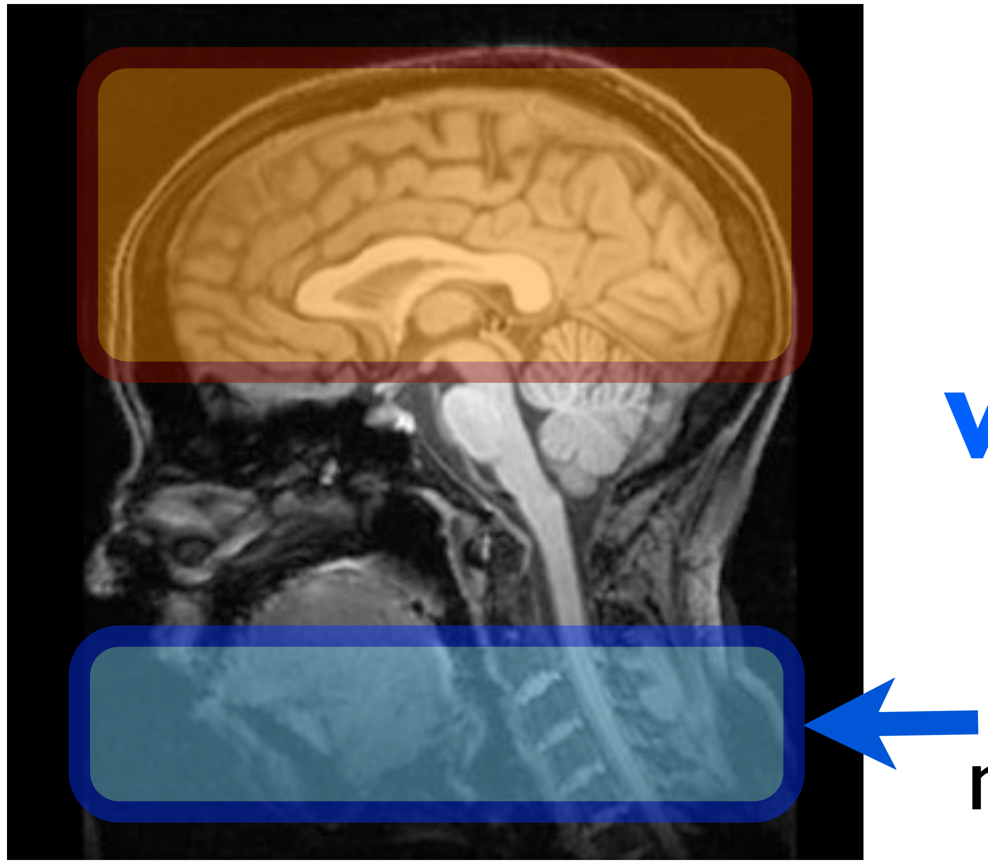
Label blood by magnetic inversion





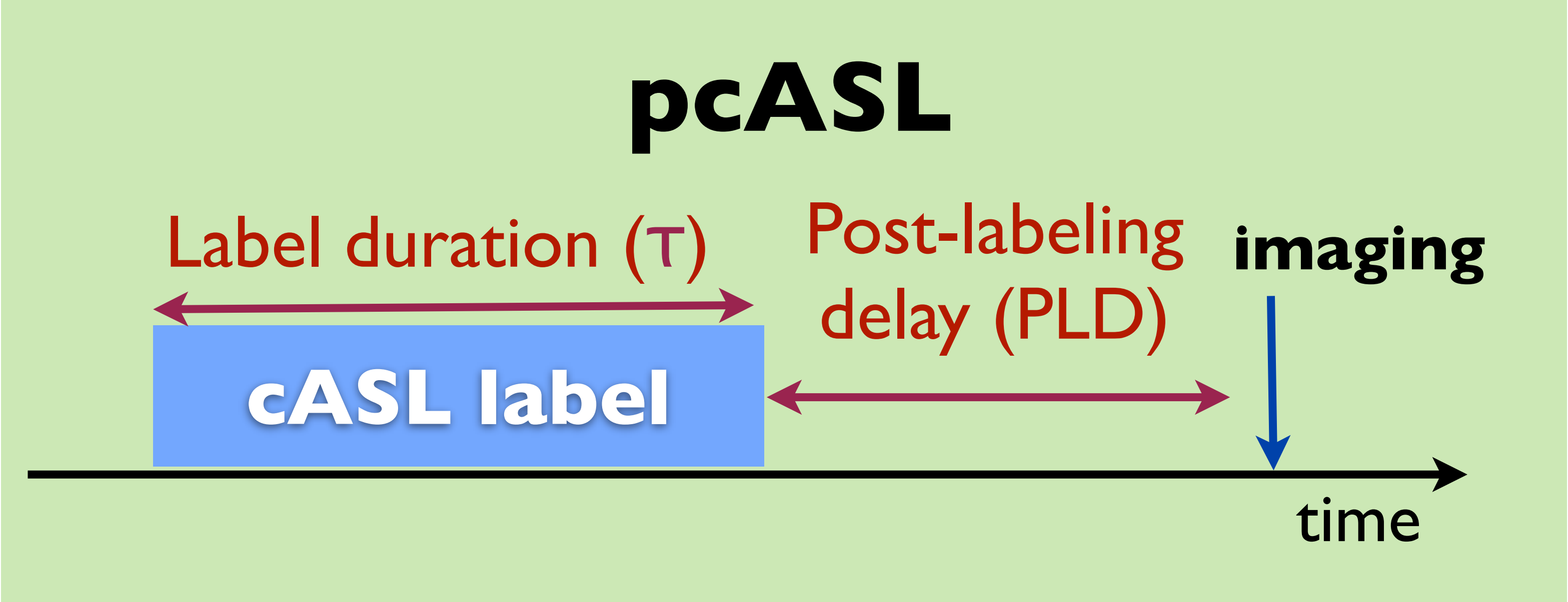
ASL ACQUISITION

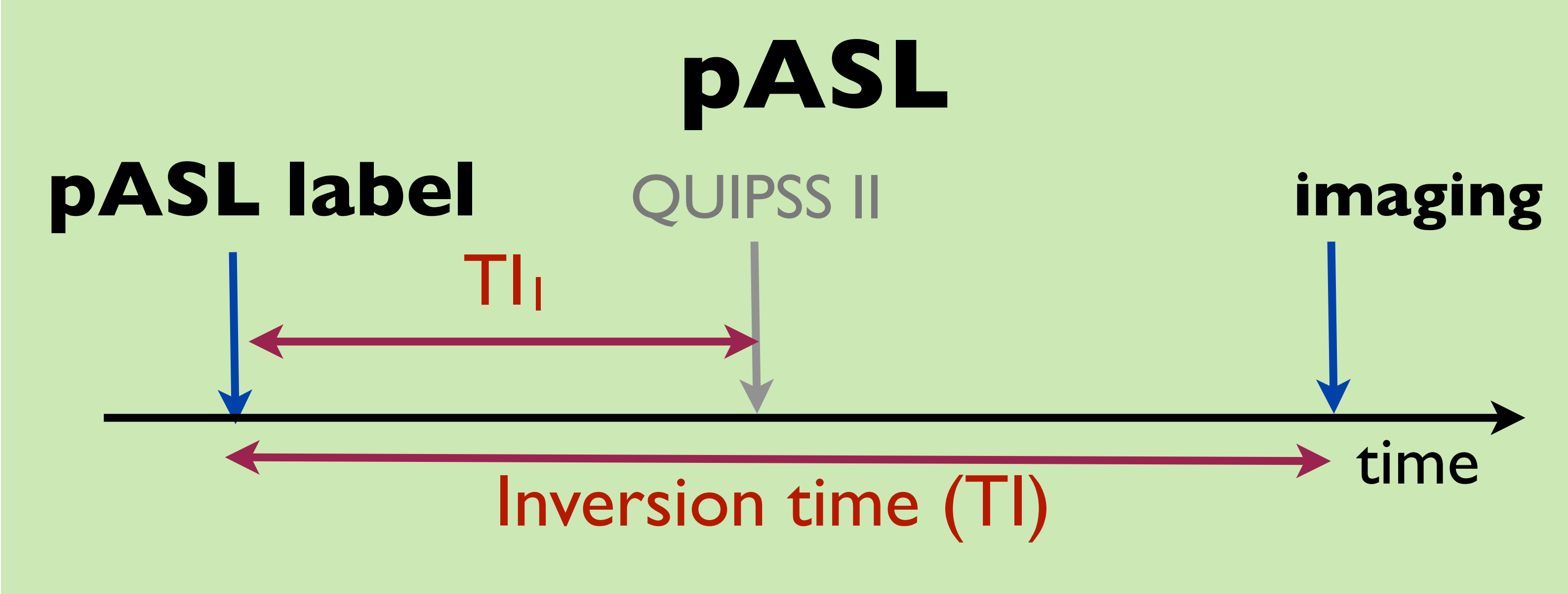
- Nuts & bolts: Bolus/label duration



Wait for blood to reach brain

Label blood by magnetic inversion



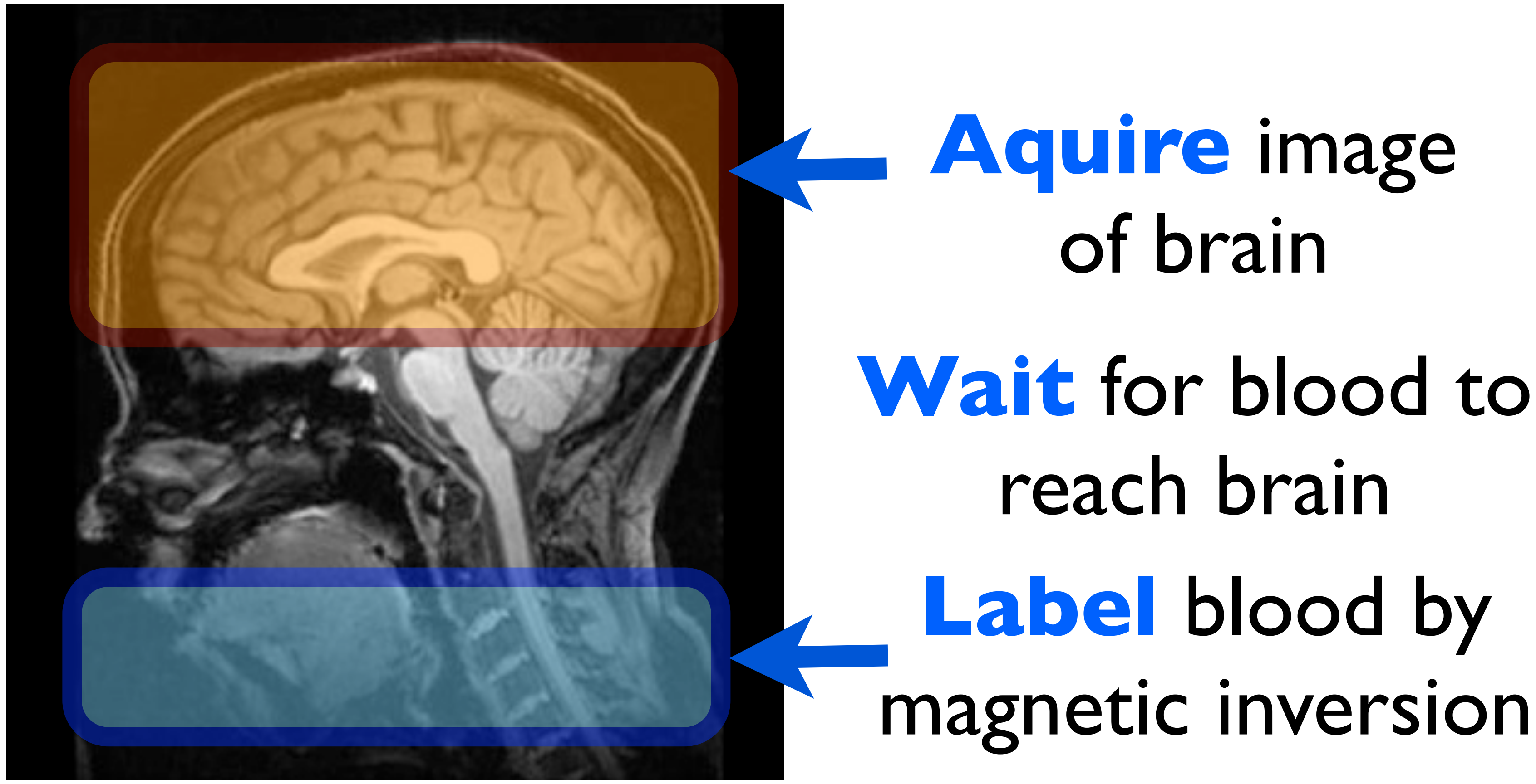


pASL

- Label duration is undefined in pASL.
- QUIPSSII pulses ‘cut off’ the end of the labeled bolus.

ASL ACQUISITION

- Buts & Bolts: Readout


Aquire image of brain

Wait for blood to reach brain

Label blood by magnetic inversion

EPI

(stack of 2D slices)
Different PLD/TI for each slice

GRASE/RARE (3D)

Higher SNR
Long echo-train: blurring

Pre-saturation

Saturate static signal at start of TR

Background suppression

Null static signal - reduce physiological noise

ASL ACQUISITION

- The ASL ‘white paper’:
  - ➡ Use pcASL where possible
    Label duration 1800 ms
    Post labeling delay ~1800 ms
  - ➡ Otherwise pASL with QUIPSSII
    Inversion time ~1800 ms
    TI_1 of 800 ms
    Slab thickness 15-20 cm
  - ➡ Ideally 3D readout.
    2D EPI an acceptable alternative.
  - ➡ Resolution:
    3-4 mm in plane.
    4-8 mm through plane.
  - ➡ Use background suppression.

Recommended Implementation of Arterial Spin Labeled Perfusion MRI for Clinical Applications: A consensus of the ISMRM Perfusion Study Group and the European Consortium for ASL in Dementia

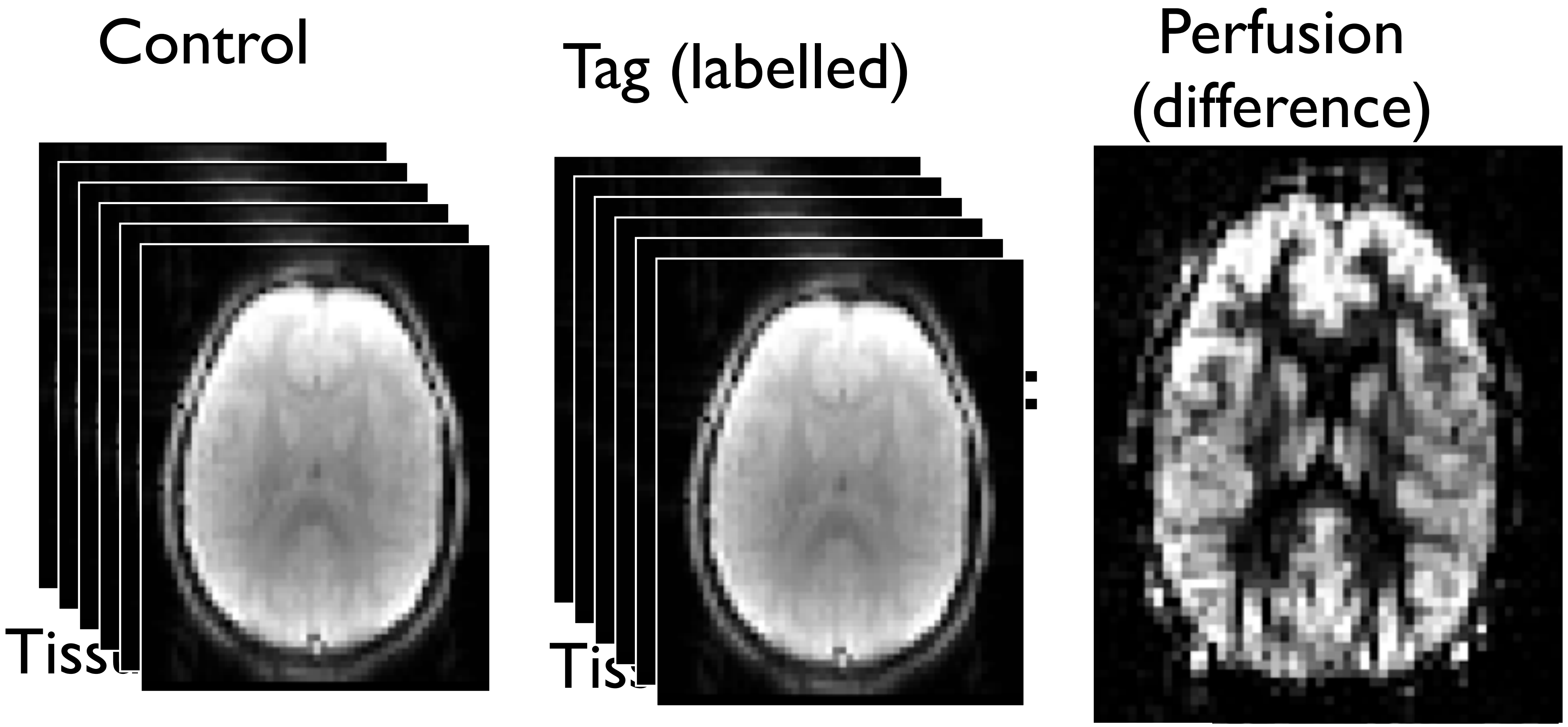
Magnetic Resonance in Medicine - in press

OUTLINE

- Acquisition
- Keep it simple!
  - ➡ Perfusion weighted images.
  - ➡ Perfusion fMRI.
- Quantitative perfusion:
  - ➡ A short course in tracer kinetics.
  - ➡ Measuring arterial blood magnetization.
- Preparing for group analysis.
- Advanced quantification:
  - ➡ Macro vascular contamination
  - ➡ Partial Volume Correction

EXAMPLE (SIMPLE)

- What I have...
  - ➡ ASL data!
- What I want...
  - ➡ A perfusion image (in this subject).
- What should I do?
  - ➡ Tag-control subtraction
  - ➡ Average



```
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asl_file --data={ASLdata.nii.gz} --ntis=1 --iaf=tc --diff --mean={diffdata_mean.nii.gz}
```

FUNCTIONAL ASL

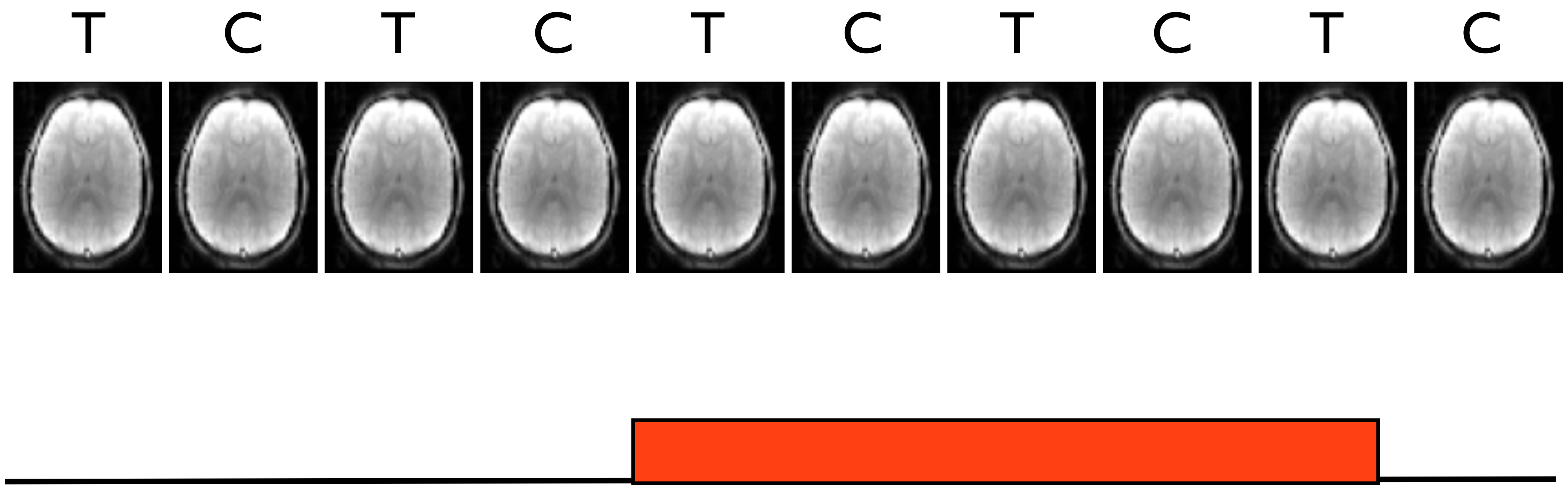
- Why use ASL for a functional experiment?
  - ➡ A direct measure of perfusion changes - physiological response.
  - ➡ (Potentially) fully quantitative - possible to calculate absolute perfusion.
  - ➡ Good for low frequency designs.

- What are the challenges?
  - ➡ SNR
  - ➡ Temporal sampling - TR and the need for tag and control scans.

  - ➡ Time series data will contain both ASL (tag-control difference) and BOLD effects (depends upon the TE used).

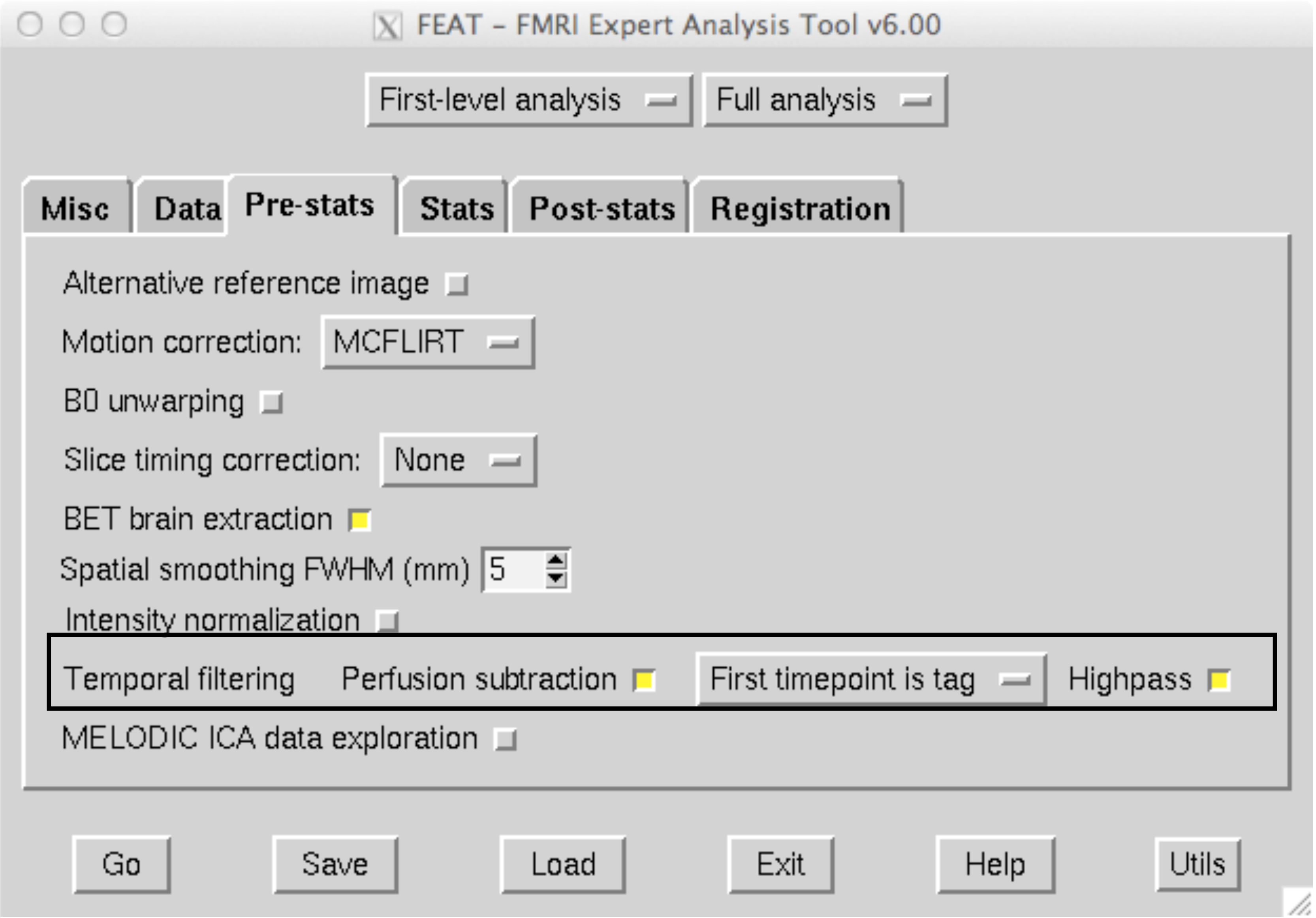
FUNCTIONAL ASL

- What I have…
  - ➡ ASL data during a functional task.
- What I want…
  - ➡ Activations
- What should I do?
  - ➡ Tag-control subtraction
  - ➡ GLM



FUNCTIONAL ASL

- Two options in FEAT
  - ➡ Do subtraction before GLM
  - ➡ (FILM prewhitening OFF)
  - ➡ ONLY considers the perfusion contribution, subtraction removes BOLD signal.



Alternative reference image ☐

Motion correction: MCFLIRT

B0 unwarping ☐

Slice timing correction: None

BET brain extraction ☑

Spatial smoothing FWHM (mm) 5

Intensity normalization ☐

Temporal filtering Perfusion subtraction ☑ First timepoint is tag Highpass ☑

MELODIC ICA data exploration ☐

```
asl_file --data={ASLdata.nii.gz} --ntis=1 --iaf=tc --diff --out={diffdata.nii.gz}
perfusion_subtract {ASLdata.nii.gz} {diffdata.nii.gz}
```

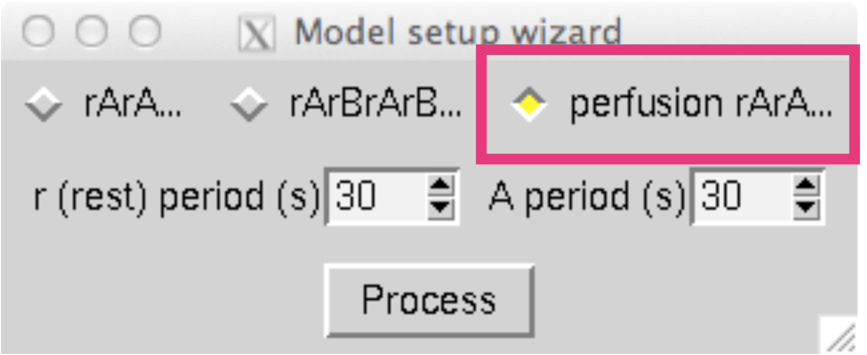
FUNCTIONAL ASL

- Two options in FEAT
  - ➡ Full model

    Includes perfusion and BOLD contributions

  - ➡ EV1 - Tag vs. Control

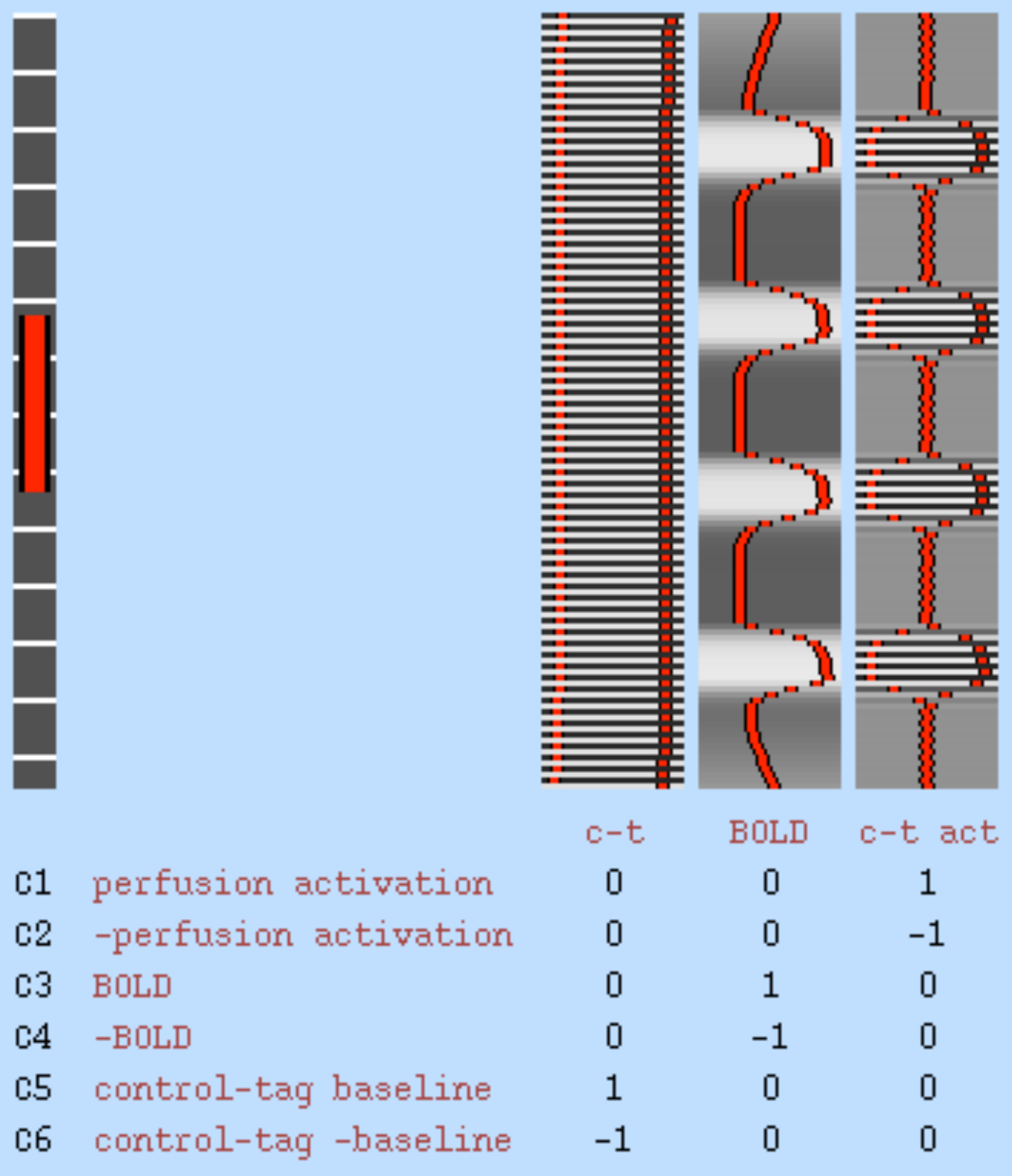
    -1 1 -1 1 -1 1 -1 1
  - ➡ EV2 - BOLD
  - ➡ EV3 - Interaction



