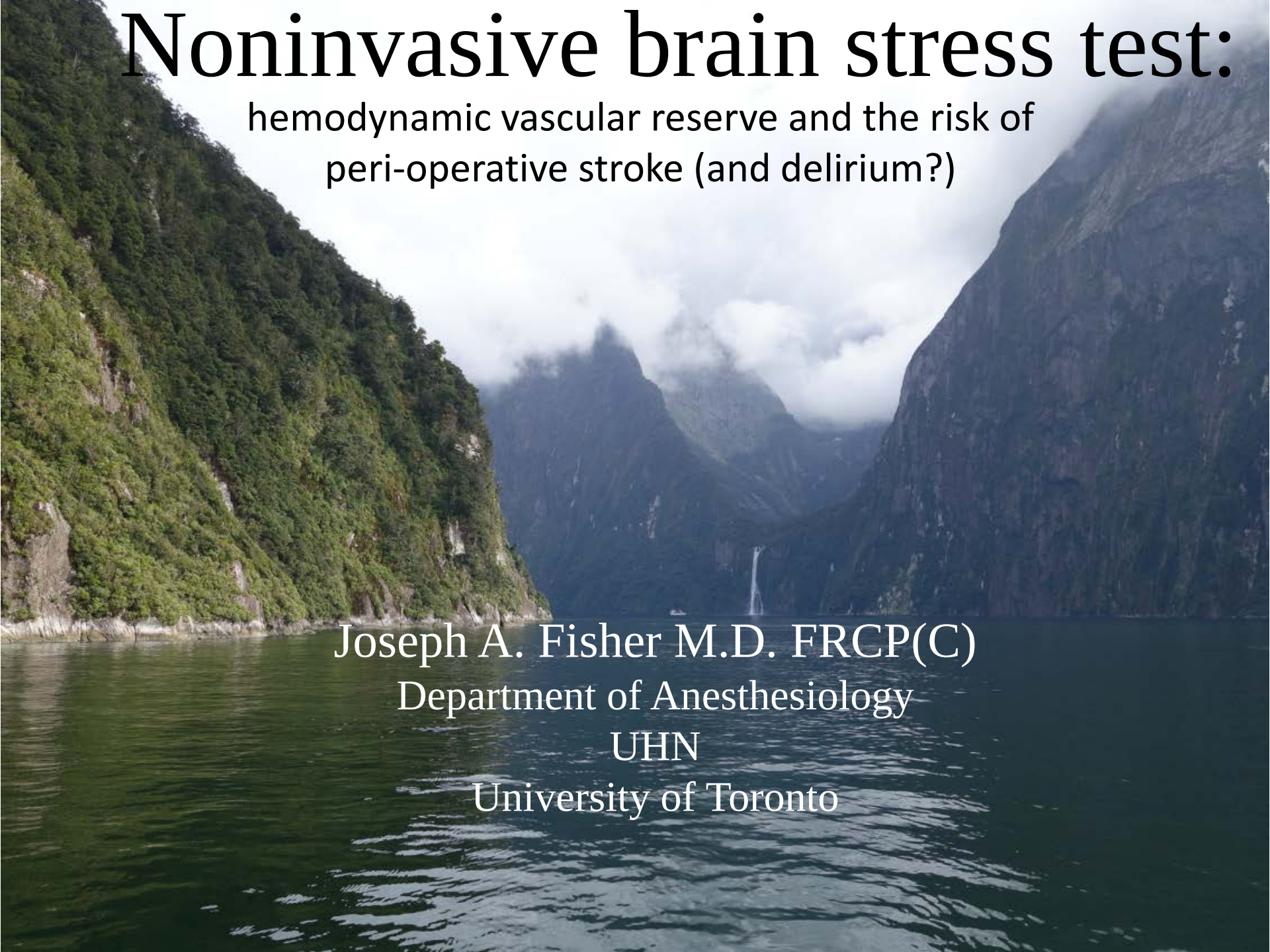
Noninvasive brain stress test:

hemodynamic vascular reserve and the risk of peri-operative stroke (and delirium?)



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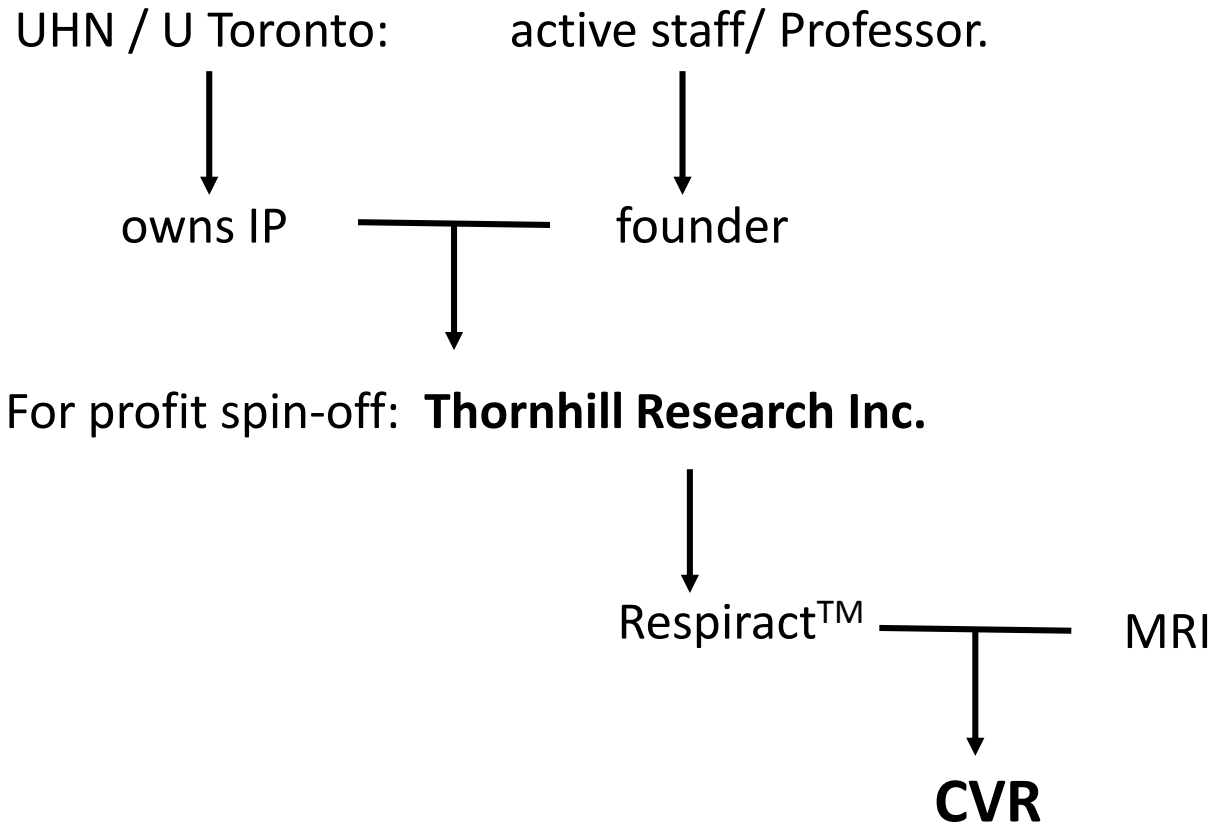
Disclosures:



Aim:

- Present a narrative summary of the dynamics of steno-occlusive cerebrovascular disease

Source:

- 19 years
- 1500 patients/scans
- Symptoatic, asymptomatic, interventions, no interventions
- Atlas of normal scans

Tools

- Precise, repeatable vasoactive stimulus: CO_2
- MRI
- Clinical data

Model: continuously updated

- Understanding neurovascular physiology
- Patho-physiology
- interpetation
- Hypothesis generation

Citations

Fisher JA, Venkatraghavan L, Mikulis DJ, Stroke Aug. 2018 in press.

Roiland R, Fisher JA, Ainslie P. Pysiological Reviews. in press.

Caveat:

Not all of my colleagues may agree with all of this talk at all times.

Some basic science

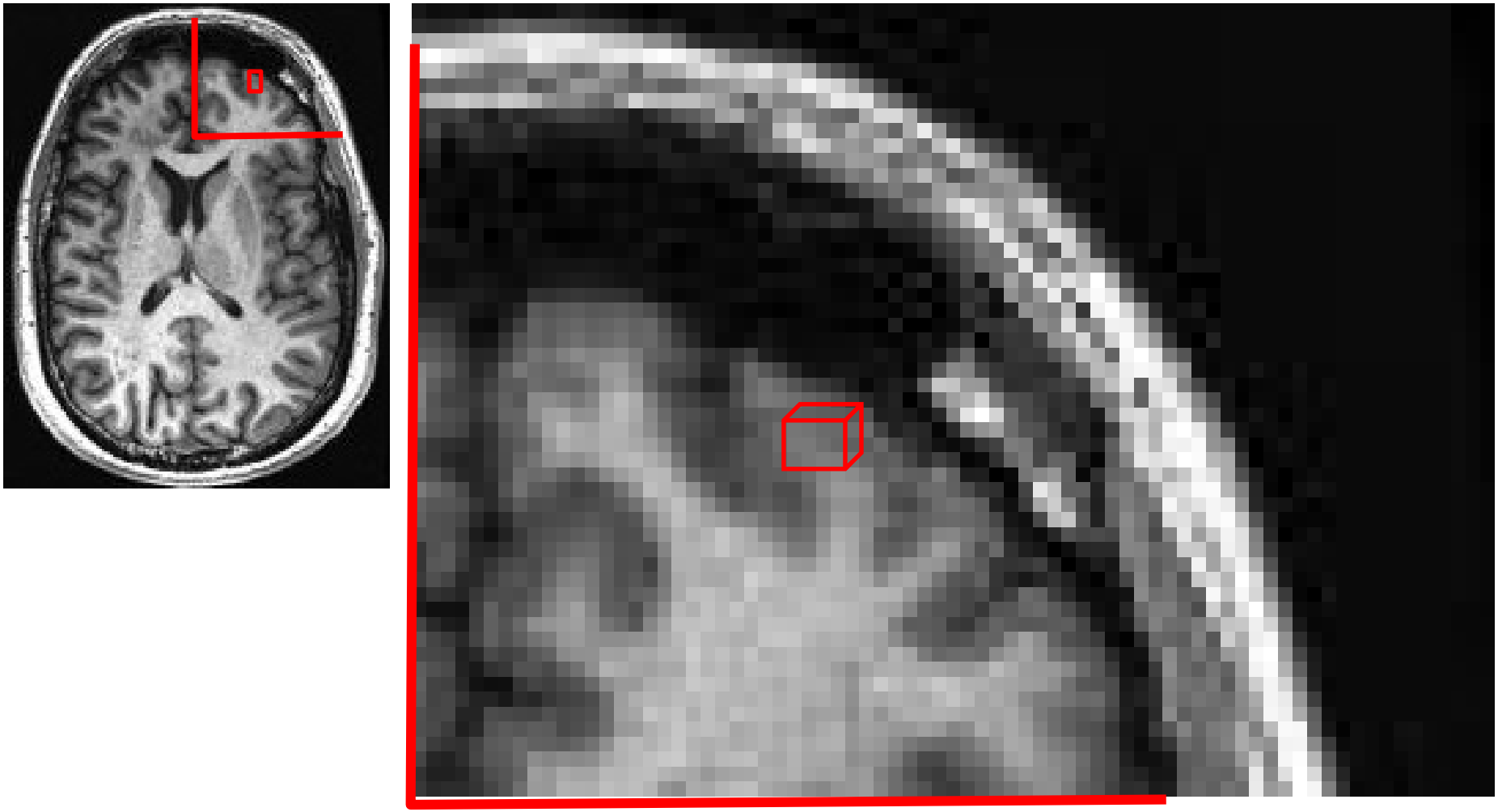
Using MRI signal (BOLD) to measure CBF

- dOHb is paramagnetic --> ↓ BOLD signal
- **high flow --> ↓ dOHb --> ↑BOLD signal**

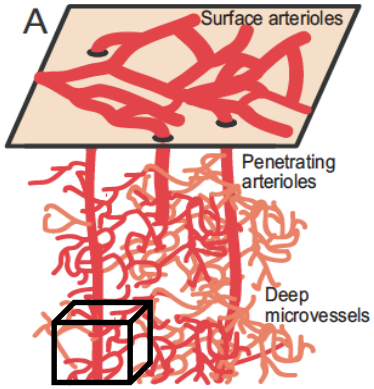
Cerebrovascular reactivity: $CVR = \frac{\Delta \text{ BOLD}}{\Delta \ PCO_2}$

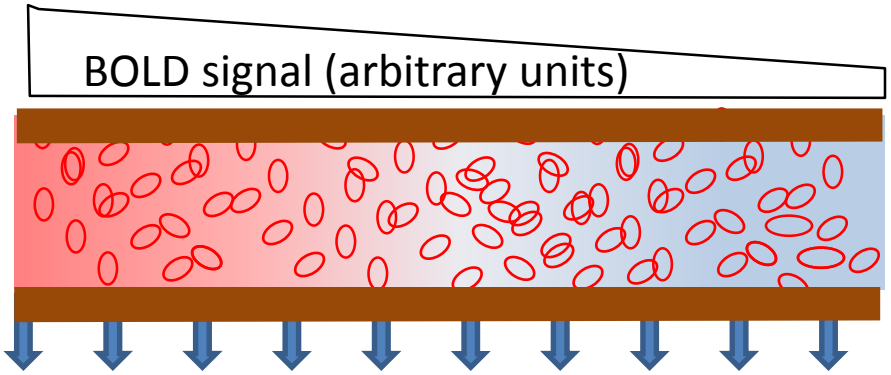
Distribution of CBF in presence of CV disease

Interrogation of voxel: 2.5 x 2.5 x 2.5



PCO_2

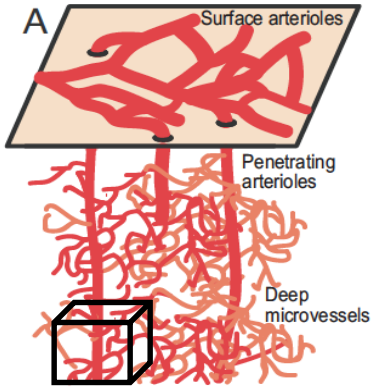




40

$CMRO_2$ constant

PCO_2



BOLD signal (arbitrary units)

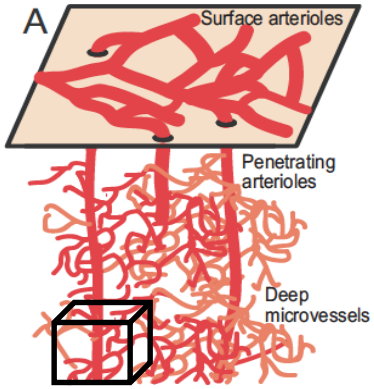
40

50

$CMRO_2$ constant

PCO_2

$$CVR = \frac{\Delta\ BOLD}{\Delta\ PCO_2}$$



BOLD signal (arbitrary units)

40

50

$CMRO_2$ constant

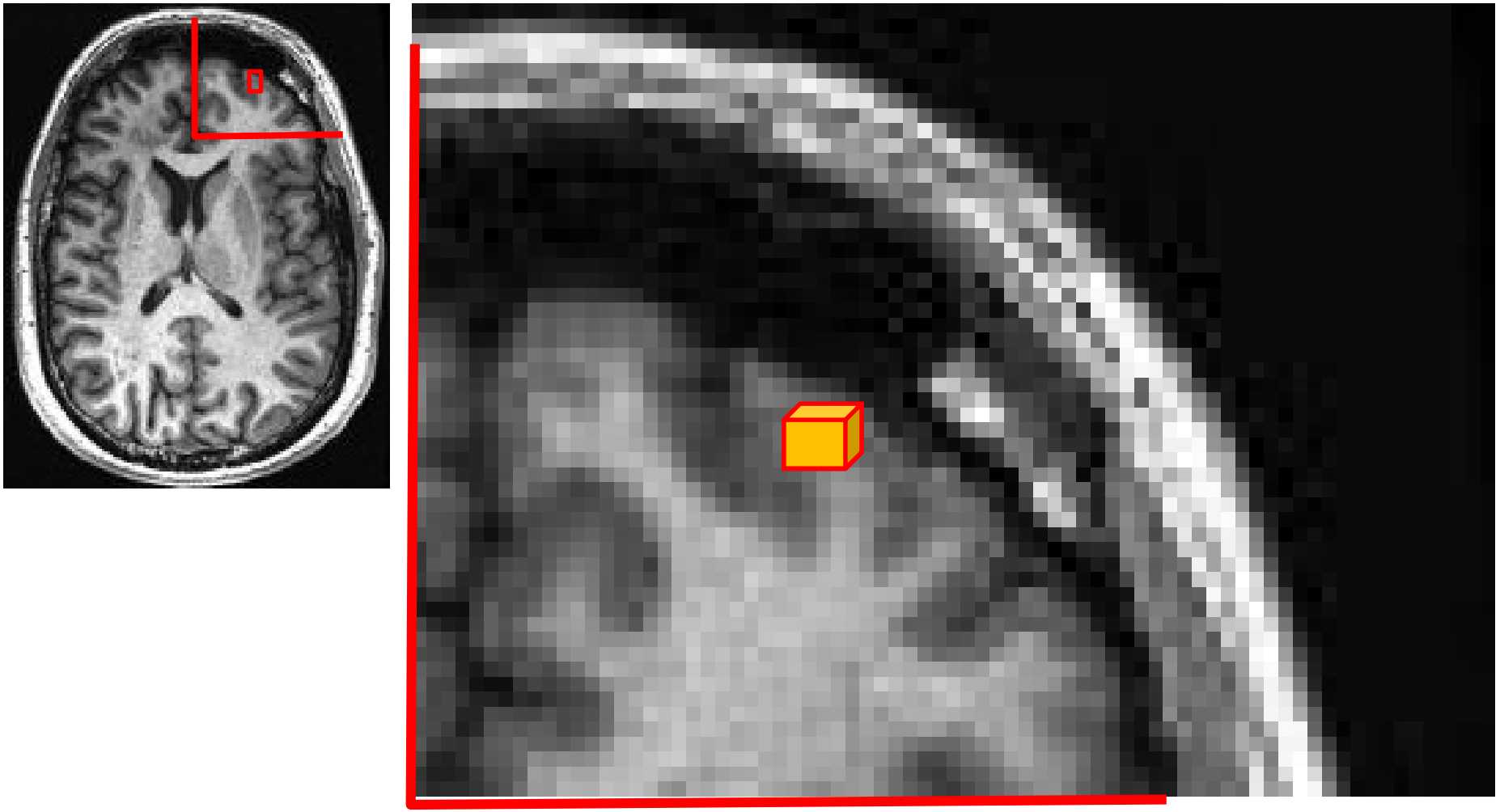
CVR =

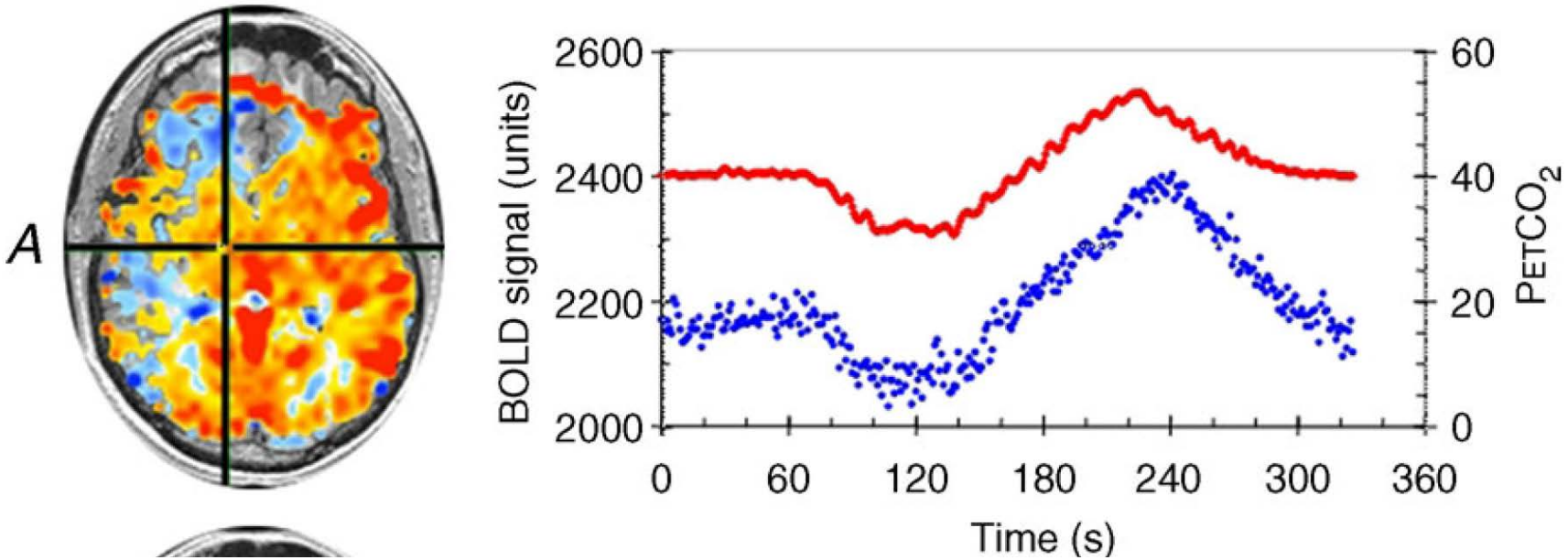
10

0.45
0.25
0
-0.25
-0.45

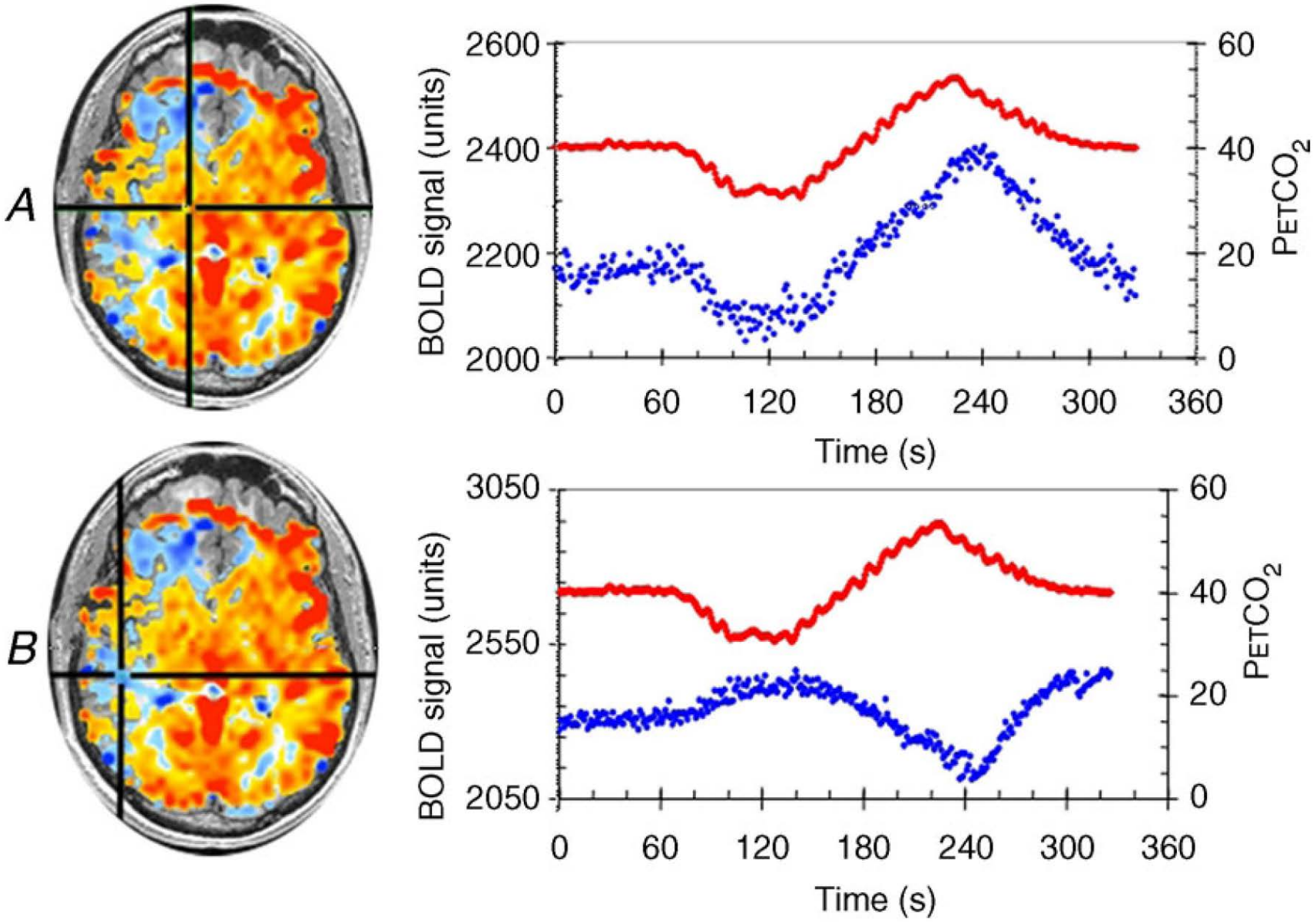
-0.70 (Δ %/ Δ mmHg)