Model setup wizard

○ rArA... ○ rArBrArB... ● perfusion rArA...

r (rest) period (s) 30 A period (s) 30



		c-t	BOLD	c-t act
C1	perfusion activation	0	0	1
C2	-perfusion activation	0	0	-1
C3	BOLD	0	1	0
C4	-BOLD	0	-1	0
C5	control-tag baseline	1	0	0
C6	control-tag -baseline	-1	0	0

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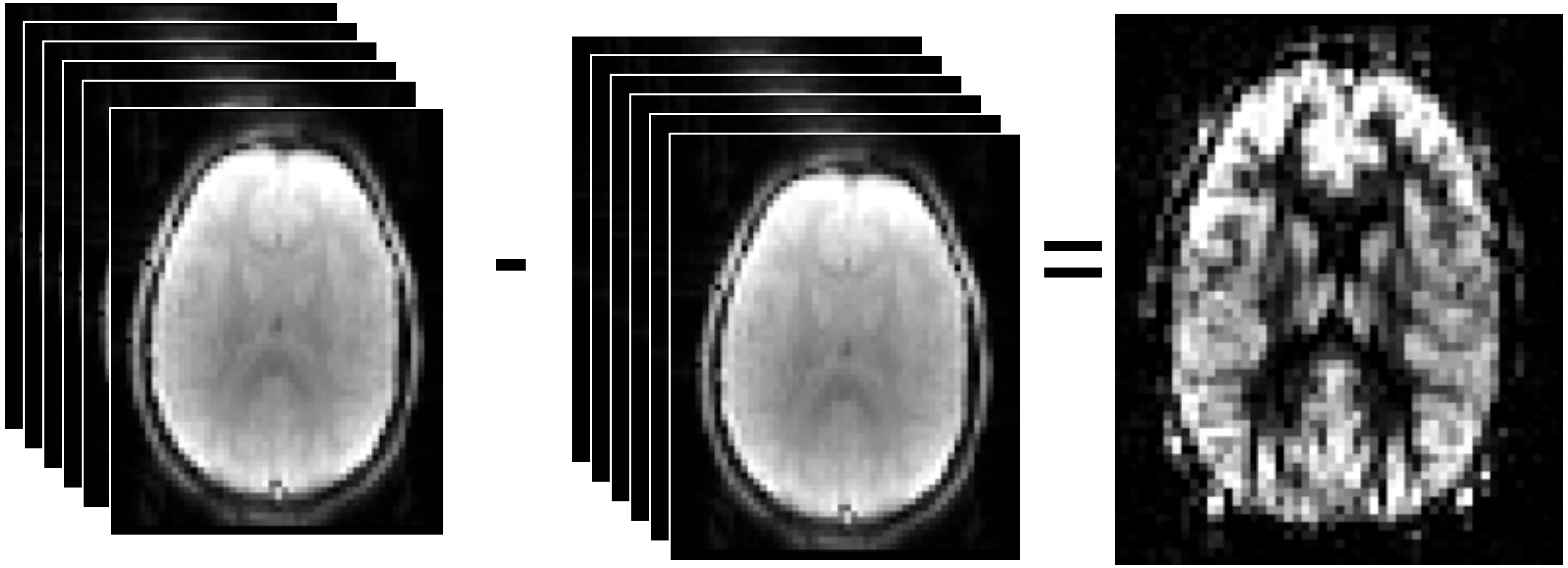
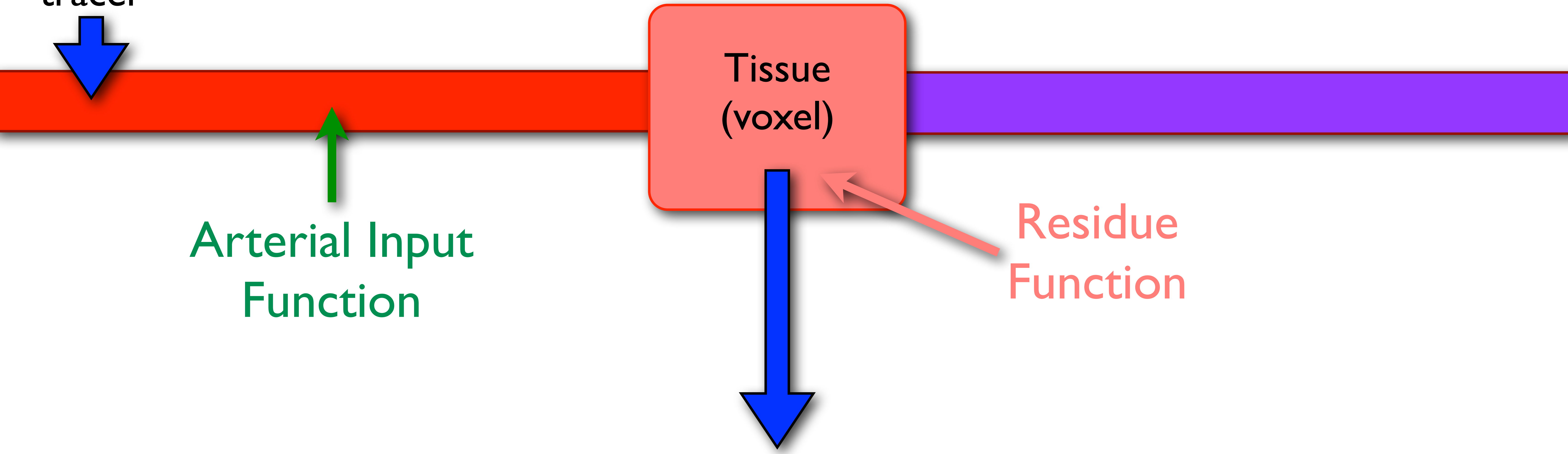
EXAMPLE

- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ←
  - ➡ M0 calculation.



KINETIC MODEL INVERSION



Introduce tracer

Tissue (voxel)

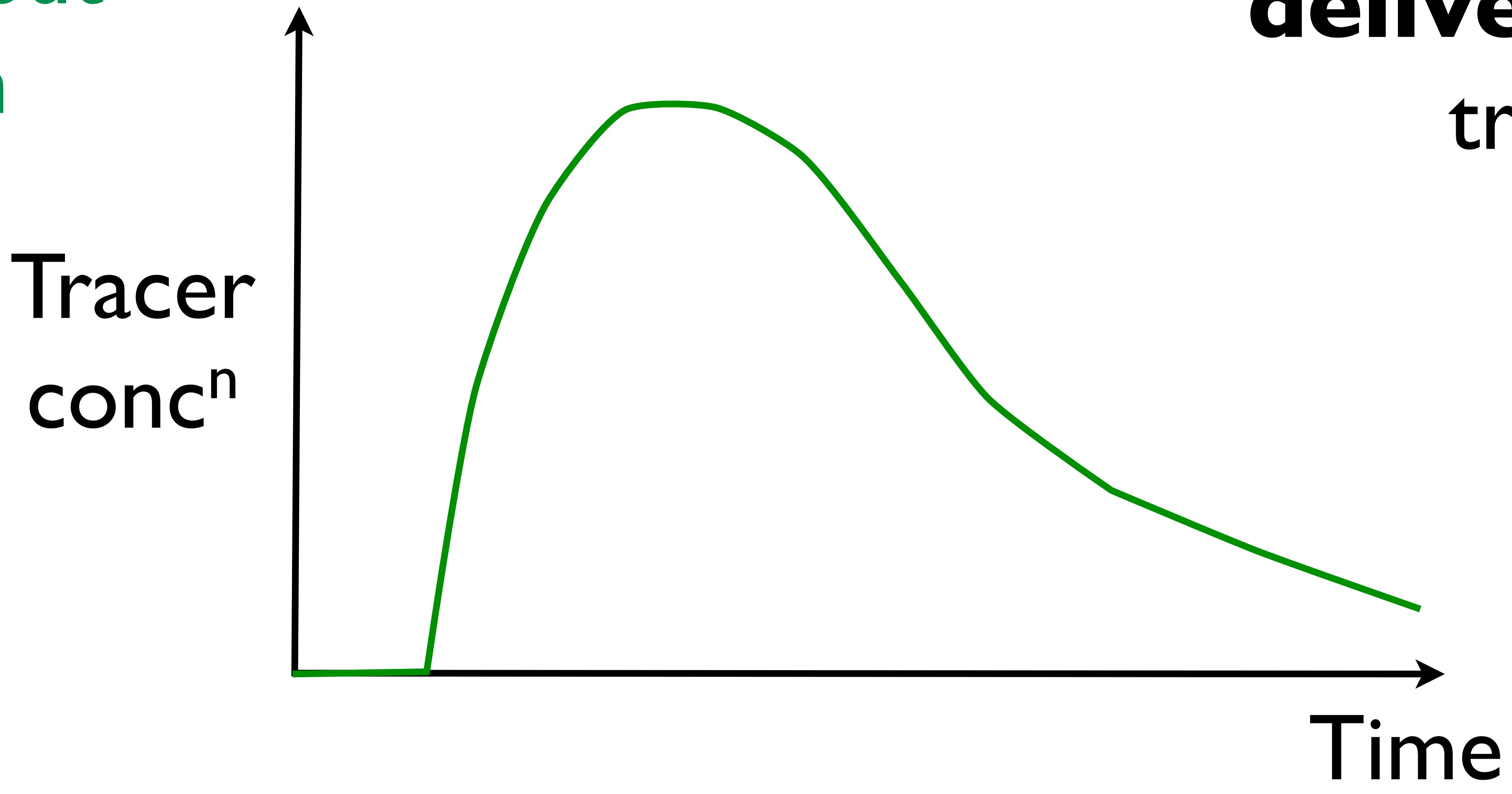
Arterial Input Function

Residue Function

$$\Delta M(t) = F \cdot AIF(t) * r(t)$$

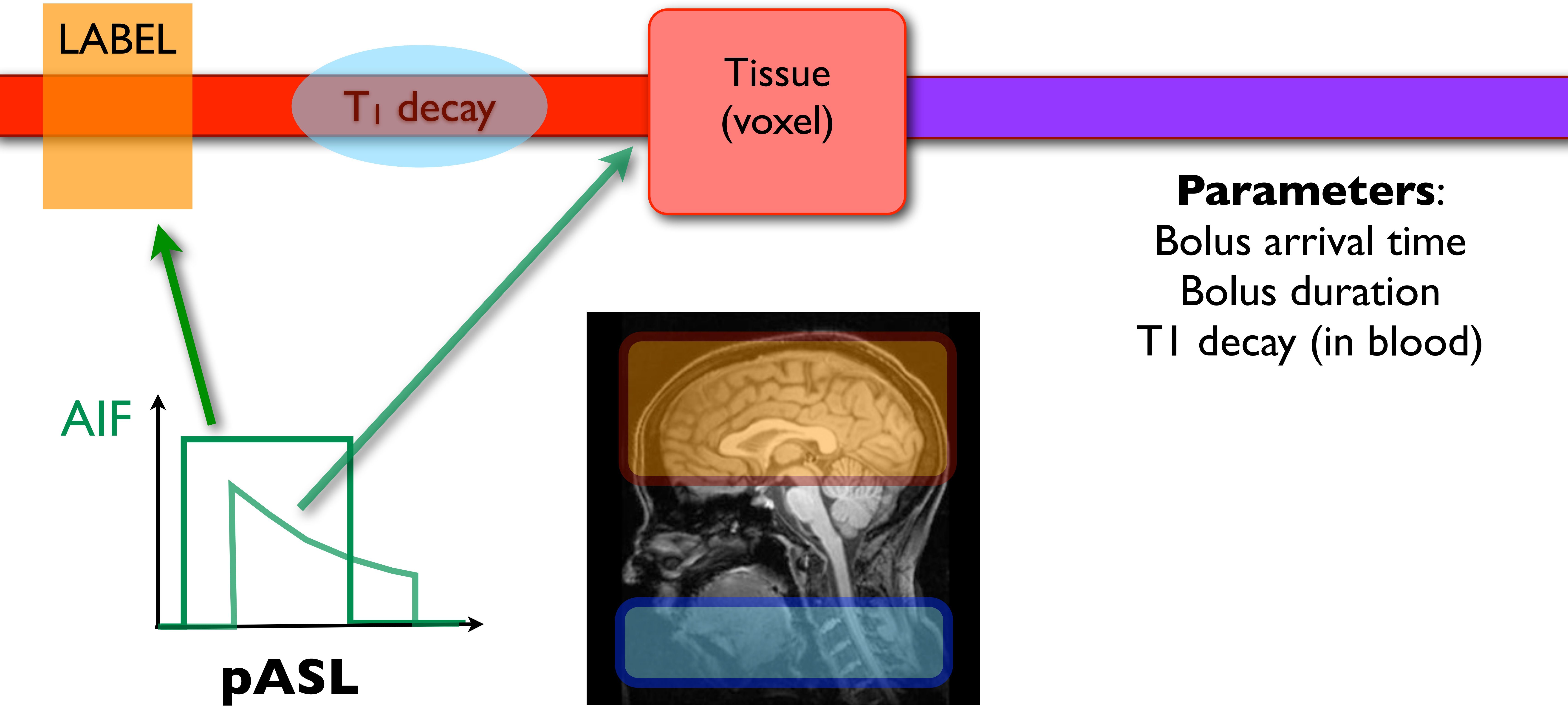
KINETIC MODEL INVERSION

Arterial Input Function



Tells us about the **delivery** of the tracer

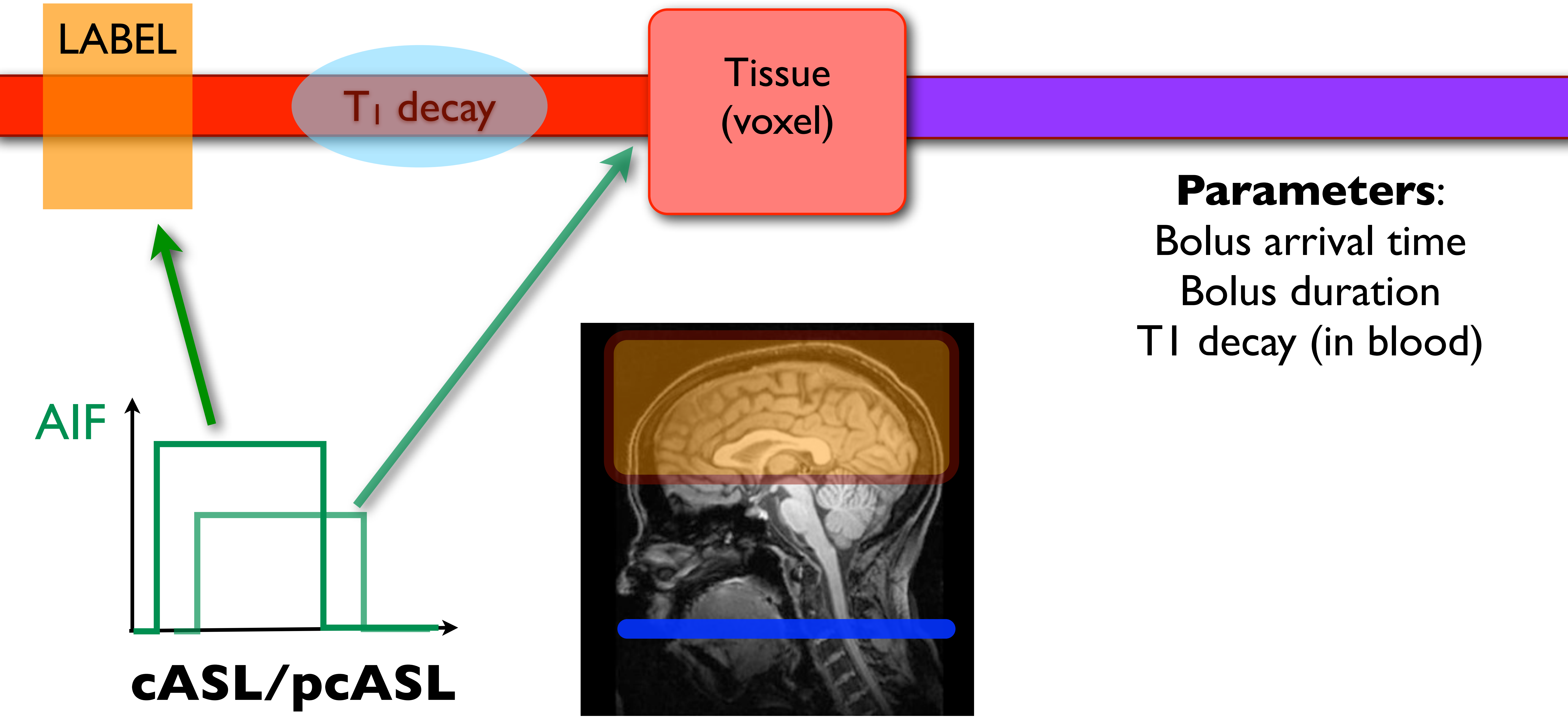
Kinetic Model Inversion



pASL

Parameters:
Bolus arrival time
Bolus duration
T1 decay (in blood)

KINETIC MODEL INVERSION



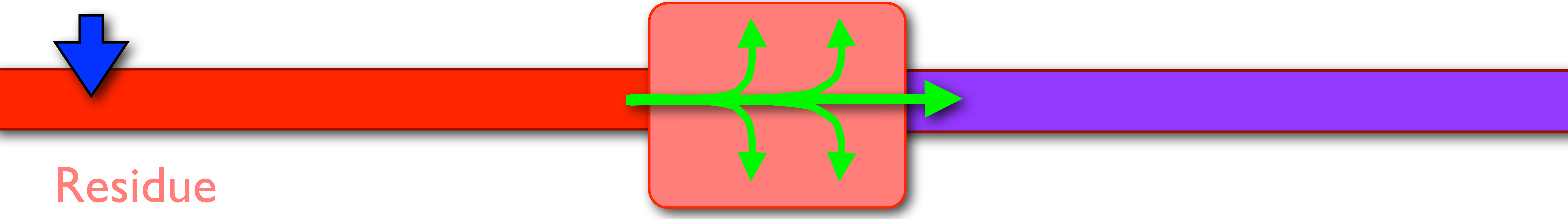
Parameters:

Bolus arrival time

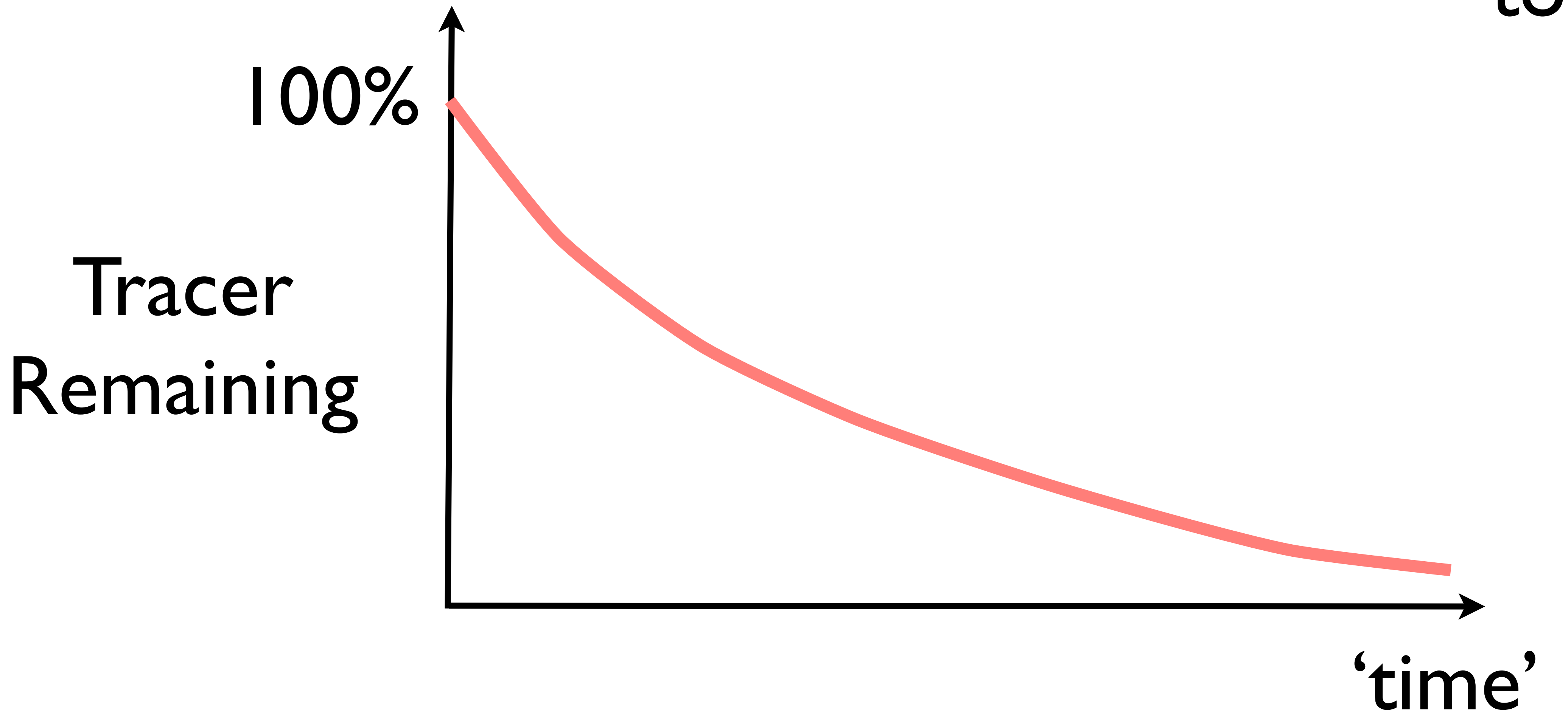
Bolus duration

T1 decay (in blood)

KINETIC MODEL INVERSION



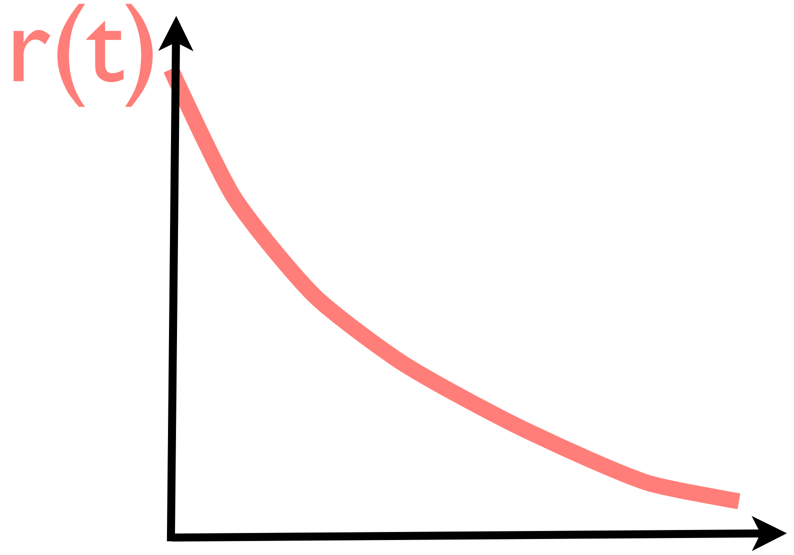
Residue Function



Tells us what happens to the tracer after is has arrived.

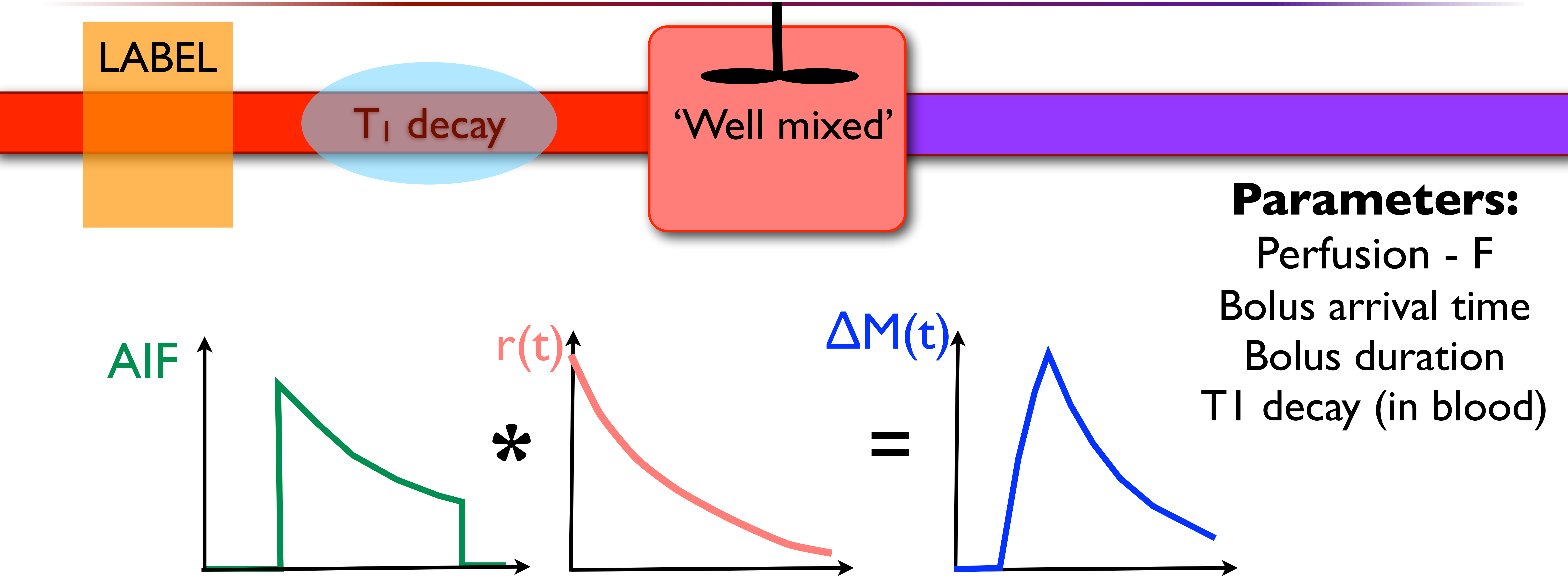
KINETIC MODEL INVERSION

- Rapid exchange: single well mixed compartment
- No spins leave the compartment
- Decay with T1



Parameters:
Bolus arrival time
Bolus duration
T1 decay (in blood)

KINETIC MODEL INVERSION



Parameters:

Perfusion - F

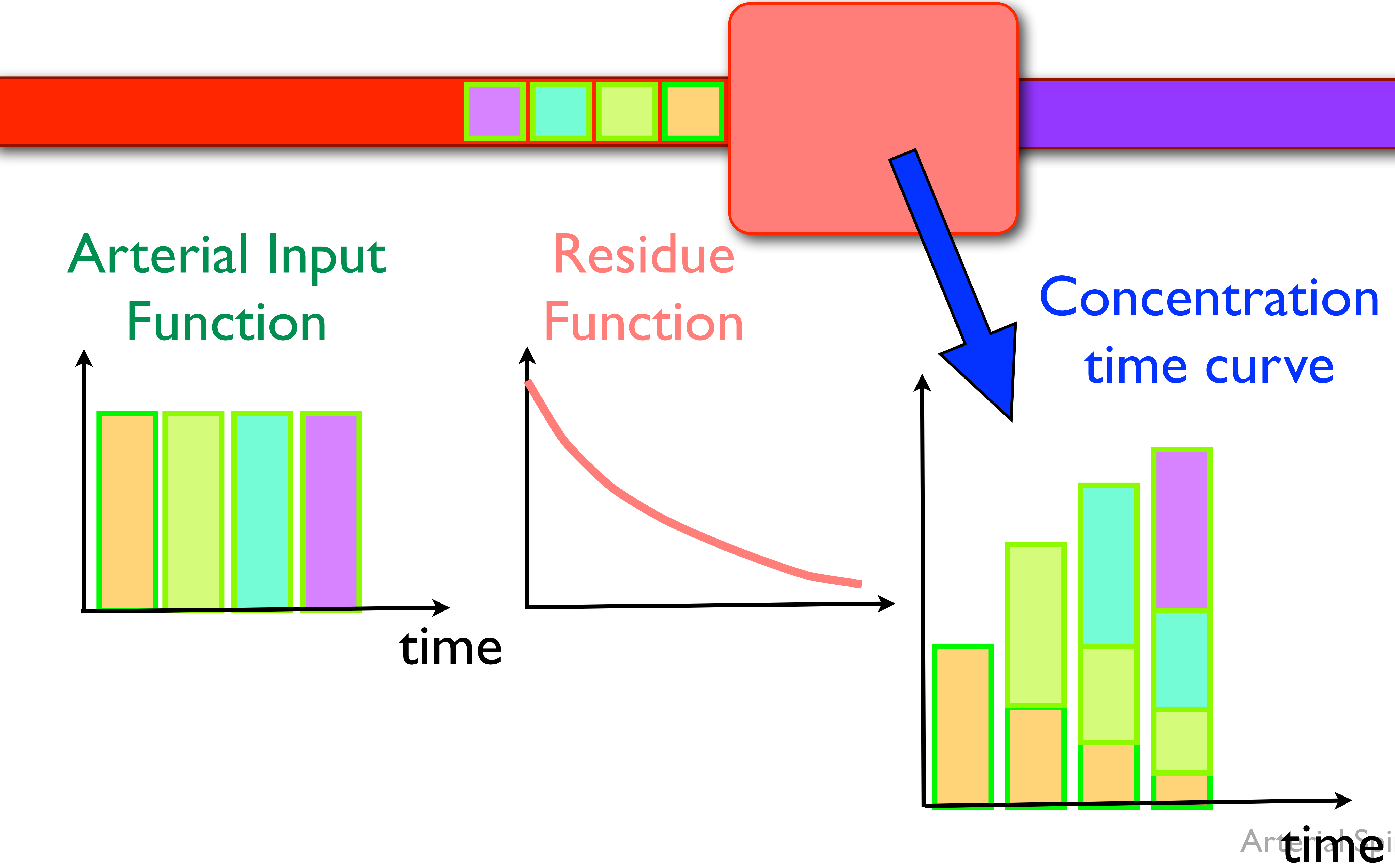
Bolus arrival time

Bolus duration

T1 decay (in blood)

$$\Delta M(t) = F \cdot AIF(t) * r(t)$$

Kinetic Model Inversion



Arterial Input Function

Residue Function

Concentration time curve

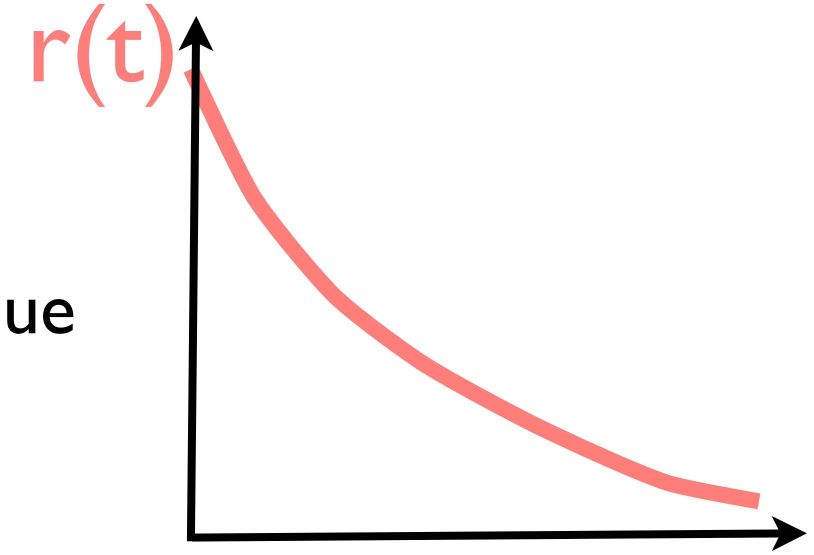
KINETIC MODEL INVERSION

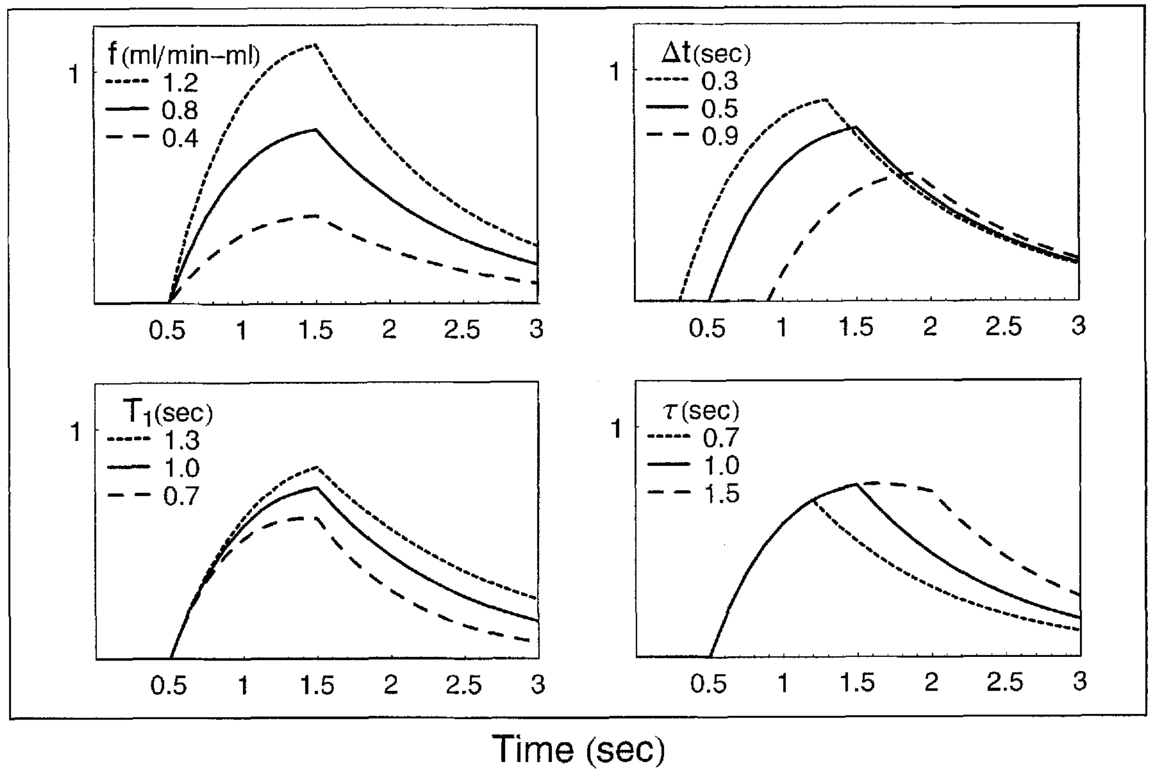

LABEL

T_{1b} decay

'Well mixed' T_{1t} decay

- The 'simple' model
  - ➡ Only one T1 value (blood)
  - ➡ Spins never leave tissue
- The 'standard' model:
  - ➡ Separate T_1 for blood and tissue ($T_{1t} < T_{1b}$).
  - ➡ Spins leave voxel at rate determined by perfusion and partition coefficient.





Buxton *et al.*, MRM 40(3), 1998.

EXAMPLE

- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ←
  - ➡ M0 calculation.

What you need to know about your data:

Labeling

pASL (pulsed)	or	pcASL (continuous)
Inversion time(s)		Post-labeling delay(s)
Bolus duration (if QUIPSS/Q2TIPS)		Labeling duration

Model

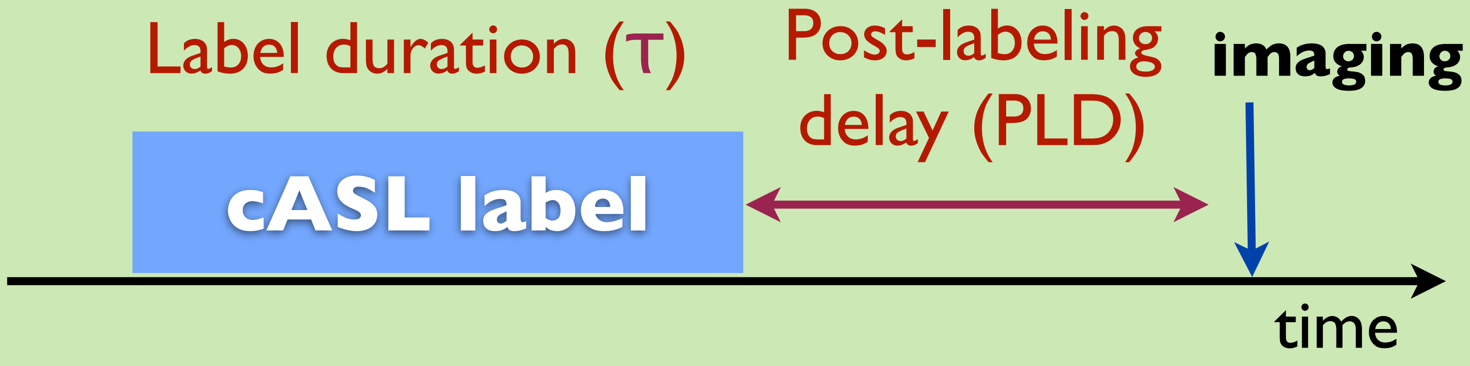
T1 (tissue and blood?)
Bolus arrival time

Kinetic Model Inversion

Analytical solutions - Simple model (ASL 'white paper'):

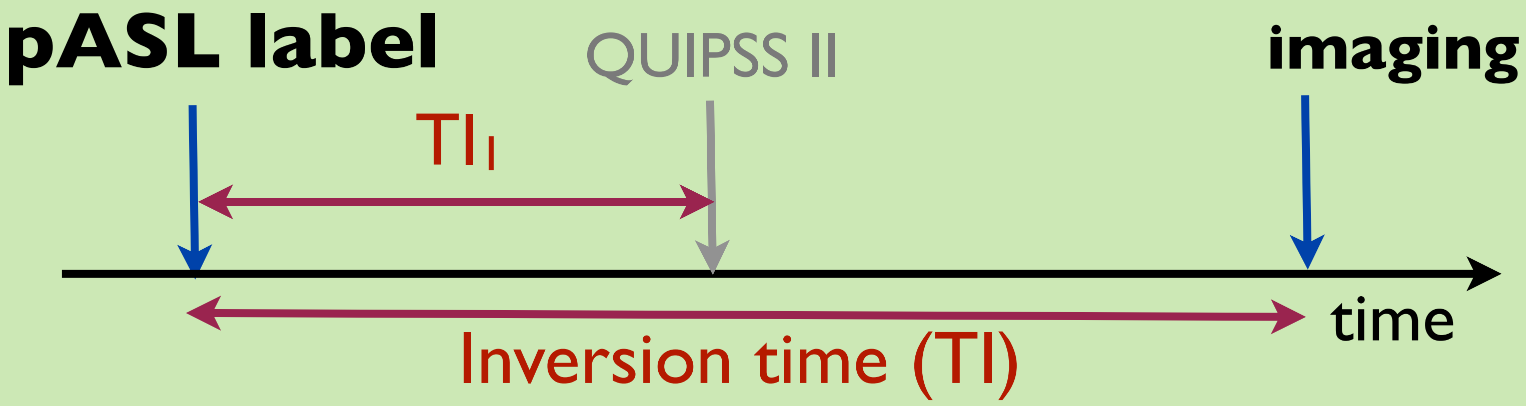
pcASL

$$\mathrm{CBF} = \frac{6000\cdot\lambda\cdot(\mathrm{SI}_{\mathrm{control}}-\mathrm{SI}_{\mathrm{label}})\cdot e^{\frac{\mathrm{PLD}}{\mathrm{T}_{1,\mathrm{blood}}}}}{2\cdot\alpha\cdot\mathrm{T}_{1,\mathrm{blood}}\cdot\mathrm{SI}_{\mathrm{PD}}\cdot(1-e^{-\frac{\tau}{\mathrm{T}_{1,\mathrm{blood}}}})}$$



pASL QUIPSS II

$$\mathrm{CBF} = \frac{6000\cdot\lambda\cdot(\mathrm{SI}_{\mathrm{control}}-\mathrm{SI}_{\mathrm{label}})\cdot e^{\frac{\mathrm{TI}}{\mathrm{T}_{1,\mathrm{blood}}}}}{2\cdot\alpha\cdot\mathrm{TI}_1\cdot\mathrm{SI}_{\mathrm{PD}}}$$



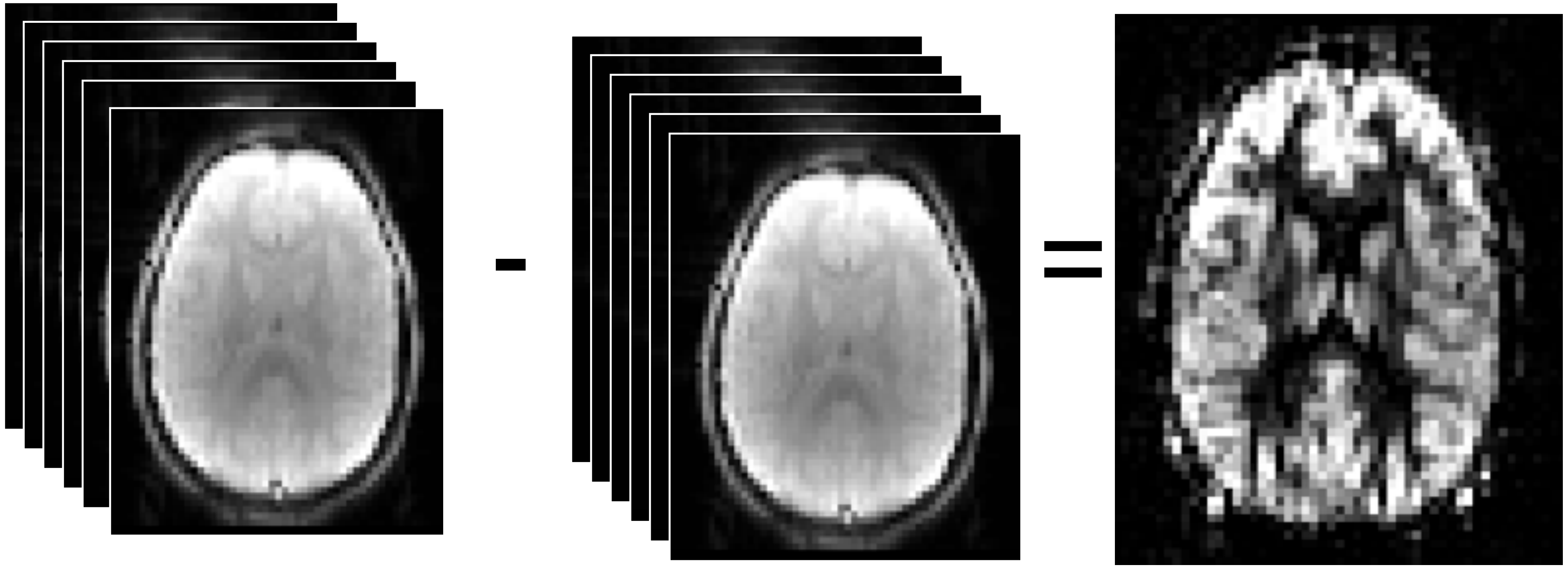
Fixed value:

T_{1blood} = 1650 ms (3T)

Assumes that BAT = 0

EXAMPLE 1

- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ←
  - ➡ M0 calculation.



pcASL with
labeling duration: 1.4 s
post-label delay: 1.0 s

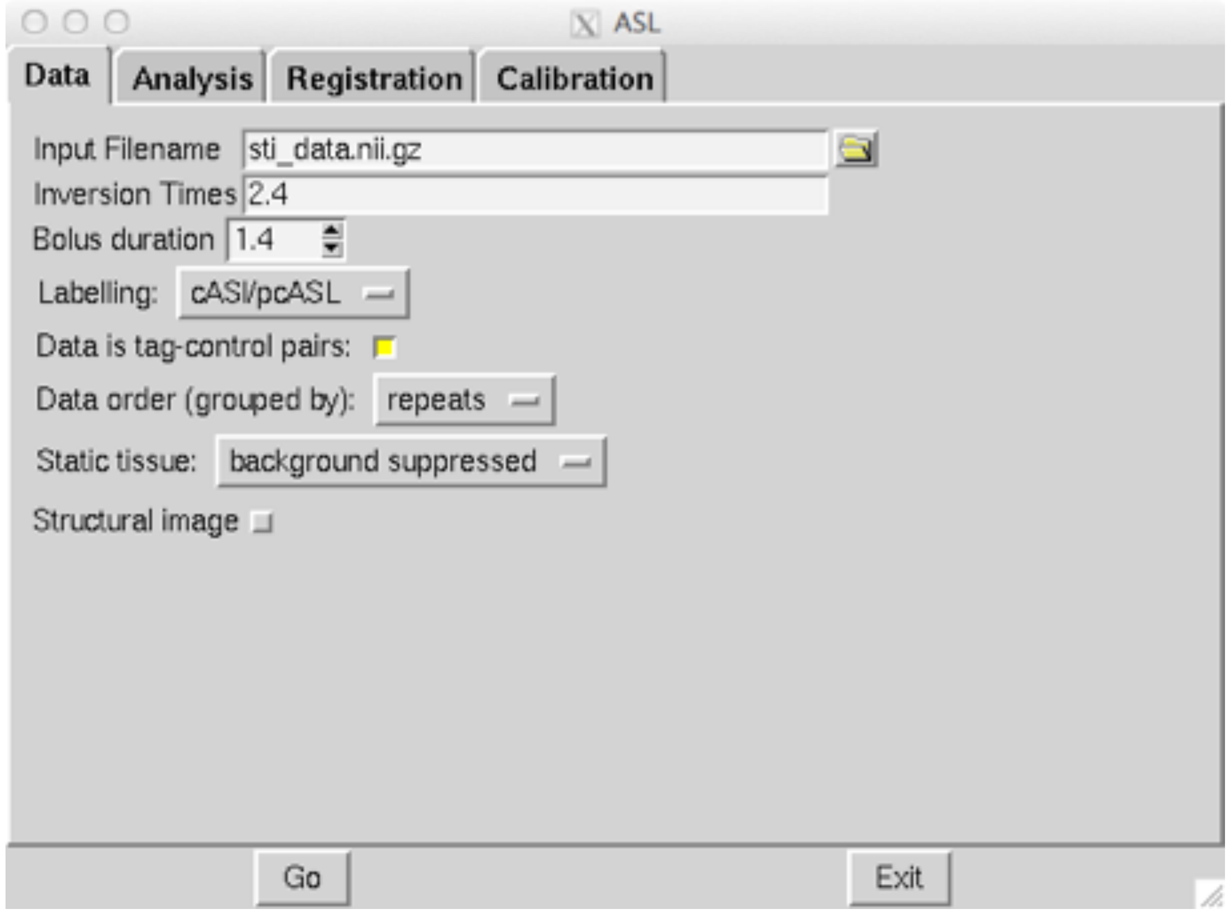
Assume
T1 (blood): 1.6 s
T1 (tissue): 1.3 s
BAT : 1.3 s

```
oxford_asl -i {ASL_diff_data.nii.gz} -o {result_dir}
  --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
```

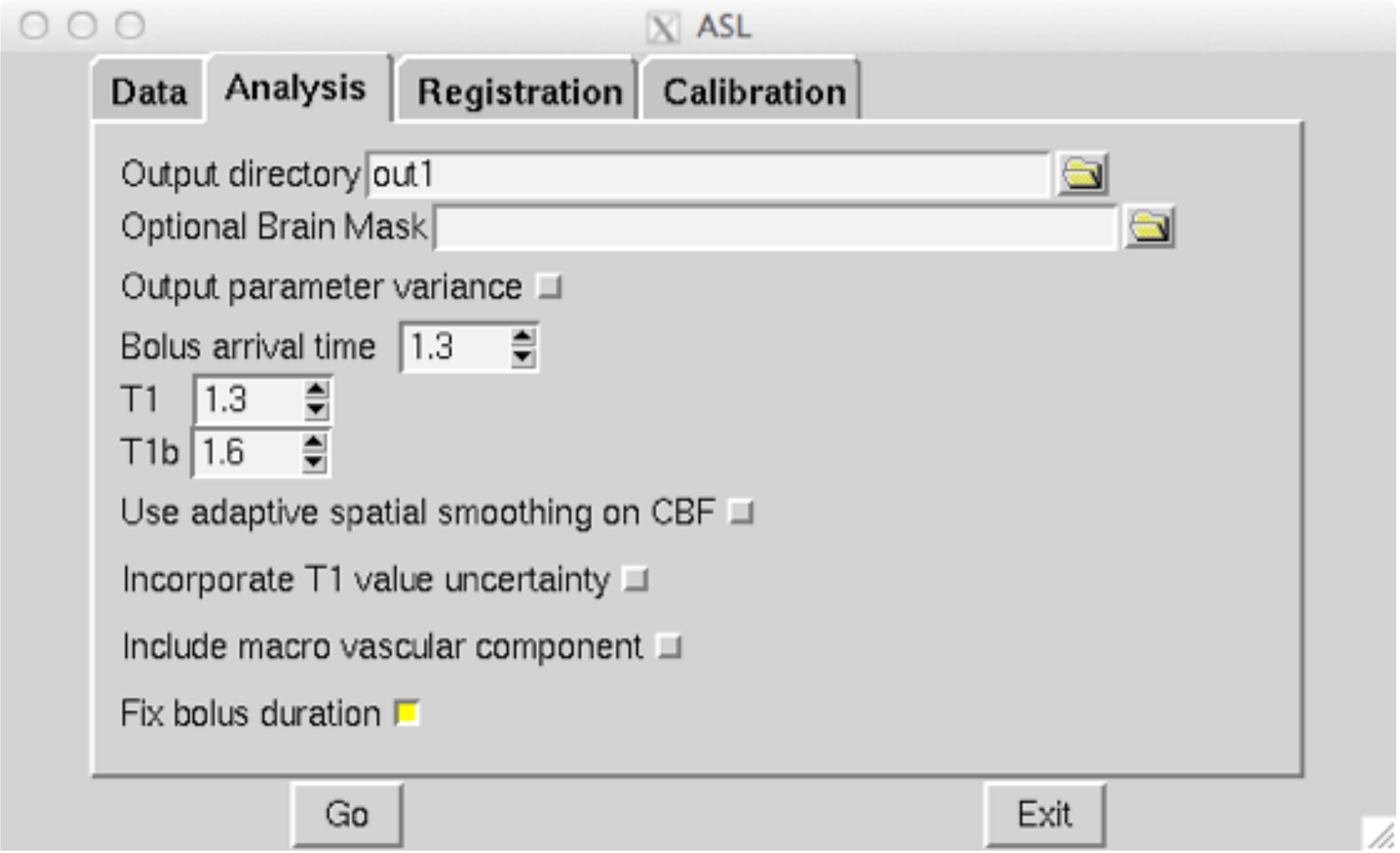
EXAMPLE 1

pcASL with
- tagging duration: 1.4 s
- post-label delay: 1.0 s

Assume
- T1 (blood): 1.6 s
- T1 (tissue): 1.3 s
- BAT : 1.3 s



Input Filename sti_data.nii.gz
Inversion Times 2.4
Bolus duration 1.4
Labelling: cASl/pcASL
Data is tag-control pairs: ☑
Data order (grouped by): repeats
Static tissue: background suppressed
Structural image ☐

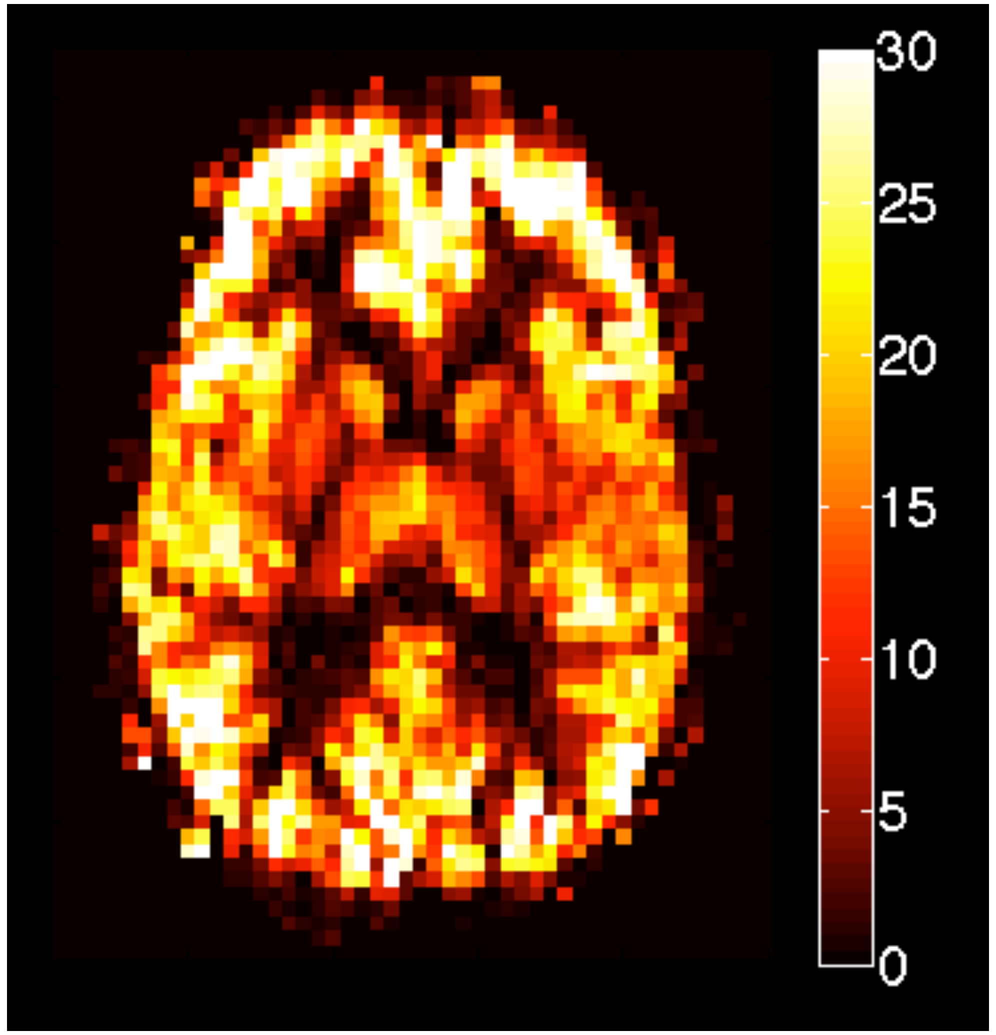


Output directory out1
Optional Brain Mask
Output parameter variance ☐
Bolus arrival time 1.3
T1 1.3
T1b 1.6
Use adaptive spatial smoothing on CBF ☐
Incorporate T1 value uncertainty ☐
Include macro vascular component ☐
Fix bolus duration ☑

```
> asl_file --data=sti_data.nii.gz --ntis=1 --iaf=tc --diff --out=sti_diffdata.nii.gz
> oxford_asl -i sti_diffdata.nii.gz -o out1
   --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
```

EXAMPLE 1

Perfusion (arbitrary units)

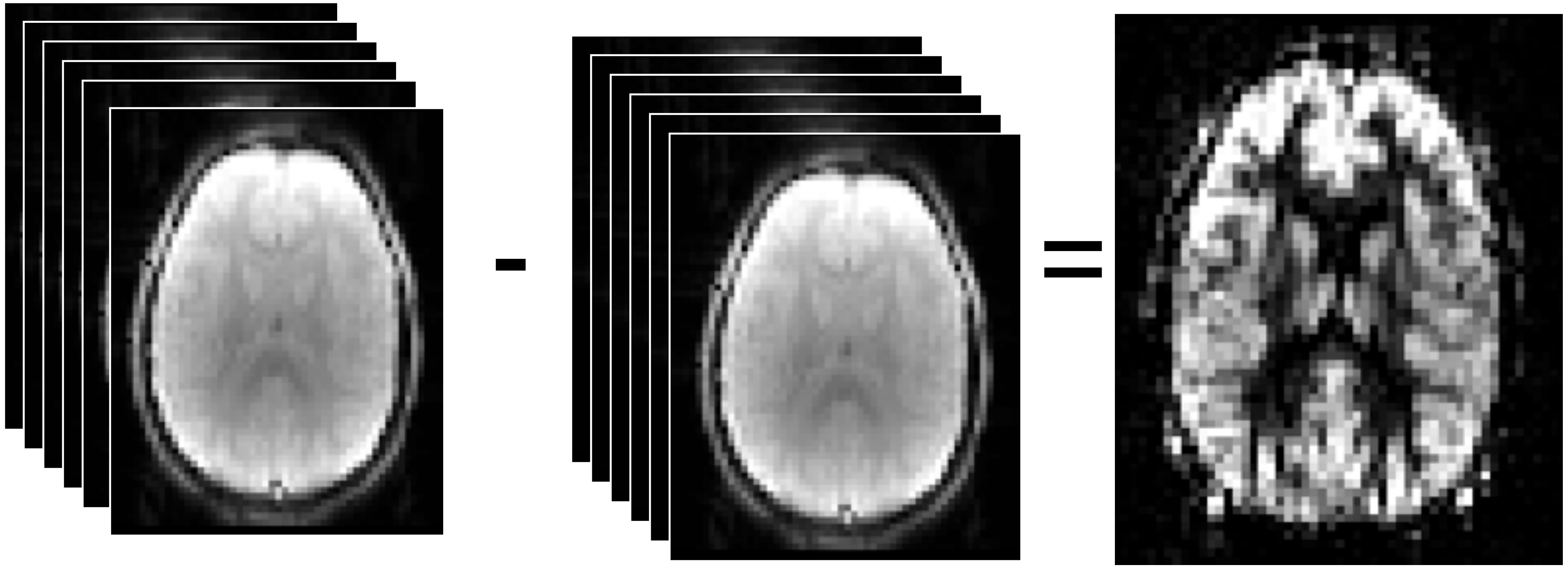


`out1/native_space/perfusion.nii.gz`

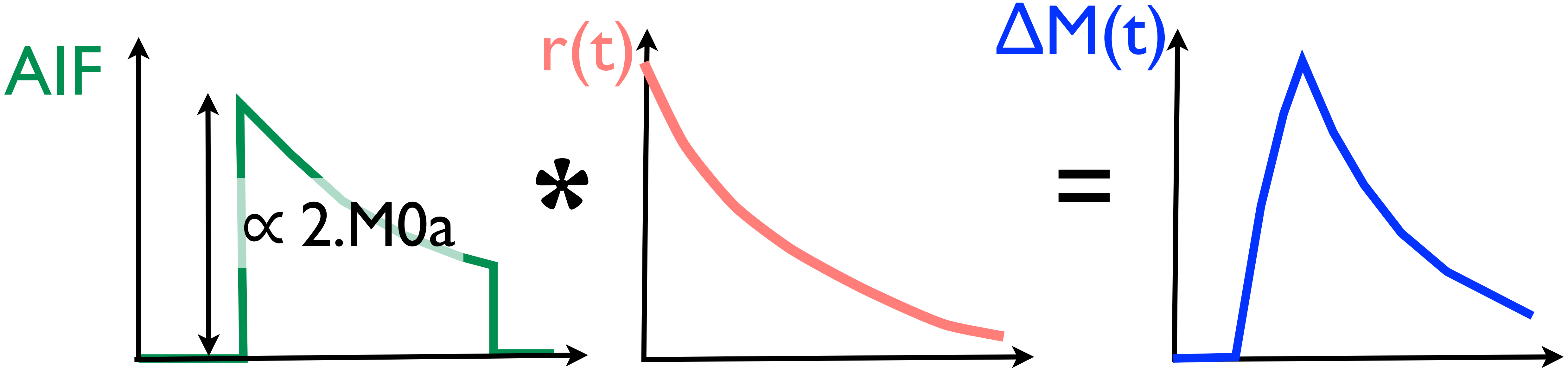
```
> asl_file --data=sti_data.nii.gz --ntis=1 --iaf=tc --diff --out=sti_diffdata.nii.gz
> oxford_asl -i sti_diffdata.nii.gz -o out1
   --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
```

Example

- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ✓
  - ➡ M0 calculation. ←



M0 Calculation



$$\Delta M(t) = 2 \cdot M0a \cdot CBF \cdot AIF(t) * r(t)$$

M0 CALCULATION

- Cannot measure M0a directly.
- indirect via brain 'tissue' magnetization.
  - ➡ Calculate M0t.