Interrogation of voxel: 2.5 x 2.5 x 2.5





Fierstra J, et al. *J Physiol* 591.23 (2013) pp 5809–5821



Fierstra J, et al. *J Physiol* 591.23 (2013) pp 5809–5821

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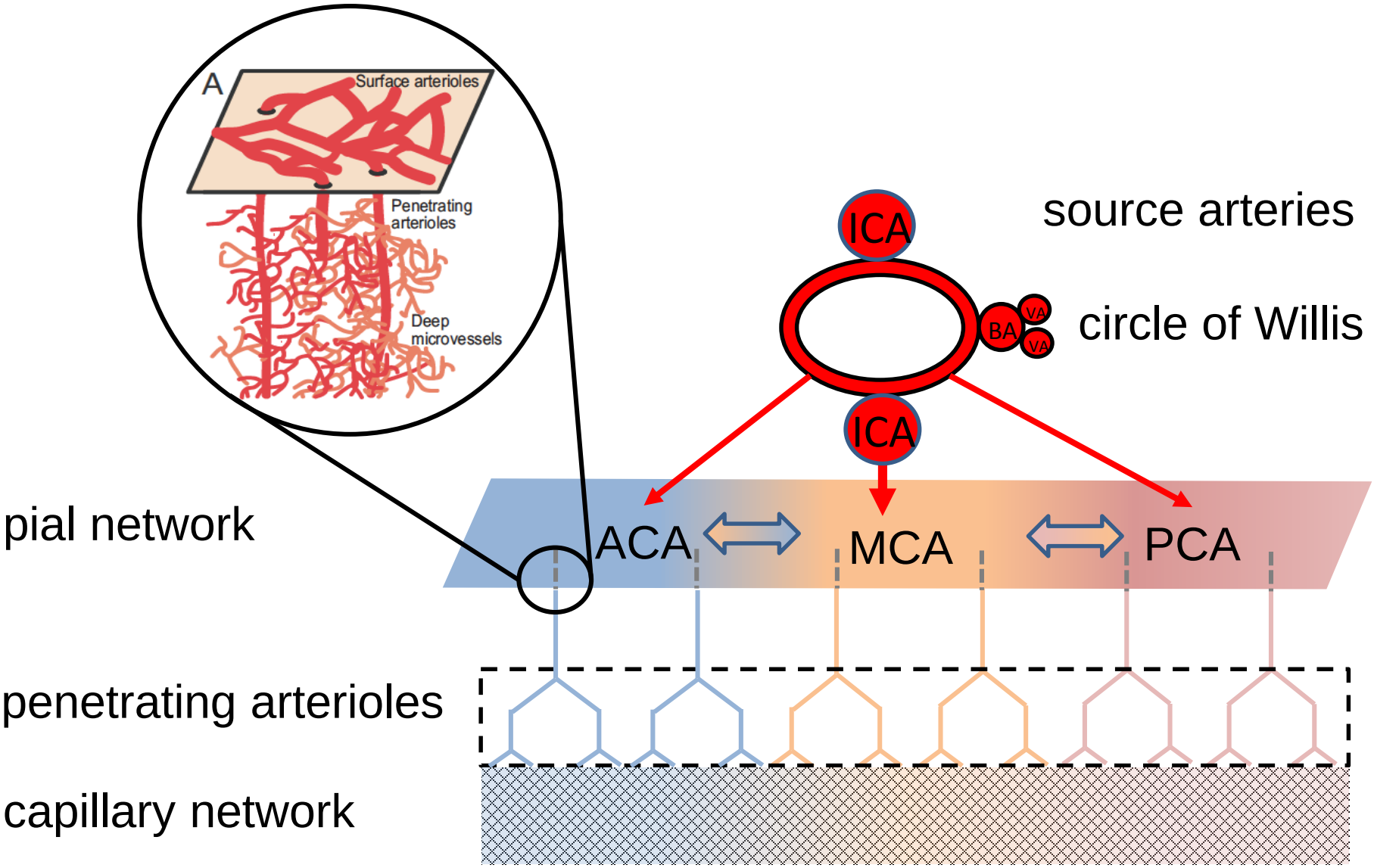
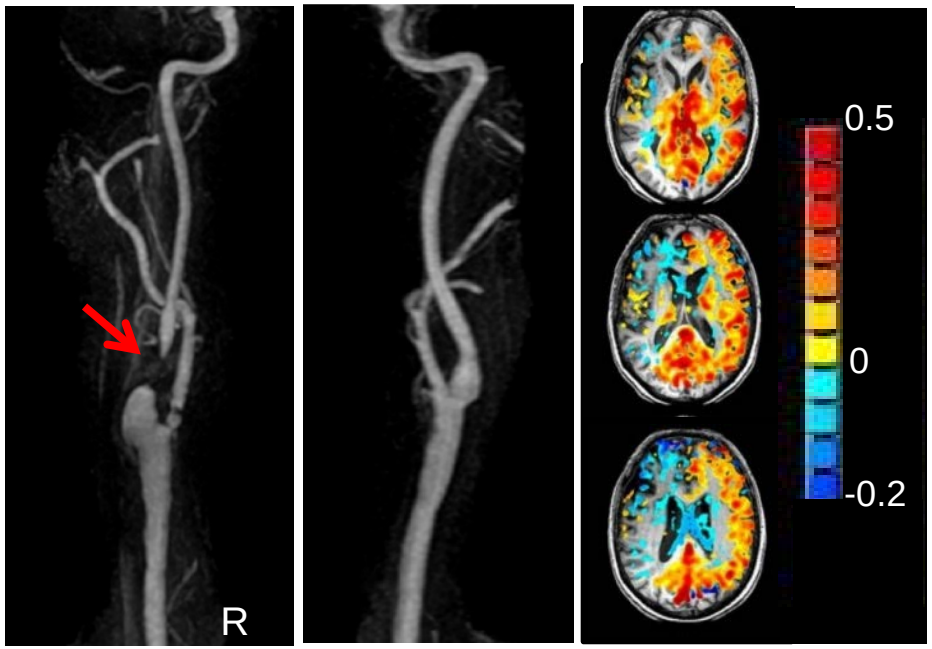
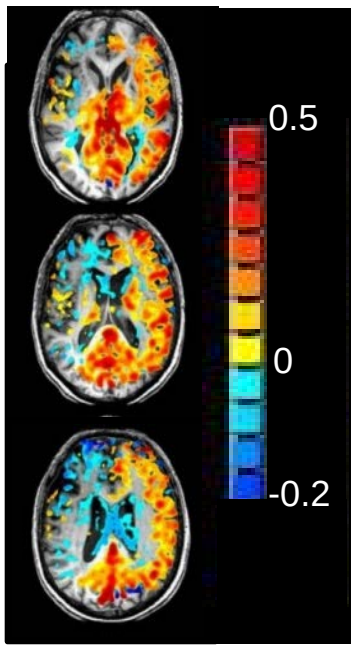
Distribution of CBF in presence of CV disease

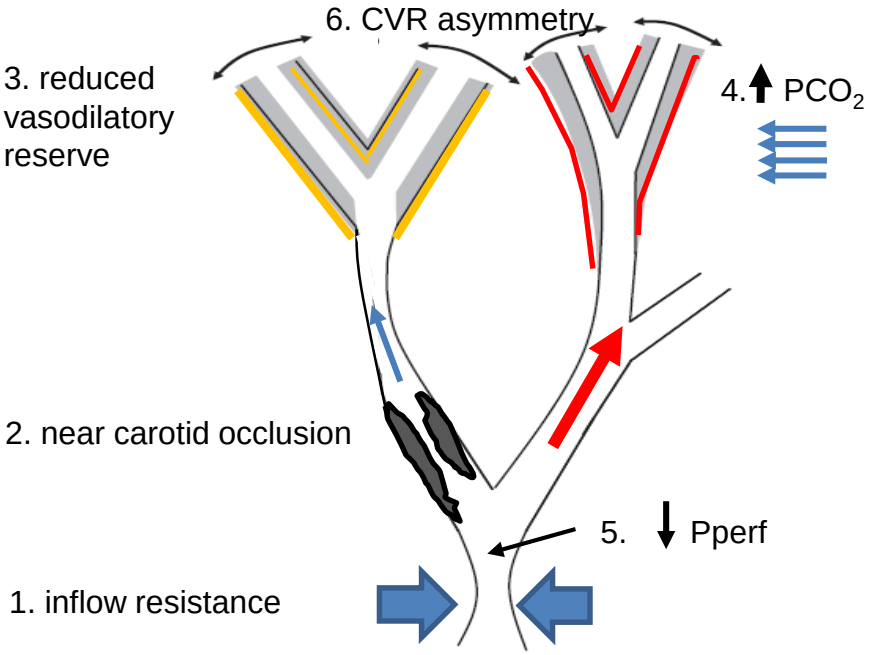
Organization of cerebral blood flow and collateral blood flow

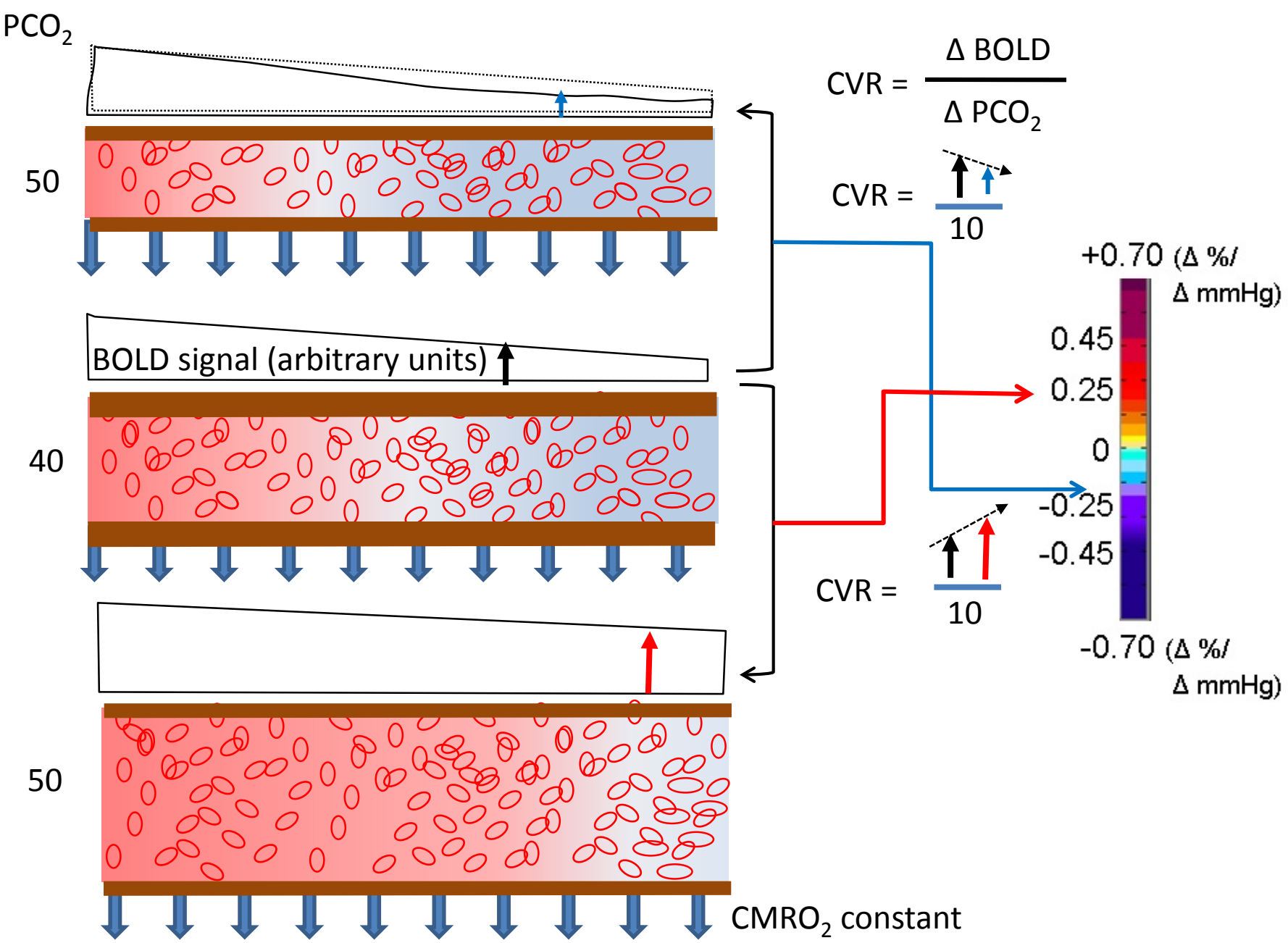


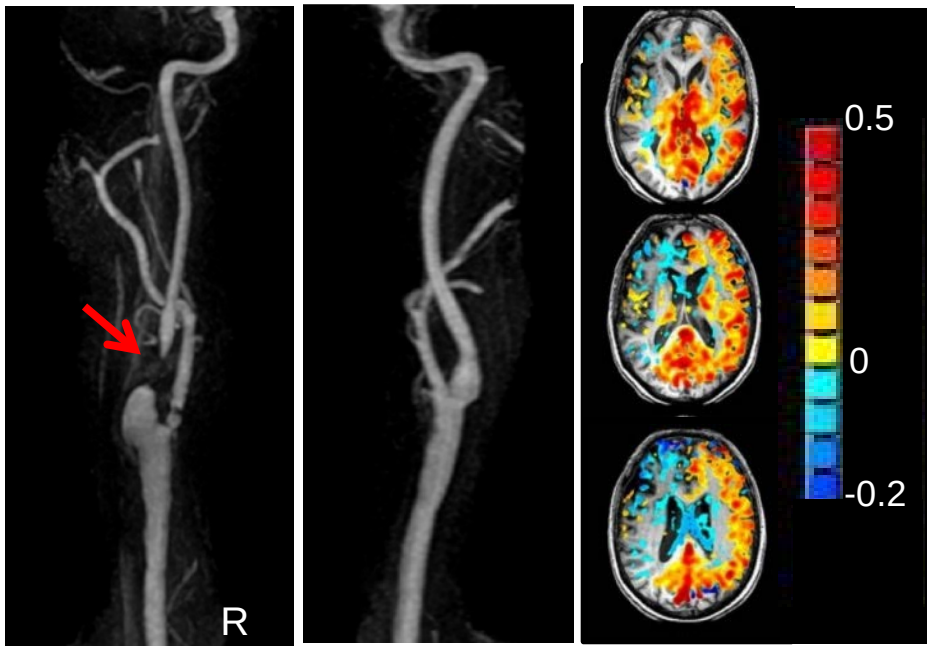

R
0.5
0
-0.2

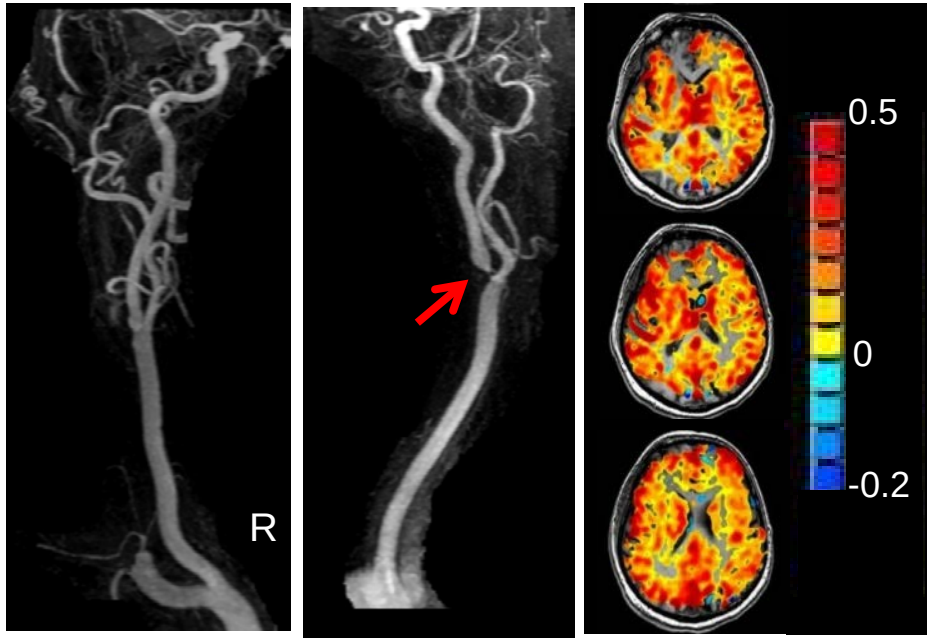

R

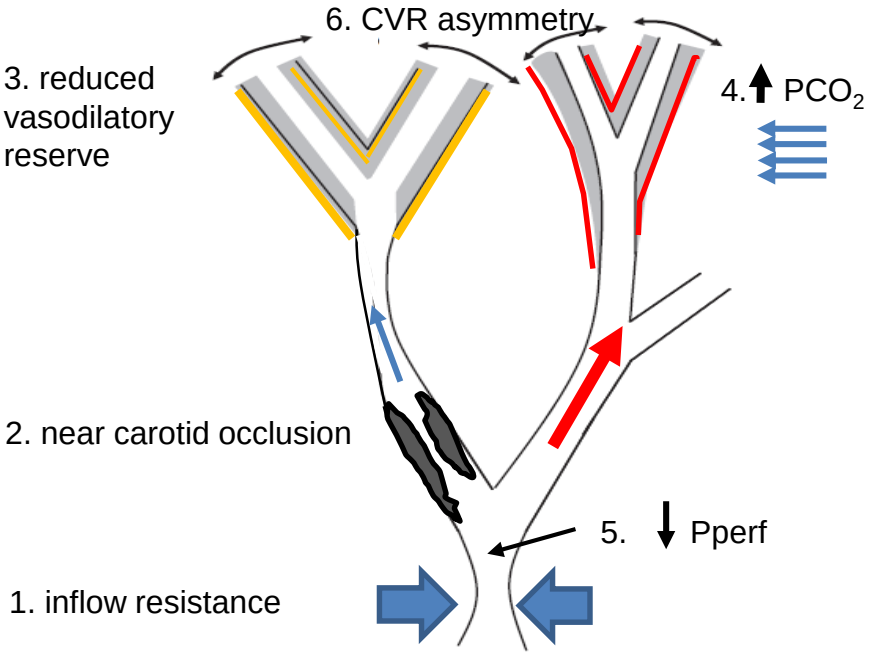

0.5
0
-0.2

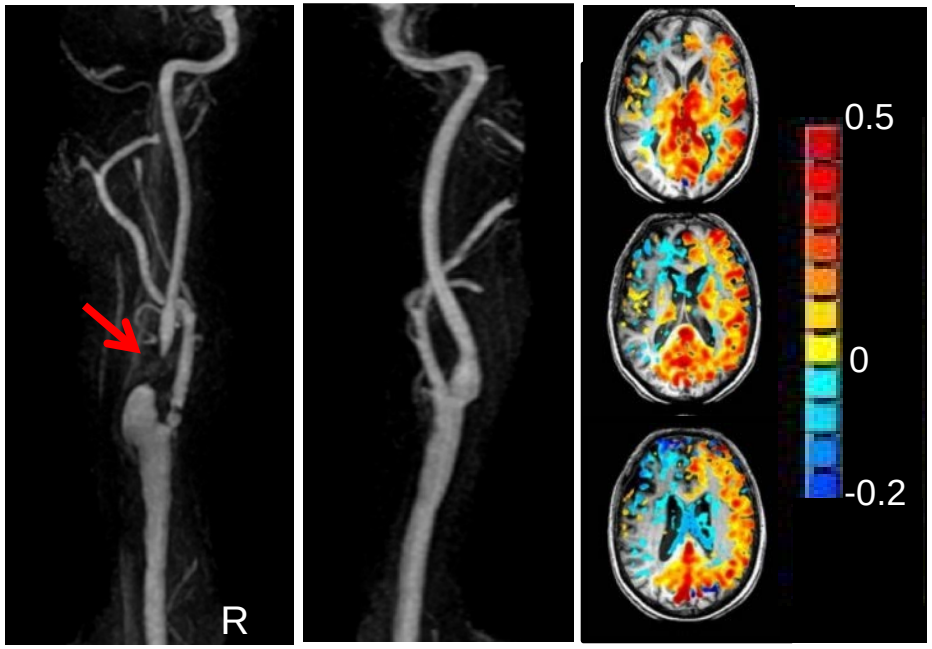

6. CVR asymmetry
3. reduced vasodilatory reserve
4. ↑ PCO2
2. near carotid occlusion
5. ↓ Pperf
1. inflow resistance

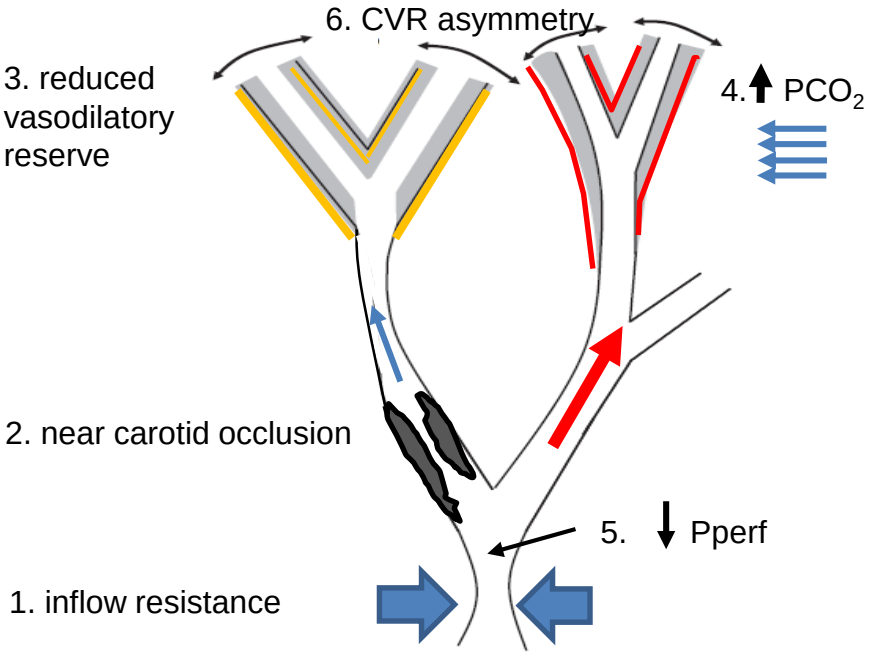

PCO2
50
BOLD signal (arbitrary units)
40
50
CMRO2 constant
CVR = Δ BOLD / Δ PCO2
CVR =
10
CVR =
10
+0.70 (Δ %/ Δ mmHg)
0.45
0.25
0
-0.25
-0.45
-0.70 (Δ %/ Δ mmHg)