    (M0 of 'tissue')
  - ➡ M0t to M0a.

Steady state magnetization

$$S = M_0\left(1 - e^{-TR/T_1}\right)$$

With pre-saturation:

$$S = M_0\left(1 - Ae^{-t/T_{1t}}\right)$$

With background suppression:

No static tissue - need separate calibration images
i.e. a control image with BGS off.

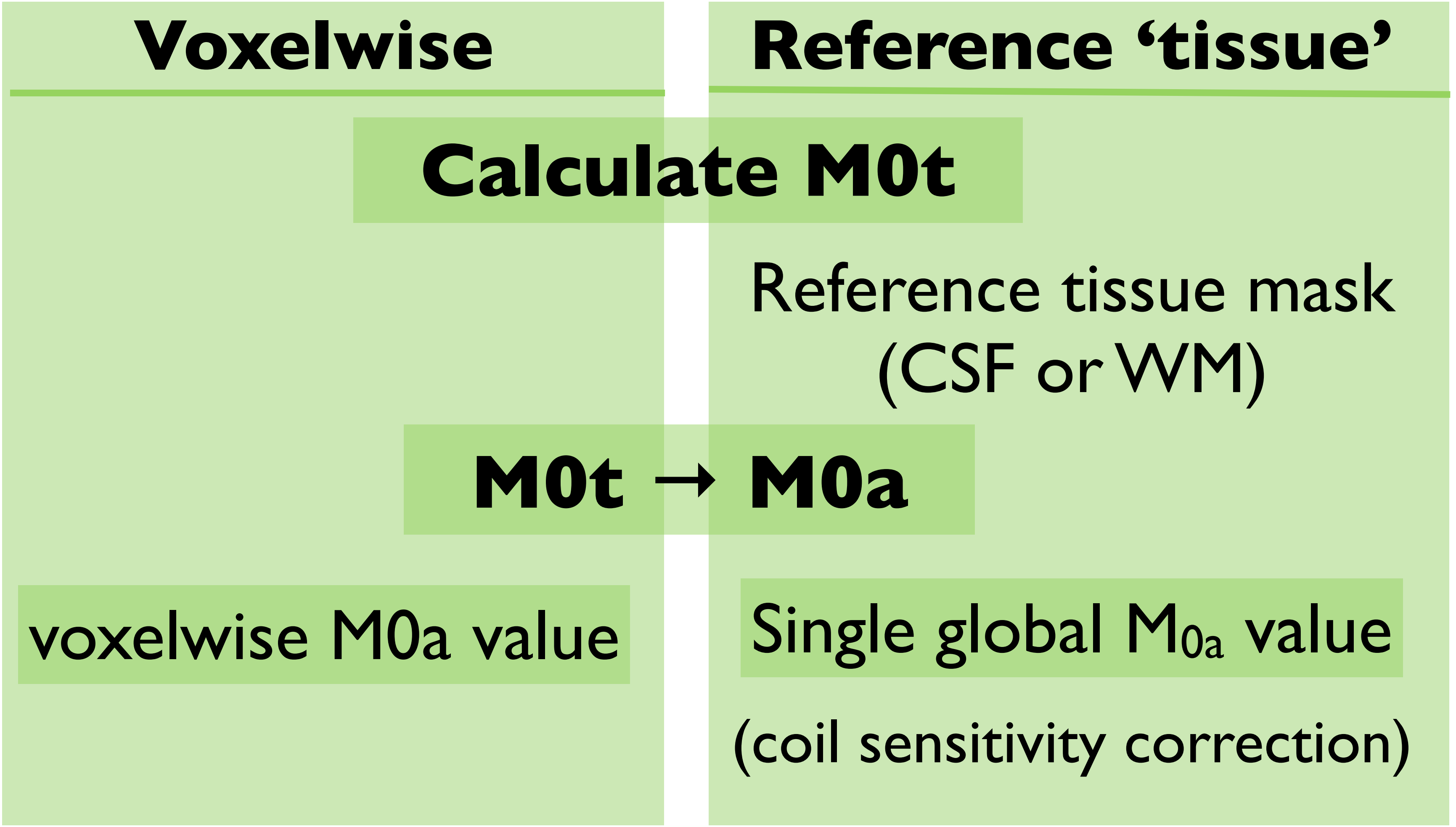
Account for relative proton densities:

$$M_{0a} = \frac{M_{0t}}{\lambda}$$

```
oxford_asl ... -c {calibration_image.nii.gz} -s {structural_image.nii.gz}
asl_calib --mode longtr ...
asl_calib --mode satrecov ...
```

M0 CALCULATION

- Cannot measure M0a directly.
- indirect via brain 'tissue' magnetization.
  - ➡ Calculate M0t.
    (M0 of 'tissue')
  - ➡ M0t to M0a.
- Practicalities
  - ➡ Reference 'tissue'?
  - ➡ Voxelwise?



Voxelwise

Reference 'tissue'

Calculate M0t

Reference tissue mask (CSF or WM)

M0t → M0a

voxelwise M0a value

Single global M_{0a} value

(coil sensitivity correction)

Perfusion (ml/100g/min) = (Perfusion / M_{0a}) * 6000

```
oxford_asl ... -c {calibration_image.nii.gz} -s {structural_image.nii.gz}
asl_calib --mode longtr ...
asl_calib --mode satrecov ...
fslmaths {perfusion.nii.gz} -div [M0a] -mul 6000 {perfusion_calib.nii.gz}
```

M0 CALCULATION

Analytical solutions - Simple model (ASL ‘white paper’):

pcASL

$$\mathrm{CBF} = \frac{6000 \cdot \lambda \cdot (\mathrm{SI}_{\mathrm{control}} - \mathrm{SI}_{\mathrm{label}}) \cdot e^{\frac{\mathrm{PLD}}{\mathrm{T}_{1,\mathrm{blood}}}}}{2 \cdot \alpha \cdot \mathrm{T}_{1,\mathrm{blood}} \cdot \mathrm{SI}_{\mathrm{PD}} \cdot \left(1 - e^{-\frac{\tau}{\mathrm{T}_{1,\mathrm{blood}}}}\right)}$$

$\alpha = 0.85$

pASL QUIPSS II

$$\mathrm{CBF} = \frac{6000 \cdot \lambda \cdot (\mathrm{SI}_{\mathrm{control}} - \mathrm{SI}_{\mathrm{label}}) \cdot e^{\frac{\mathrm{TI}}{\mathrm{T}_{1,\mathrm{blood}}}}}{2 \cdot \alpha \cdot \mathrm{TI}_1 \cdot \mathrm{SI}_{\mathrm{PD}}}$$

$\alpha = 0.98$

Perfusion (ml/100g/min) = (Perfusion / M_{0a}) * 6000

A ‘voxelwise’ approach:

$M_{0a} = M_{0t} / \lambda = SI_{PD} / \lambda$ with $\lambda = 0.9$ ml/g

SI_{PD} is a proton density weighted image with ‘long’ TR

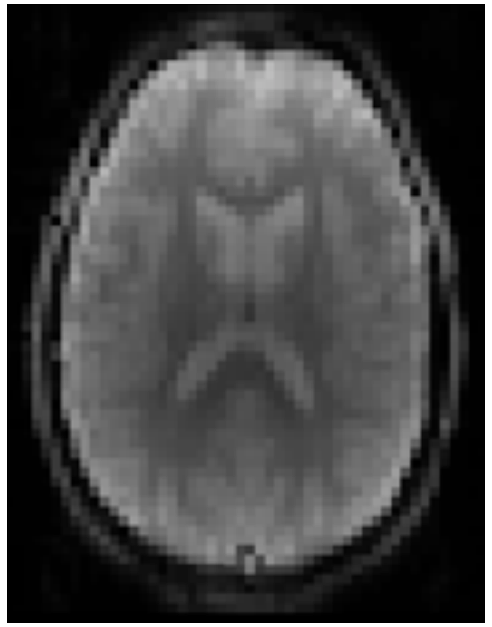
For TR < 5s correct using: $S = M_0\left(1 - e^{-TR/T_1}\right)$

EXAMPLE 2

- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ✓
  - ➡ M0 calculation. ←

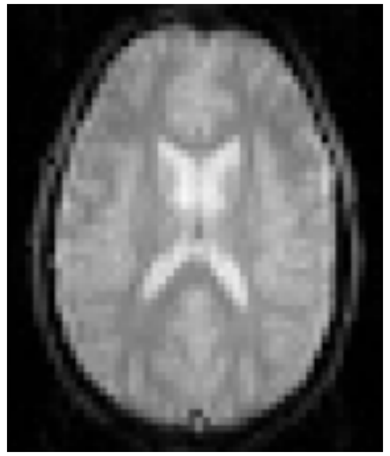
Background suppression on

Calibration image



Steady state
TR = 6 s

Calibration
reference

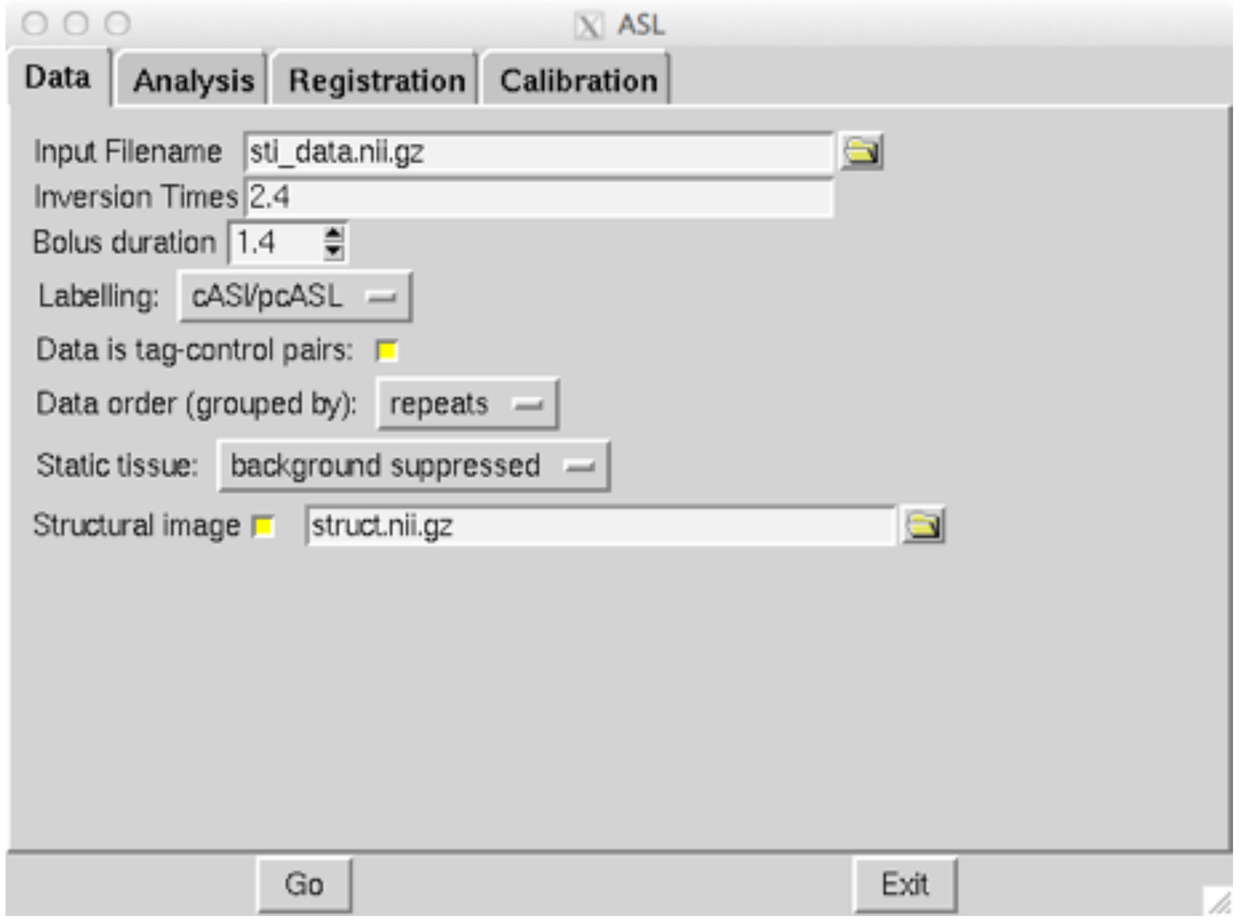


```
oxford_asl -i {ASL_diff_data.nii.gz} -o {result_dir}
  --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
  -c {calibration_image.nii.gz} --tr 6 --cref {calibration_reference.nii.gz}
  -s {structural_image} --regfrom {calibration_image)
```

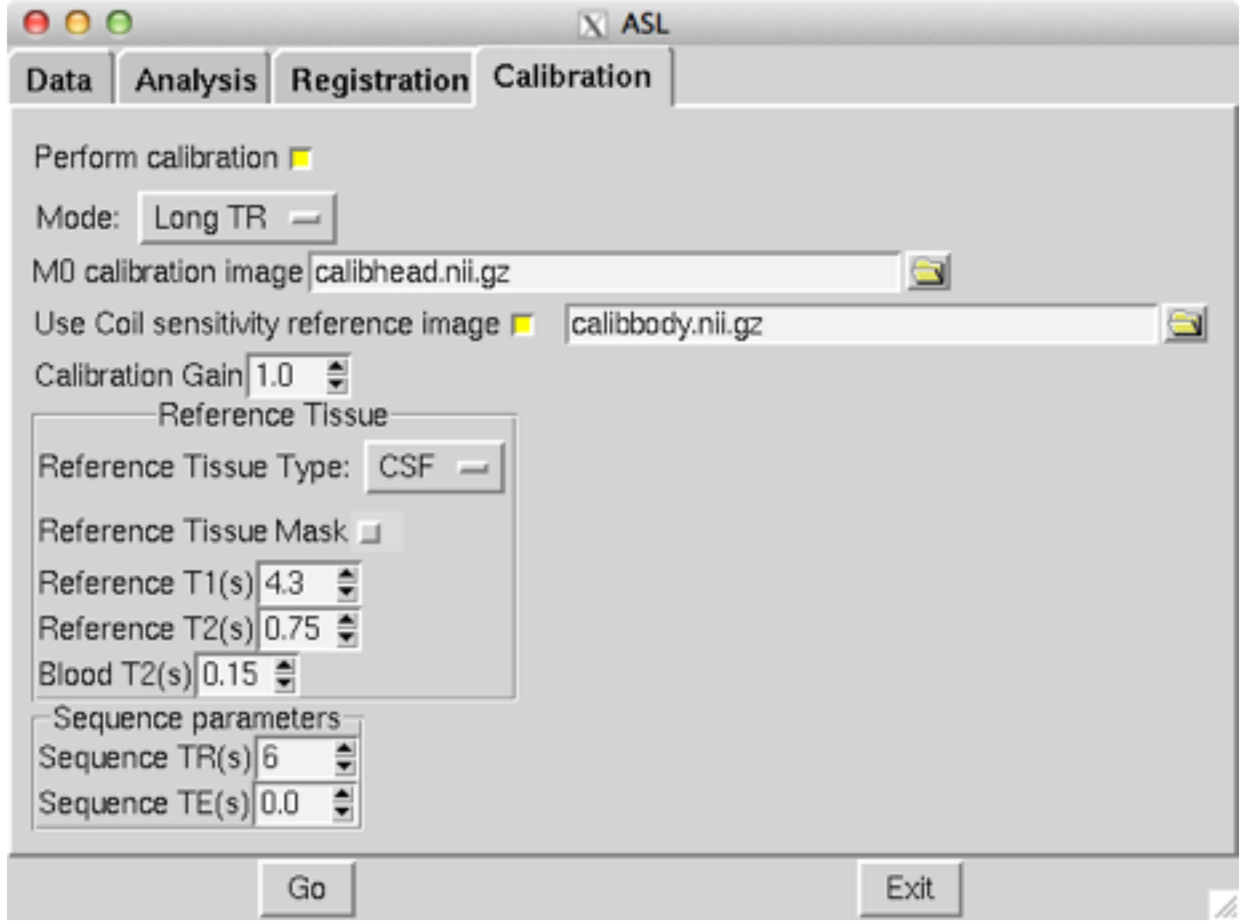
EXAMPLE 2

pcASL with
 tagging duration: 1.4 s
 post-label delay: 1.0 s

Calibration image with TR = 6 s
Calibration reference (body coil)



Input Filename: sti_data.nii.gz
Inversion Times: 2.4
Bolus duration: 1.4
Labelling: cASl/pcASL
Data is tag-control pairs: ☑
Data order (grouped by): repeats
Static tissue: background suppressed
Structural image ☑ struct.nii.gz



Perform calibration ☑
Mode: Long TR
M0 calibration image: calibhead.nii.gz
Use Coil sensitivity reference image ☑ calibbody.nii.gz
Calibration Gain: 1.0

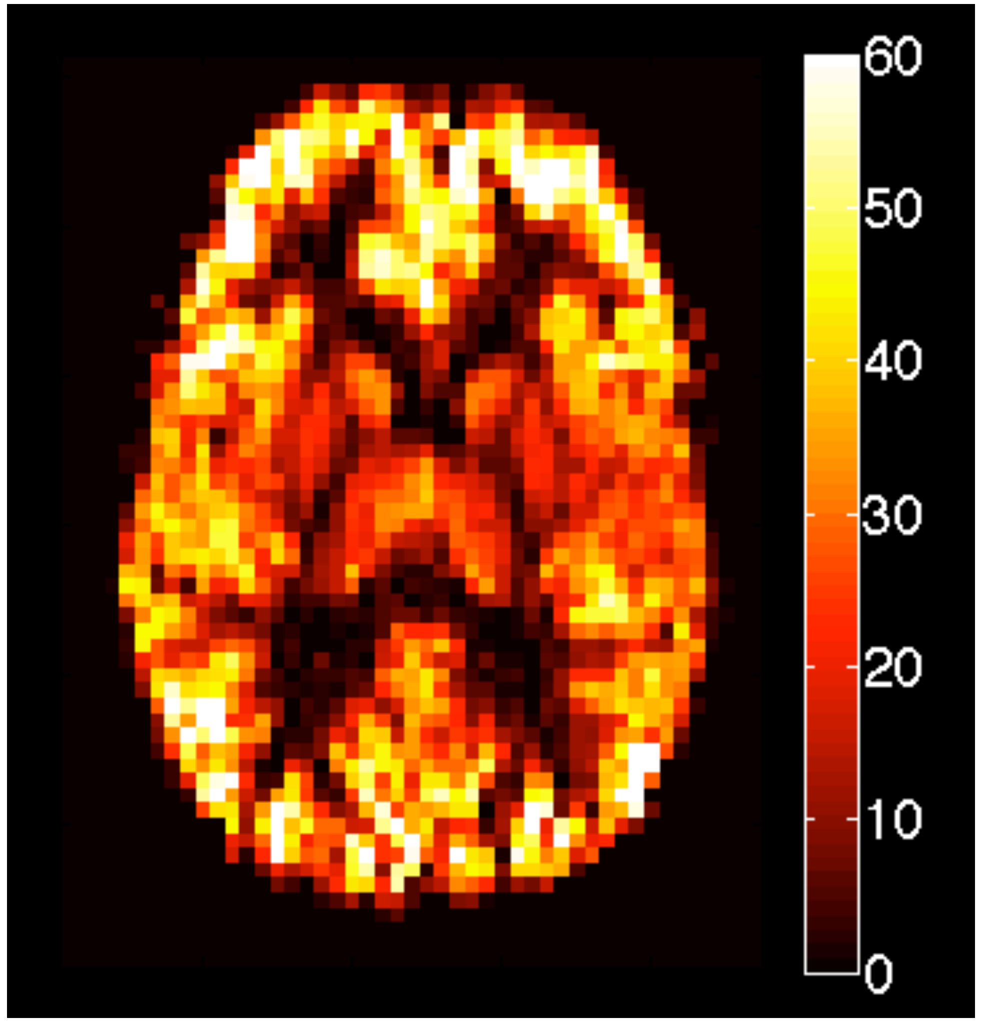
Reference Tissue
Reference Tissue Type: CSF
Reference Tissue Mask ☐
Reference T1(s): 4.3
Reference T2(s): 0.75
Blood T2(s): 0.15

Sequence parameters
Sequence TR(s): 6
Sequence TE(s): 0.0

```
> oxford_asl -i sti_diffdata.nii.gz -o out2
    --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
    -c calibhead.nii.gz --tr 6 --cref calibbody.nii.gz
    -s struct.nii.gz --regfrom calibhead.nii.gz
```

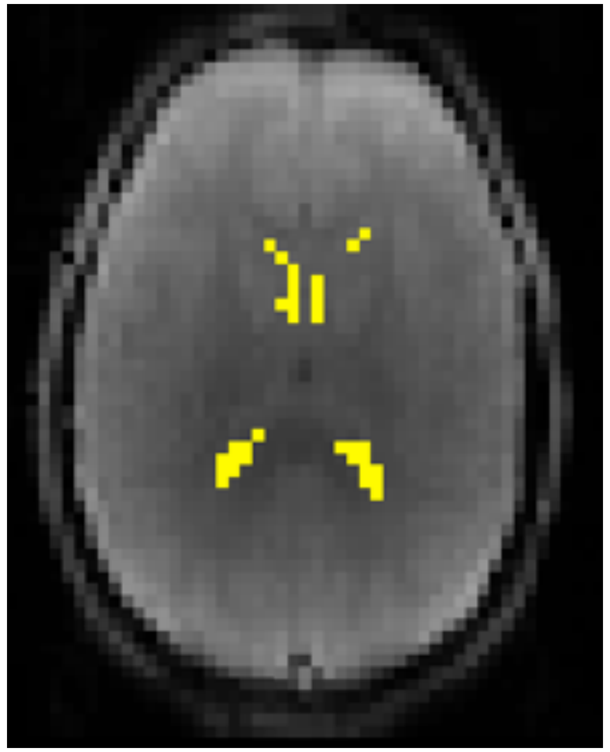
EXAMPLE 2

Perfusion (ml/100g/min)



out2/native_space/perfusion_calib.nii.gz

Calibration: CSF mask



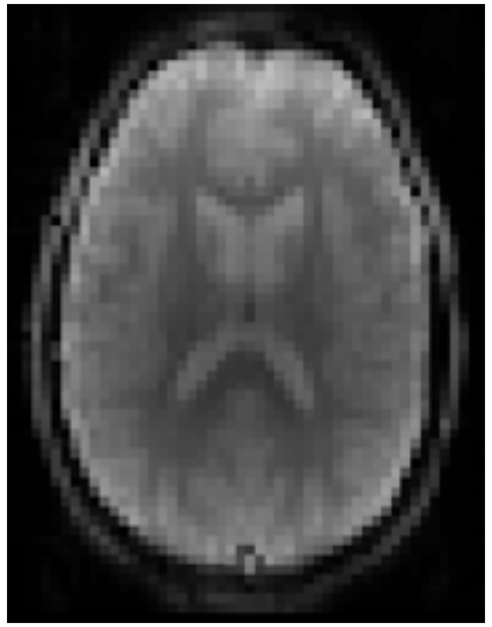
out2/calibration/refmask.nii.gz
(overlaid on raw data)

```
> oxford_asl -i diffdata.nii.gz -o out2
    --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
    -c calibhead.nii.gz --tr 6 --cref calibbody.nii.gz
    --s struct.nii.gz --regfrom calibhead.nii.gz
```

EXAMPLE 2B

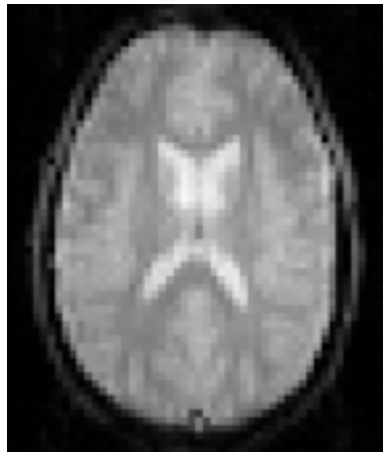
- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ✓
  - ➡ M0 calculation. ←

Calibration image

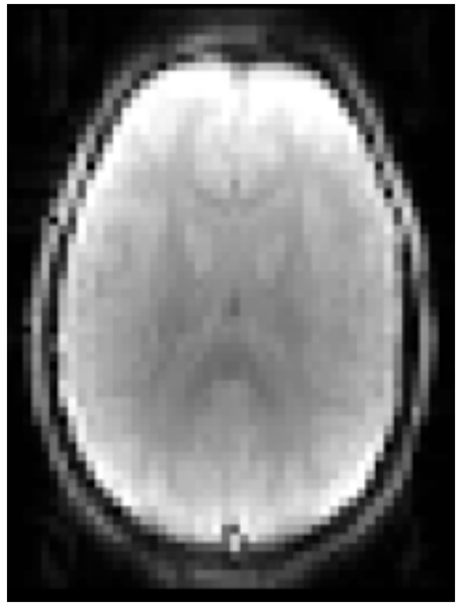


Steady state
TR = 6 s

Calibration reference



Control image



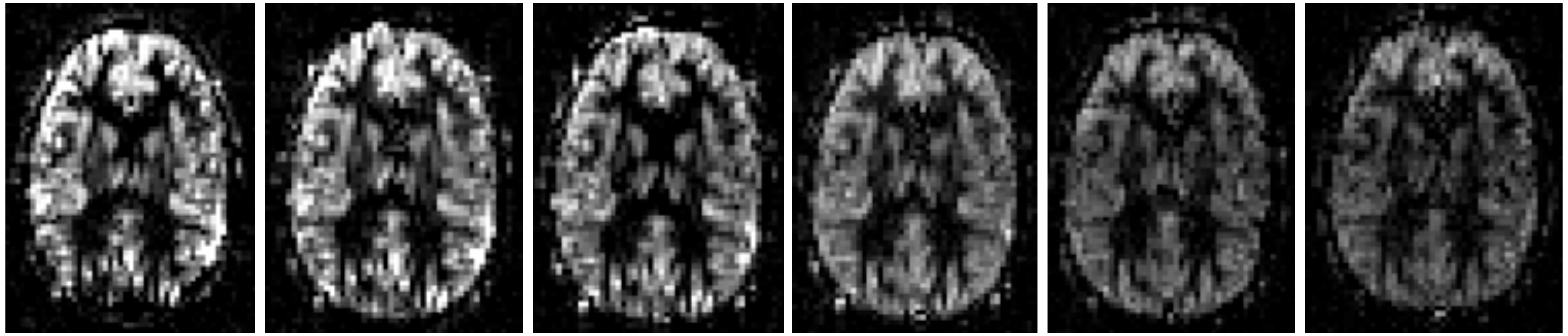
Saturation recovery
t = 2.4 s

```
asl_calib -c {calibration_image / control_image} -s {Structural_image}
  -t {asl2struct.mat} --tissref csf -o {out_dir}
    --mode longtr --tr 6   /   --mode satrecov --tis 2.4
```

EXAMPLE 3

- What I have...
  - ➡ ASL data - multi-TI/PLD
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction.
  - ➡ Kinetic model inversion.
  - ➡ M0 calculation.

pcASL with
labeling duration: 1.4 s
post-label delays: 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 s



TI: 1.65 1.9 2.15 2.4 2.65 2.9

Kinetic Model Inversion

Parameters:

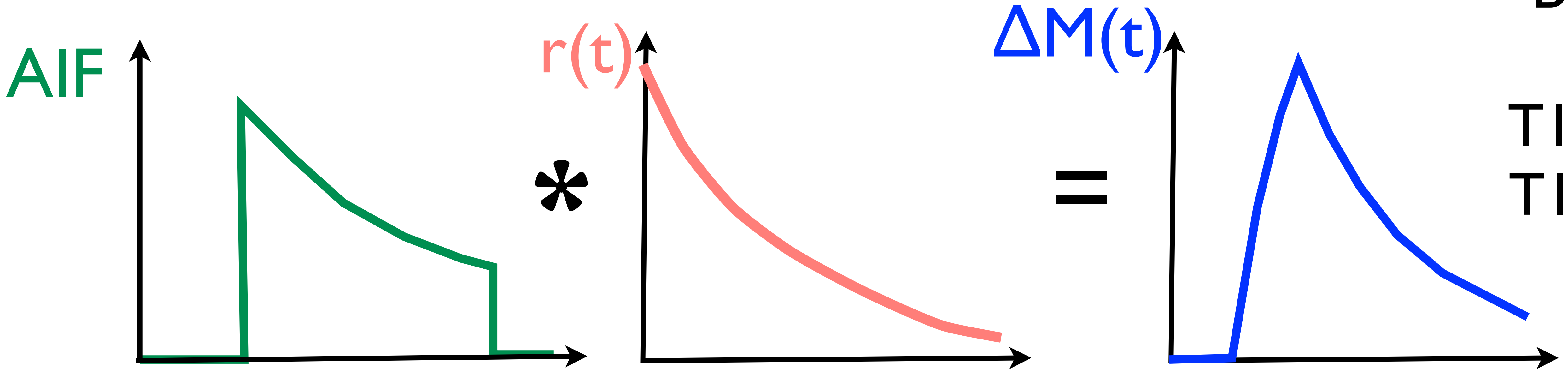
Perfusion - F

Bolus arrival time

Bolus duration

T1 decay (in blood)

T1 decay (in tissue)



$$\Delta M(t) = F \cdot AIF(t) * r(t)$$

KINETIC MODEL INVERSION

Parameters:

Perfusion - F

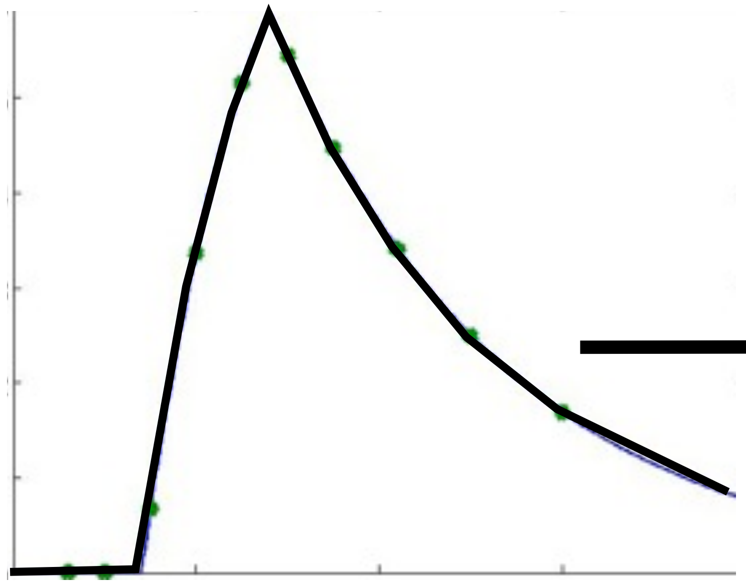
Bolus arrival time

Bolus duration

$T_{1\,\mathrm{tissue}}$

$T_{1\,\mathrm{blood}}$

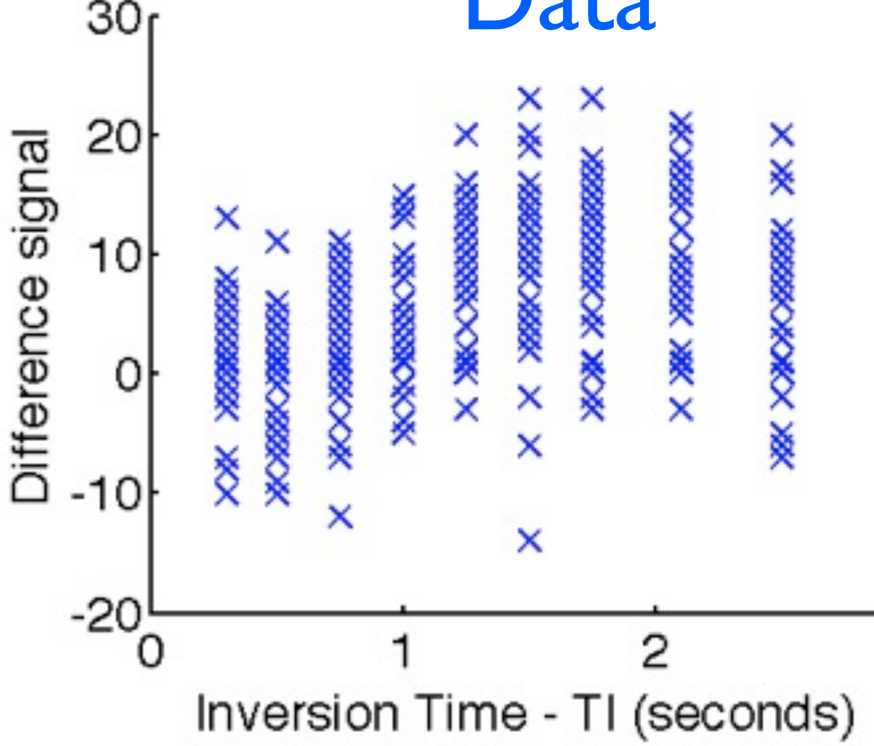
Model



white noise

⊕

Data



Single-TI/PLD

Analytic solution

Multi-TI/PLD

Non-linear fitting
(least squares)

Bayesian inference (BASIL)

Chappell et al., IEEE TSP 57(1), 2009.

Kinetic Model Inversion

- Perfusion
  - ➡ Want to know this - **variable**
- Bolus/Arterial arrival time
  - ➡ Want to correct for this - **variable**

but limited to a sensible range

- Bolus/Label duration
  - ➡ Set by sequence - **fixed**

might not be that well fixed, pASL?

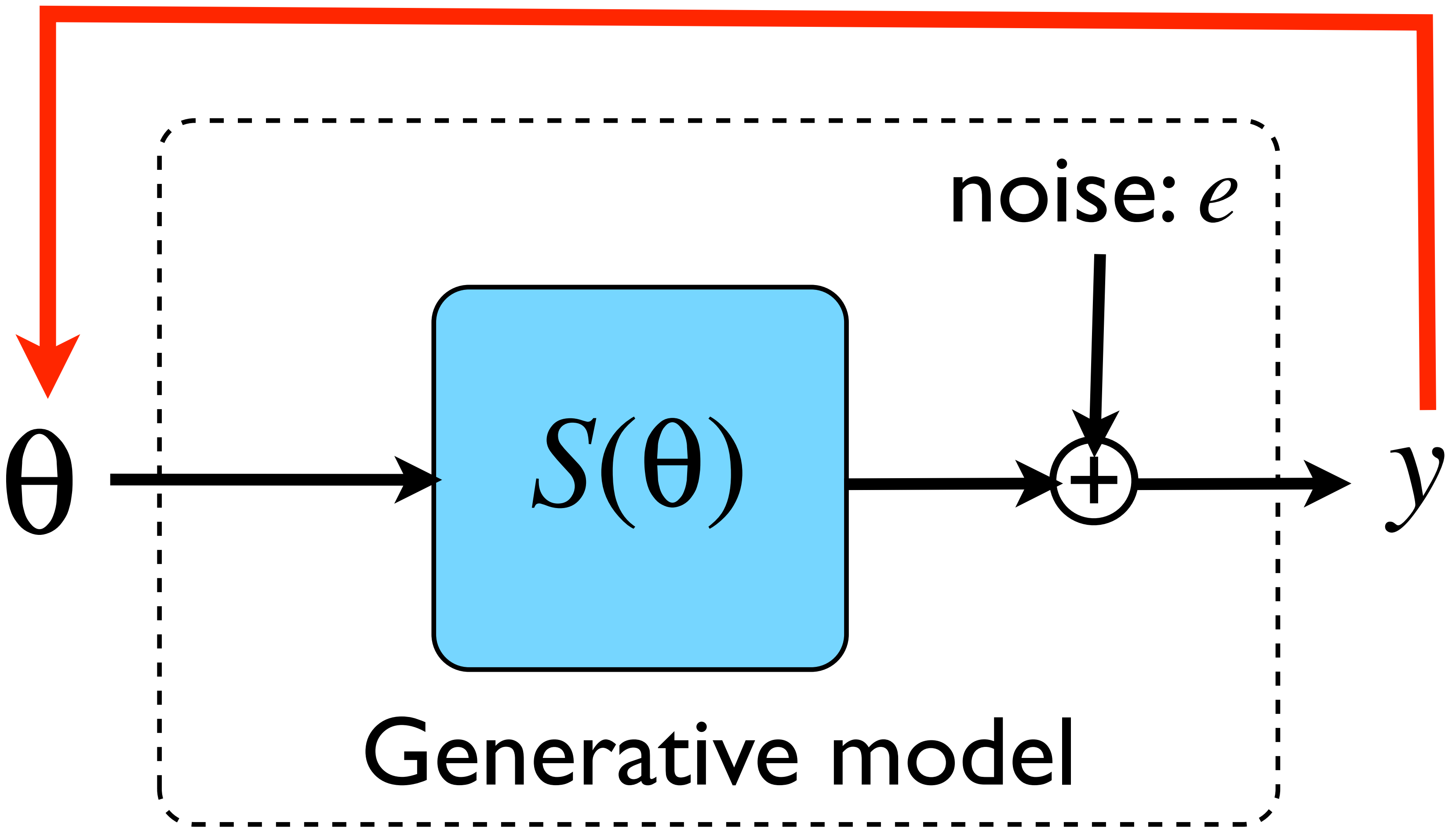
- T_1 tissue
  - ➡ 1.3 s at 3T - **fixed**
- T_1 blood

Doesn't T_1 vary a bit?

  - ➡ 1.66 at 3T - **fixed**

KINETIC MODEL INVERSION

- Bayesian 'inversion'



θ

$S(\theta)$

noise: e

y

Generative model

Posterior:

$\Pr(\theta \mid y)$

Likelihood:

$\Pr(y \mid \theta)$

KINETIC MODEL INVERSION

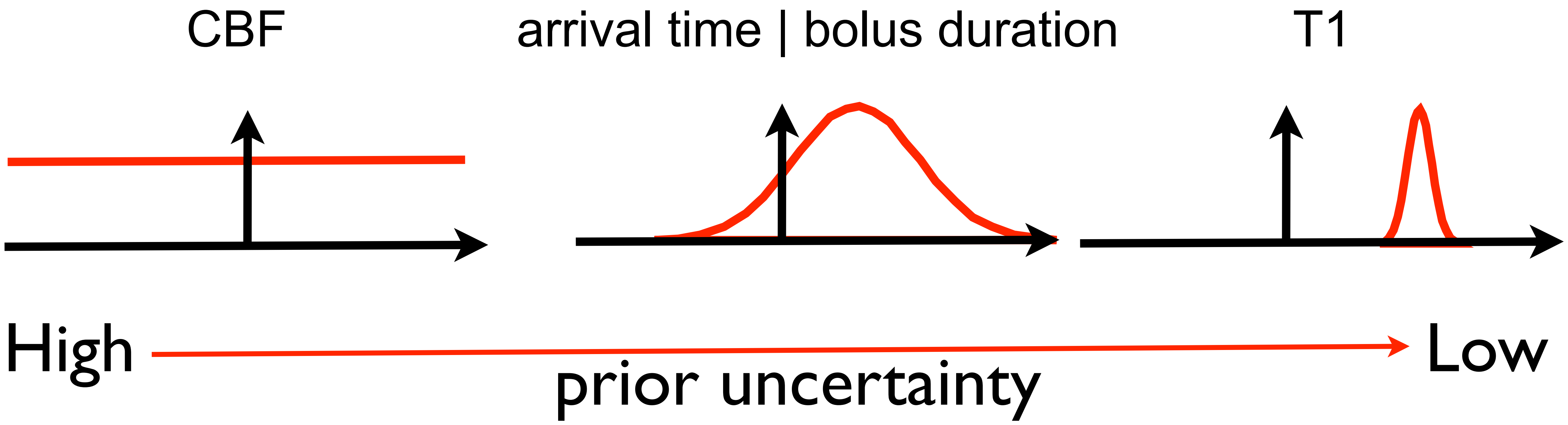
- Bayesian ‘inversion’:

$$\underbrace{\Pr(\theta \mid y)}_{\text{Posterior}} = \frac{\overbrace{\Pr(y \mid \theta)}^{\text{Likelihood}}\overbrace{\Pr(\theta)}^{\text{Prior}}}{\underbrace{\Pr(y)}_{\text{Evidence}}}$$

$$\Pr(\theta \mid y) \propto \Pr(y \mid \theta)\Pr(\theta)$$

Kinetic Model Inversion

- Incorporate presence (or absence) of existing knowledge about parameters.
  - ➡ define prior probability distributions on all the parameters.



Kinetic Model Inversion

Priors:

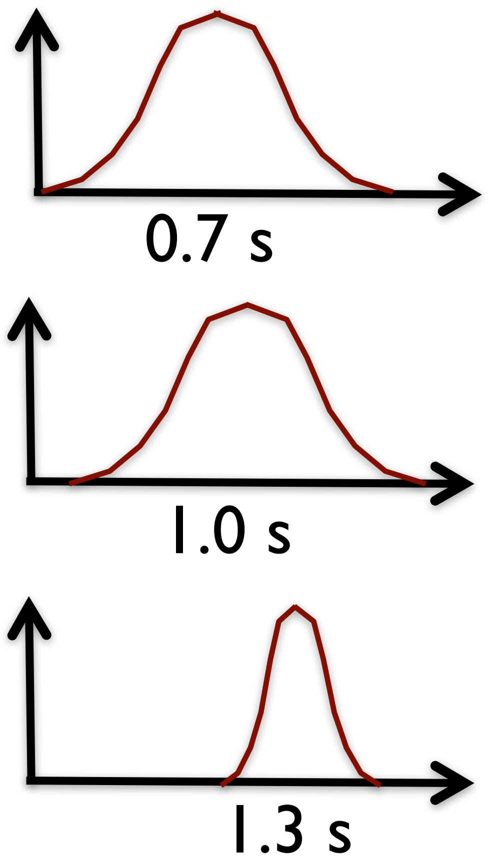
Perfusion

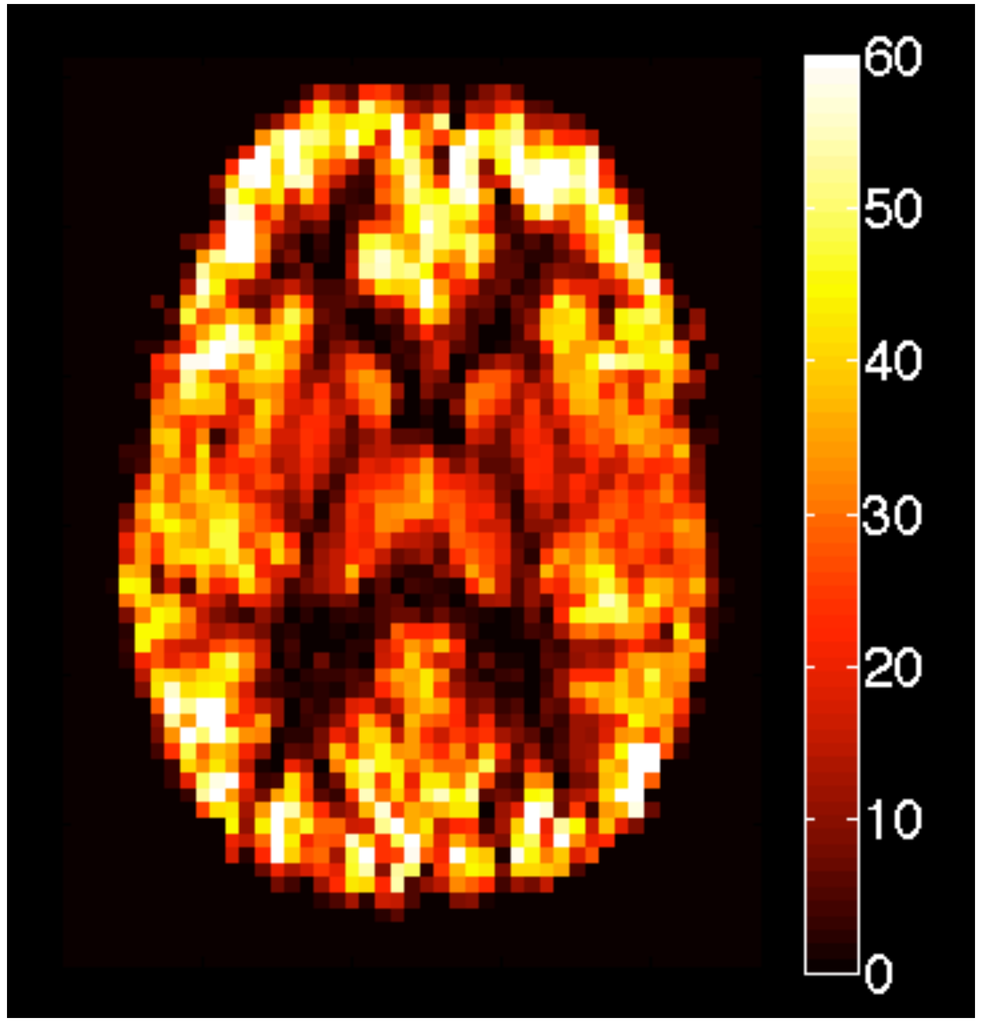
Bolus arrival time

Bolus duration

TI

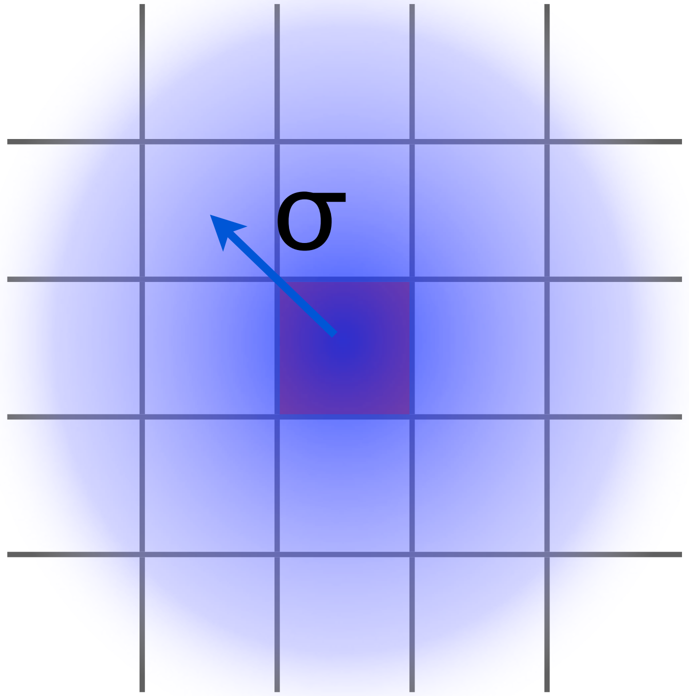
Spatial





Spatial prior:

Prior distribution for perfusion in voxel defined over its neighbours

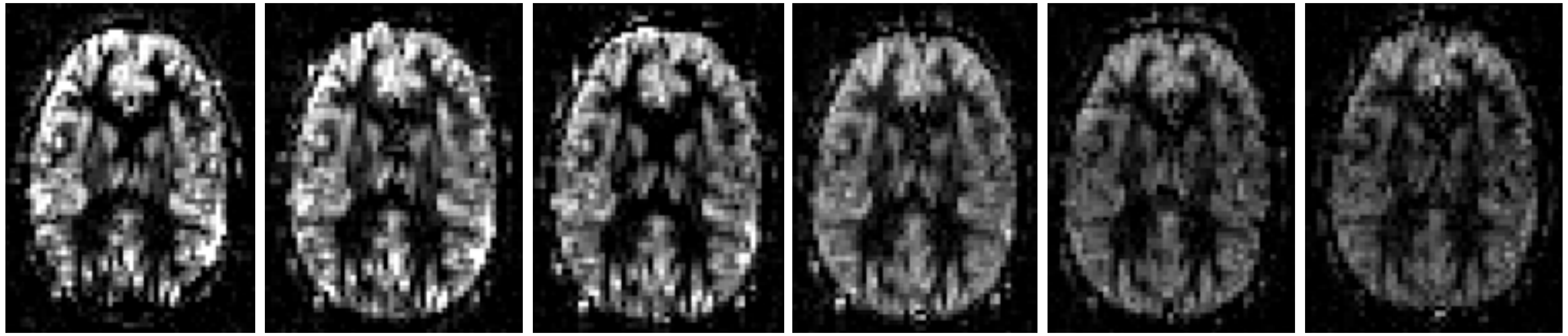


σ - spatial scale of prior (determined from the data)

EXAMPLE 3

- What I have...
  - ➡ ASL data - multi-TI/PLD
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction.
  - ➡ Kinetic model inversion.
  - ➡ M0 calculation.

pcASL with
labeling duration: 1.4 s
post-label delays: 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 s



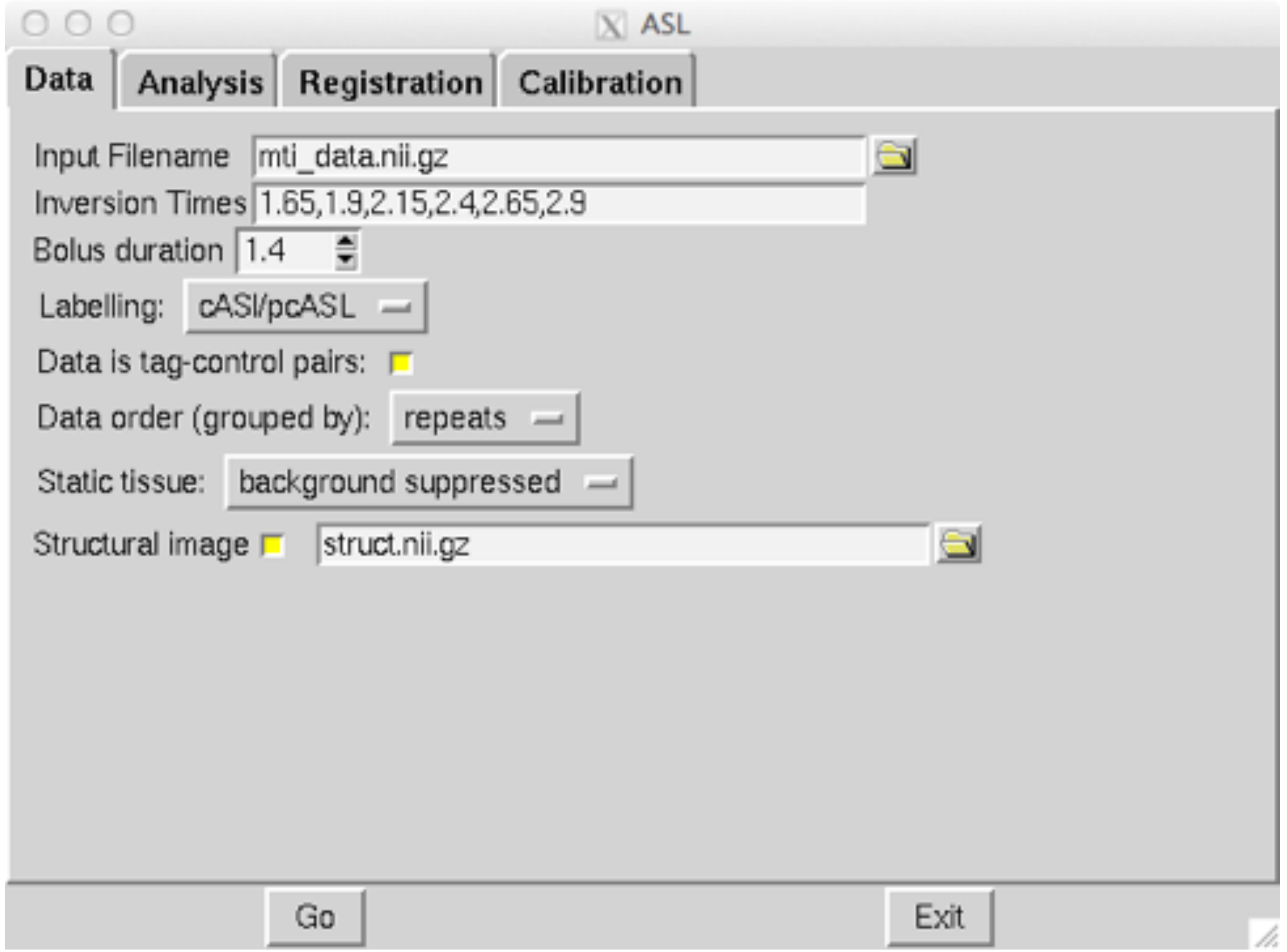
```
oxford_asl -i {ASL_diff_data.nii.gz} -o {result_dir}
  --casl --tis 1.65,1.9,2.15,2.4,2.65,2.9 --bolus 1.4 --bat 1.3 --artoff --fixbolus
  -c {calibration_image.nii.gz} --tr 6 --cref {calibration_reference.nii.gz}
  -s {structural_image.nii.gz} --regfrom {calibration_image.nii.gz)
```

Example 3

pcASL with

tagging duration: 1.4 s

post-label delays: 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 s



Input Filename mti_data.nii.gz

Inversion Times 1.65,1.9,2.15,2.4,2.65,2.9

Bolus duration 1.4

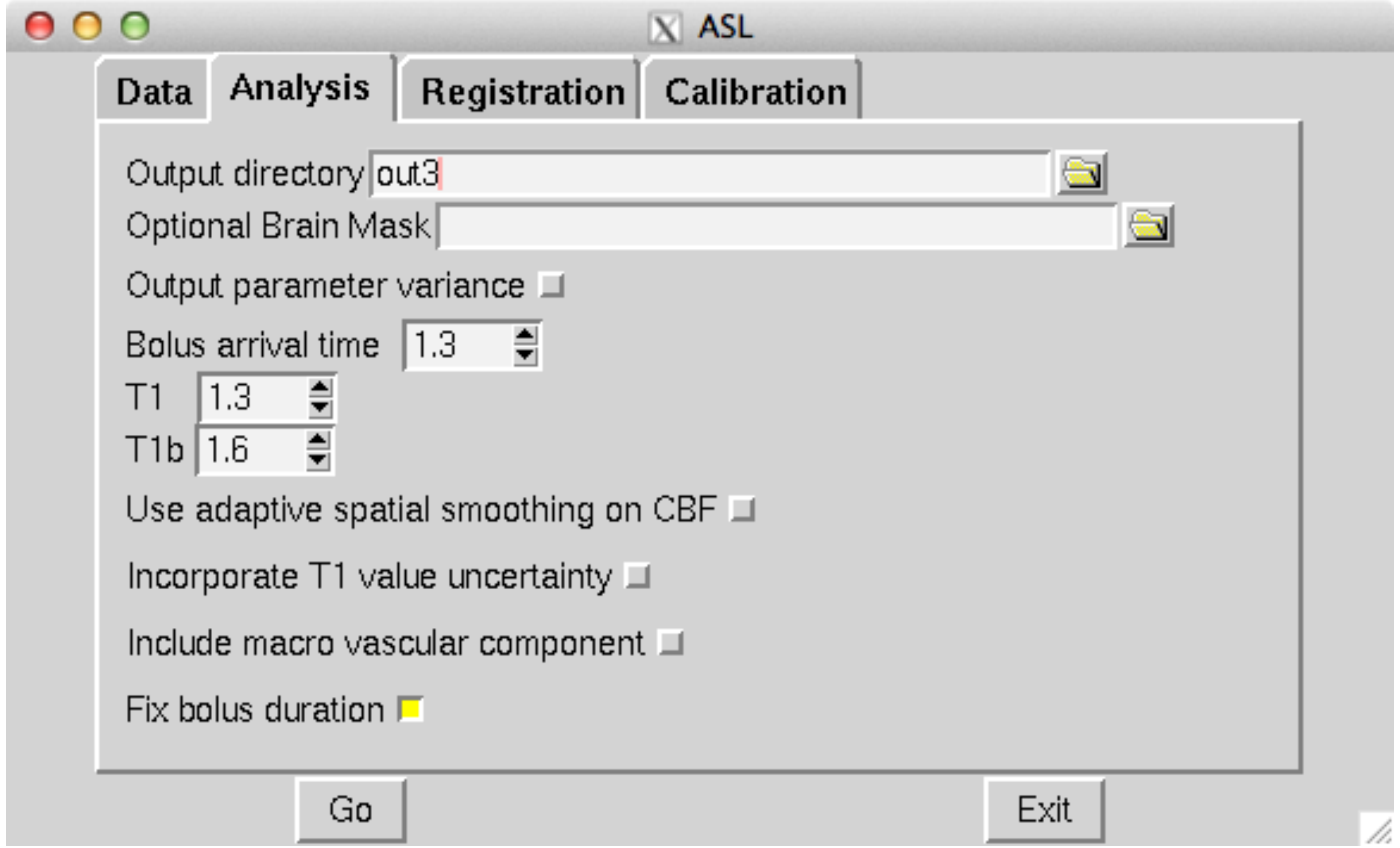
Labelling: cASl/pcASL

Data is tag-control pairs: ☑

Data order (grouped by): repeats

Static tissue: background suppressed

Structural image ☑ struct.nii.gz



Output directory out3

Optional Brain Mask

Output parameter variance ☐

Bolus arrival time 1.3

T1 1.3

T1b 1.6

Use adaptive spatial smoothing on CBF ☐

Incorporate T1 value uncertainty ☐

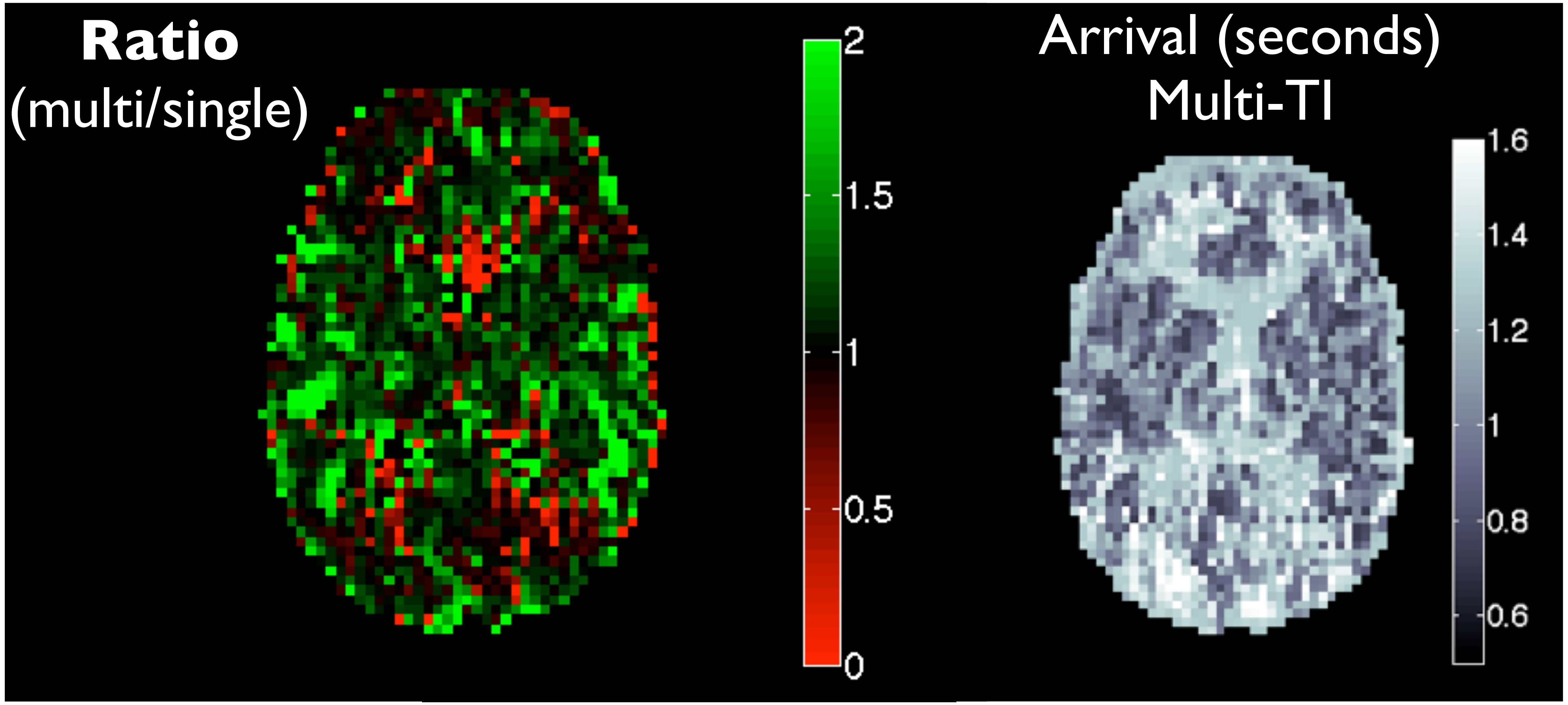
Include macro vascular component ☐

Fix bolus duration ☑

```
> asl_file --data=mti_data.nii.gz --ntis=6 --iaf=tc --diff --out=mti_diffdata --obf=rpt
> oxford_asl -i diffdata.nii.gz -o out3 --casl --tis 1.65,1.9,2.15,2.4,2.65,2.9
  --bolus 1.4 --bat 1.3 --artoff --fixbolus -c calibhead.nii.gz --tr 6
  --cref calibbody.nii.gz -s struct.nii.gz --regfrom calibhead.nii.gz
```