R
0.5
0
-0.2


R
0.5
0
-0.2


6. CVR asymmetry
3. reduced vasodilatory reserve
4. ↑ PCO_2
2. near carotid occlusion
5. ↓ Pperf
1. inflow resistance


R
0.5
0
-0.2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4. PCO_2
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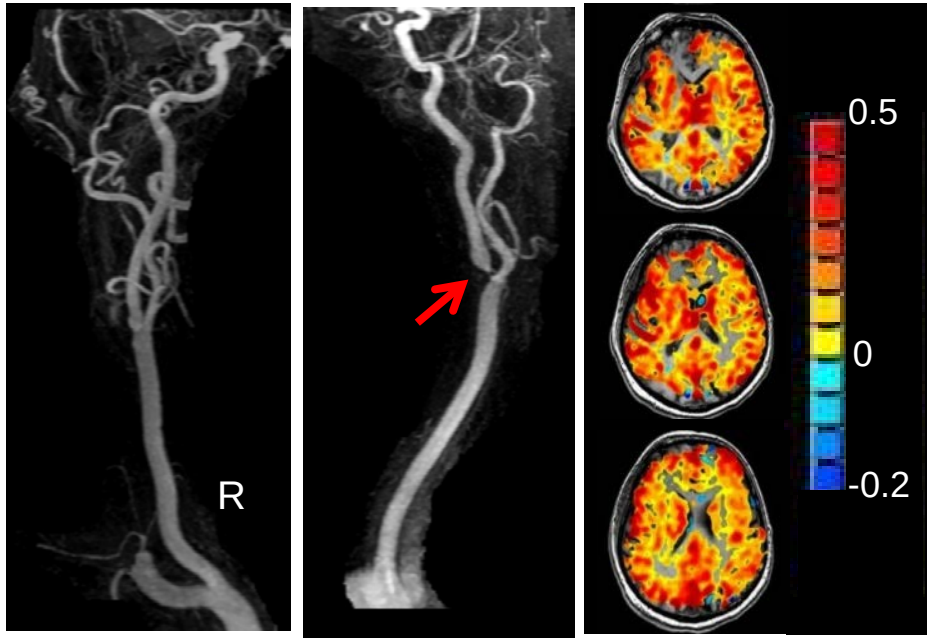
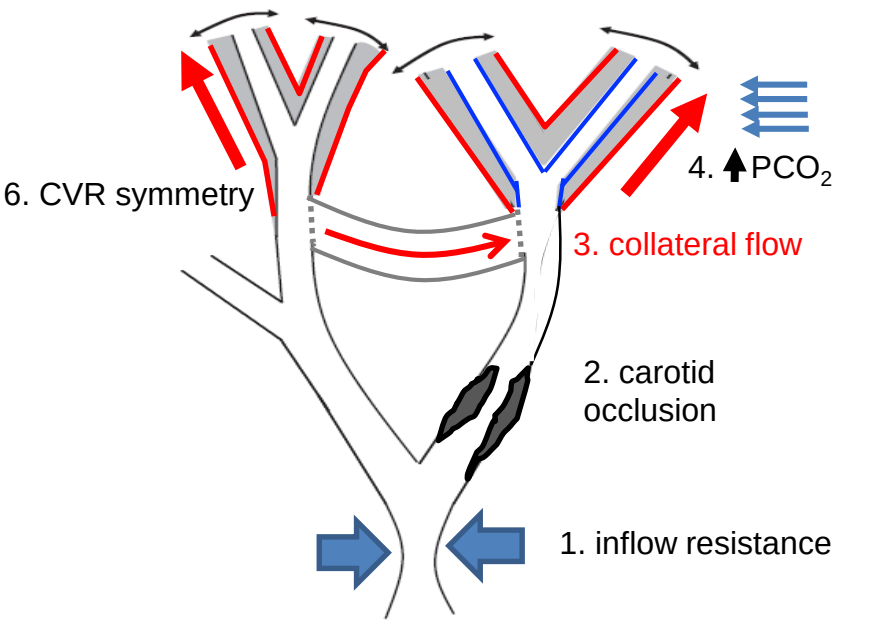
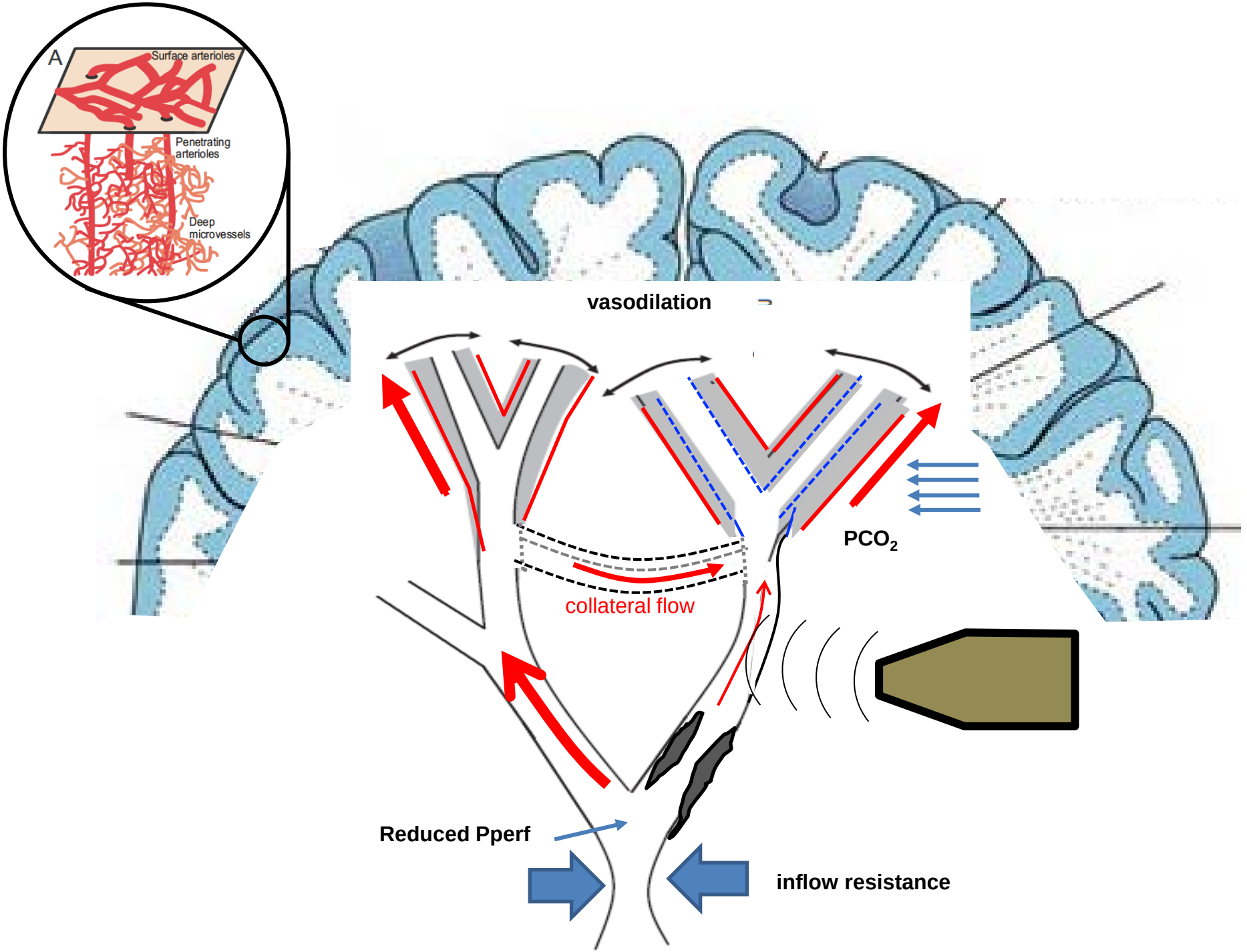
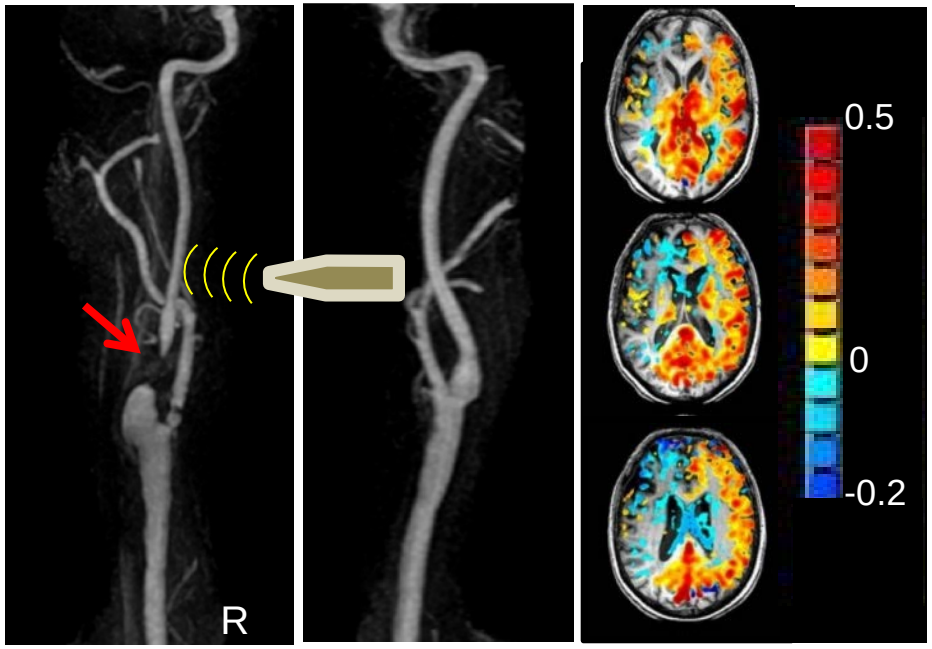
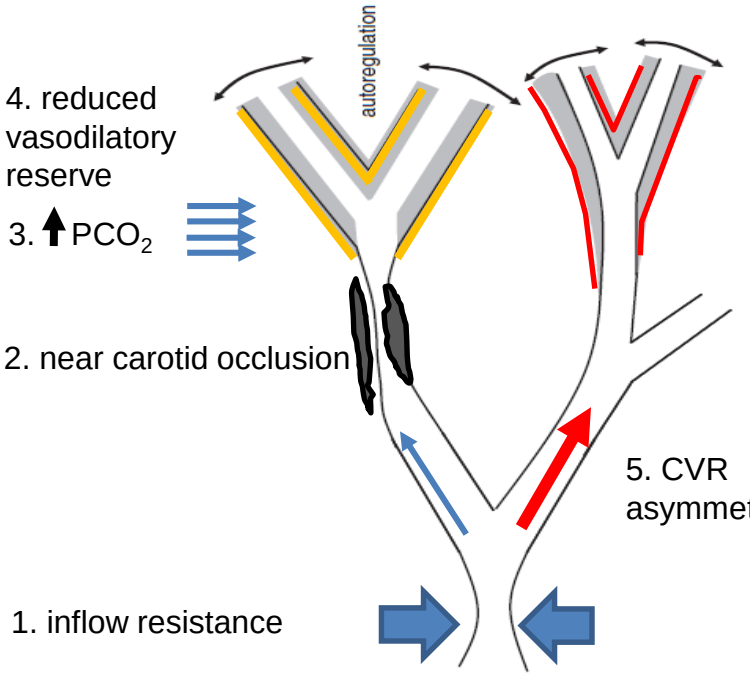
1. inflow resistance

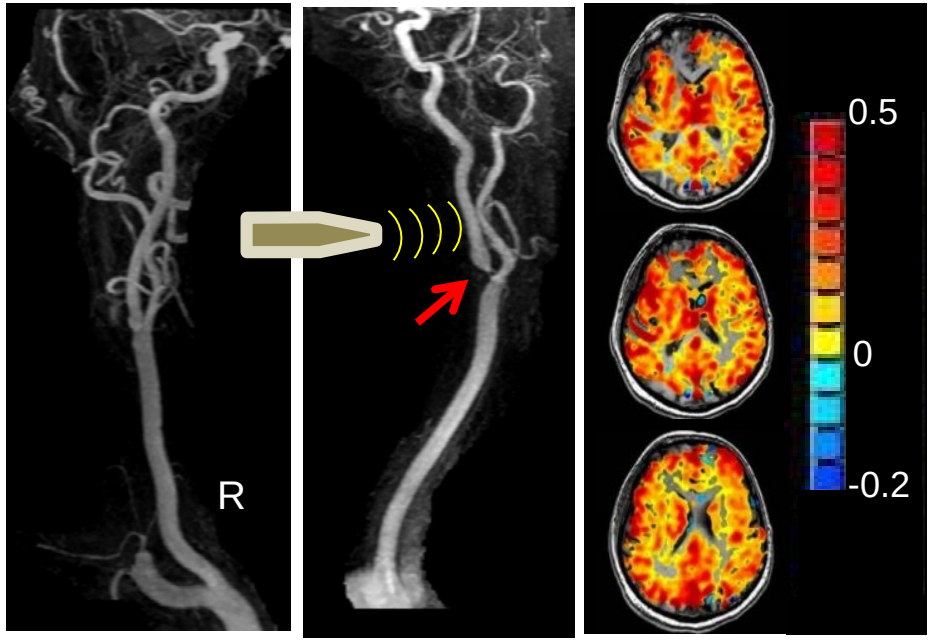

R
0.5
0
-0.2

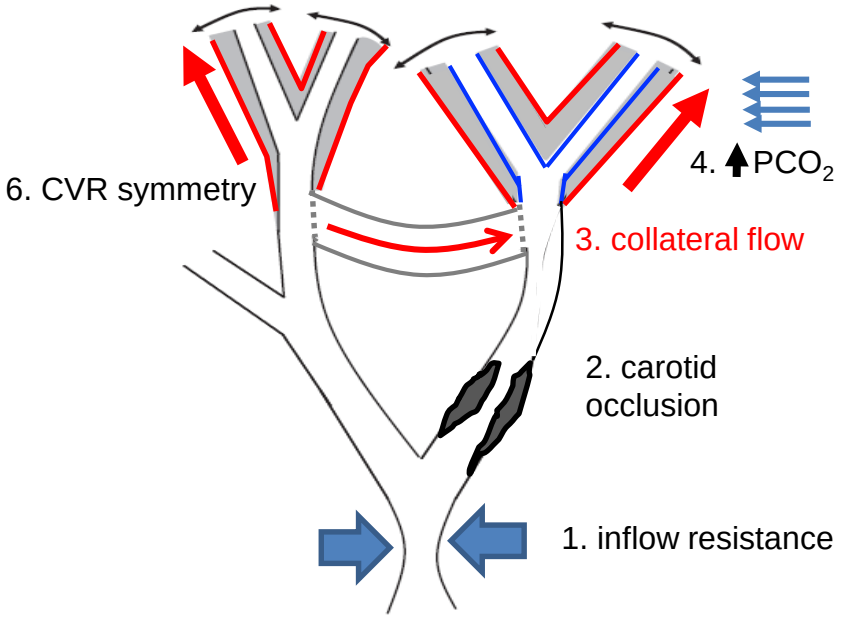

5. equal bilateral vasodilatory reserve
6. CVR symmetry
4. PCO_2
3. collateral flow
2. carotid occlusion
1. inflow resistance


A
Surface arterioles
Penetrating arterioles
Deep microvessels
vasodilation
PCO2
collateral flow
Reduced Pperf
inflow resistance


R
0.5
0
-0.2


autoregulation
4. reduced vasodilatory reserve
3. ↑PCO2
2. near carotid occlusion
5. CVR asymmetry
1. inflow resistance


R
0.5
0
-0.2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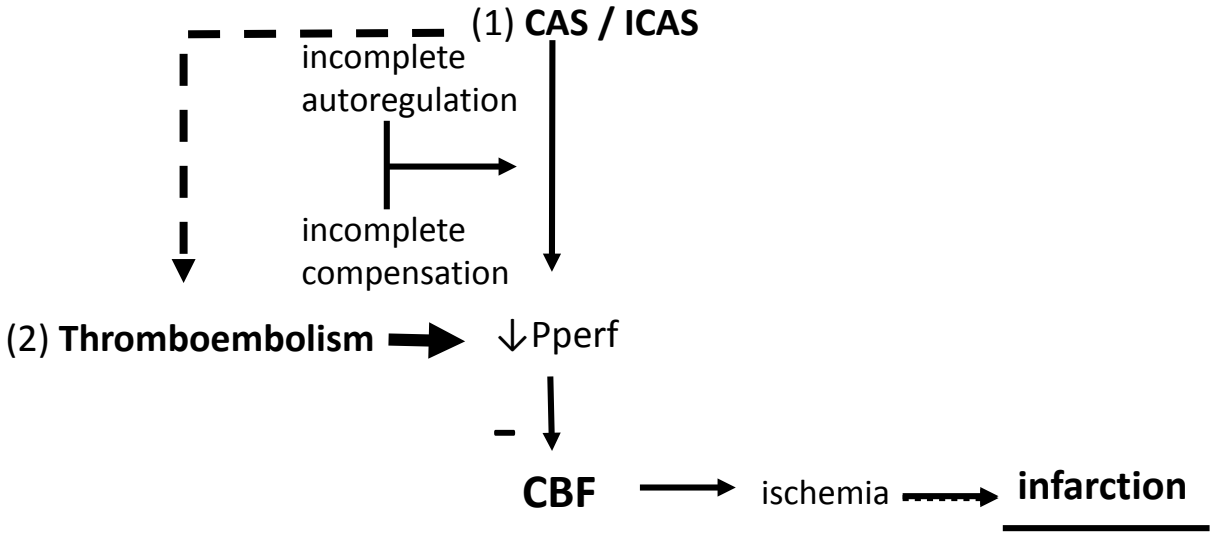
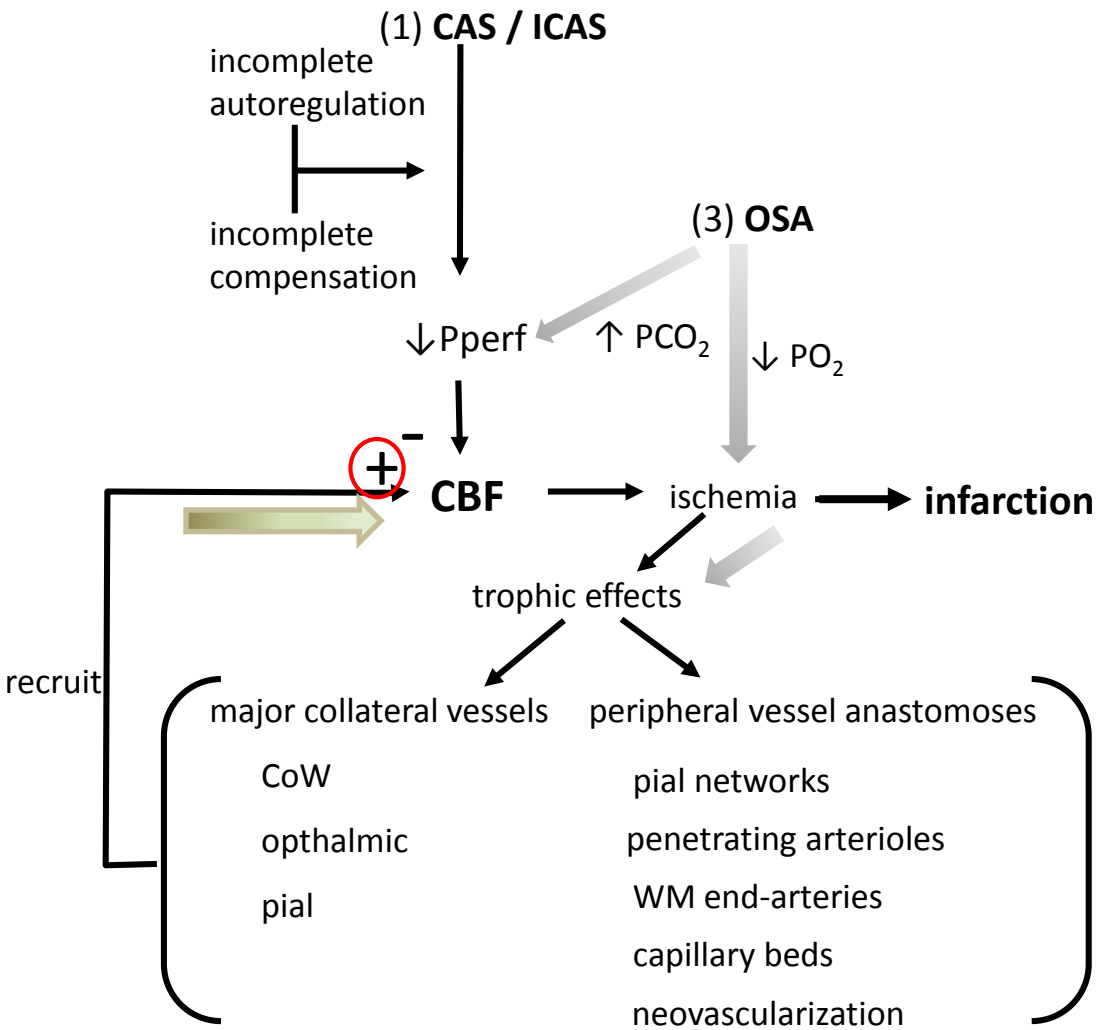
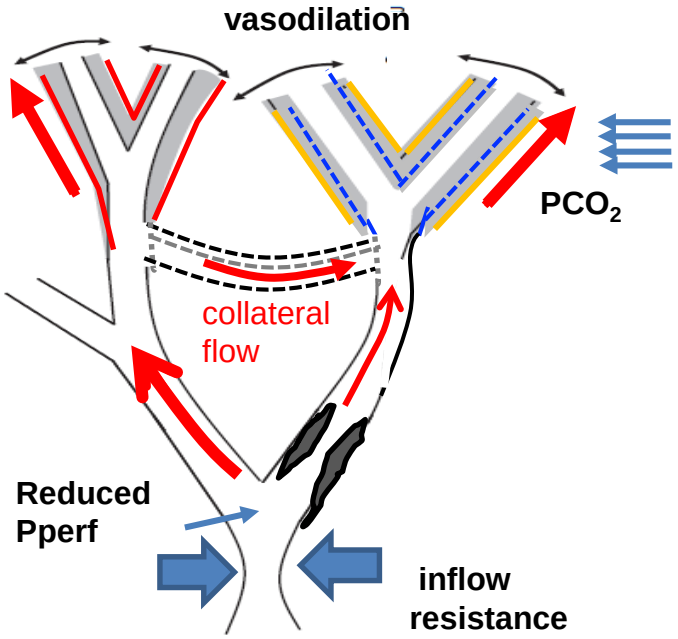
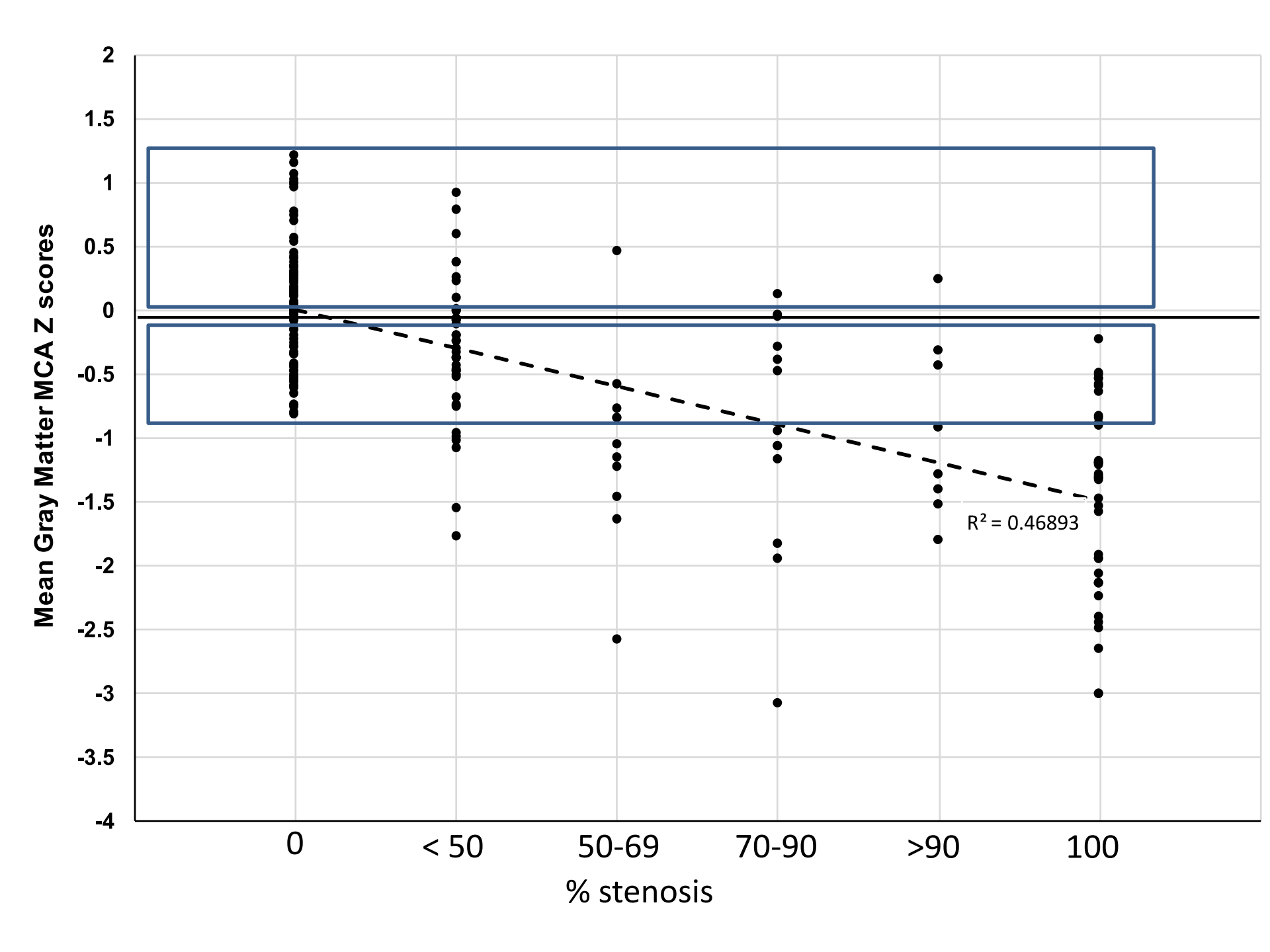

(1) CAS / ICAS
incomplete autoregulation
incomplete compensation
(2) Thromboembolism
↓Pperf
CBF
ischemia
infarction


(1) CAS / ICAS
incomplete autoregulation
incomplete compensation
(3) OSA
↓Pperf
↑ PCO_2
↓ PO_2
+
-
CBF
ischemia
infarction
trophic effects
recruit
major collateral vessels
CoW
opthalmic
pial
peripheral vessel anastomoses
pial networks
penetrating arterioles
WM end-arteries
capillary beds
neovascularization

What causes TIA if CASO but CVR is "normal"

With stenosis CVR is never above mean of normal: always in the lower range




Mean Gray Matter MCA Z scores
2
1.5
1
0.5
0
-0.5
-1
-1.5
-2
-2.5
-3
-3.5
-4
R² = 0.46893
0
< 50
50-69
70-90
>90
100
% stenosis

What causes TIA if CASO but CVR is "normal"

With stenosis CVR is always in the lower range

Collateral blood flow isn't automatic: needs to be recruited when ↓ flow --> symptoms

What is risk of stroke with CASO and "normal" CVR?