SINGLE-TI VS MULTI-TI

- Data:
  - ➡ pcASL
  - ➡ tagging duration: 1.4 s
  - ➡ Single-TI
    post-label delay: 1.5 s
    Assume BAT of 1.3 s
  - ➡ Multi-TI
    PLDs: 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 s



```
out1/native_space/perfusion_calib.nii.gz
out3/native_space/perfusion_calib.nii.gz
out3/native_space/arrival.nii.gz
```

OUTLINE

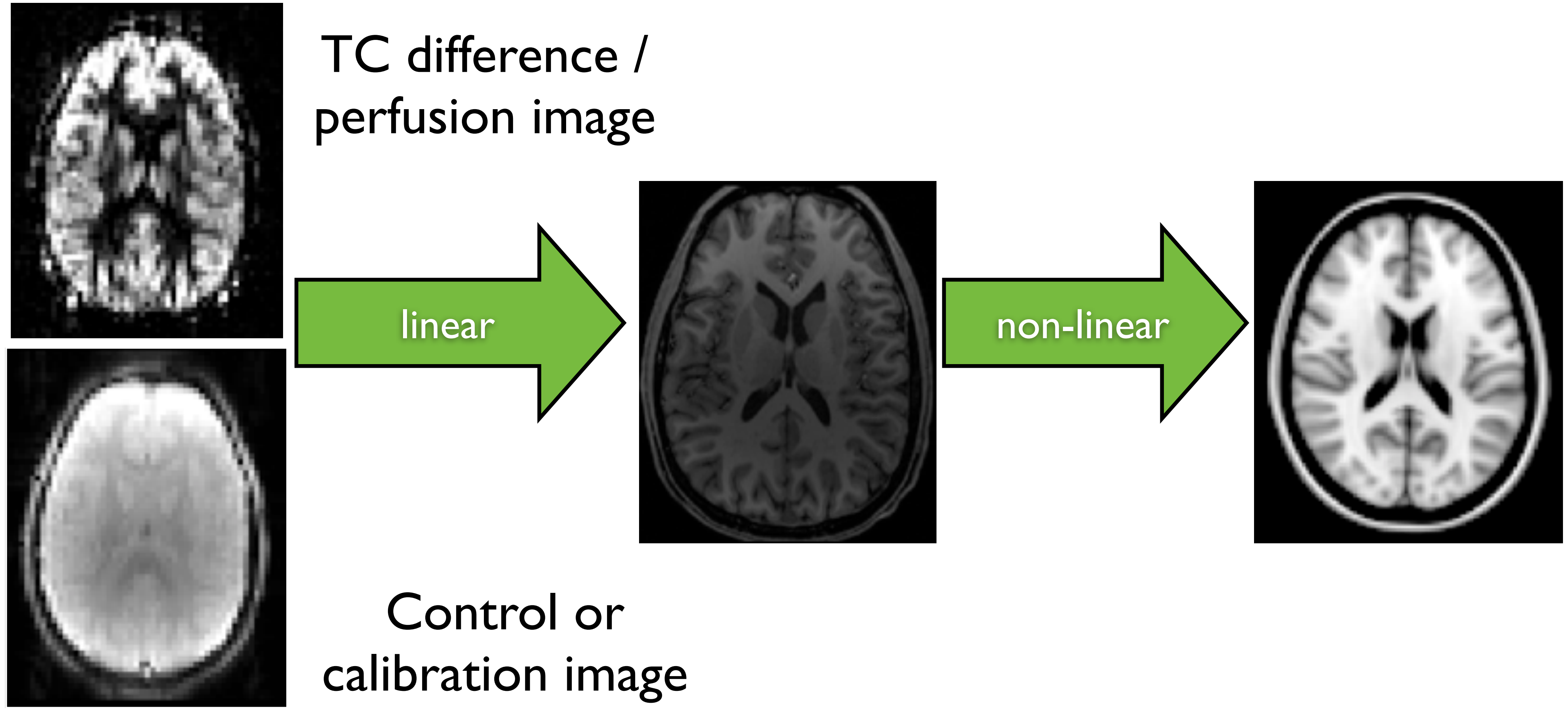
- Acquisition
- Keep it simple!
  - ➡ Perfusion weighted images.
  - ➡ Perfusion fMRI.
- Quantitative perfusion:
  - ➡ A short course in tracer kinetics.
  - ➡ Measuring arterial blood magnetization.
- Preparing for group analysis.
- Advanced quantification:
  - ➡ Macro vascular contamination
  - ➡ Partial Volume Correction

PREPARING FOR GROUP ANALYSIS

- Group analysis and quantitative comparisons between individuals requires consistent representation
- **Consistent geometry:**
  - ➡ 'Spatial' normalization (registration)
  - ➡ Transform perfusion map to a common space, e.g. MNI152
- **Consistent intensity:**
  - ➡ Quantitive maps - perfusion in ml/100g/min.
  - ➡ Intensity normalization to a reference.

PREPARING FOR GROUP ANALYSIS

- Registration to 'standard' space
  - ➡ ASL → Structural
    linear - 6 DOF
  - ➡ Structural → Standard
    linear - 12 DOF
    non-linear



TC difference / perfusion image

linear

non-linear

Control or calibration image

```
oxford_asl ... --s {structural_image.nii.gz} -t {struct2std.mat}
  --regfrom {control/calibration_image.nii.gz)
```

See also: `asl_reg, flirt, fnirt`

PREPARING FOR GROUP ANALYSIS

- **Quantitative maps**
  - ➡ requires estimate of M0a - ‘calibration’ data.
- Pros:
  - ➡ An absolute scale - can potentially relate to physiology
  - ➡ Ought to be able to set consistent thresholds

    e.g. perfusion < 20 ml/100g/min is ischaemia
- Cons:
  - ➡ Requires calibration information.
  - ➡ Global perfusion appears to be quite variable between individuals.

- **Intensity normalization:**
  - ➡ requires a ‘reference’.

    e.g. a brain structure: thalamus

    e.g. a ‘global’ value: mean in GM or WM
- Pros:
  - ➡ No need for calibration.

    NB still might want coil sensitivity correction.
  - ➡ Removes inter subject variability in ‘global’ perfusion.
- Cons:
  - ➡ Relies on a consistent reference.

GROUP ANALYSIS

- ROI
  - ➡ GM / WM(?)

    partial volume issues
  - ➡ Structures
- Voxelwise
- Designs
  - ➡ Group mean
  - ➡ Group differences/paired differences
- Statistics
  - ➡ Linear model
  - ➡ Permutation testing

Absolute perfusion:

A direct physiological measurement

e.g. Asllani et al., JCBFM, 28, 2008.

A consistent baseline (c.f BOLD)

e.g. Wang et. al, MRM, 49, 2003.

Inter subject and inter session variability

e.g Gevers et al., JCBFM, 31, 2011.
Petersen et al., NeuroImage, 49(1), 2011.

Arrival time (multi-TI/PLD):

Potential confound

An extra quantitative measurement

e.g. Bokkers et al., AJNR, 29(9), 2008.
MacIntosh et al, AJNR, 33(10), 2012.

```
Feat (higher-level analysis)
Randomise
```

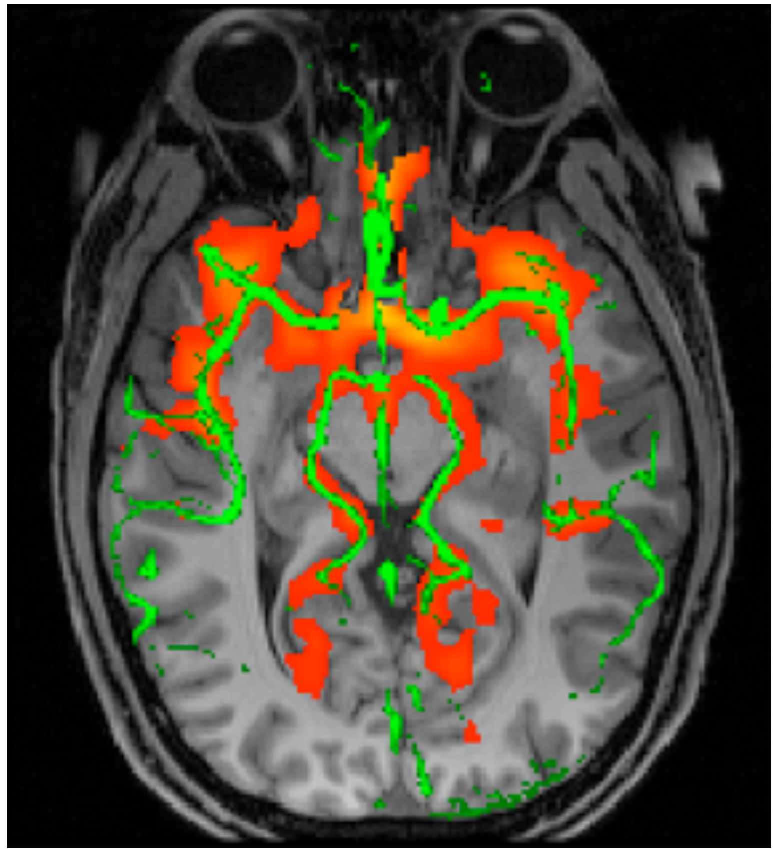
OUTLINE

- Acquisition
- Keep it simple!
  - ➡ Perfusion weighted images.
  - ➡ Perfusion fMRI.
- Quantitative perfusion:
  - ➡ A short course in tracer kinetics.
  - ➡ Measuring arterial blood magnetization.
- Preparing for group analysis.
- Advanced quantification:
  - ➡ Macro vascular contamination
  - ➡ Partial Volume Correction

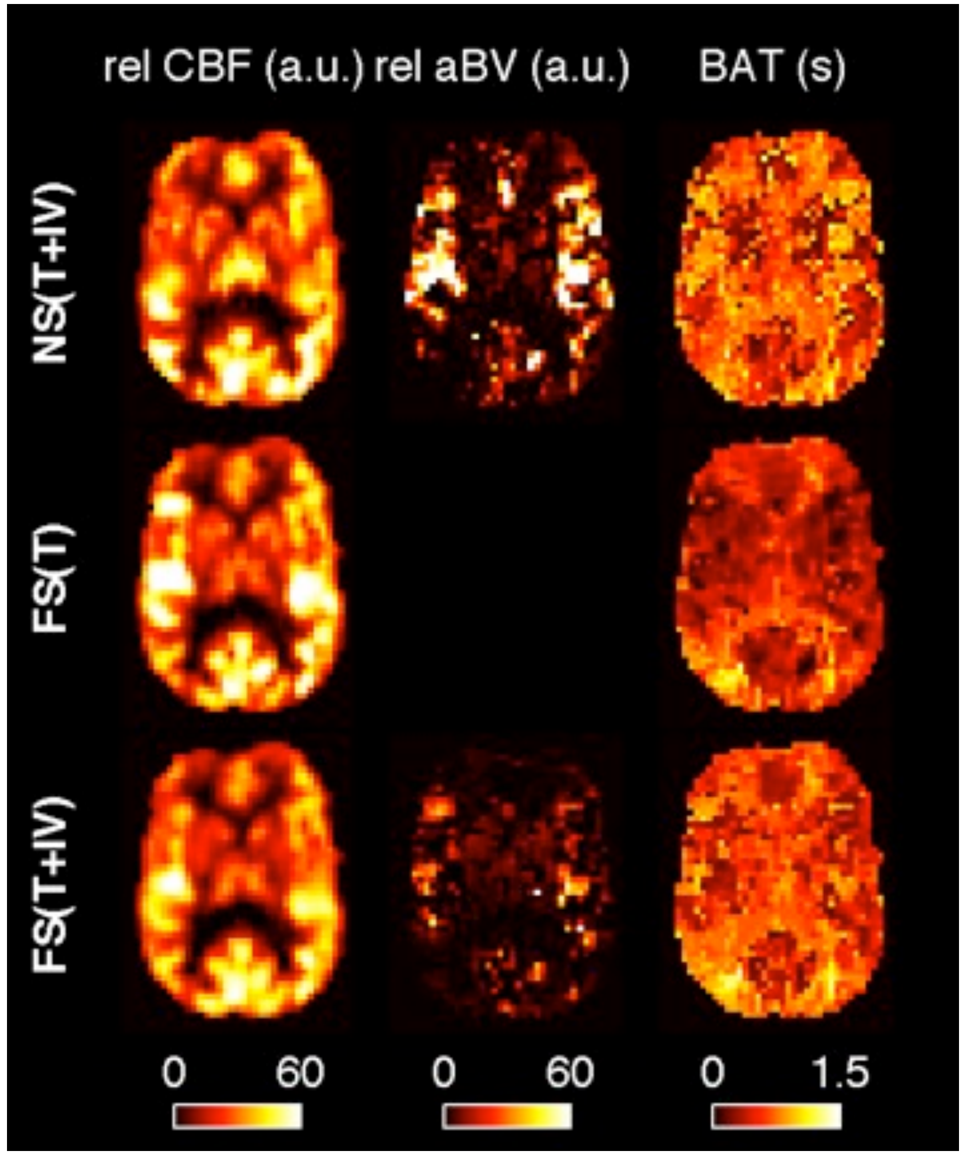
ADVANCED: MACRO VASCULAR CONTAMINATION

- Early TIs may contain label still within larger arteries.
  - ➡ perfusion overestimation

- Use long TI/PLD(s)
- Use flow suppressing gradients
- Include in model - multi-TI data
  - ➡ provides estimate of arterial blood volume



aBV and TOF MIP



`oxford_asl:` MV component included by default, use `--artoff` to turn off

Ye et al., MRM 37(2), 1997.
Chappell et al., MRM 63(5), 2010.

ADVANCED: MACRO VASCULAR CONTAMINATION

- An extended model for ASL:

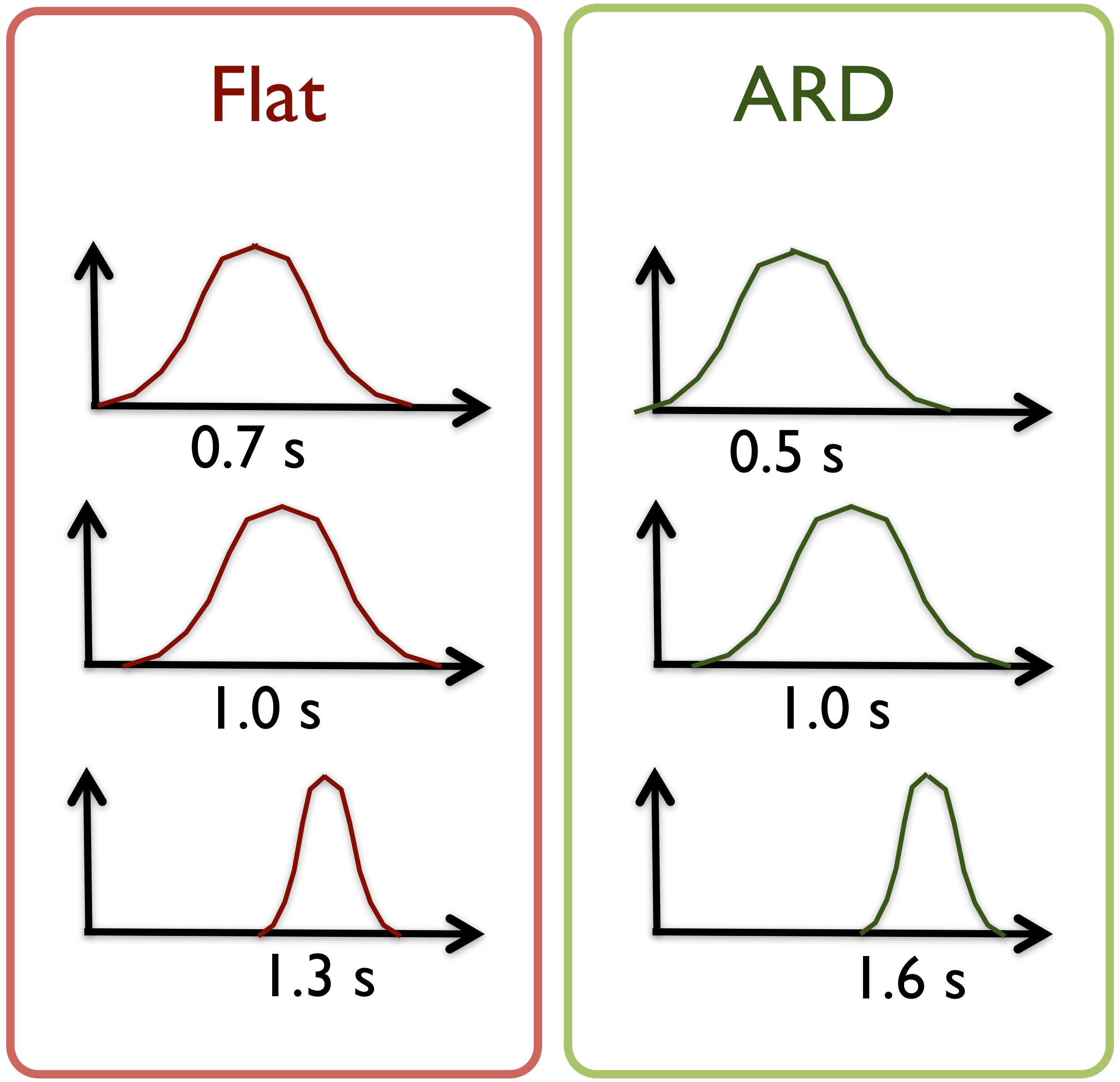
$$\Delta M(t) = CBF\ \Delta M_{tiss}(t) + aBV\ \Delta M_{IV}(t)$$

CBF/aBV

Bolus arrival time

Bolus duration

T1

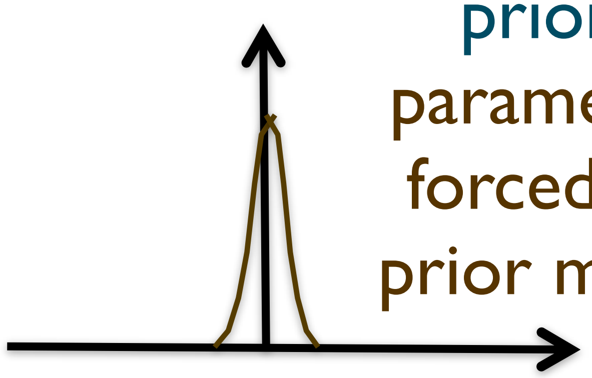


ARD prior: ~N(0,*v*)

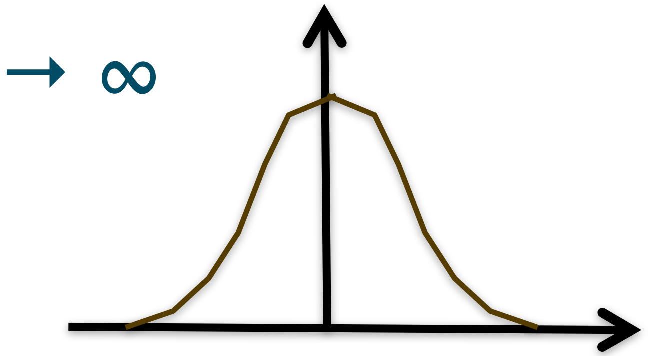
v determines the **relevance** of the prior. *v* is determined from the data.

v → 0

Restrictive prior: parameter forced to prior mean



v → ∞

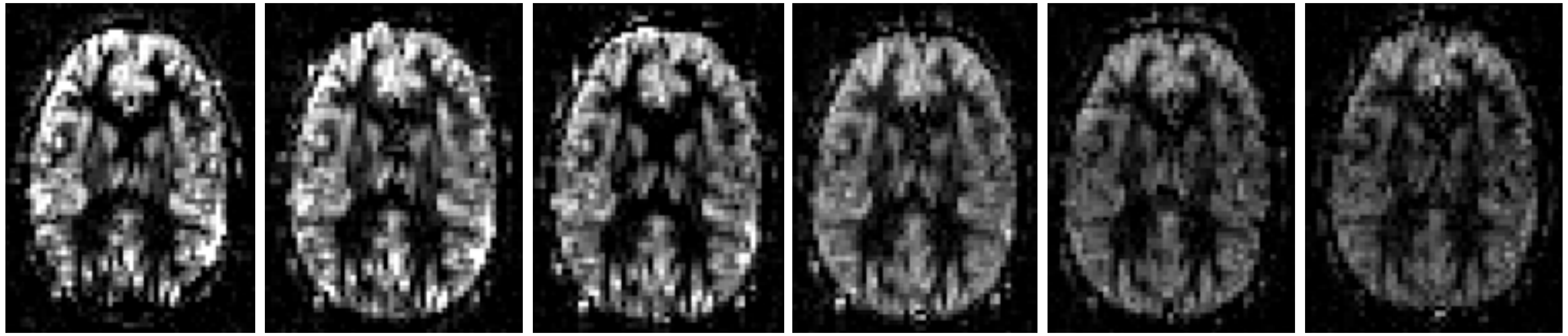


Liberal prior: parameter free to be estimated from data

EXAMPLE 4

- What I have...
  - ➡ ASL data - multi-TI/PLD
  - ➡ (calibration images)
- What I want...
  - ➡ Perfusion in ml/100g/min
  - ➡ **Arterial blood volume in ml/ml.**
- What should I do?
  - ➡ Tag-control subtraction.
  - ➡ Kinetic model inversion.
  - ➡ M0 calculation.

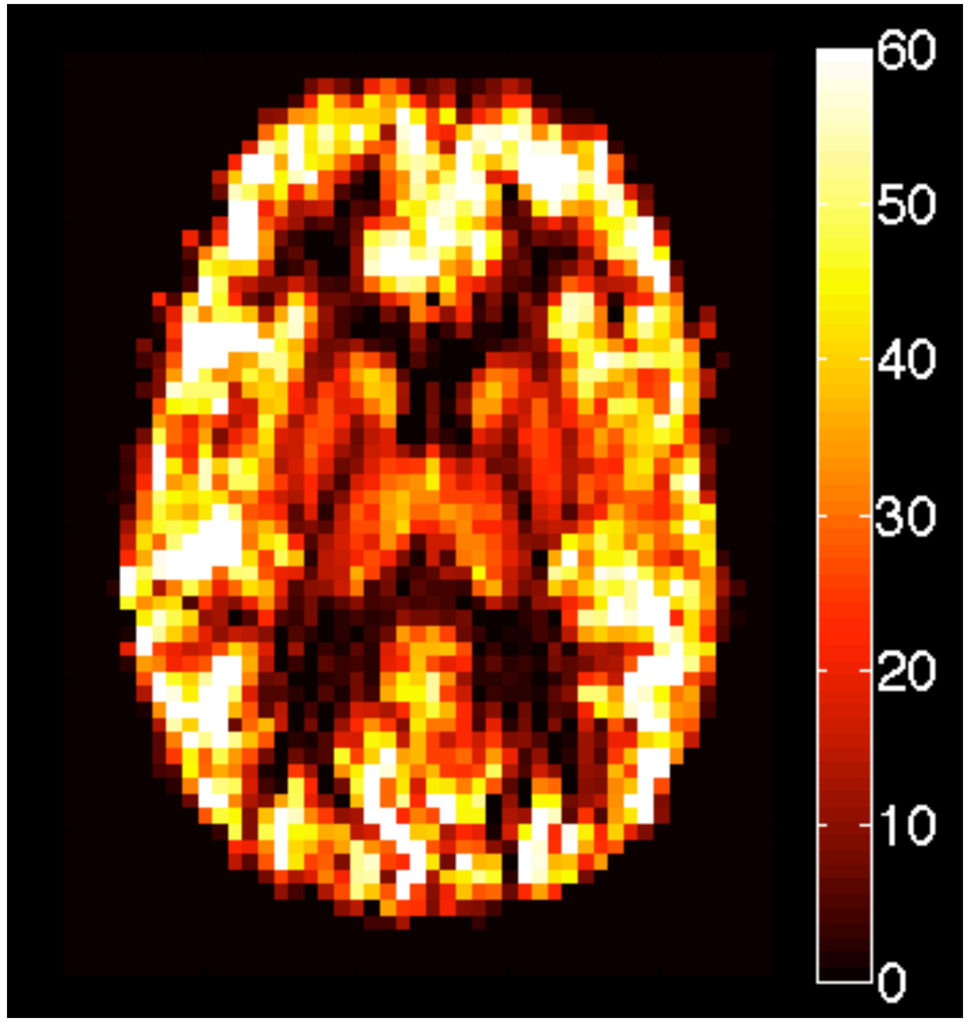
pcASL with
labeling duration: 1.4 s
post-label delays: 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 s



```
oxford_asl -i {ASL_diff_data.nii.gz} -o {out4}
  --casl --tis 1.65,1.9,2.15,2.4,2.65,2.9 --bolus 1.4 --bat 1.3 ~~--artoff~~ --fixbolus
  -c {calibration_image.nii.gz} --tr 6 --cref {calibration_reference.nii.gz}
  -s {structural_image.nii.gz} --regfrom {calibration_image.nii.gz)
```

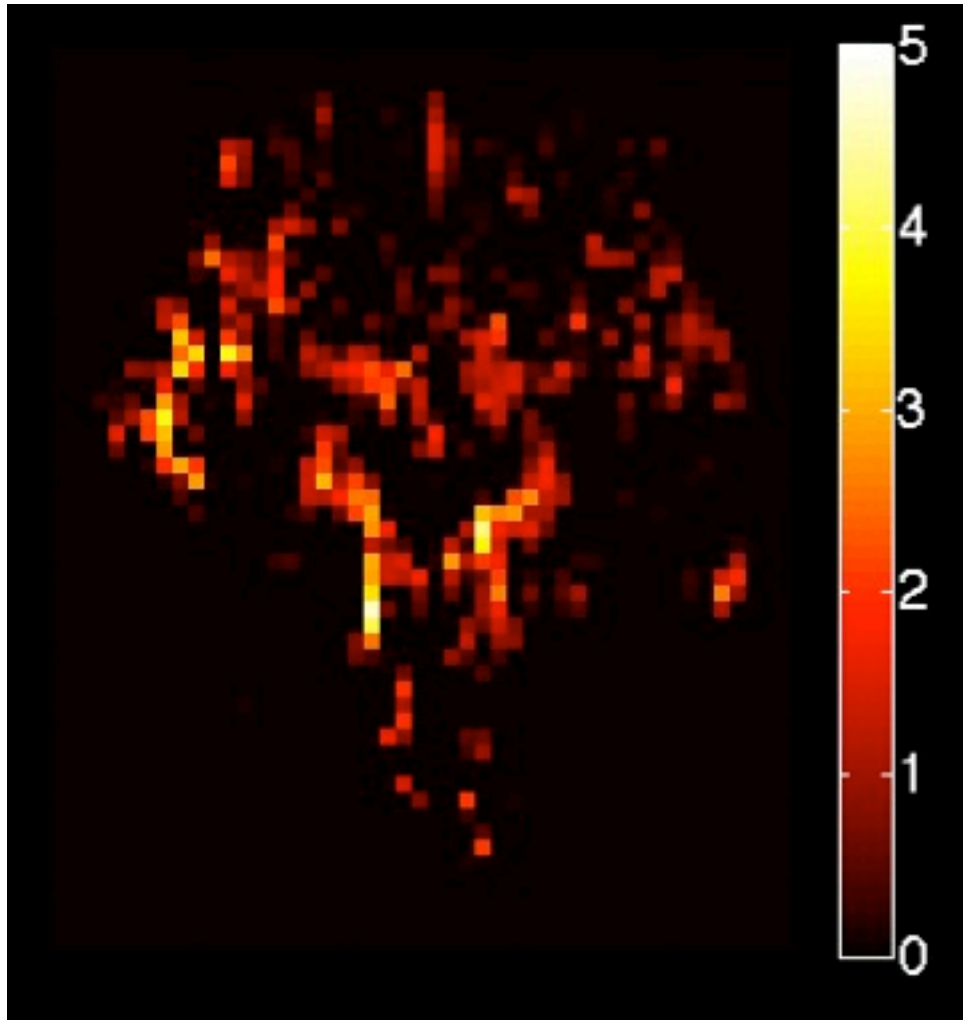
EXAMPLE 4

Perfusion ml/100g/min



middle slice

Arterial blood volume % (ml/ml * 100)



lower slice ~ Circle of Willis

```
out2/native_space/perfusion_calib.nii.gz
out4/native_space/aCBV_calib.nii.gz
```

ADVANCED: PARTIAL VOLUME CORRECTION

- Partial voluming of grey and white matter inevitable.
- Leads to GM perfusion underestimation
  - ➡ WM perfusion < GM
  - ➡ WM blood arrival > GM

- Correction
  - ➡ PV estimates from segmentation of structural image.