N CVR Protective: drops in flow give symptoms but protected by

surges in collateral flow

ischemic pre-conditioning

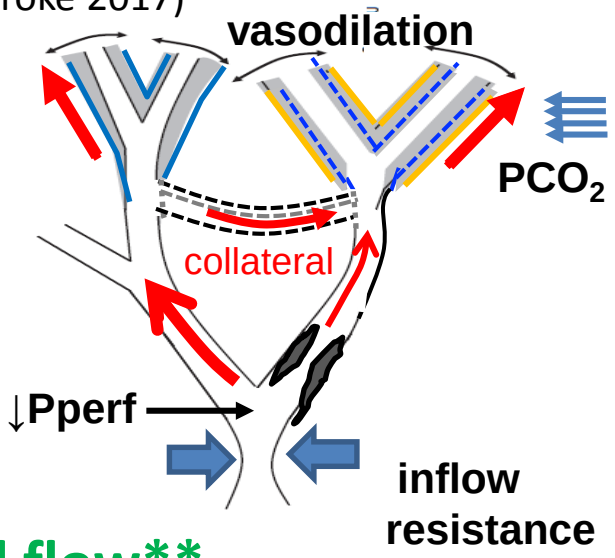
Can still stroke:

Obstruction/hypotension: too big, too sudden, too long

Reassuring:

collateral blood flow results in greater tolerance of ischemia and faster, greater recovery

- softer, less occlusion with clot, (Alves HC, et al. Stroke 2017)
- partial perfusion;
- smaller infarct;
- longer viability of brain;
- time for clot retrieval;
- rPA gets through



'time since stroke' is one criterion. More important: ****presence of collateral blood flow****

Why do people with < 50% have TIA?

Distal territory is always a bit hypoperfused because compensation is not perfect.

Small perturbations in flow (reduced BP, raises in PCO_2) --> ↓ reserve --> symptoms.

What is their CVR?

May be abnormal!

What is their risk of stroke if CVR is abnormal?

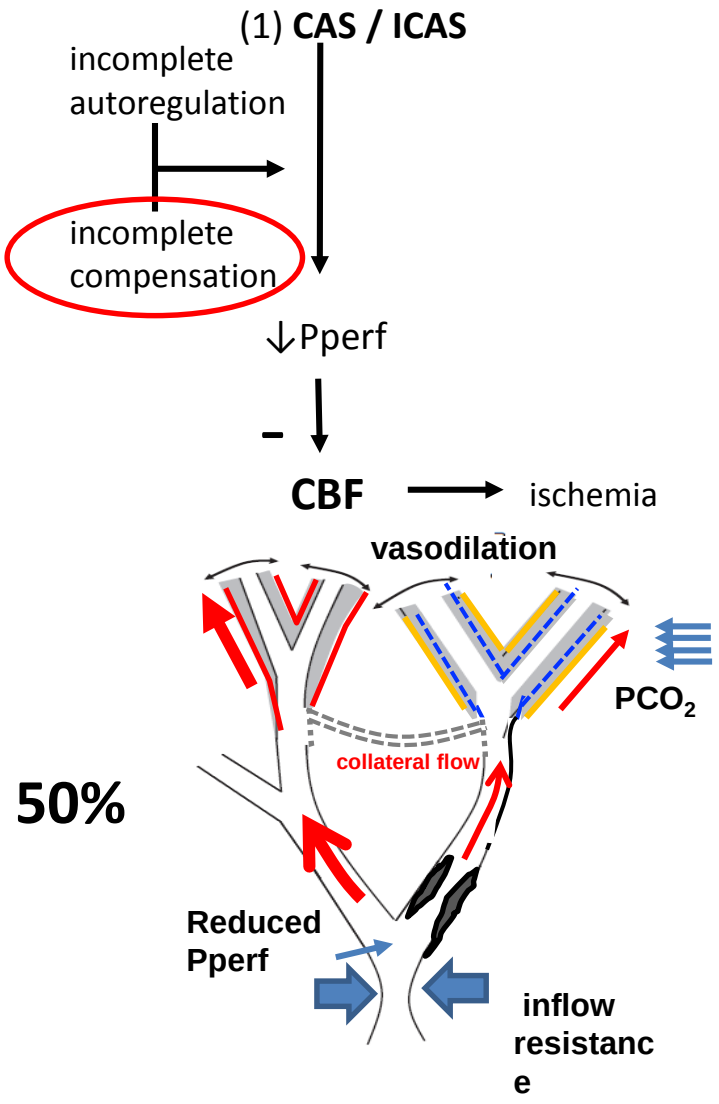
clearly hemodynamic effect of lesion
And inadequate collateral blood flow

Higher risk

What is the risk of stroke if CVR is normal?

No hemodynamic effect of lesion
Or has collateral blood flow

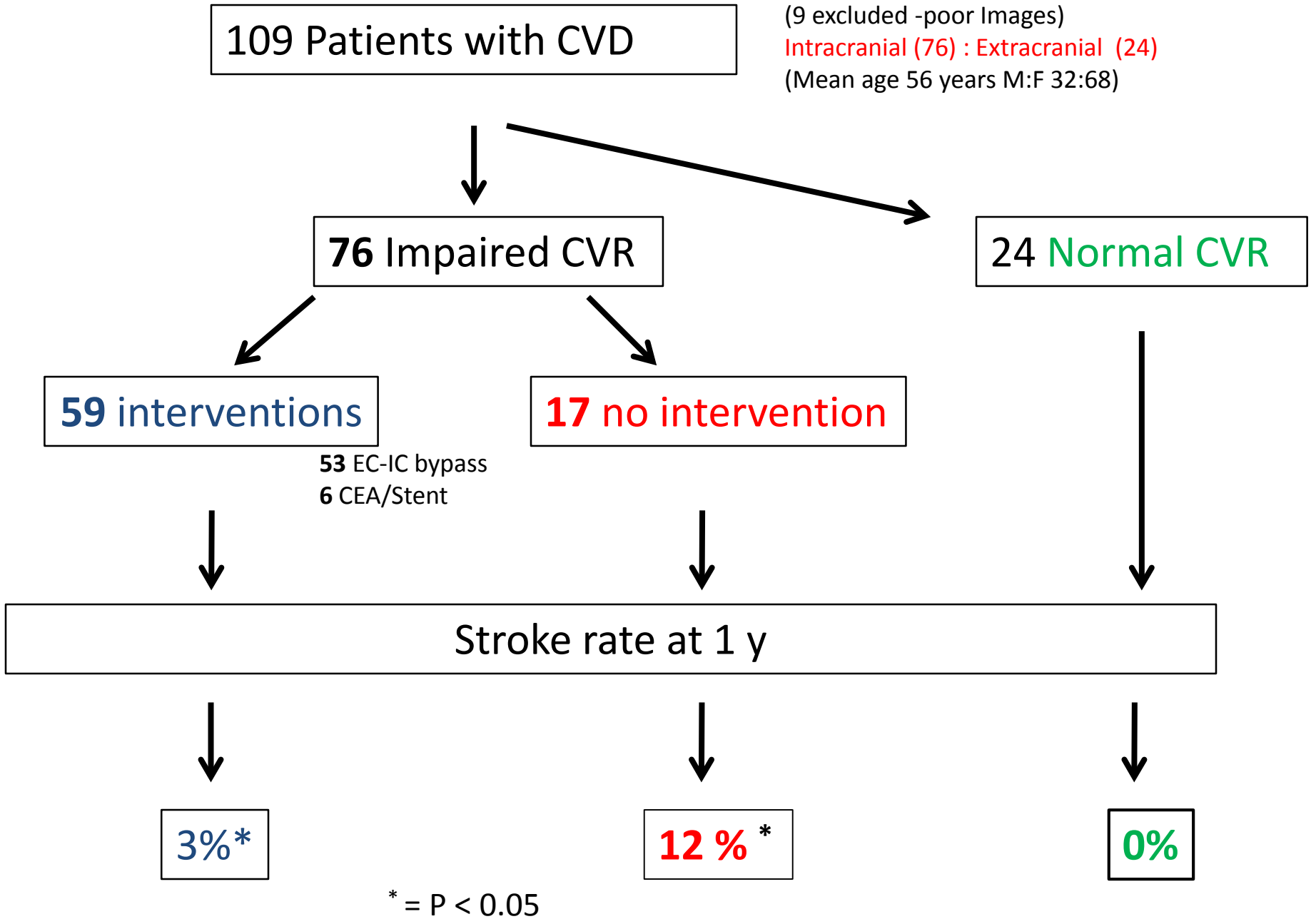
Low risk



CVR helps assign risk even if lesion < 50%

CVR marks risk for stroke

Case series of patients with cerebrovascular disease from our database at UHN, U of Toronto



Cerebrovascular reactivity predicts stroke in high-grade carotid artery disease

Neurology 83 October 14, 2014

Matthias Reinhard, MD
Guido Schwarzer, PhD
Matthias Briel, MD, MSc
Claudia Altamura, MD
Paola Palazzo, MD
Alice King, PhD
Natan M. Bornstein, MD
Nils Petersen, MD
Edith Motschall
Andreas Hetzel, MD
Randolph S. Marshall, MD, MS
Catharina J.M. Klijn, MD, PhD
Mauro Silvestrini, MD
Hugh S. Markus, FRCP
Fabrizio Vernieri, MD

754 patients
Follow up 750 d

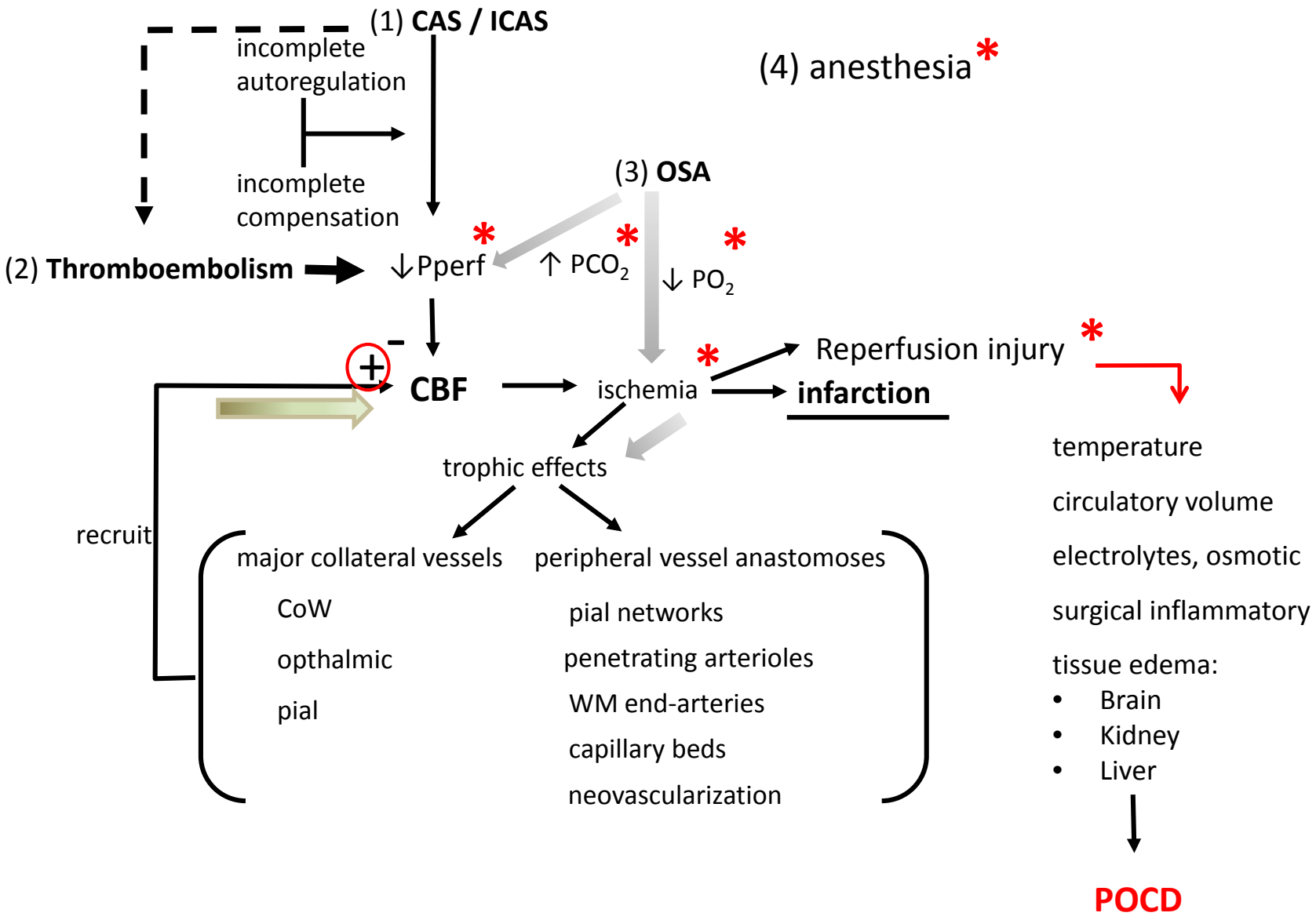
- 49 TIA
- 59 stroke

…Given the advances in modern optimized medical therapy, identifying a subset of patients at high risk is thus of increasing importance.

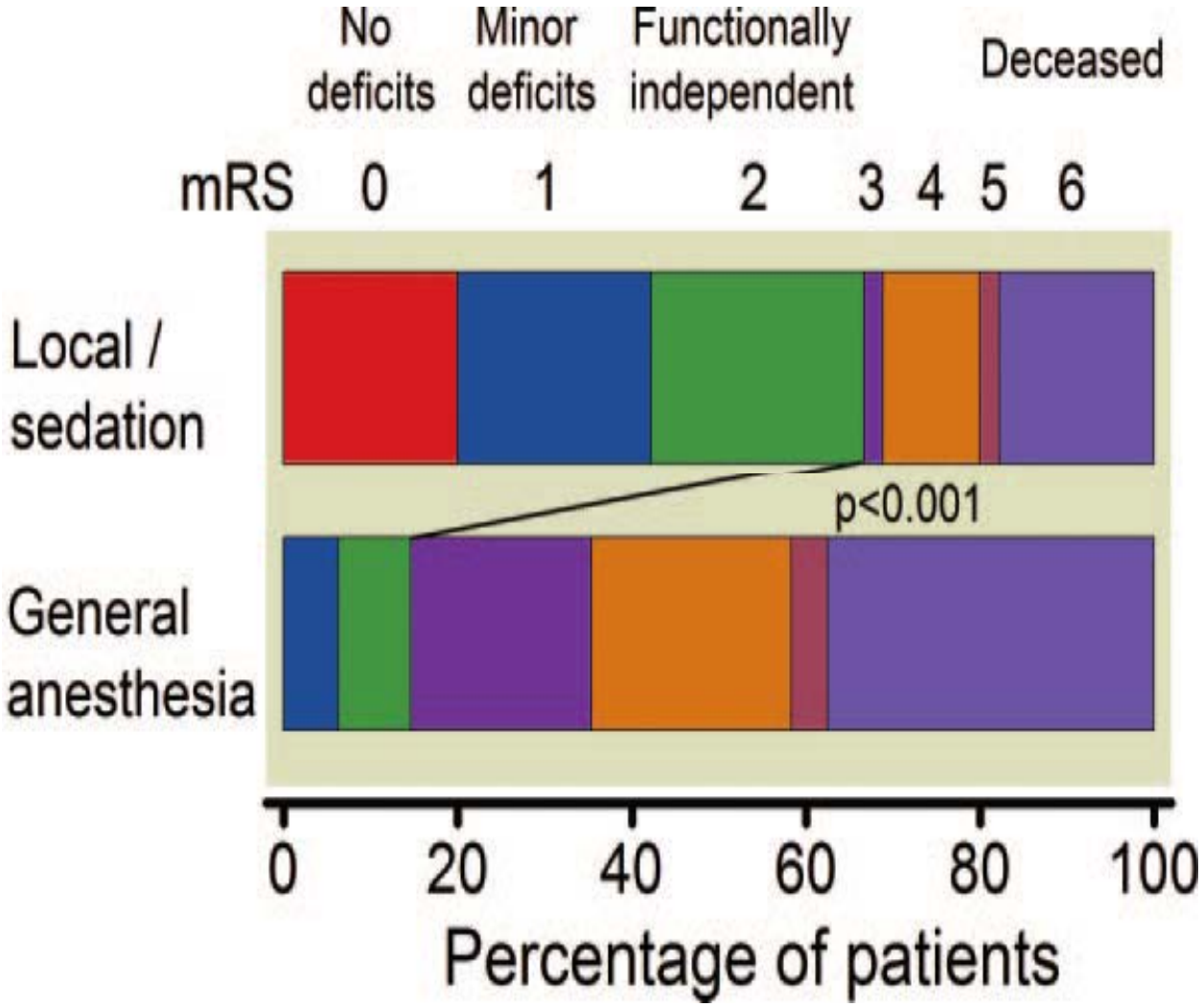
Table 3 Prognostic effect of impaired CO_2 reactivity in severe carotid stenosis or occlusion

Parameter	Adjusted HR (95% CI)	p Value
Clinical endpoint: ipsilateral stroke		
Impaired CO2R (pCi <20%)	3.69 (2.01-6.77)	<0.0001
Age	1.08 (1.04-1.12)	0.0001
Female sex	1.22 (0.69-2.17)	0.50
Carotid occlusion vs 70%-99% stenosis	2.34 (0.66-8.28)	0.19
Contralateral stenosis ≥70%	0.77 (0.26-2.22)	0.62
Symptoms within previous 3 months	2.71 (1.07-6.86)	0.035
Clinical endpoint: ipsilateral stroke or TIA		
Impaired CO2R (pCi <20%)	2.65 (1.72-4.09)	<0.0001
Age	1.04 (1.02-1.07)	0.001
Female sex	1.40 (0.91-2.16)	0.13
Carotid occlusion vs 70%-99% stenosis	1.03 (0.50-2.15)	0.93
Contralateral stenosis ≥70%	0.57 (0.32-1.02)	0.06
Symptoms within previous 3 months	3.31 (1.80-6.10)	0.0001
Parameter	**Coefficient (95% CI)**	**p Value**
Clinical endpoint: ipsilateral stroke		
pCi (per 10% decrease, continuous values)	1.64 (1.33-2.02)	<0.0001
Age, y	1.08 (1.04-1.12)	<0.0001
Female sex	1.28 (0.72-2.29)	0.40
Carotid occlusion vs 70%-99% stenosis	1.59 (0.44-5.80)	0.48
Contralateral stenosis ≥70%	0.65 (0.23-1.88)	0.43
Symptoms within previous 3 months	2.08 (0.81-5.34)	0.13
Clinical endpoint: ipsilateral stroke or TIA		
pCi (per 10% decrease, continuous values)	1.33 (1.18-1.50)	<0.0001
Age, y	1.04 (1.02-1.07)	0.00051
Female sex	1.44 (0.93-2.23)	0.102
Carotid occlusion vs 70%-99% stenosis	0.90 (0.43-1.90)	0.79
Contralateral stenosis ≥70%	0.54 (0.30-0.97)	0.038
Symptoms within previous 3 months	3.12 (1.69-5.77)	0.00027

Anesthetic implications


(1) CAS / ICAS
incomplete autoregulation
incomplete compensation
(2) Thromboembolism
(3) OSA
(4) anesthesia *
↓Pperf
↑ PCO_2
↓ PO_2
CBF
ischemia
Reperfusion injury
infarction
trophic effects
recruit
major collateral vessels
CoW
opthalmic
pial
peripheral vessel anastomoses
pial networks
penetrating arterioles
WM end-arteries
capillary beds
neovascularization
temperature
circulatory volume
electrolytes, osmotic
surgical inflammatory
tissue edema:
Brain
Kidney
Liver
POCD

Anesthsia for endovascular procedures



Davis et al. Anesthesiology 2012; 116:396 – 405

*keep PCO_2 constant and MAP (91 mmHg) constant throughout

Outcome: <u>Same as conscious sedation</u>

GA advantages:

- Neuroprotective effects of reduced CMRO2 with vapors
- Longer arrival to groin puncture…but faster groin puncture to retrieval

(*Henden et al. Stroke. 2017;48:1601-1607)

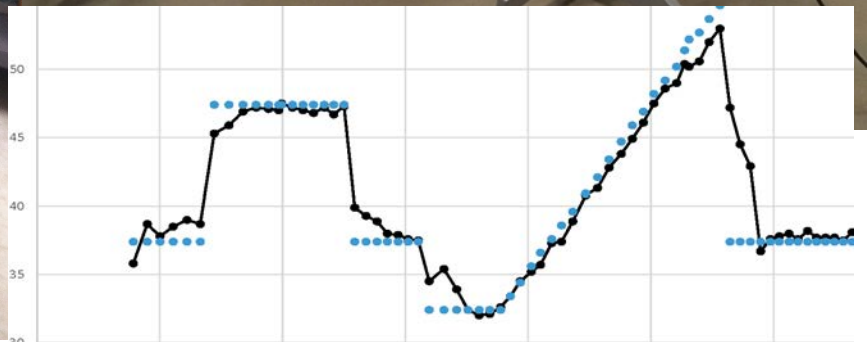
Summary

To standardize the brain stress test:

We began by standardizing the stimulus…

If it was so easy…others would…

PCO_2



Clinical progress:

- **Definition of normal CVR**;
- Can localize *and quantitate* abnormal CVR in a single patient;
- Can follow repeat CVR in *individual* subject to assess:
  - progress of lesions over time
  - result of therapeutic interventions
- *data compatible across centers:

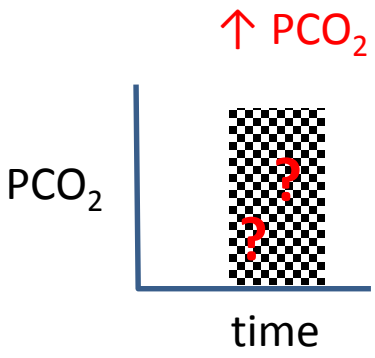
  Establish a database across centers
- **Clinical model for assessment and management of risk of stroke**

Chief Scientist

Joe.fisher@utoronto.ca

https://bigadventure2016.tumblr.com

Tight co-relation between time course and amplitude of PCO_2 and BOLD



Breath hold

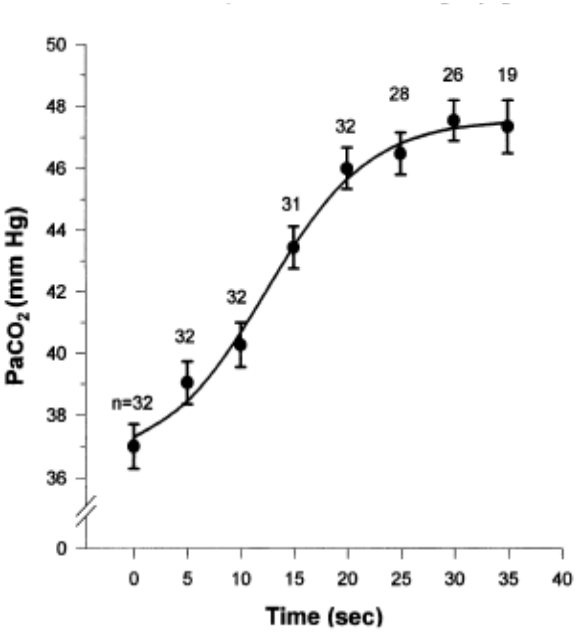
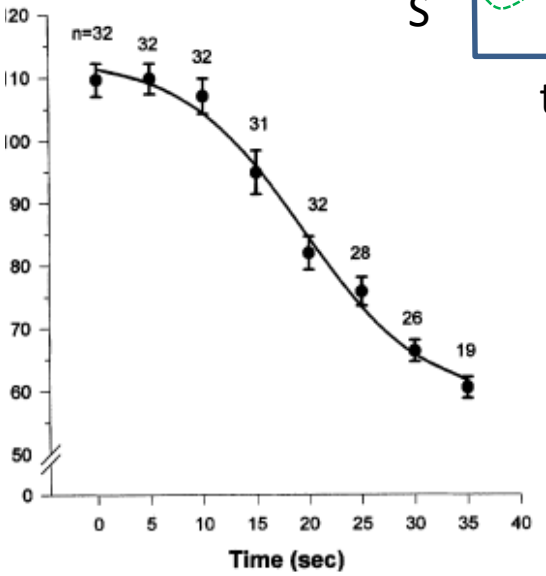
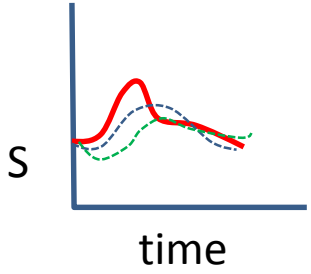


FIGURE 4. In this graph, the composite mean arterial P_{CO_2} (mm Hg) vs time (seconds) during breath-holding from FRC for all eight subjects is shown. Error bars refer to the SEM. The number above each point refers to the number of $PaCO_2$ values used to calculate the mean. The curvilinear line shown is that from equation 2.

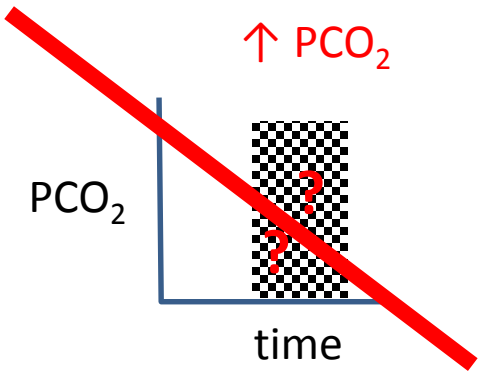


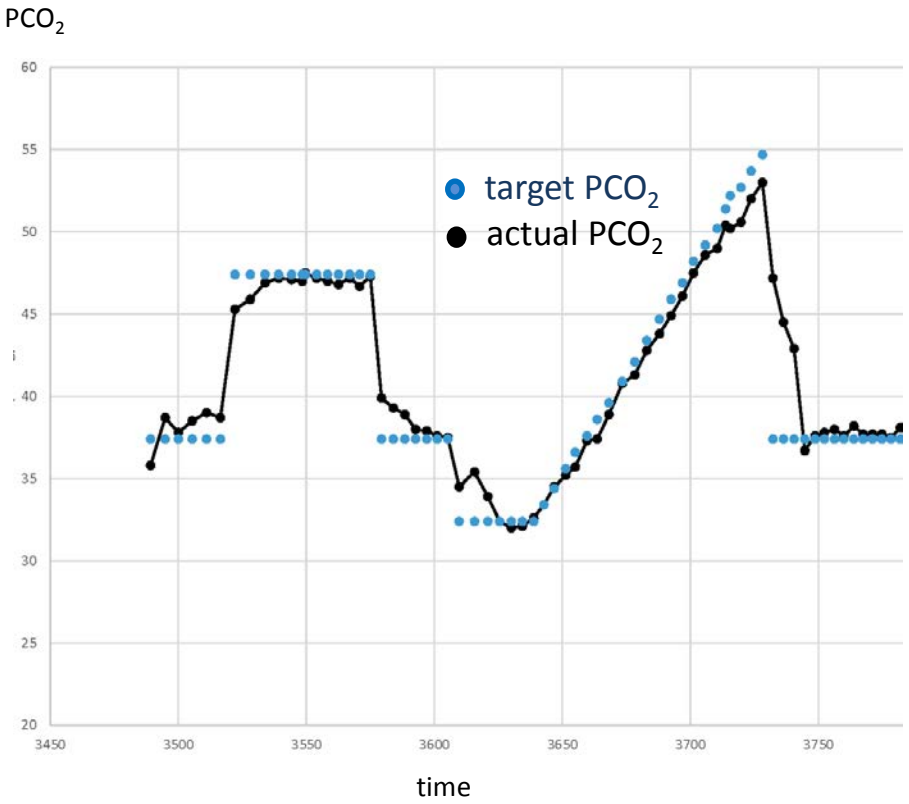
E 2. In this graph, the composite mean arterial P_{O_2} (mm Hg) ie (seconds) during breath-holding from FRC for all eight ts is shown. Error bars refer to the SEM. The number above oint refers to the number of PaO_2 values (n) used to calcu- ie mean. The curvilinear line shown is that from equation 1.

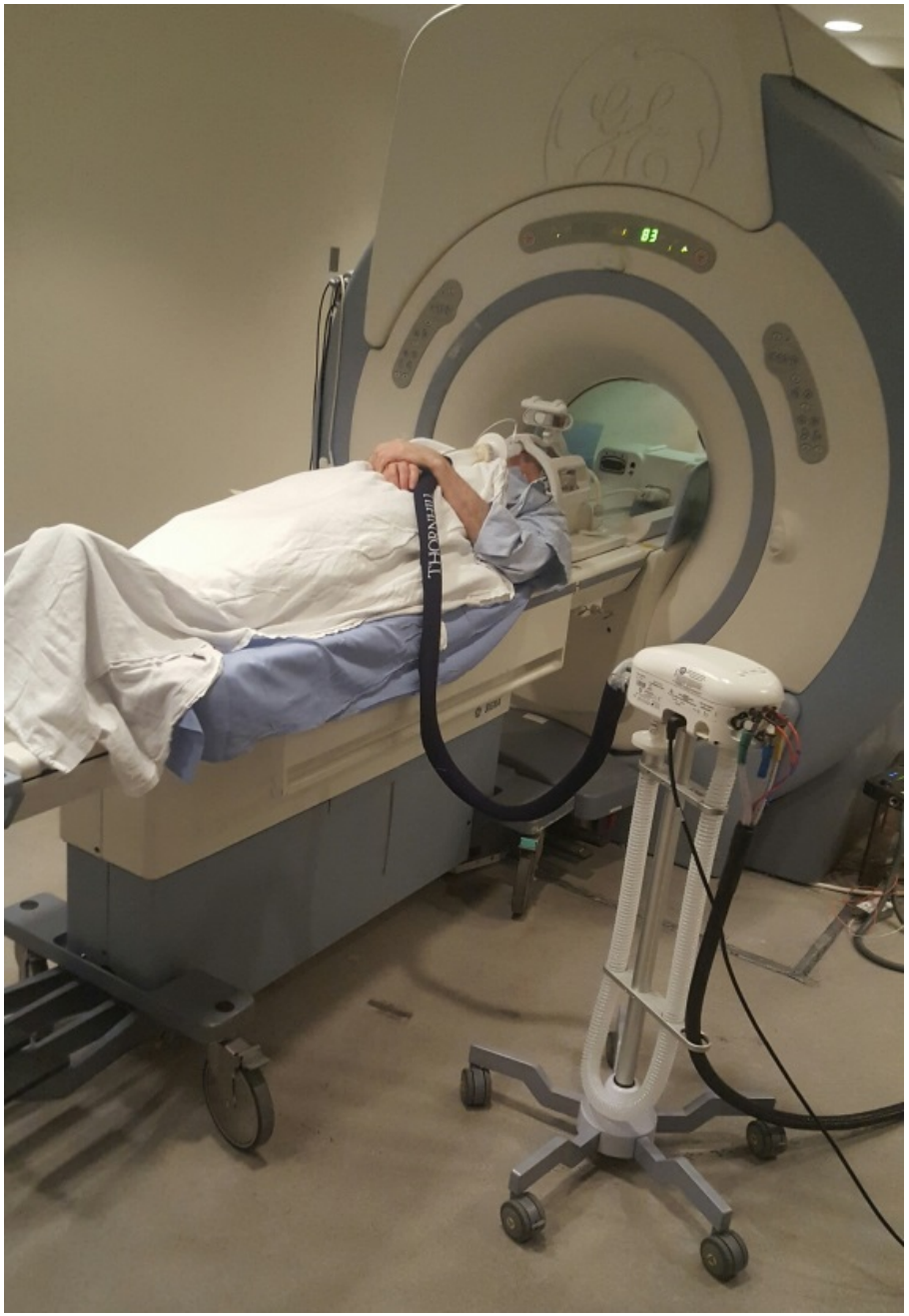


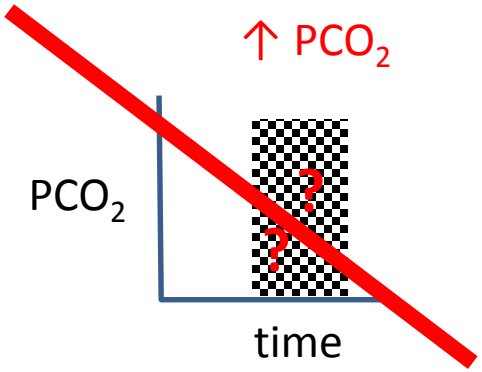
Sasse et al. Chest 1996; 110: 958 - 64

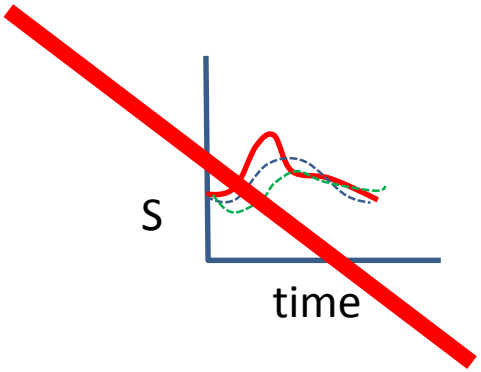
Tight co-relation between time course and amplitude of PCO_2 and BOLD

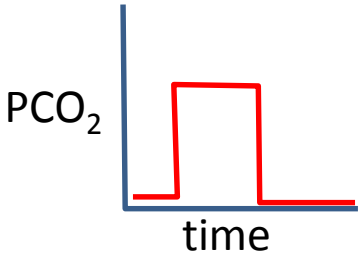


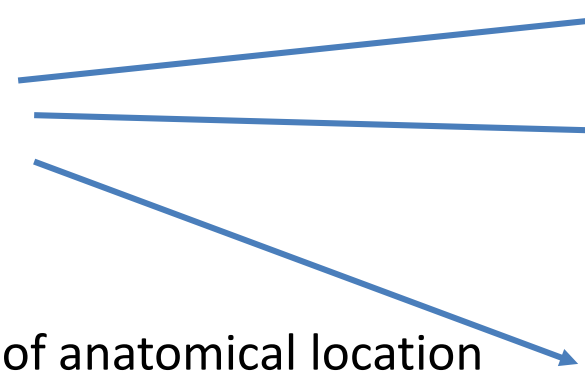


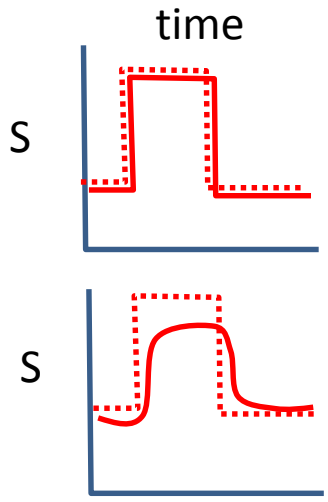






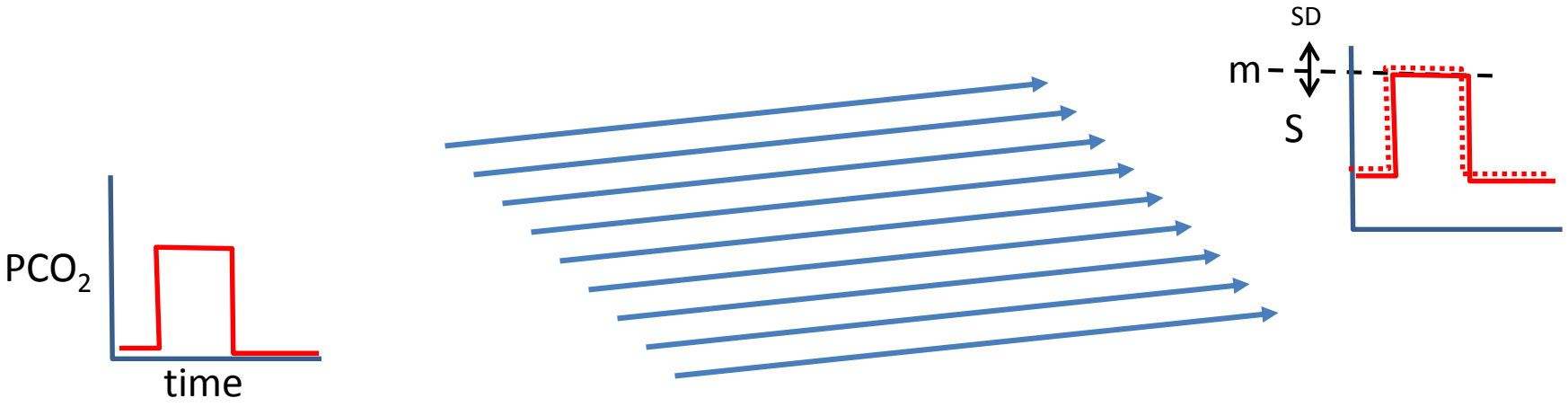


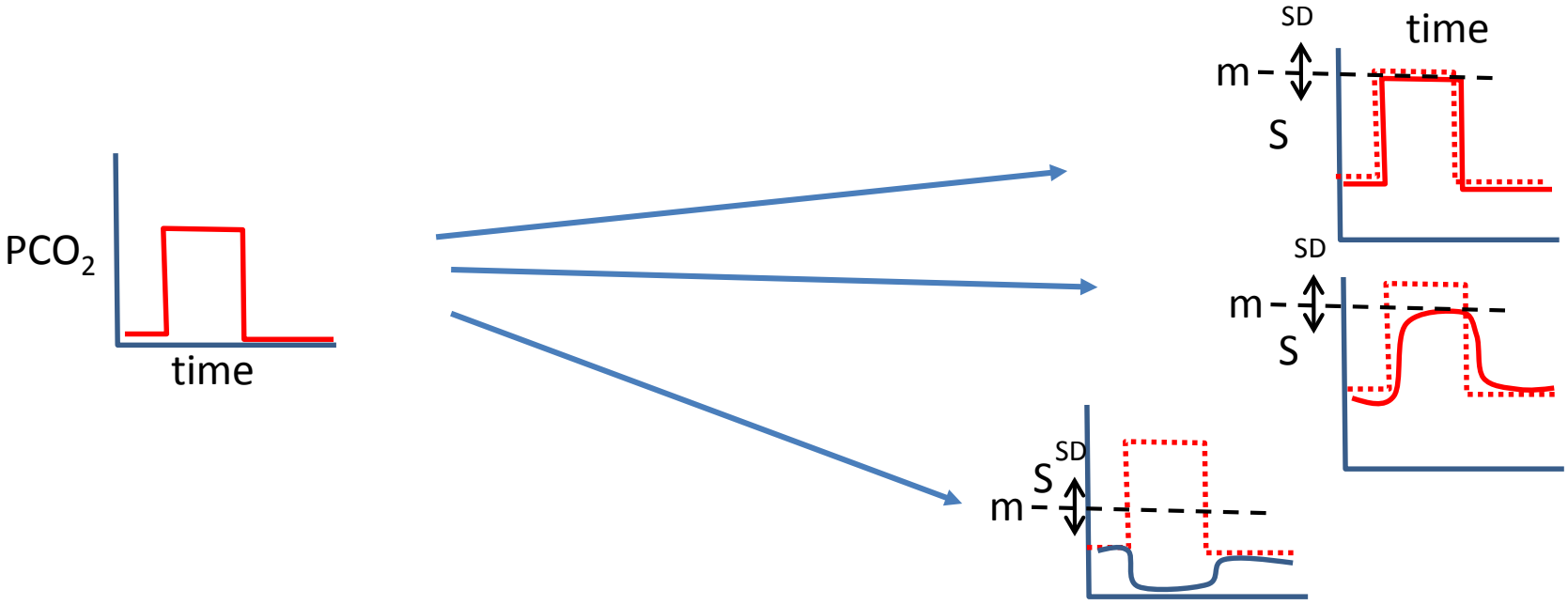




BUT: CVR is also a function of anatomical location

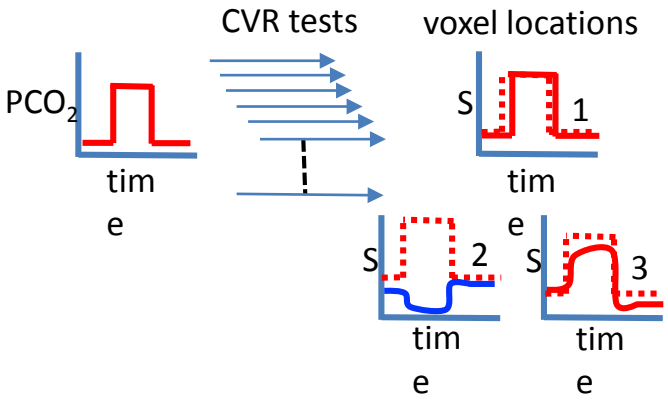
…so how do we know which is normal for THAT location?


PCO2
time
SD
m
S

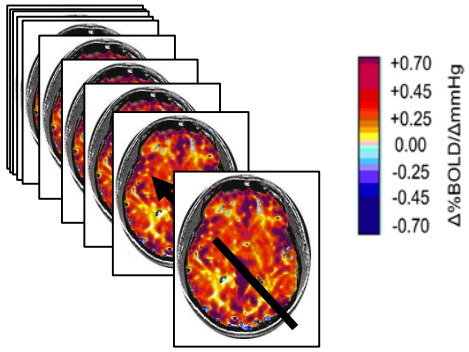

PCO2
time
SD
time
m
S
SD
m
S
SD
S
m

Z-map Construction

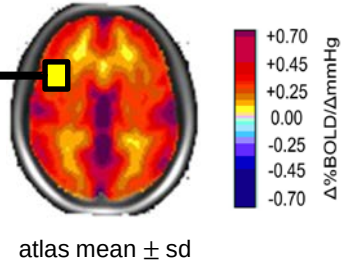
1. Perform CVR tests with standard stimulus in cohort



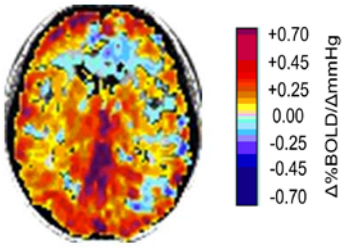
2. Coregister all subject scans to standard space



3. Atlas of subject mean and standard deviation for each corresponding voxel



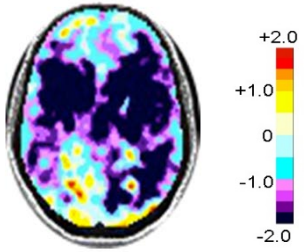
atlas mean ± sd



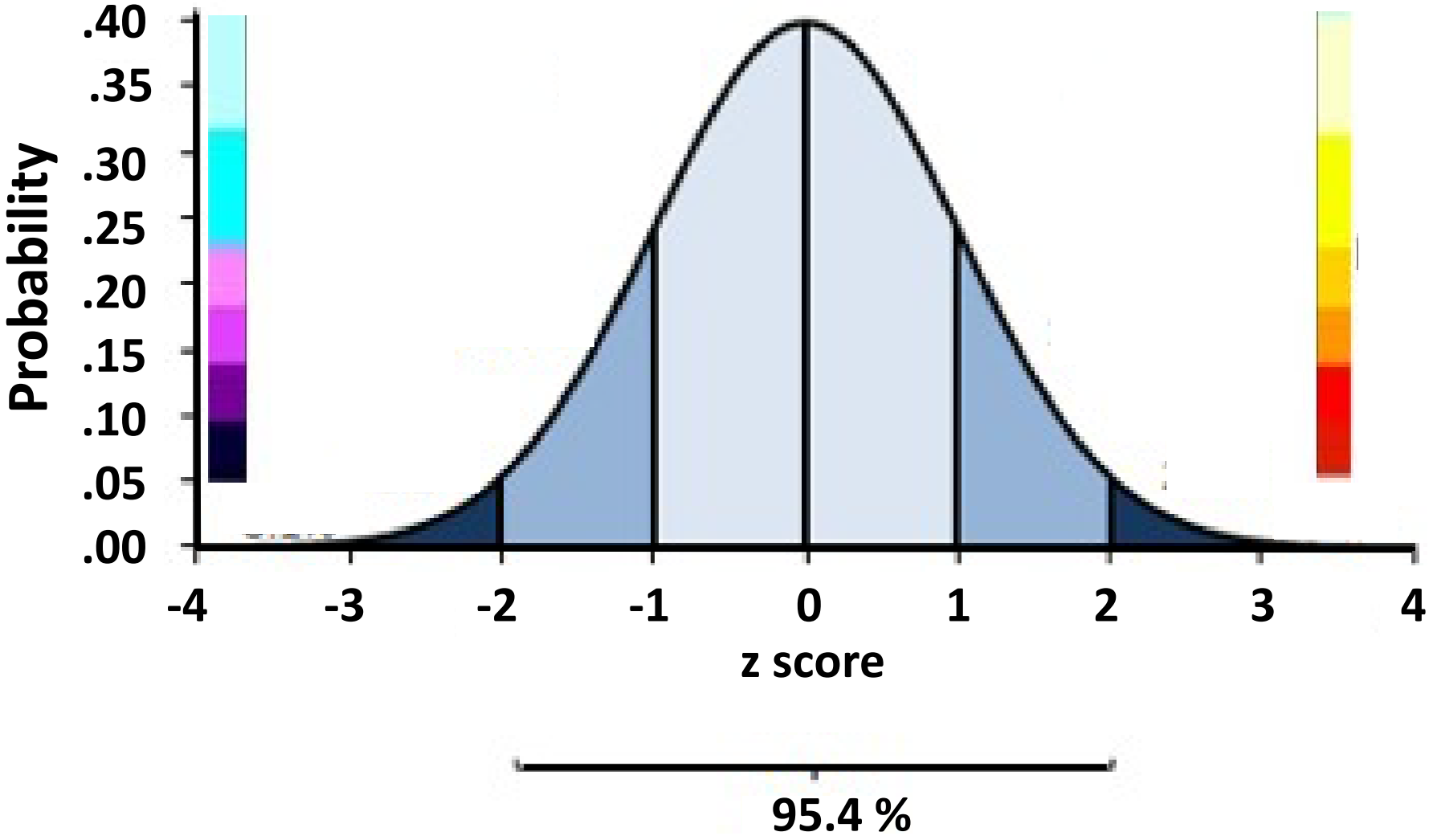
4. Patient CVR with same standard stimulus as cohort

$$z = \frac{[CVR] - M}{\sigma}$$

5. Calculate z score for each voxel



6. Map and color code z scores to anatomical scans creating z-map


Probability
.40
.35
.30
.25
.20
.15
.10
.05
.00
-4
-3
-2
-1
0
1
2
3
4
z score
95.4 %

CVR: a Brain stress test:

1) How does it work?

2) Making it clinical

Size: matters

Variability of stimulus: -> variability of CVR result

Normalize for anatomical location

Optimize resolution of test-test changes

3) Clinical implications:

Research tool → individualized Dx → research tool

True test of hemodynamic significance

Test of efficacy of intervention

CREST 2?

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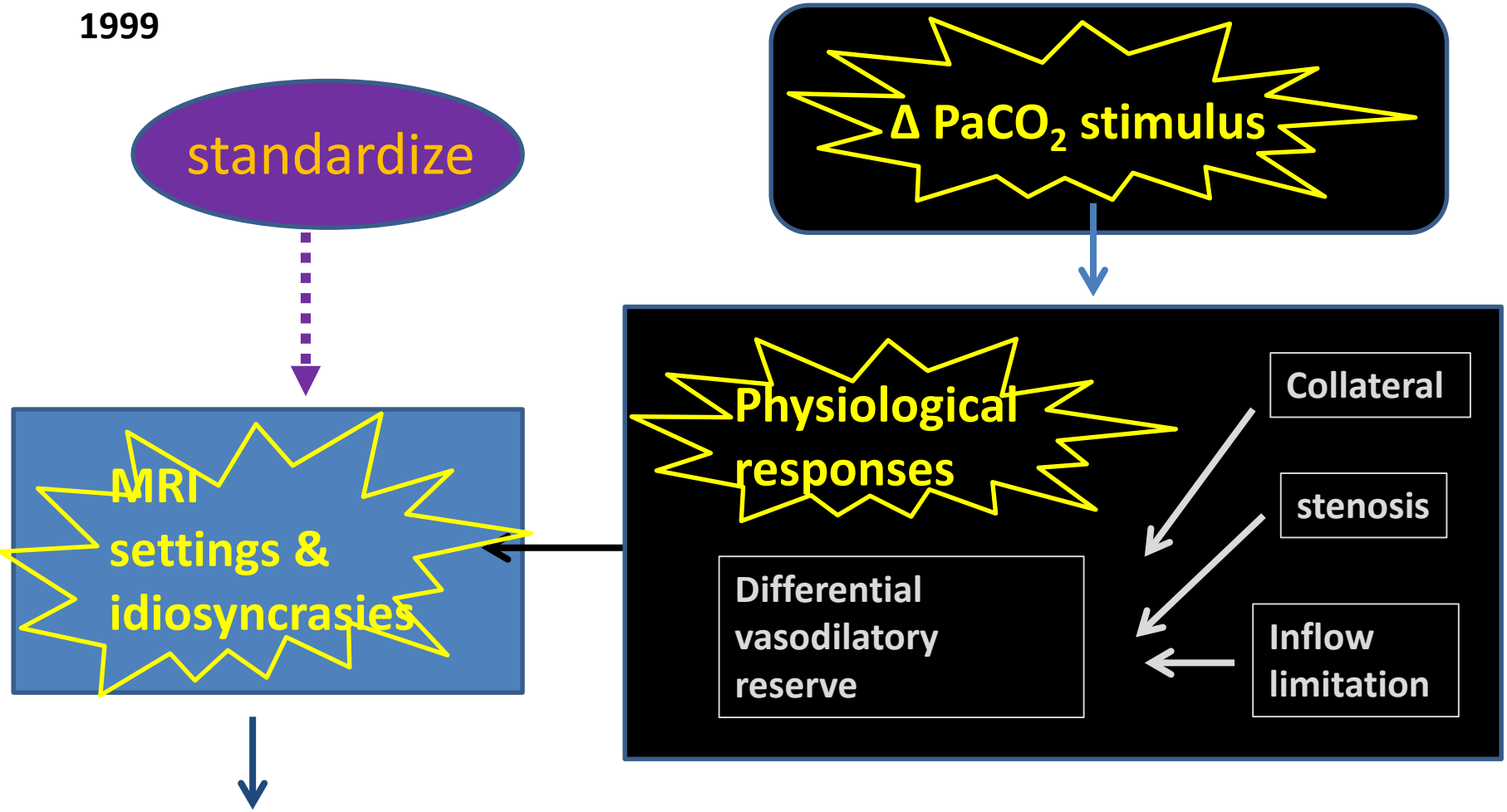
CVR: measuring it right

1999

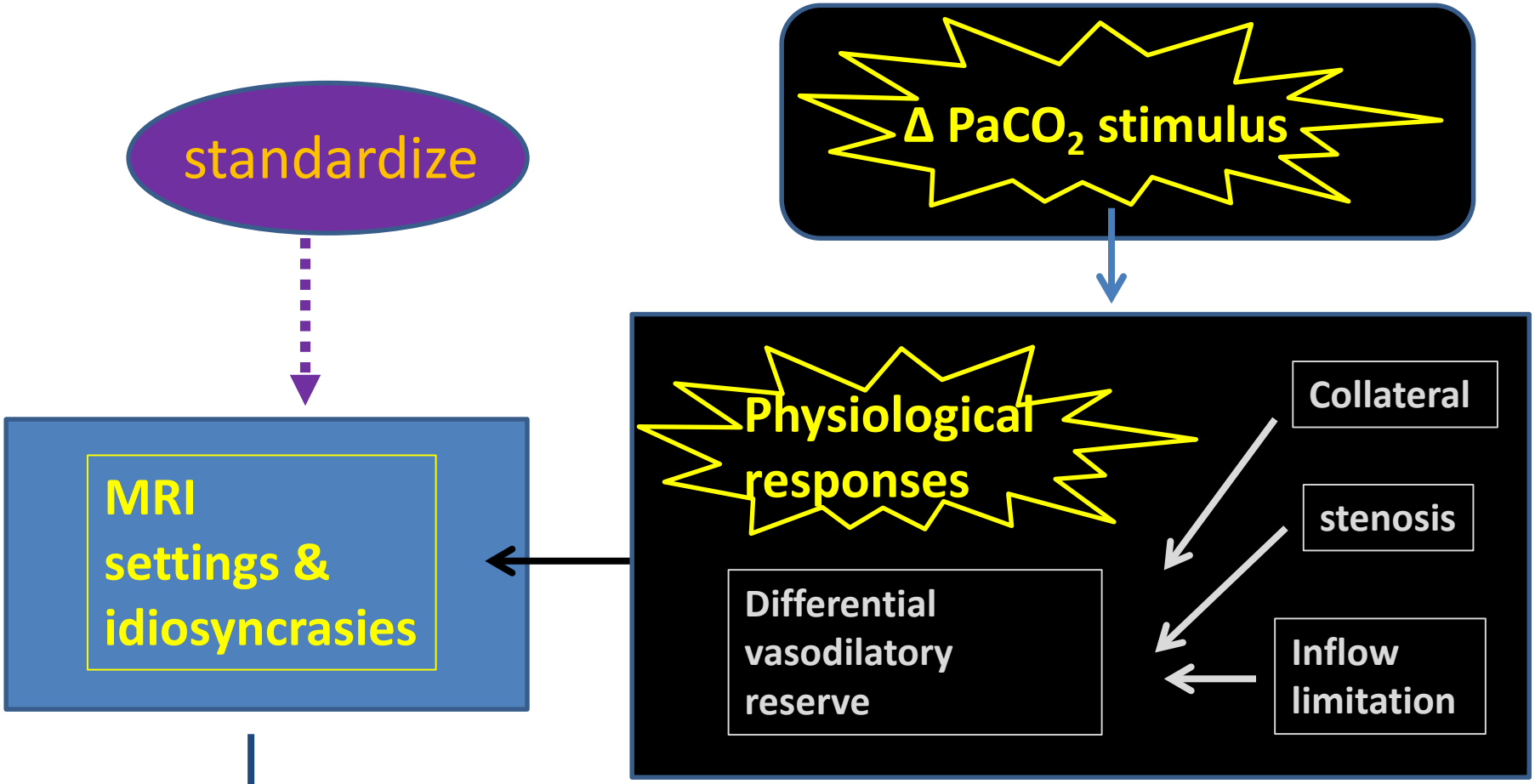


CVR/steal

$$CVR = \frac{\Delta \text{ BOLD}}{\Delta \text{ } PCO_2}$$

Interpretation:

- high specificity for S-I-C-K
- Low sensitivity!
  - No gradation in severity
  - Poor localization



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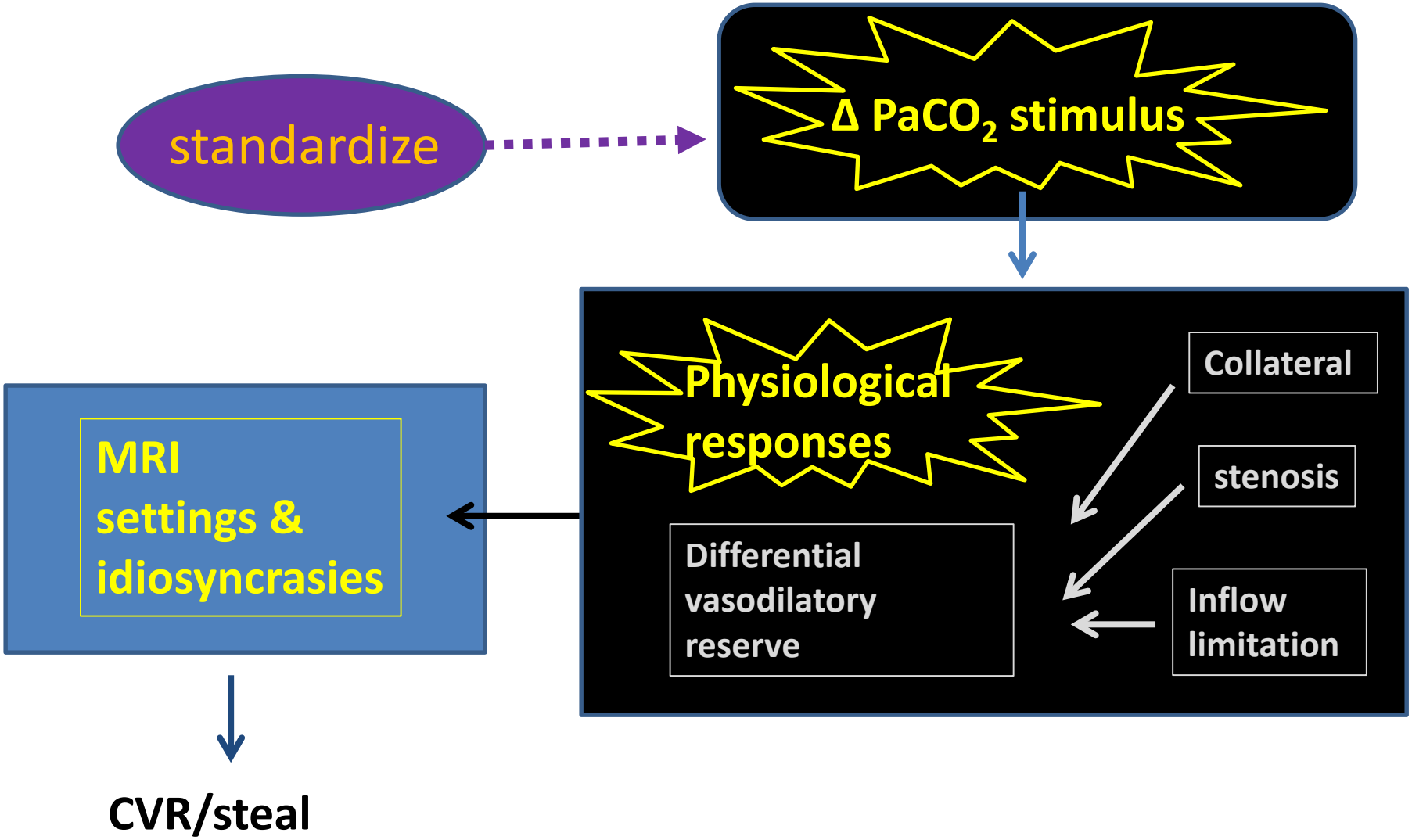
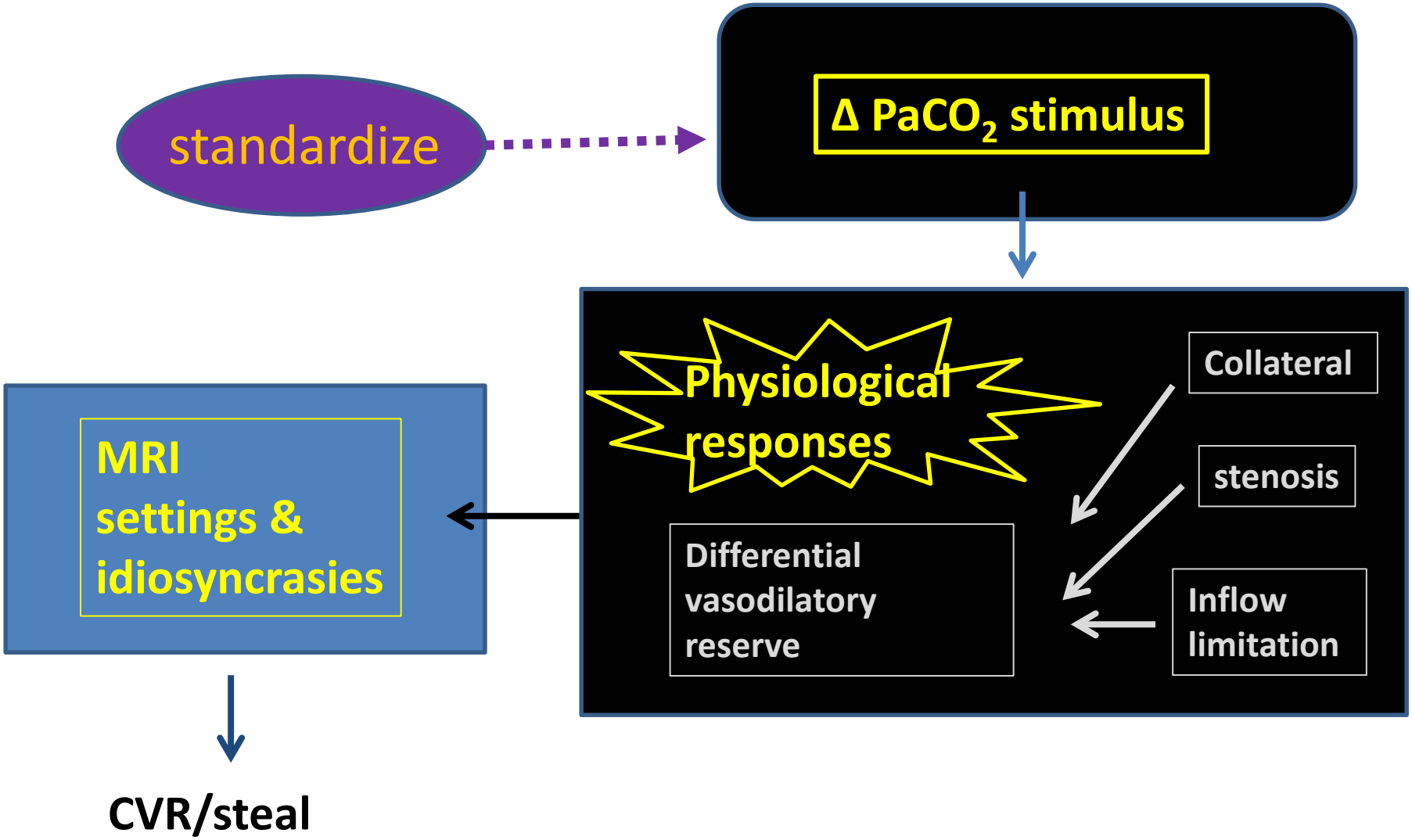

standardize
Δ PaCO2 stimulus
Physiological responses
Collateral
stenosis
Inflow limitation
Differential vasodilatory reserve
MRI settings & idiosyncrasies
CVR/steal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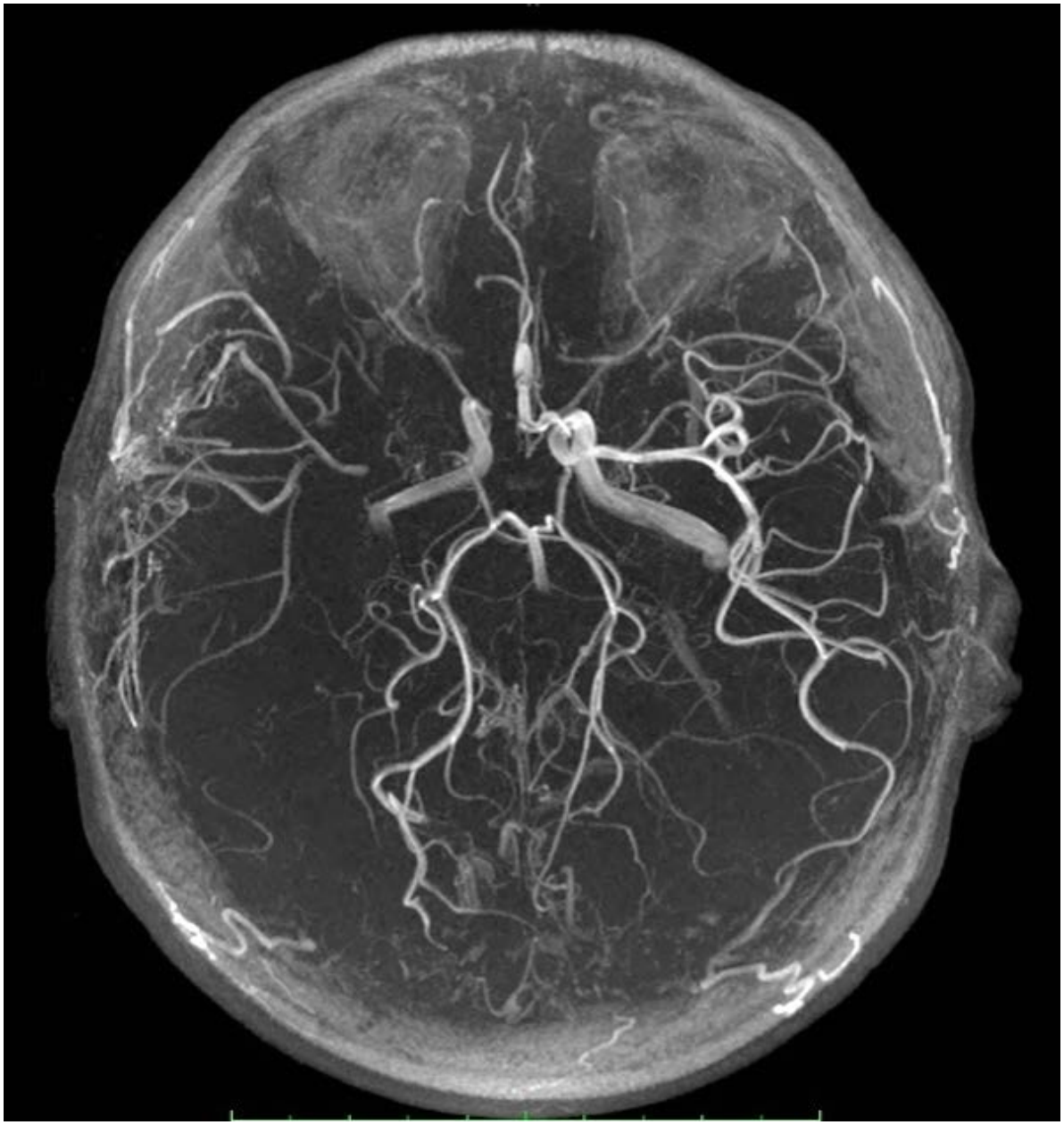
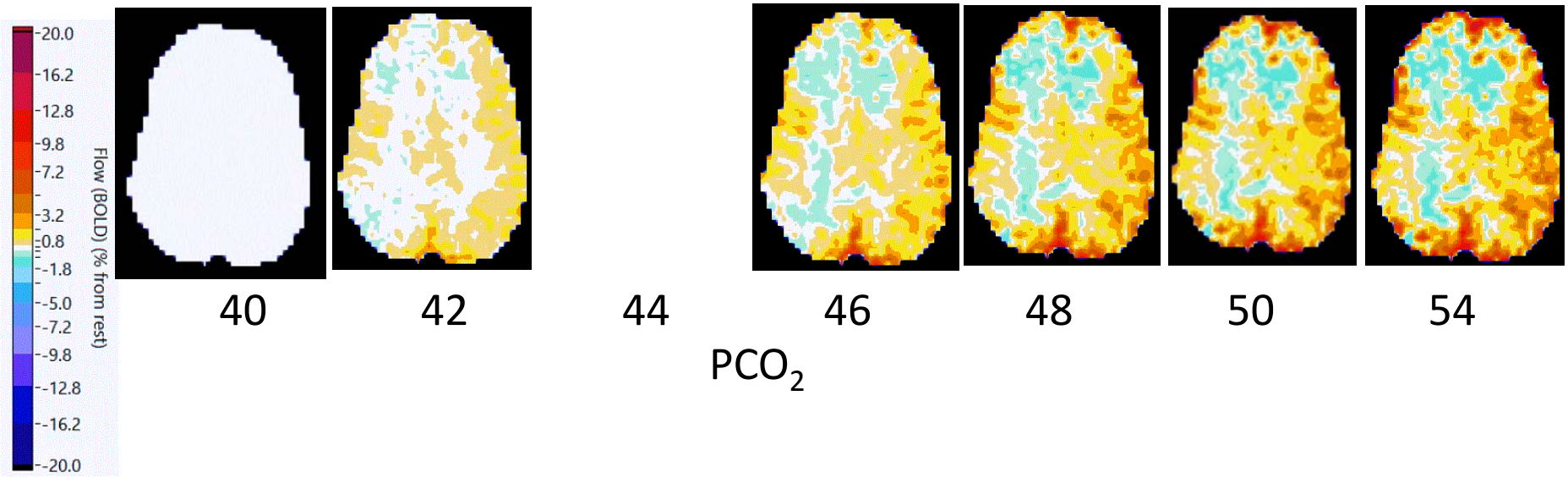
CREST 2?