    Note: partial volume estimates NOT a hard segmentation or probabilities.
  - ➡ Make separate GM and WM perfusion estimates in every voxel.

    An under determined problem.

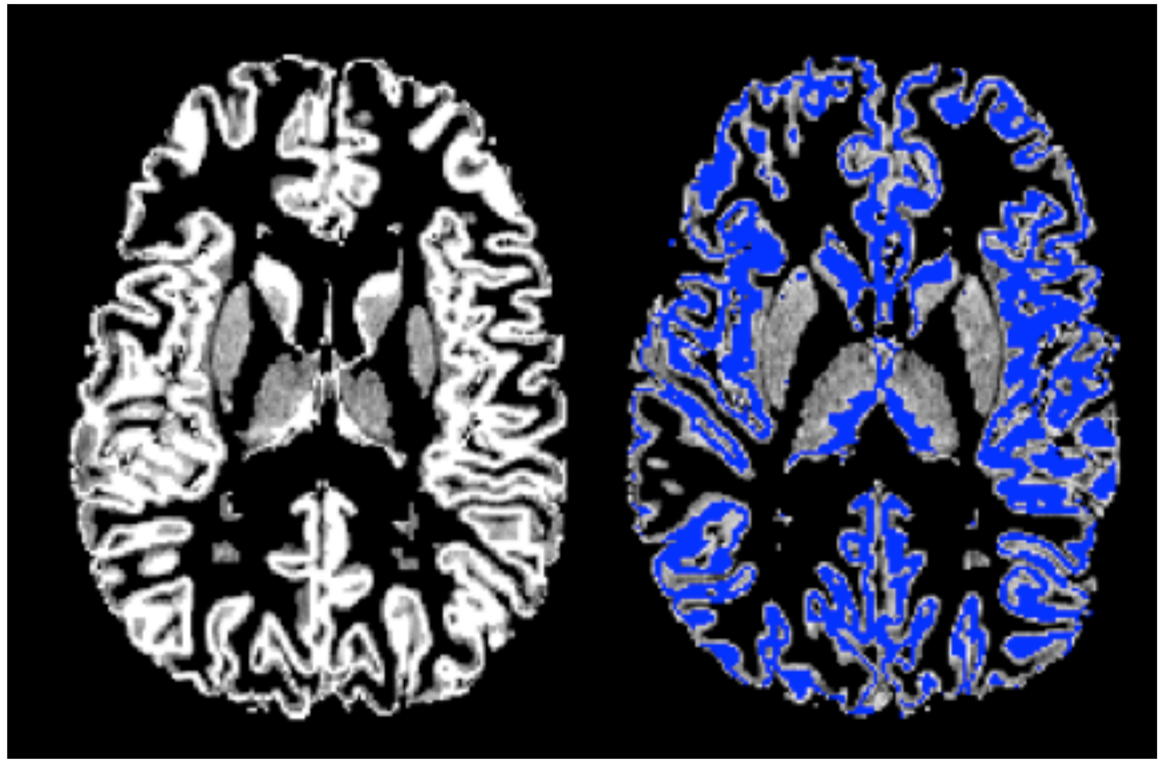
ADVANCED: PARTIAL VOLUME CORRECTION

- Does it matter that much?
  - ➡ Resolution of ASL ~ 3 x 3 x 5 mm
  - ➡ Cortical thickness ~ 2 - 4 mm
- Unlikely to have many pure GM or WM voxels in the cortex

Structural resolution

Partial Volume Estimate

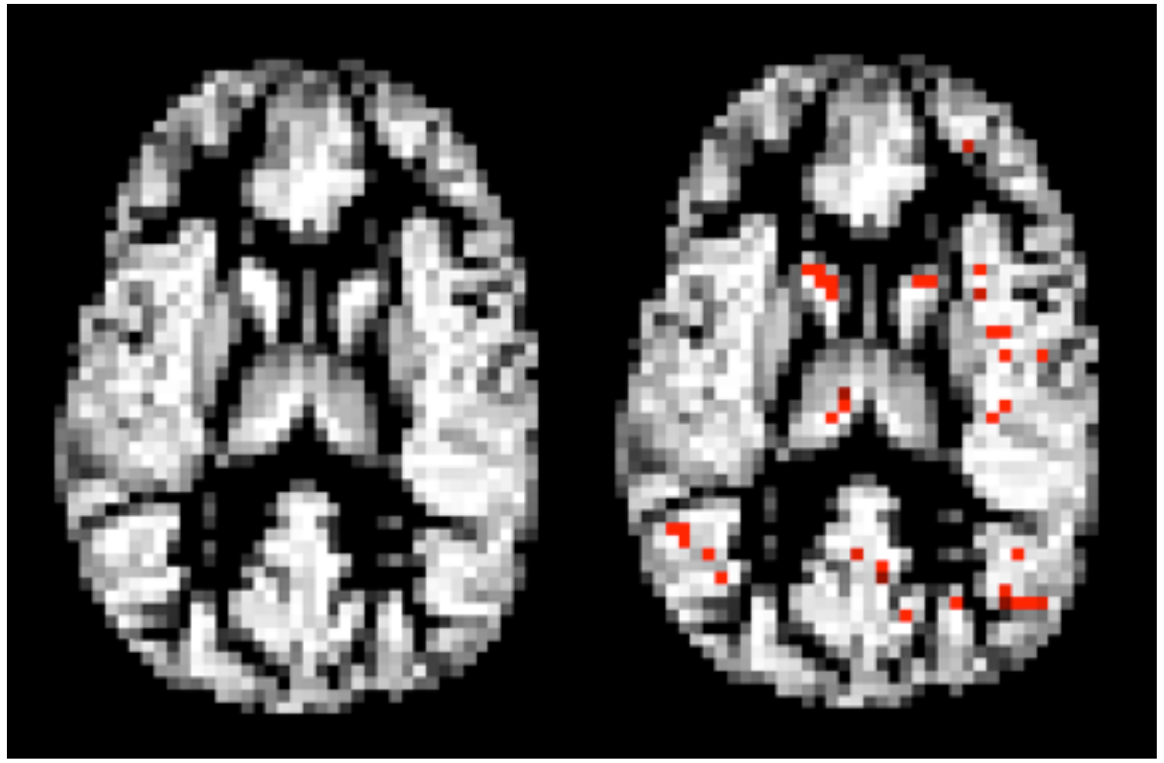
Threshold at 90%



ASL resolution

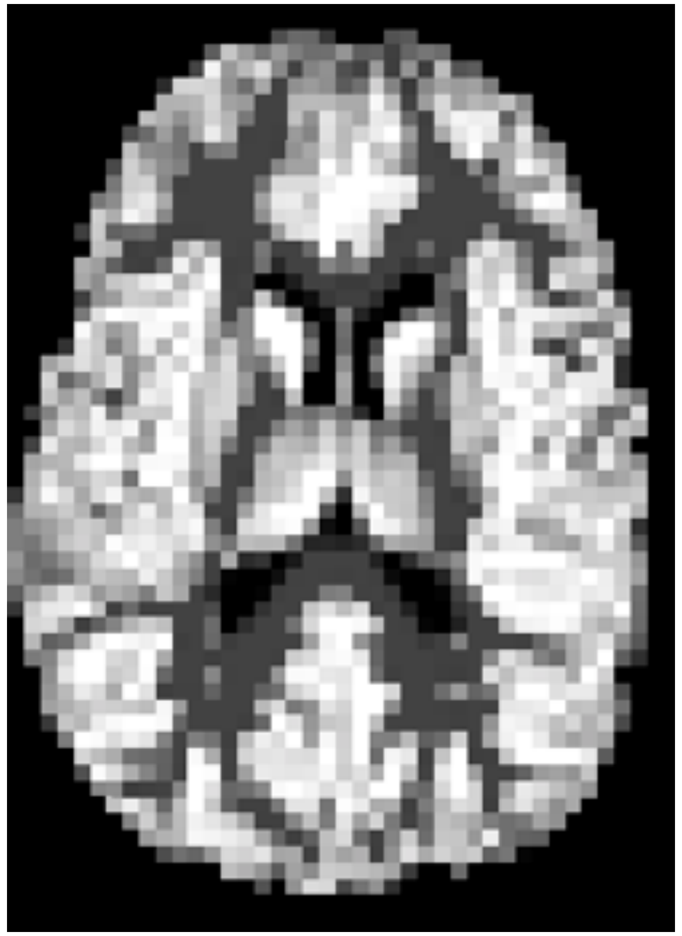
Partial Volume Estimate

Threshold at 90%

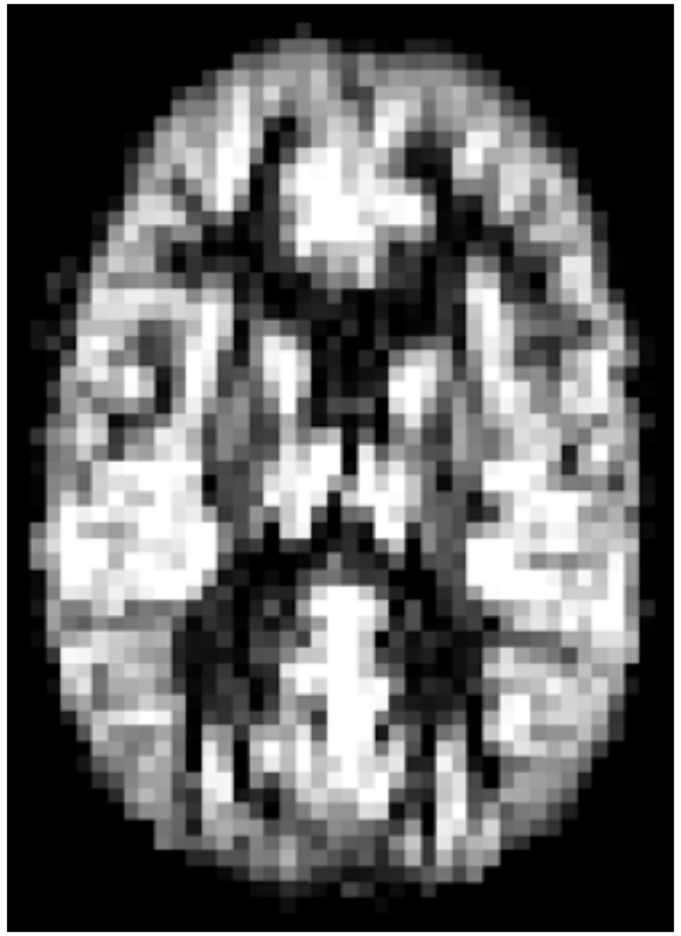


ADVANCED: PARTIAL VOLUME CORRECTION

- Does it matter that much?
  - ➡ Resolution of ASL ~ 3 x 3 x 5 mm
  - ➡ Cortical thickness ~ 2 - 4 mm
- What is this?



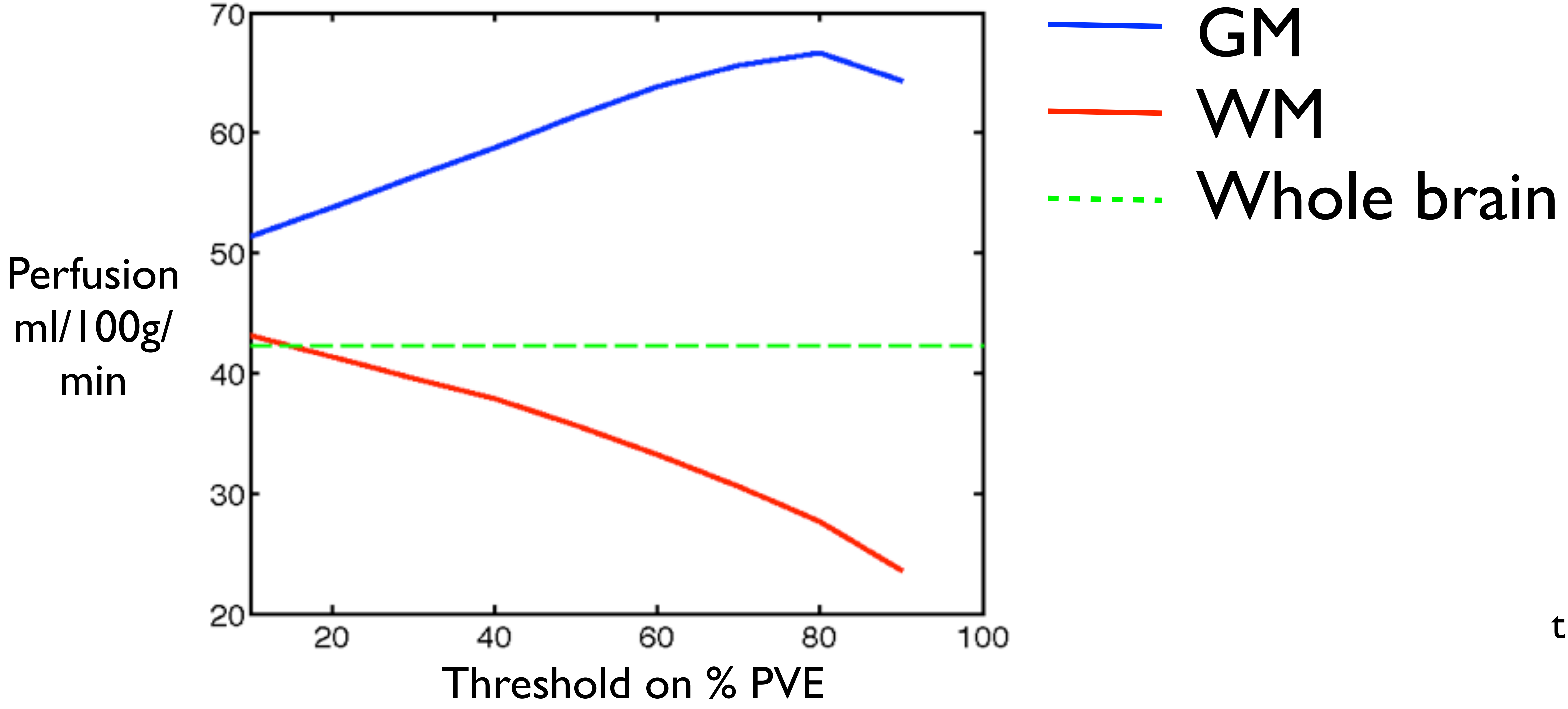
60 * PVE_{GM} + 10 * PVE_{WM}



Estimated perfusion from ASL

Advanced: Partial Volume Correction

- What do we mean when we report GM or WM perfusion?

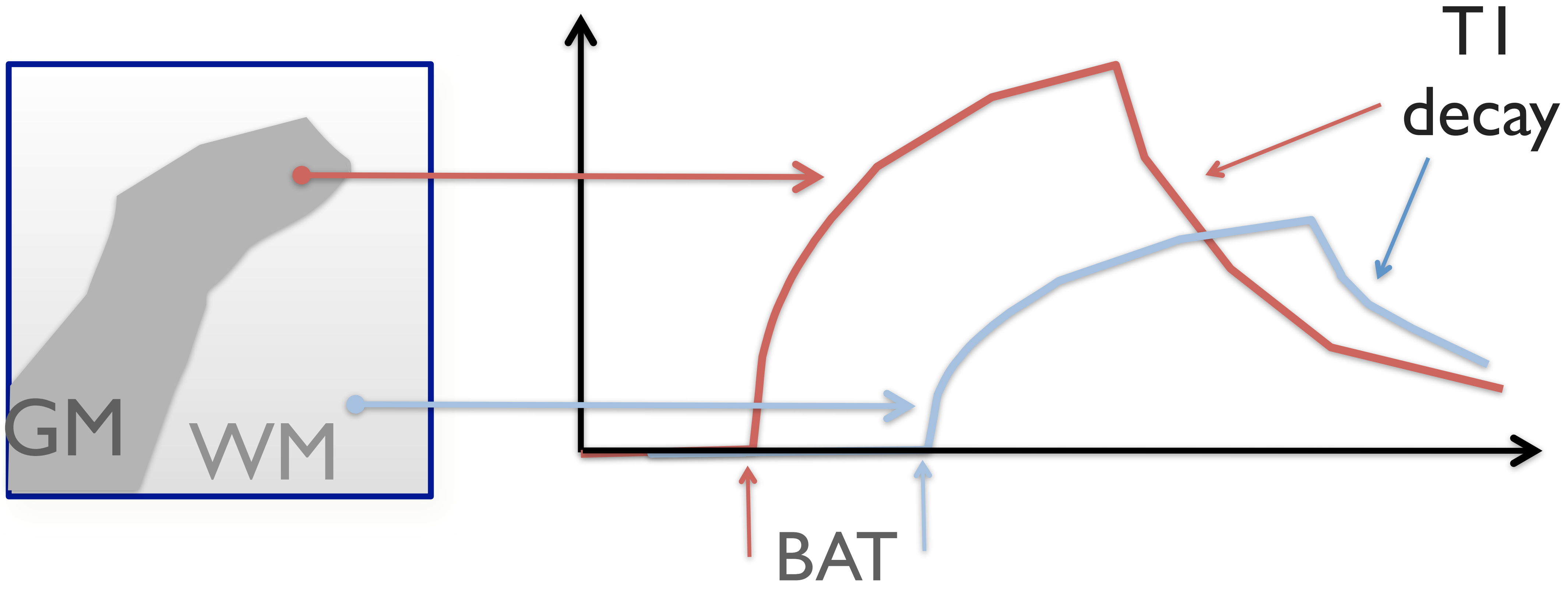


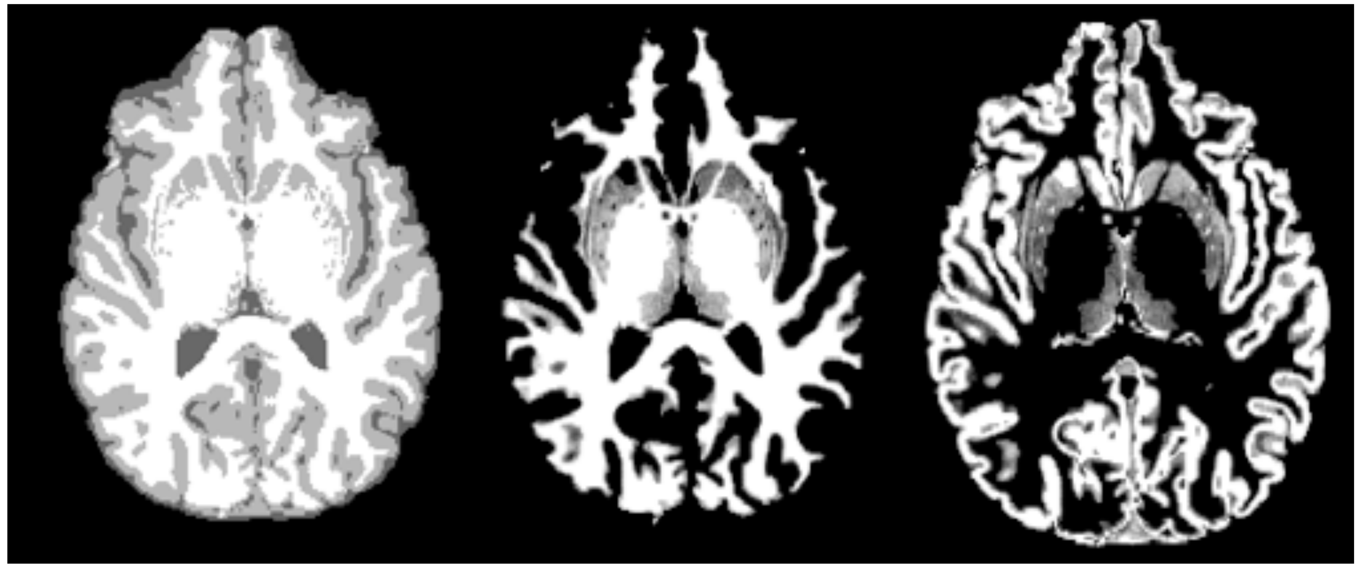
GM mask threshold at 90%

```
oxford_asl ... --report
```

ADVANCED: PARTIAL VOLUME CORRECTION

- Partial volume correction exploiting kinetic data:





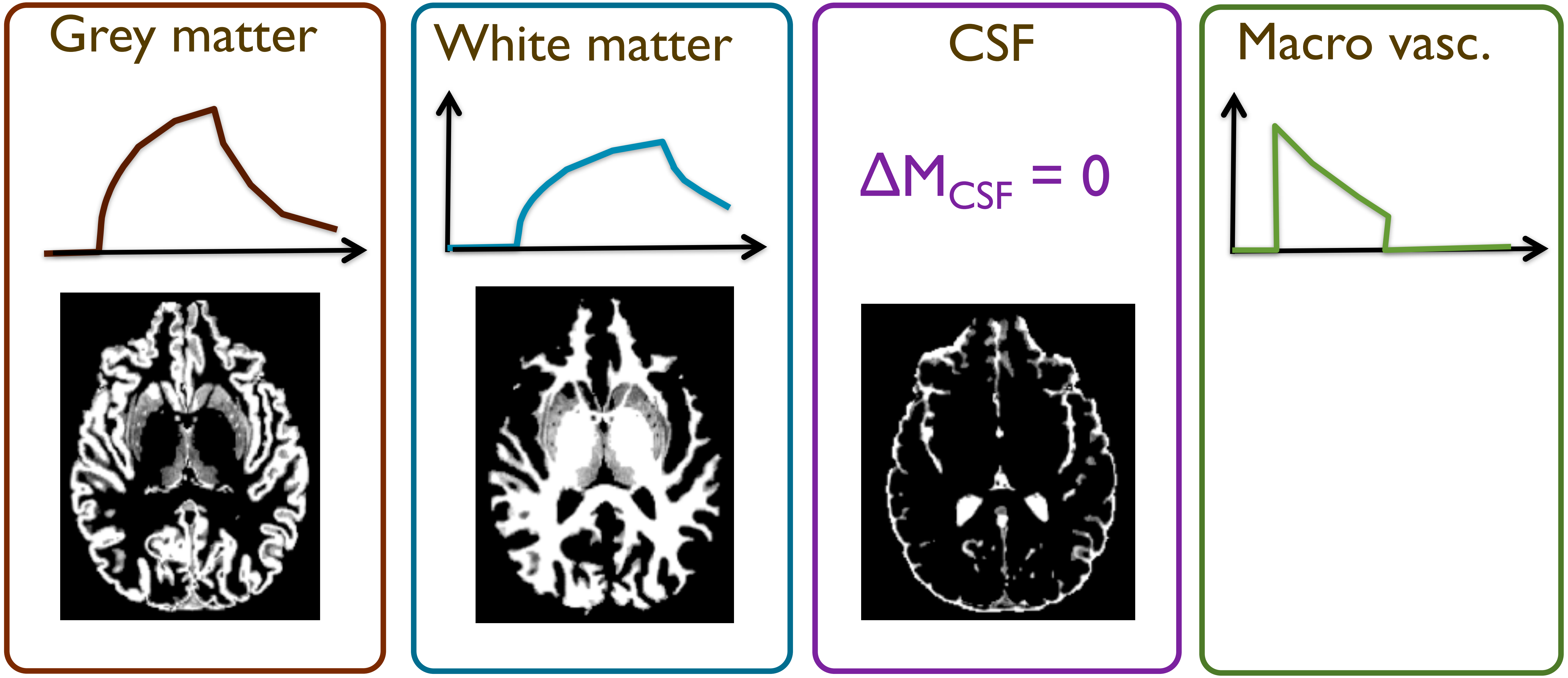
➡ CBF: GM > WM

➡ Bolus arrival: WM > GM

ADVANCED: PARTIAL VOLUME CORRECTION

- Multi-component model:

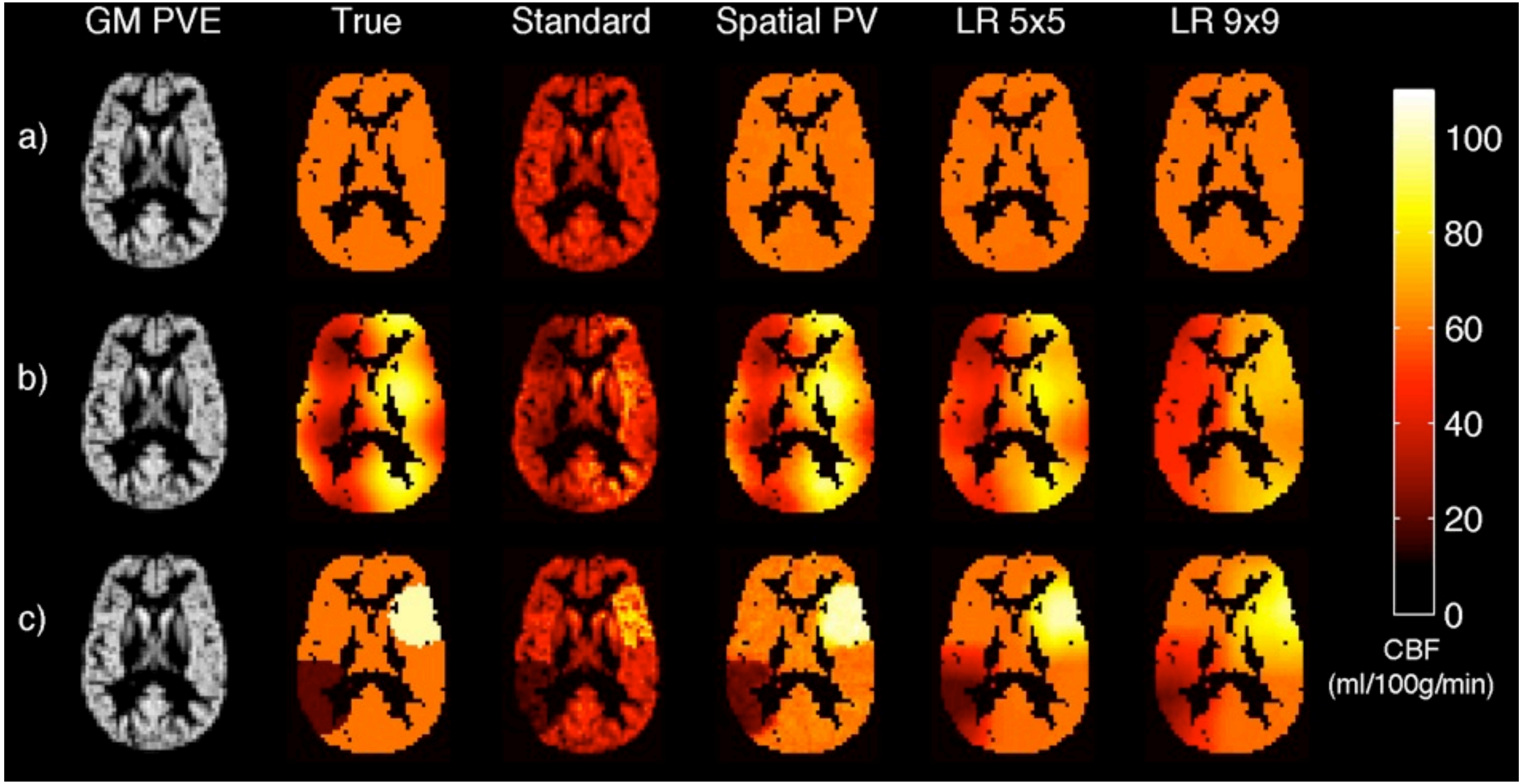
$$\Delta M(t) = PV_{GM}\Delta M_{GM}(t) + PV_{WM}\Delta M_{WM}(t) + PV_{CSF}\Delta M_{CSF}(t) + aBV\,\Delta M_{MV}(t)$$



$$\Delta M_{CSF} = 0$$

- Spatial priors on CBF for GM and WM

ADVANCED: PARTIAL VOLUME CORRECTION

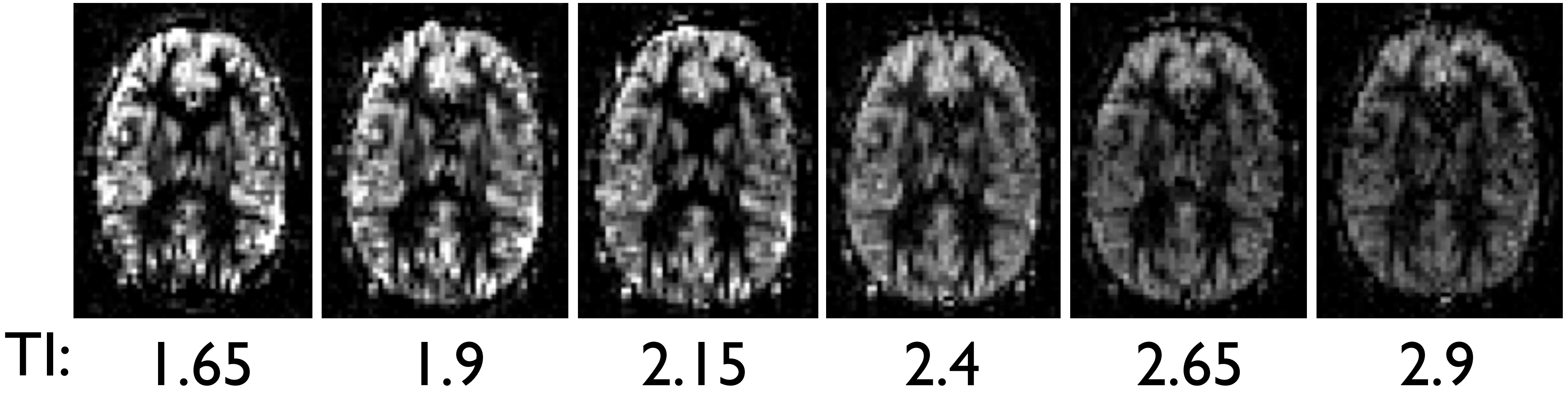


Chappell et al., MRM 65(4), 2011.

EXAMPLE 5

- What I have...
  - ➡ ASL data - multi-TI/PLD
  - ➡ (calibration images)
- What I want...
  - ➡ Grey matter perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction.
  - ➡ Kinetic model inversion.
  - ➡ M0 calculation.
  - ➡ Partial volume correction

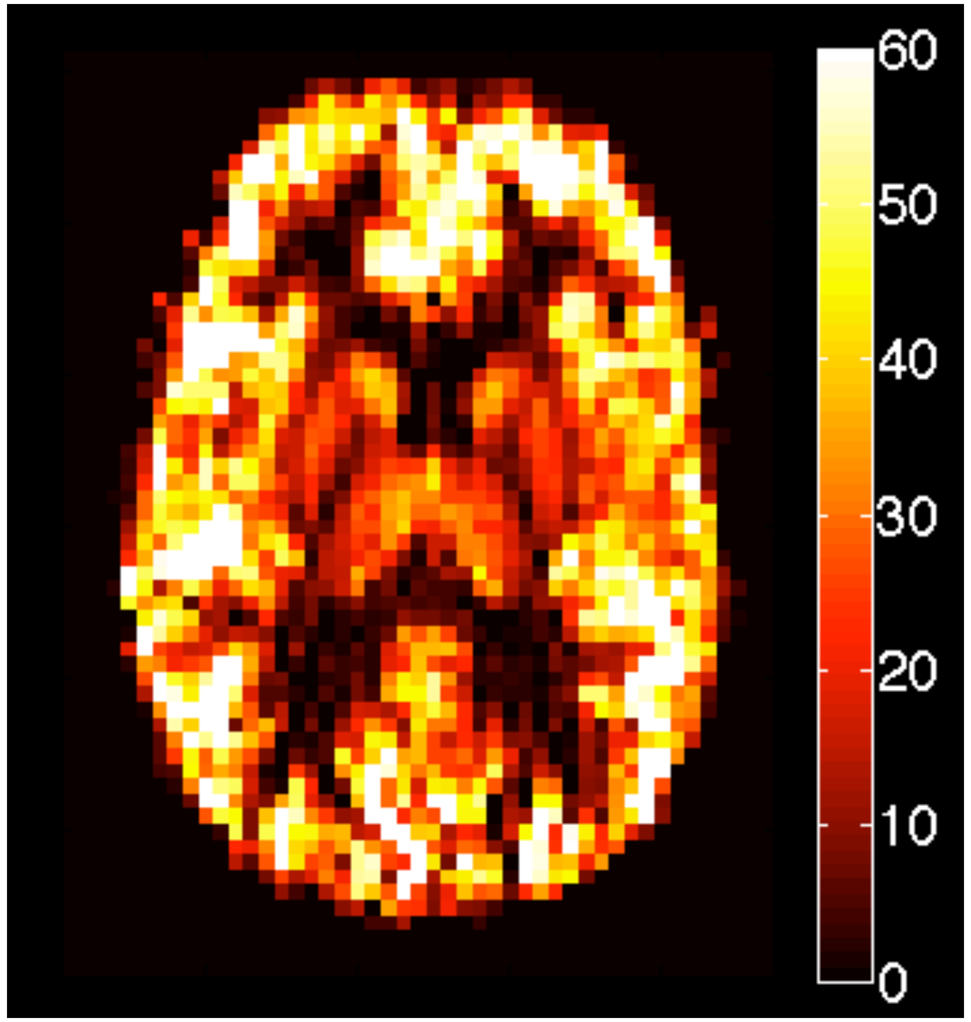
pcASL with
labeling duration: 1.4 s
post-label delays: 0.25, 0.5, 0.75, 1.0, 1.25, 1.5 s



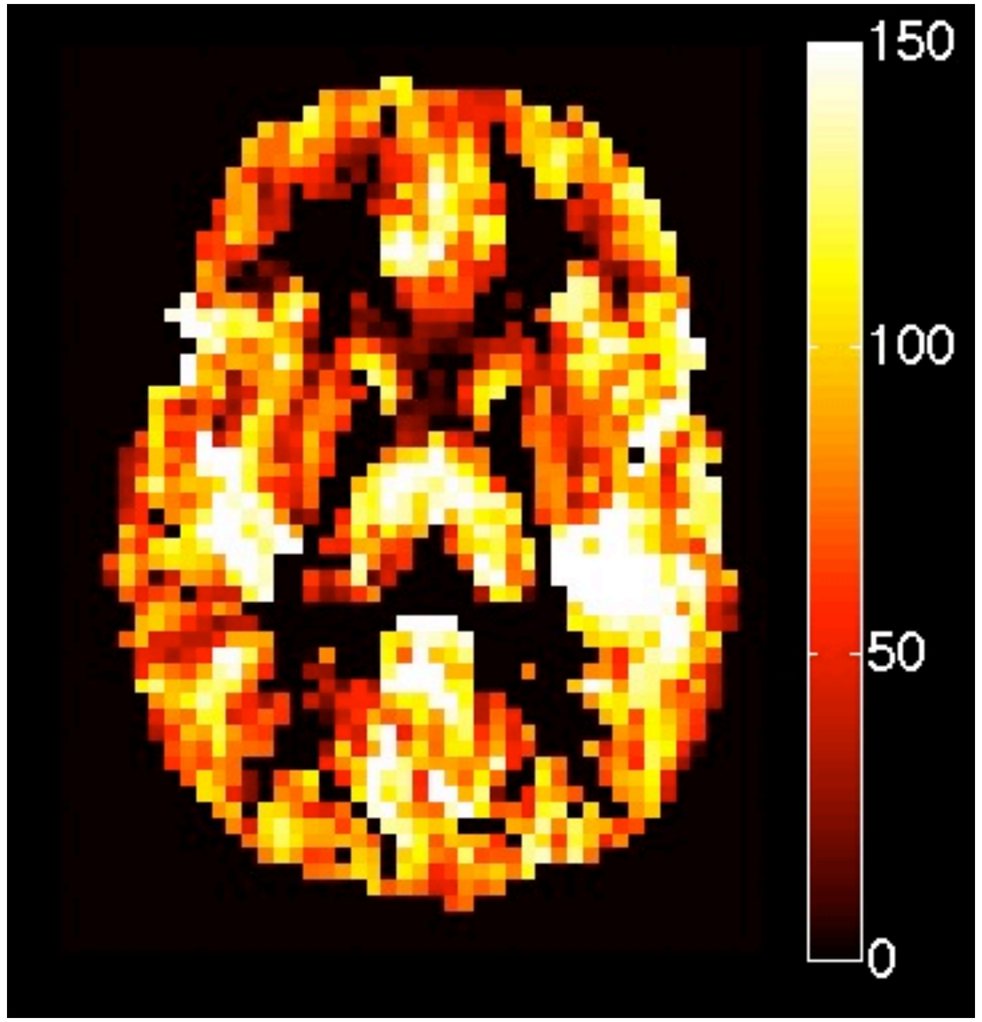
```
oxford_asl -i {ASL_diff_data.nii.gz} -o {out_dir}
  --casl --tis 1.65,1.9,2.15,2.4,2.65,2.9 --bolus 1.4 --bat 1.3 --artoff --fixbolus
  -c {calibration_image.nii.gz} --tr 6 --cref {calibration_reference.nii.gz}
  -s {structural_image.nii.gz} --regfrom {calibration_image.nii.gz) --pvcorr
```

EXAMPLE 5

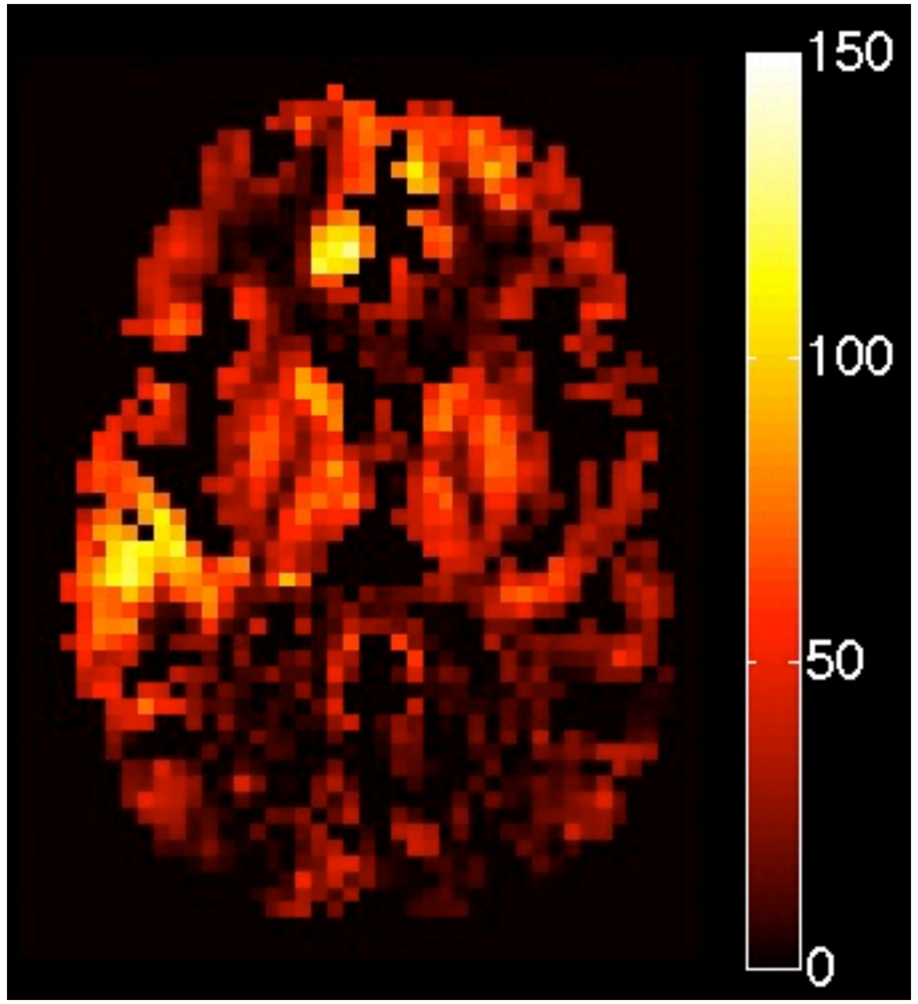
Perfusion (uncorrected)
ml/100g/min



Grey matter perfusion
ml/100g/min



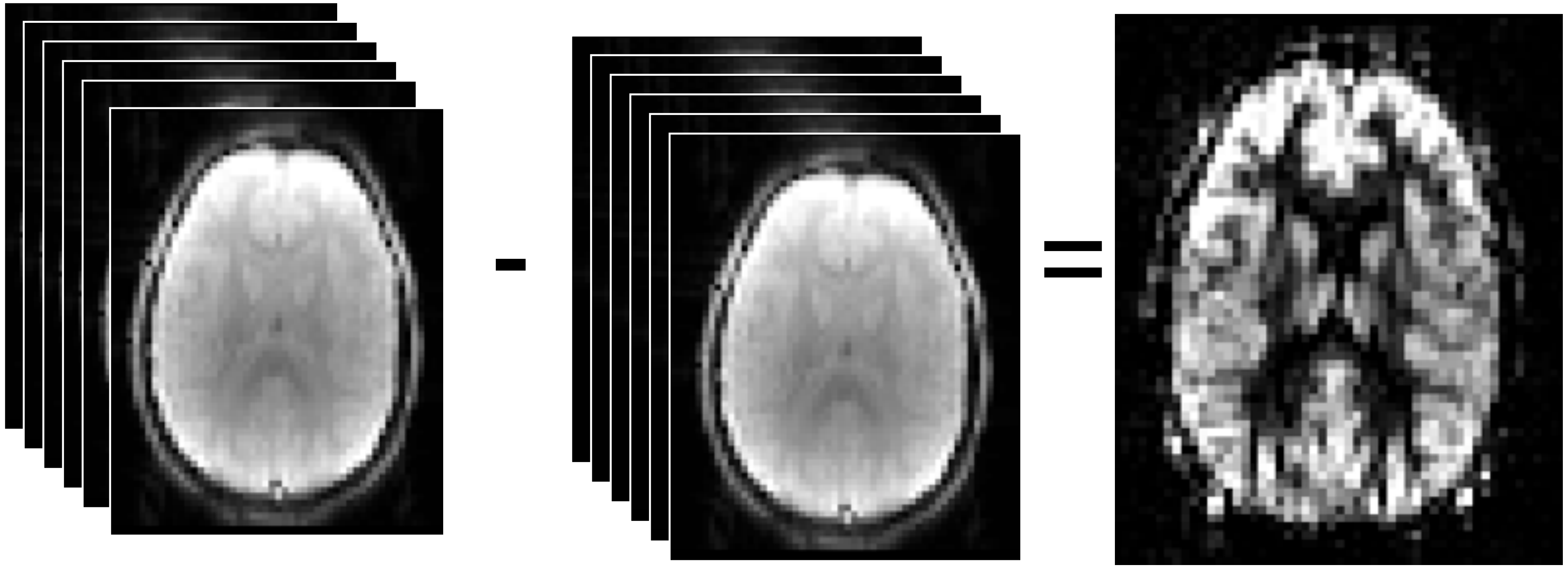
White matter perfusion
ml/100g/min



```
out2/native_space/perfusion_calib.nii.gz
out5b/native_space/perfusion_calib_masked.nii.gz
out5b/native_space/perfusion_wm_calib_masked.nii.gz
```

EXAMPLE 5B

- What I have...
  - ➡ ASL data
  - ➡ (calibration images)
- What I want...
  - ➡ Grey matter perfusion in ml/100g/min
- What should I do?
  - ➡ Tag-control subtraction. ✓
  - ➡ Kinetic model inversion. ←
  - ➡ M0 calculation.
  - ➡ Partial volume correction



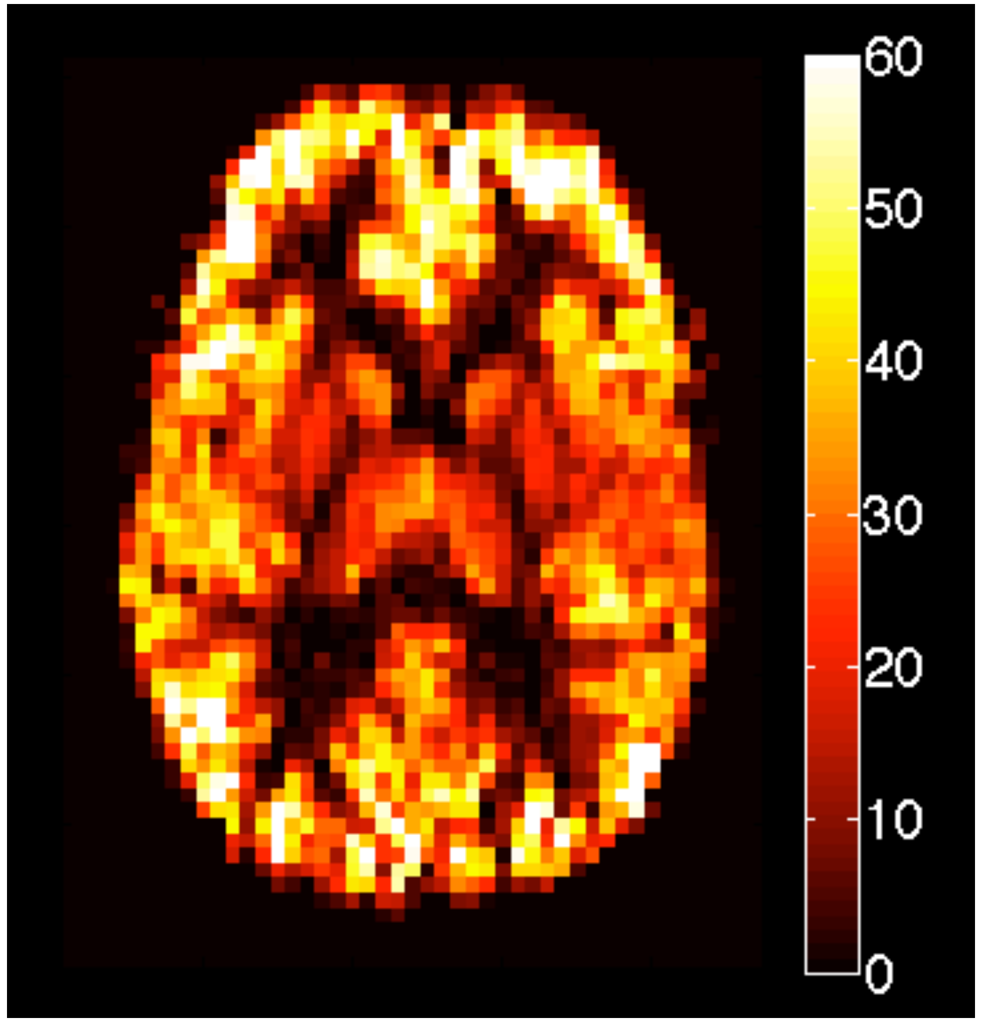
pcASL with
labeling duration: 1.4 s
post-label delay: 1.0 s

Assume
T1 (blood): 1.6 s
T1 (tissue): 1.3 s
BAT : 1.3 s

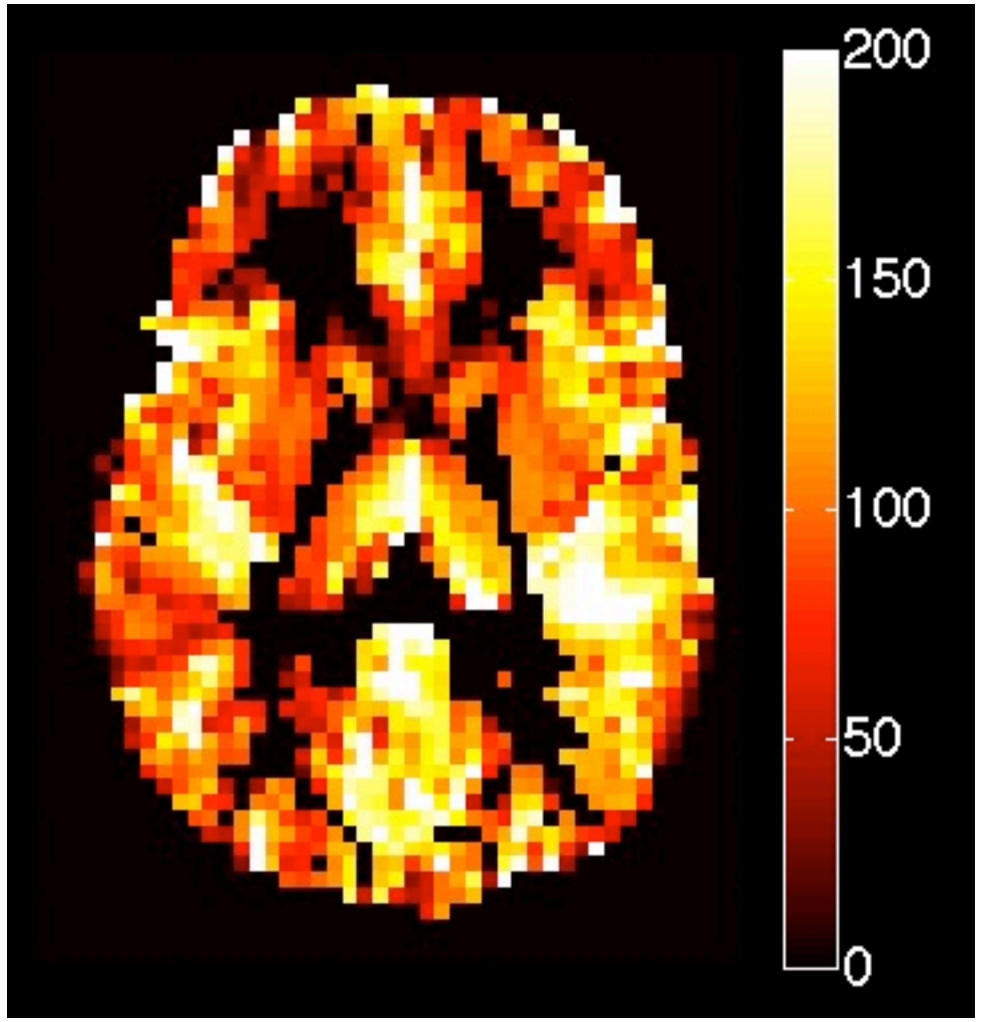
```
oxford_asl -i {ASL_diff_data.nii.gz} -o {out_dir}
  --casl --tis 2.4 --bolus 1.4 --bat 1.3 --artoff --fixbolus
  -c {calibration_image.nii.gz} --tr 6 --cref {calibration_reference.nii.gz}
  -s {structural_image.nii.gz} --regfrom {calibration_image.nii.gz) --pvcorr
```

EXAMPLE 5B

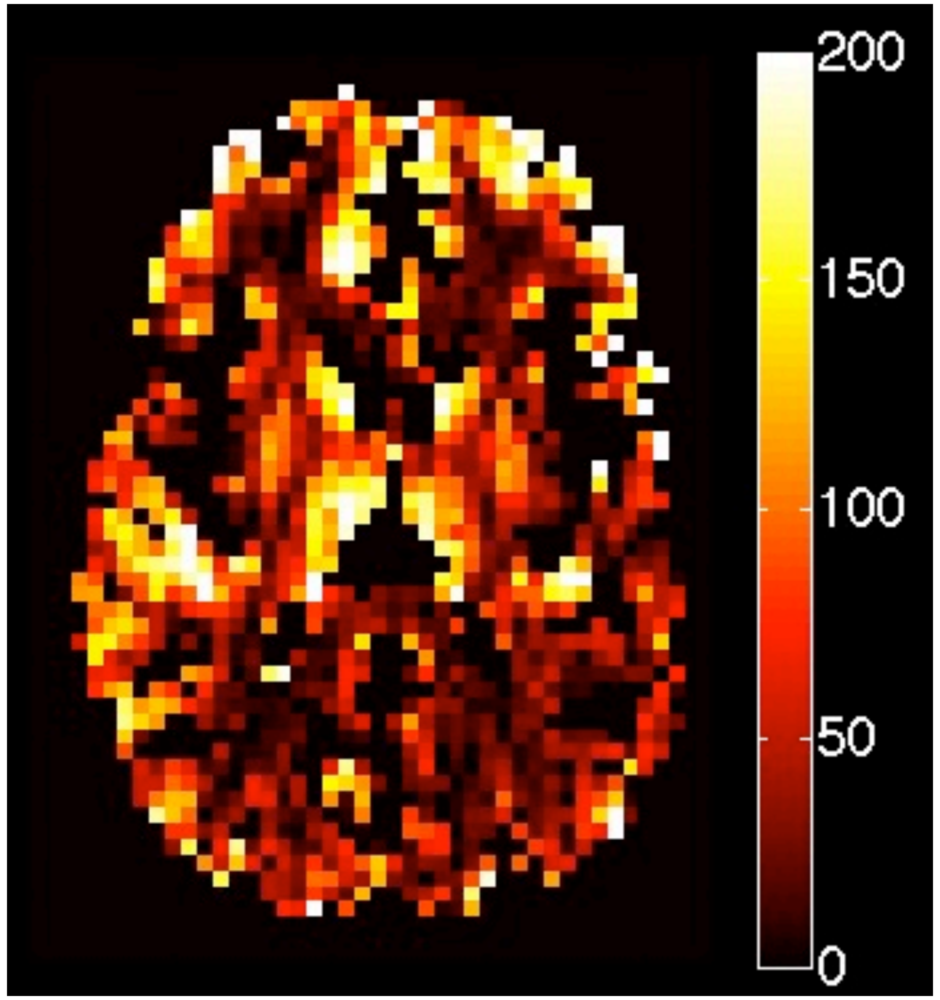
Perfusion (uncorrected)
ml/100g/min



Grey matter perfusion
ml/100g/min



White matter perfusion
ml/100g/min



```
out2/native_space/perfusion_calib.nii.gz
out5b/native_space/perfusion_calib_masked.nii.gz
out5b/native_space/perfusion_wm_calib_masked.nii.gz
```

FSL: The FMRIB Software Library (v5.0)

- ➡ BASIL: www.fmrib.ox.ac.uk/fsl/basil

  User guide & tutorials

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- FMRIB, Oxford
  - ➡ Peter Jezzard
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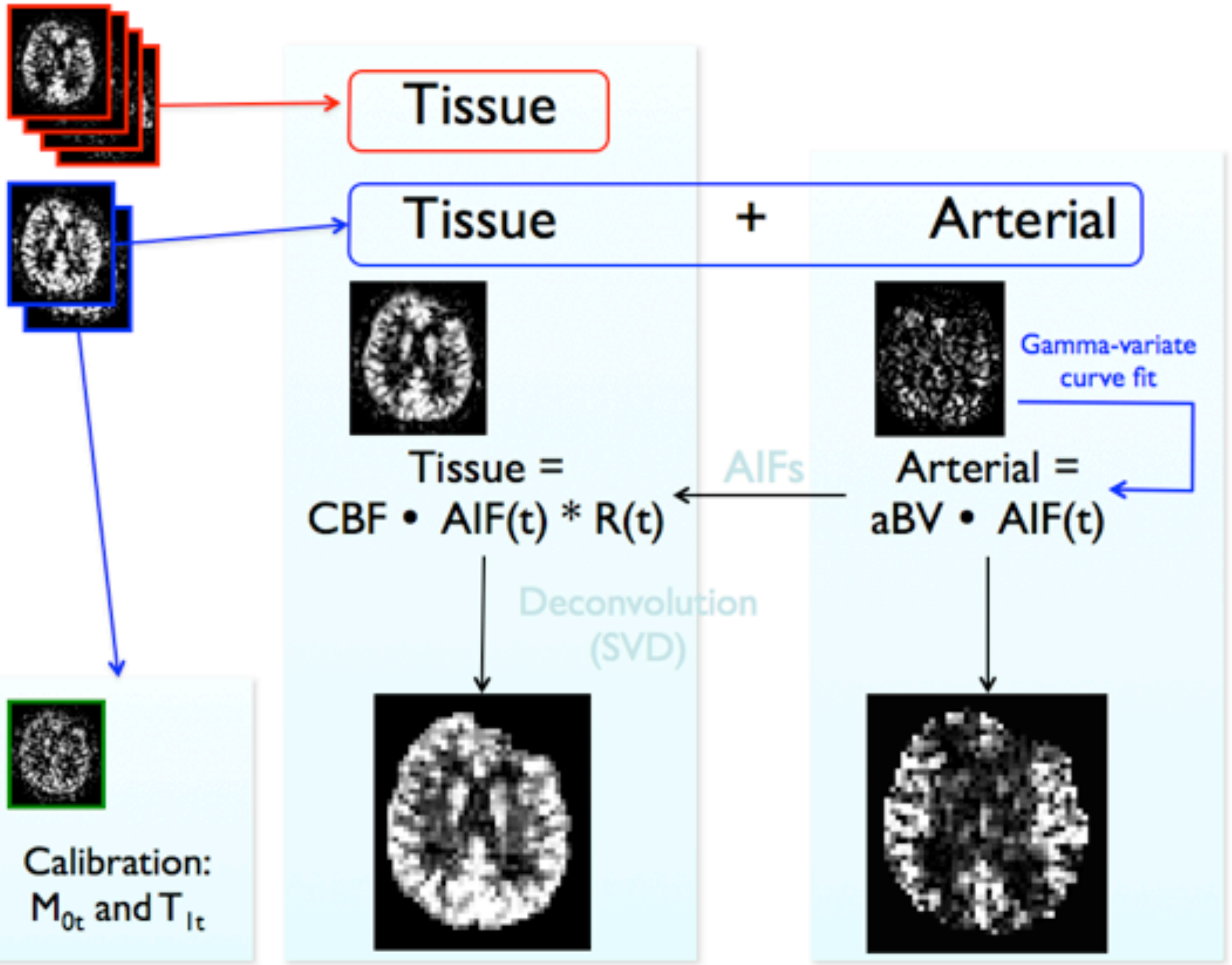
- Xavier Golay (UCL, London)
- Esben Petersen (Utrecht)
- Marco Castellaro (Padova)
- Ilaria Boscolo Galazzo (Verona)

SPECIAL: QUASAR

- QUASAR
  - ➡ multi-TI pASL acquisition.
  - ➡ Mixture of flow suppression on and off.
  - ➡ Saturation recovery control images

- Analysis
  - ➡ model-based - include MV component
  - ➡ model-free - numerical deconvolution (c.f. DSC)



```
quasil -i {QUASAR_image} -o {out_dir}
quasil -i {QUASAR_image} -o {out_dir} --mfree
```

Petersen et al., MRM 55(2),2006.
Chappell et al., MRM e-print, 2013.