18 M Dx ‘moyamoya’



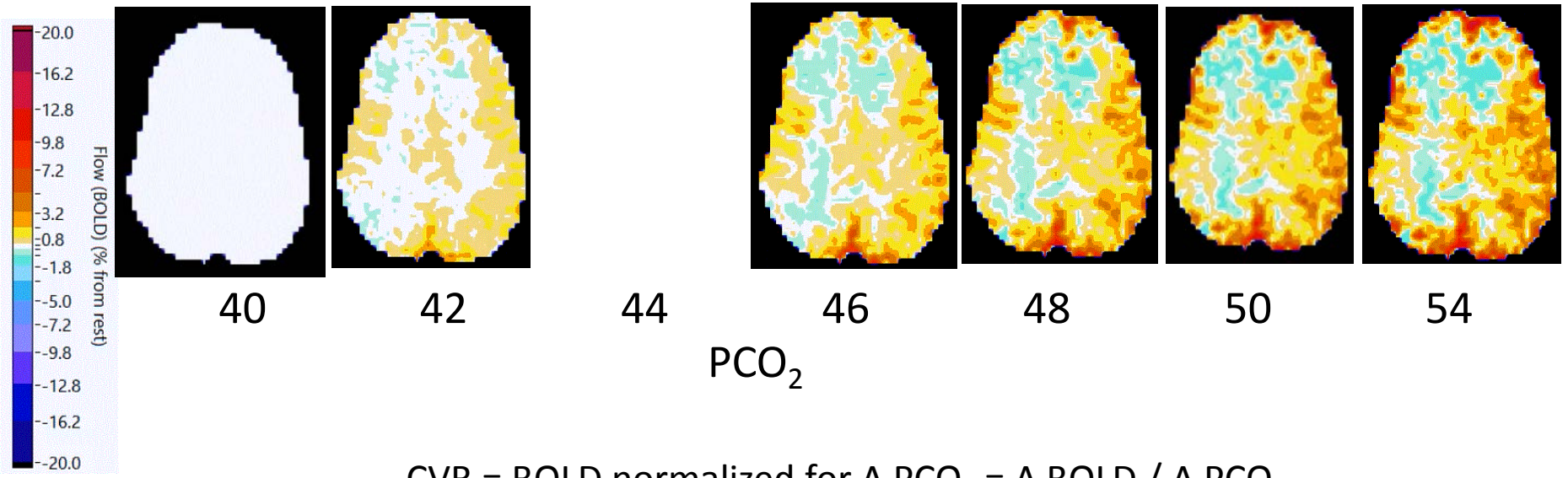
Δ BOLD

Δ BOLD as a function of PCO_2

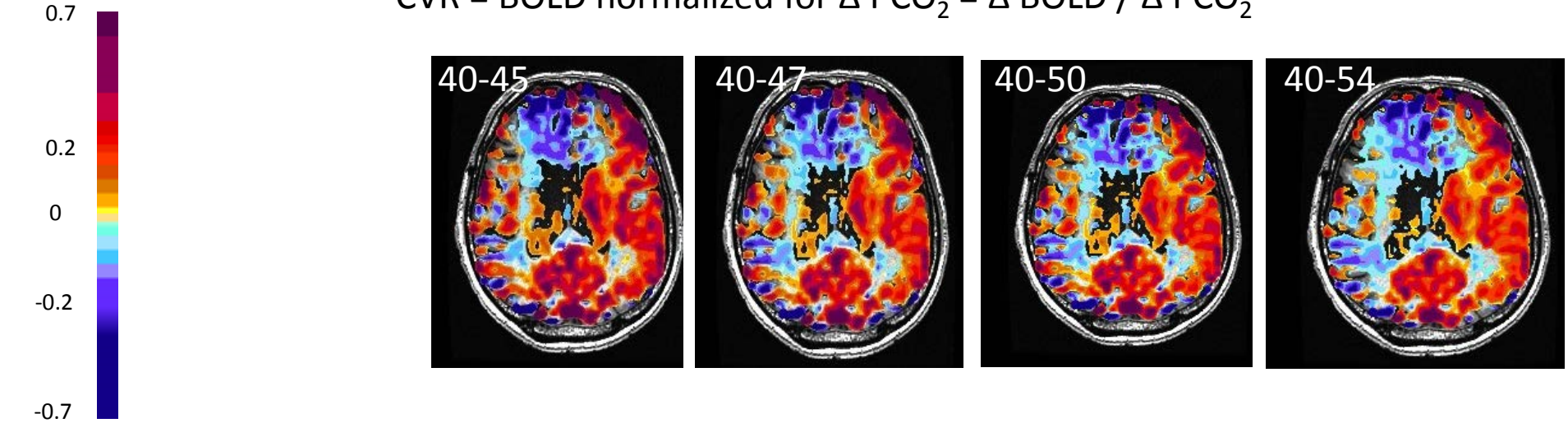


Δ BOLD

Δ BOLD as a function of PCO_2



CVR = BOLD normalized for Δ PCO_2 = Δ BOLD / Δ PCO_2



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CREST 2?

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Standardized between centers
Consistent between tests

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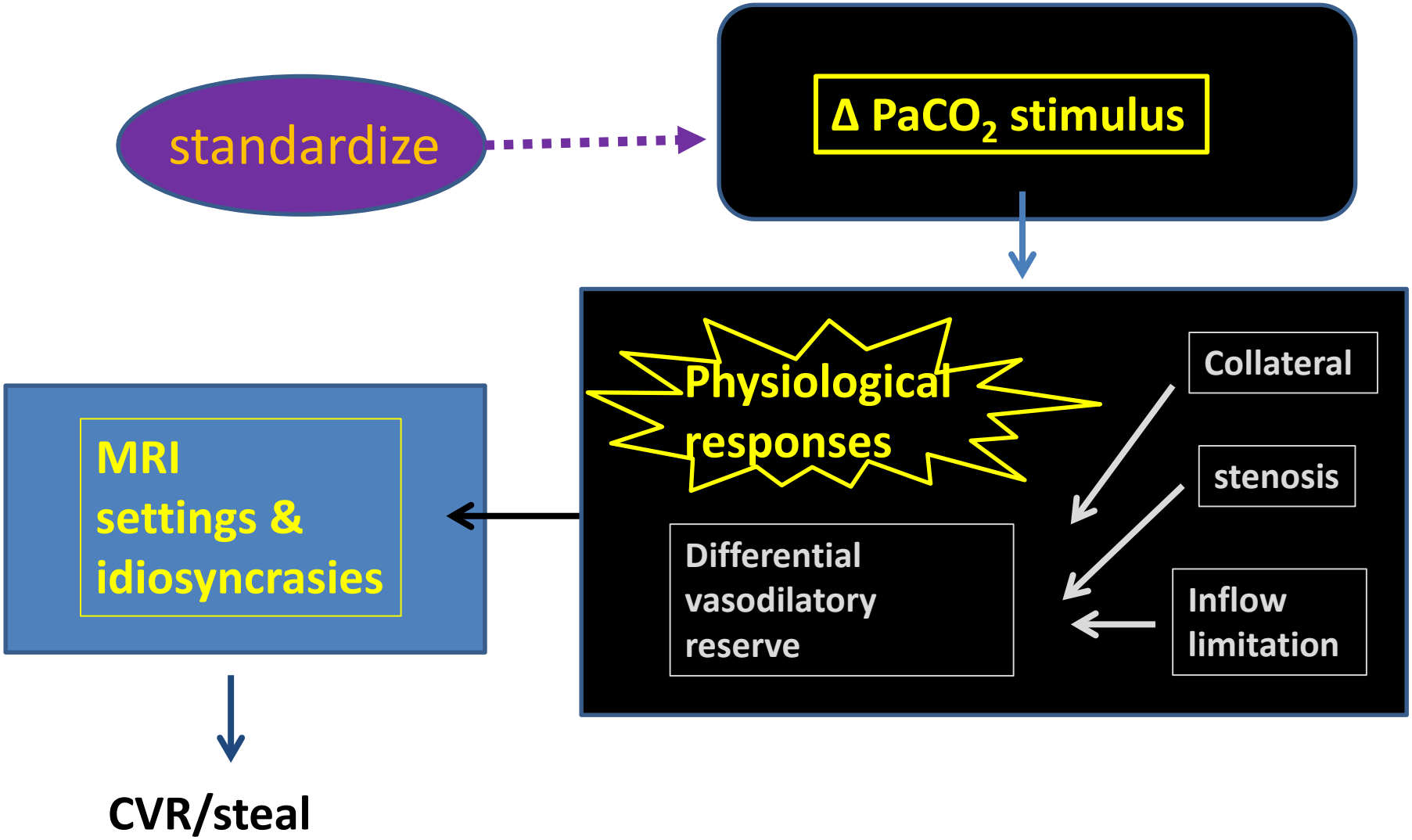
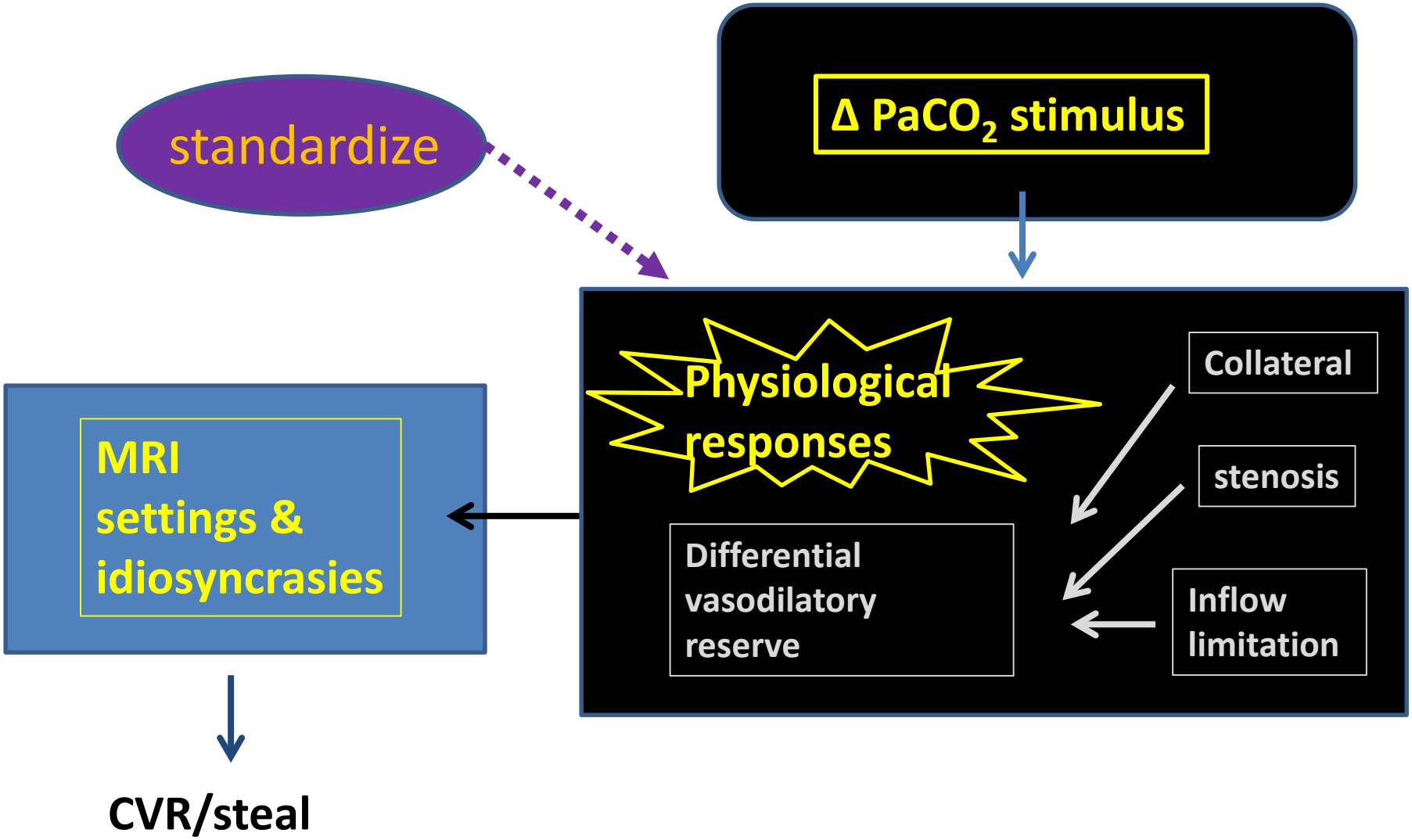

standardize
Δ PaCO2 stimulus
Physiological responses
Collateral
stenosis
Inflow limitation
Differential vasodilatory reserve
MRI settings & idiosyncrasies
CVR/steal


standardize
Δ PaCO2 stimulus
Physiological responses
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stenosis
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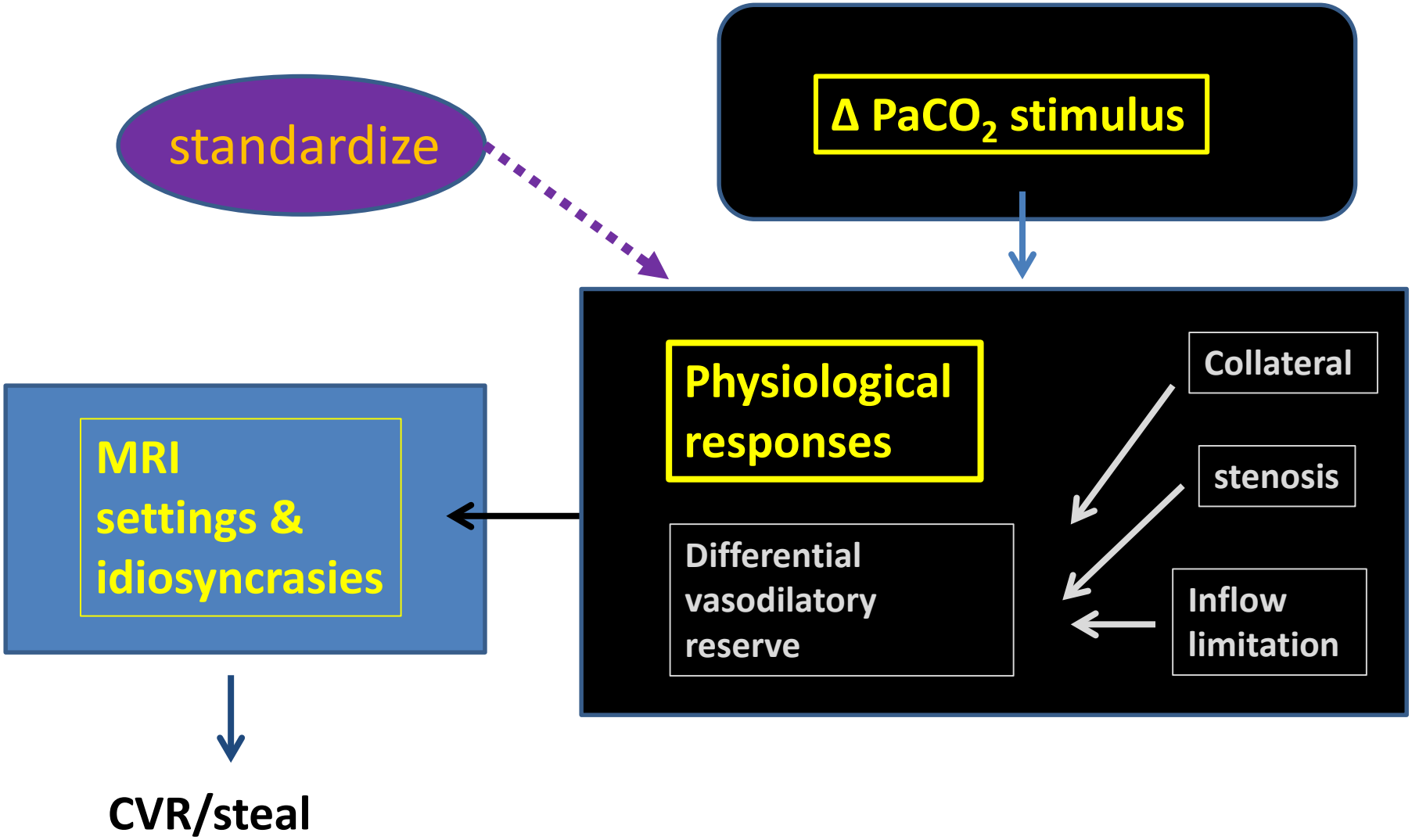
CVR/steal


standardize
Δ PaCO2 stimulus
Physiological responses
Collateral
stenosis
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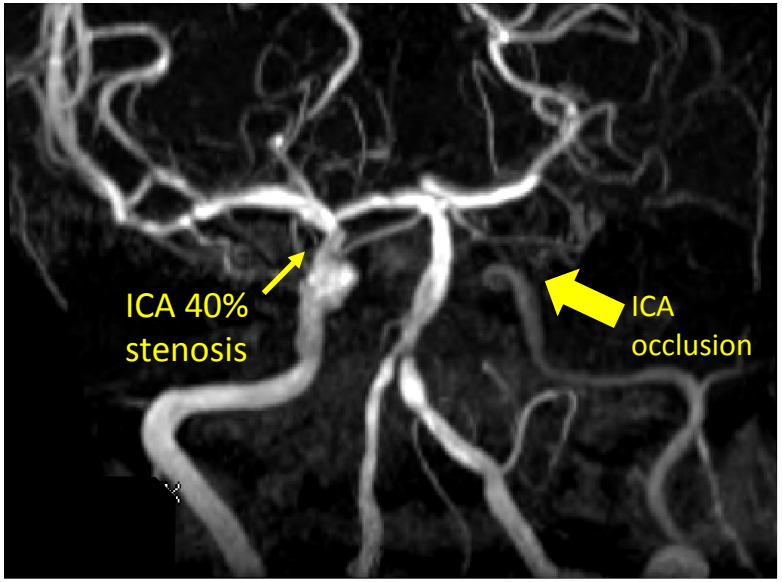
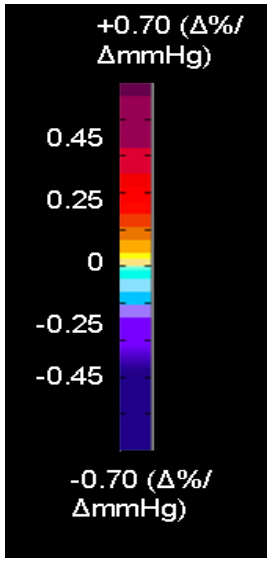
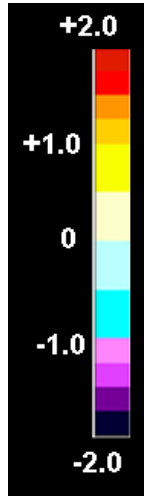
MRI settings & idiosyncrasies
CVR/steal

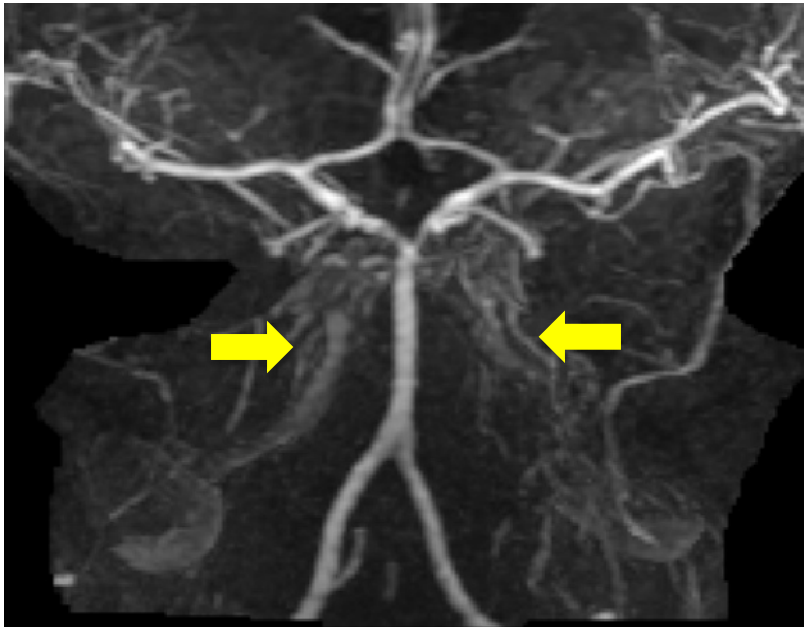

ICA 40%
stenosis
ICA
occlusion


R


L

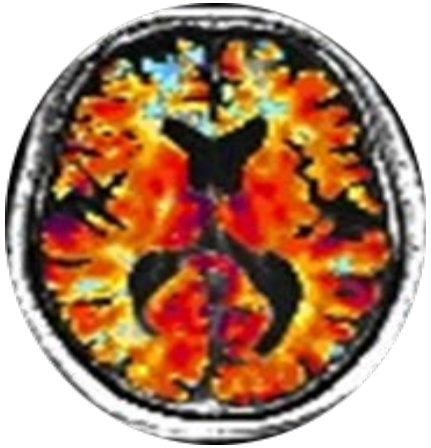

+0.70 (Δ%/
ΔmmHg)
0.45
0.25
0
-0.25
-0.45
-0.70 (Δ%/
ΔmmHg)

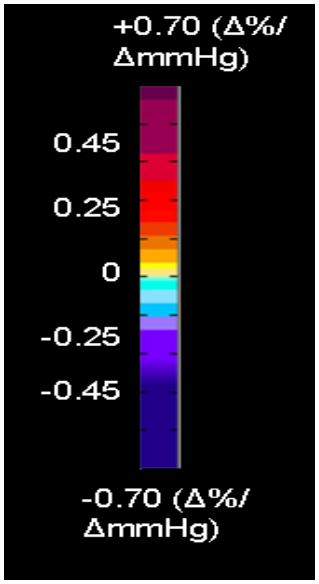

+2.0
+1.0
0
-1.0
-2.0

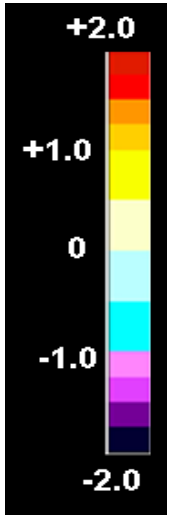



R

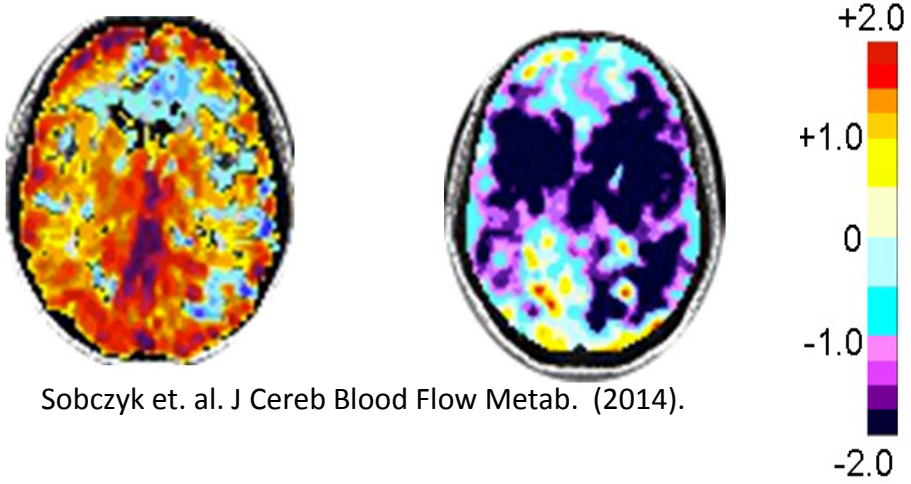

L




+0.70 (Δ%/ ΔmmHg)
0.45
0.25
0
-0.25
-0.45
-0.70 (Δ%/ ΔmmHg)


+2.0
+1.0
0
-1.0
-2.0

42 year old female with bilateral Moyamoya



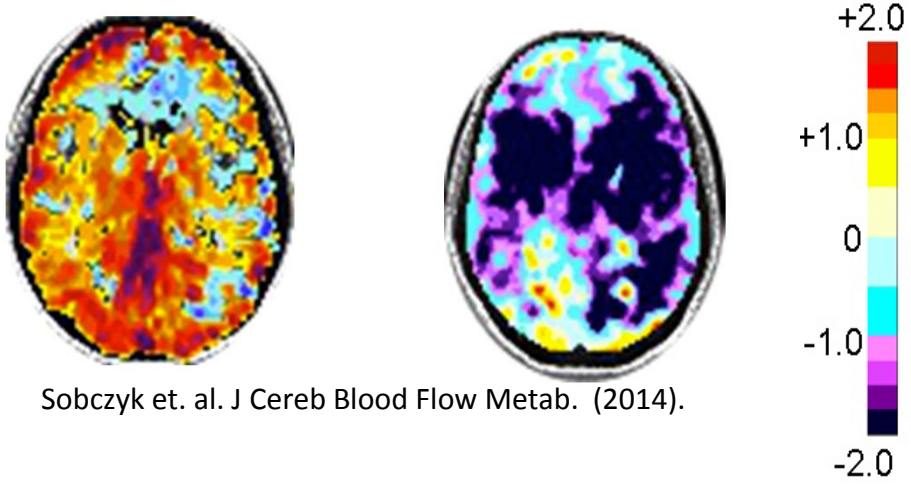
Sobczyk et. al. J Cereb Blood Flow Metab. (2014).

How far have we come with z scores?

CVR is:

- Normalized for anatomical location
- Can be normalized for age, sex, [other: e.g., Dx, Rx]

42 year old female with bilateral Moyamoya



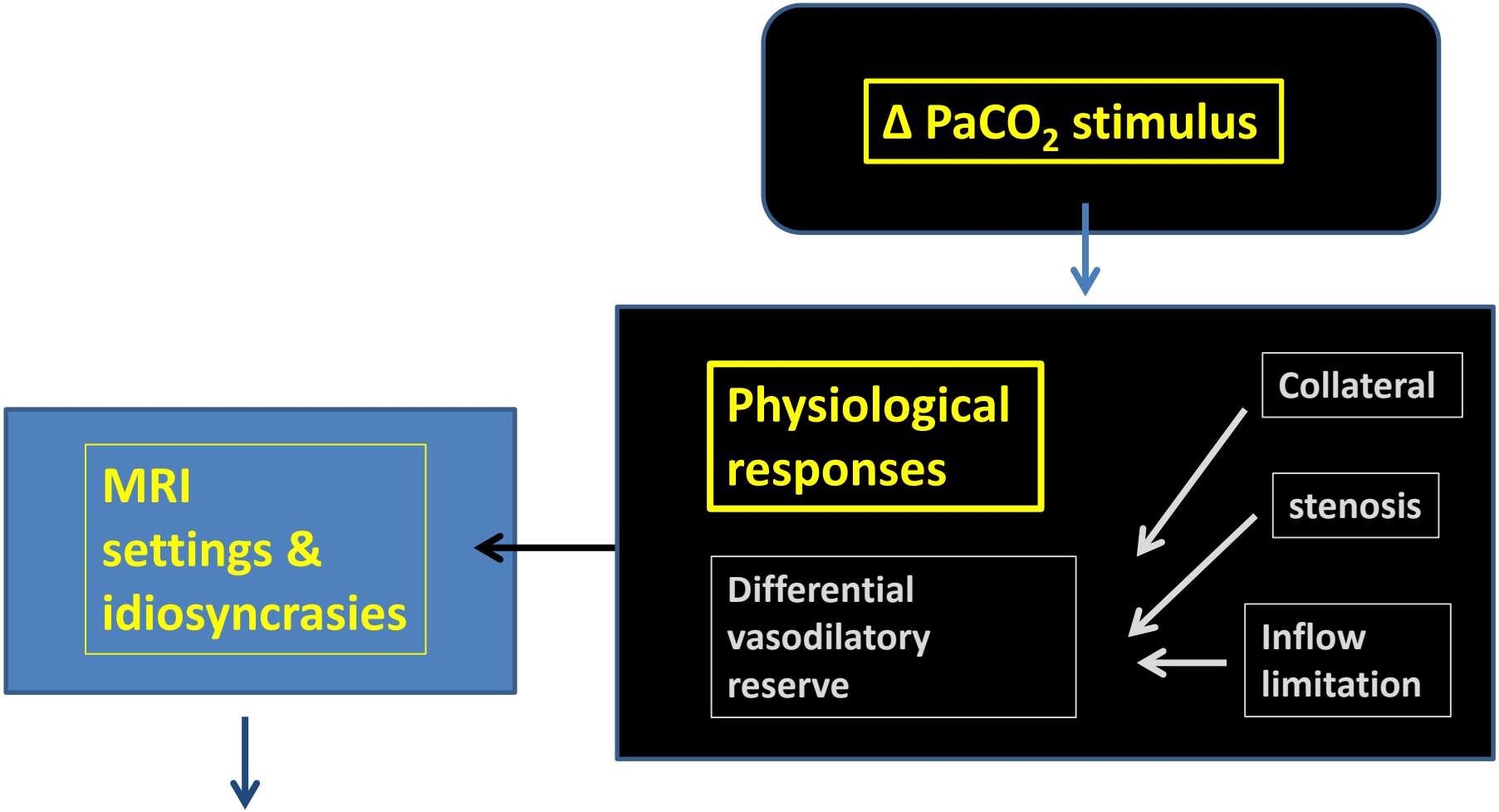
Sobczyk et. al. J Cereb Blood Flow Metab. (2014).

How far have we come with z scores?

CVR is:

- Normalized for anatomical location
- Can be normalized for age, sex, [other: e.g., Dx, Rx]
- Is comparable between scanners, institutions, MR sequences, type of CO_2 stress*

* As long as CO_2 (amplitude, pattern), and MR sequence are the <u>same</u> in the 'atlas' and in the test!



CVR/steal

Normalized for anatomical location

Interpretation:

- ~~high~~ specificity ~~for S-I-C-K~~
- ~~Low~~ sensitivity!
  - ~~No~~ gradation in severity
  - ~~Poor~~ localization

CVR: a Brain stress test

1) How does it work?

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Optimize resolution of test-test changes

3) Clinical implications:

Research tool → individualized Dx:

True test of hemodynamic significance

Test of efficacy of intervention

CREST 2?

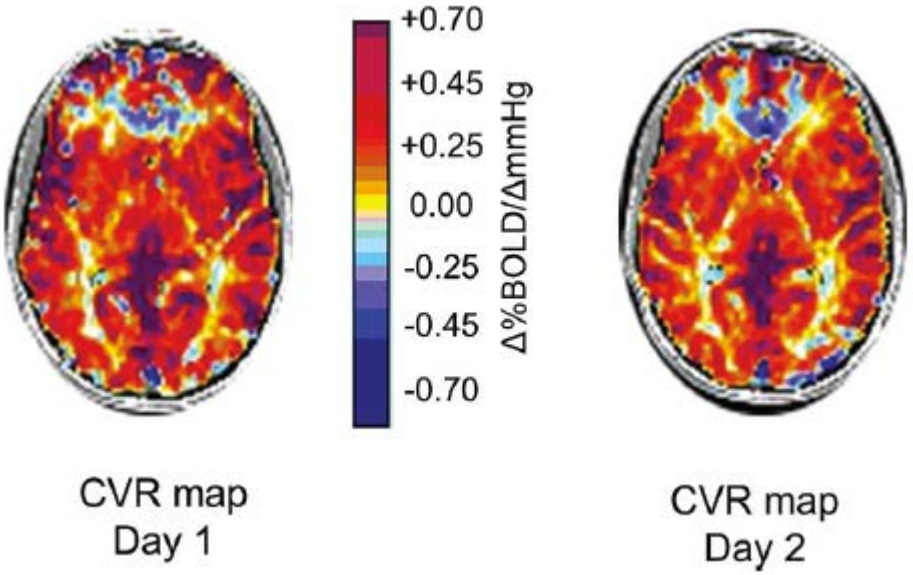
Normalized between patients
Standardized between centers
Consistent between tests

Longitudinal data:

Repeat tests in single subject

- Natural history of disease
- Effect of interventions

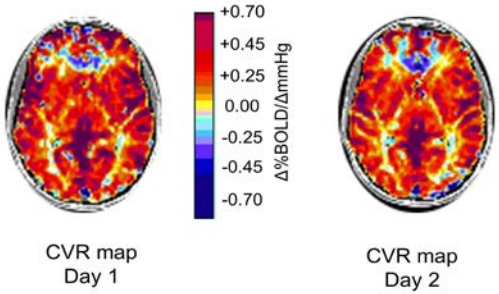
Test-retest CVR one healthy subject



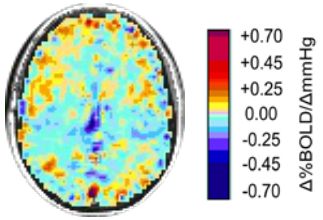
Sobczyk et al. AJNR Am J Neuroradiol 37:818 –24 May 2016

ID z-map Construction

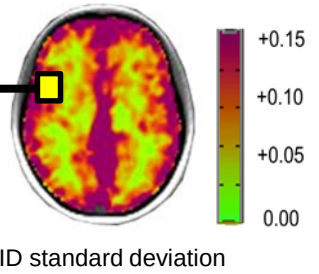
1. Healthy subjects test-retest CVR

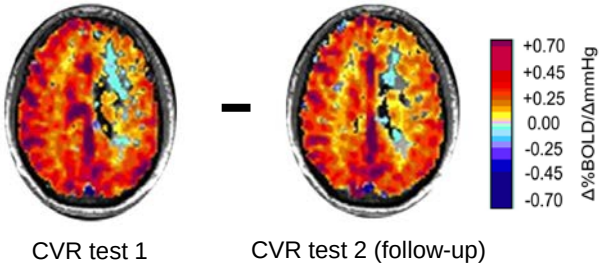


2. CVR test 2- CVR test 1 for each healthy subject



3. Atlas of healthy subjects mean and standard deviation of interval differences (ID)

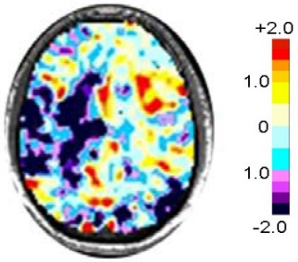




4. Patient CVR test 2 – CVR test 1

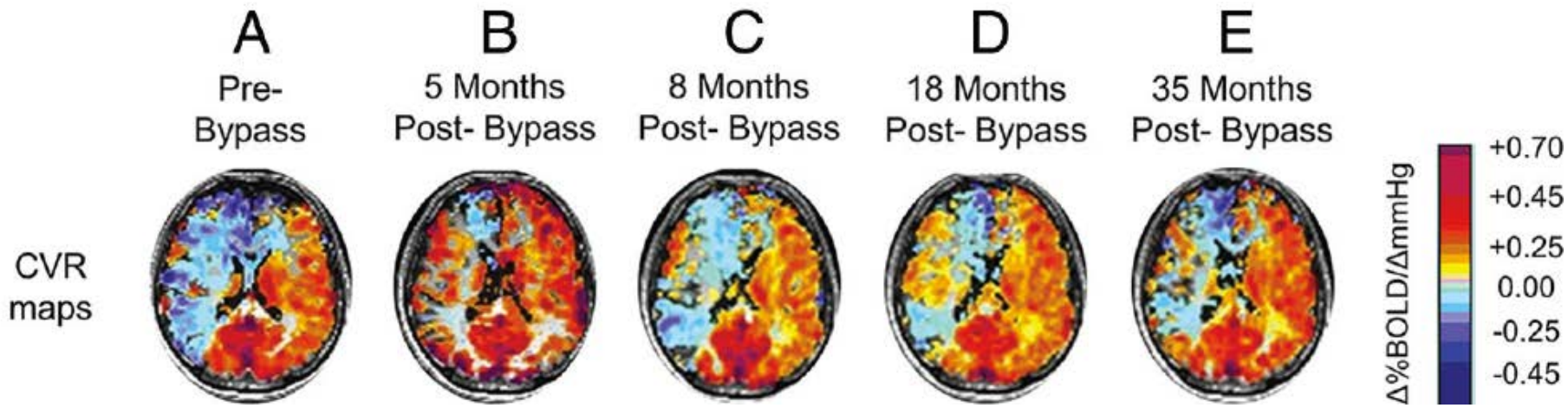
$$\text{ID - } z = \frac{[\Delta CVR] - \Delta M(0)}{\sigma}$$

5. Calculate ID z scores



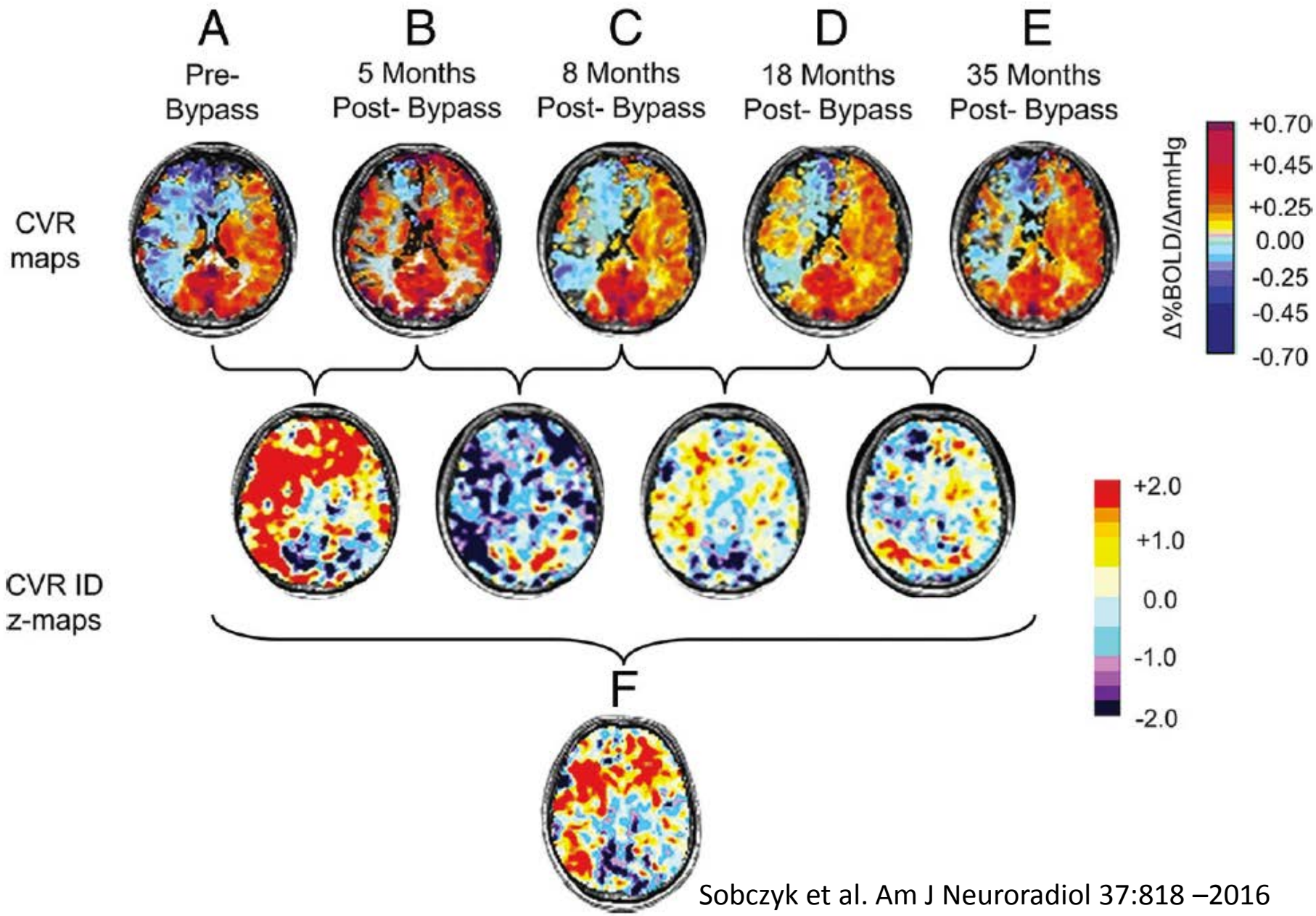
6. Map ID z scores to anatomical scans creating ID z-maps

56 M with bilateral ICA stenosis and R EC-IC bypass

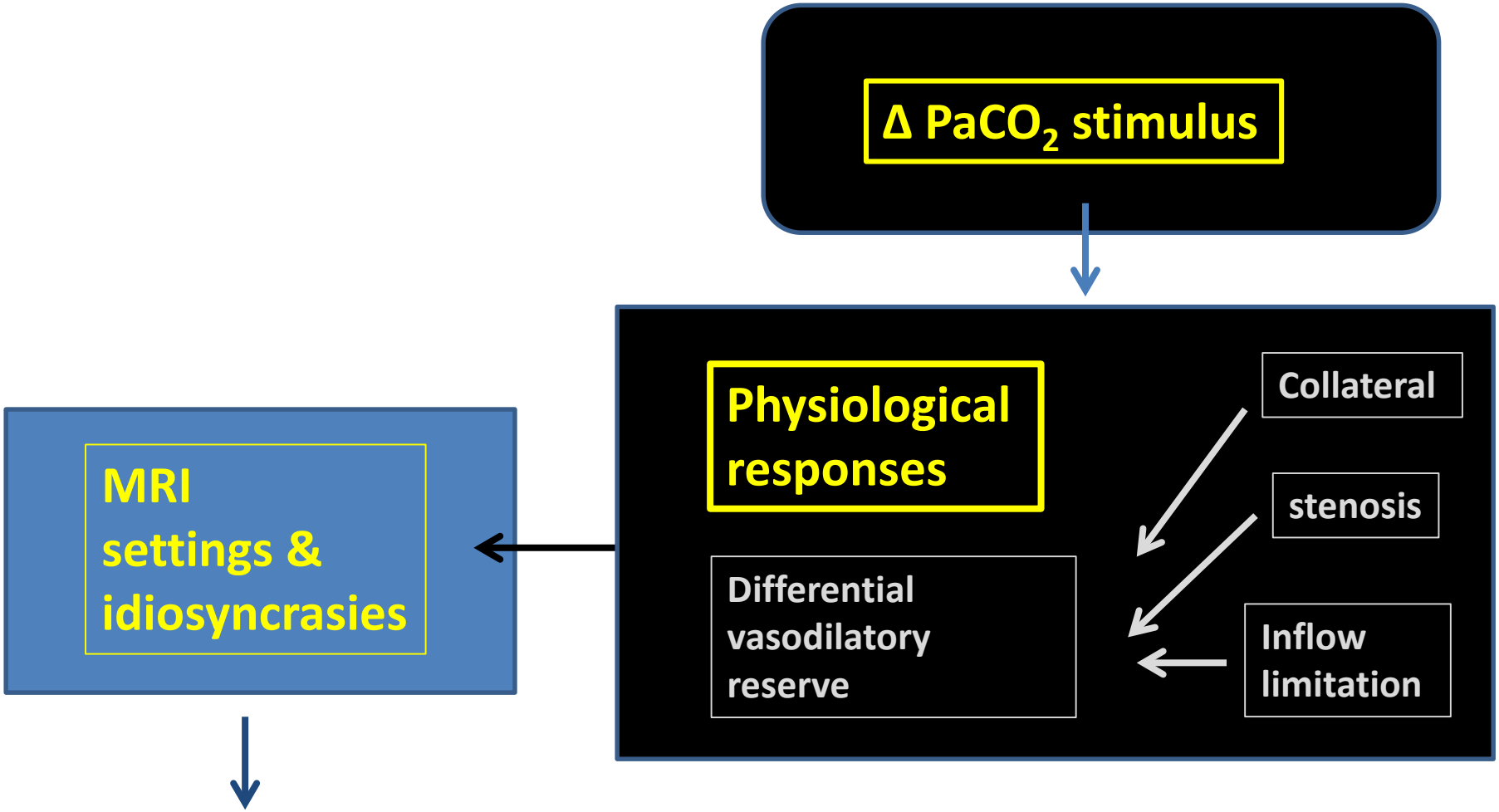


Sobczyk et al. Am J Neuroradiol 37:818 –2016

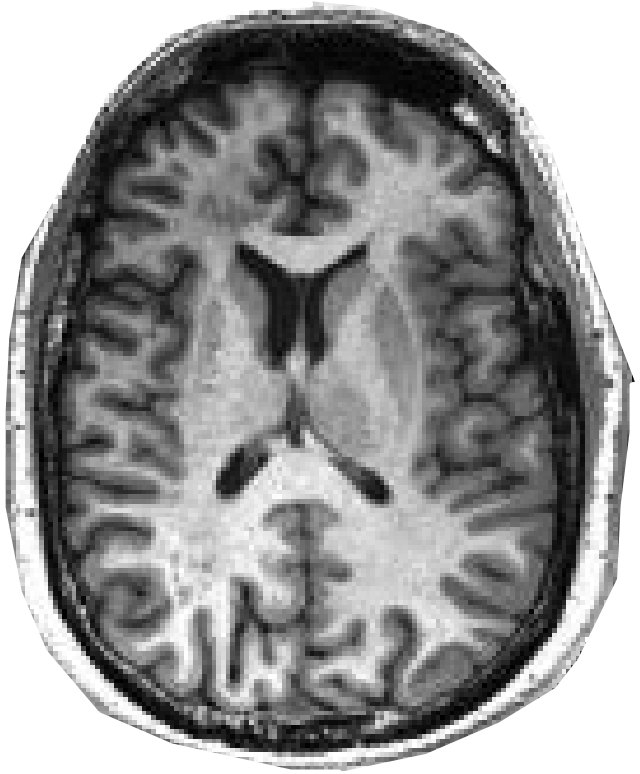
56 M with bilateral ICA stenosis and R EC-IC bypass



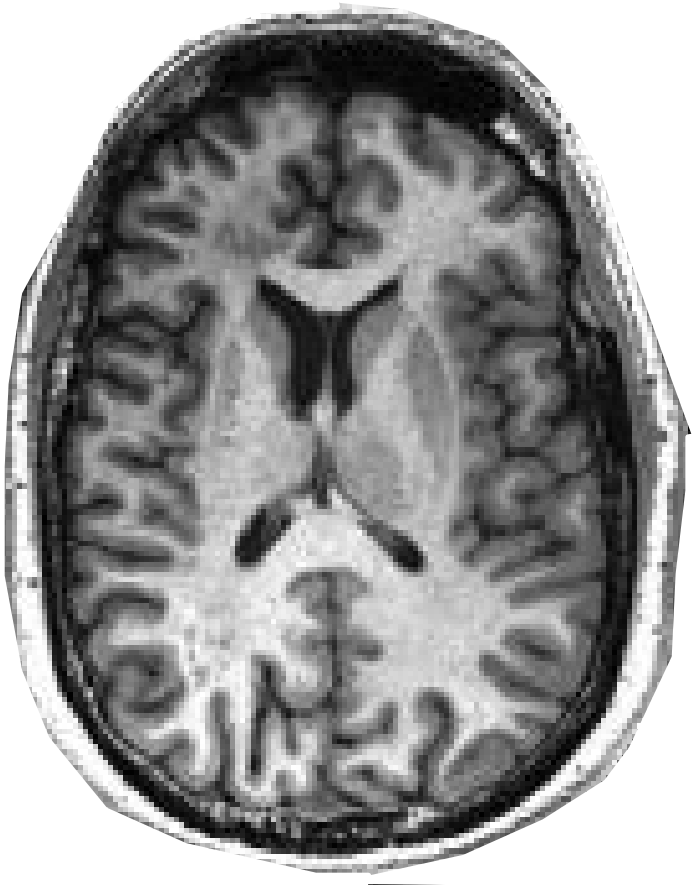
Sobczyk et al. Am J Neuroradiol 37:818 –2016


Δ PaCO2 stimulus
Physiological responses
Collateral
stenosis
Differential vasodilatory reserve
Inflow limitation
MRI settings & idiosyncrasies
CVR/steal
Normalized for anatomical location
Interpretation:
high specificity for S-I-C-K
Low sensitivity!
No gradation in severity
Poor localization
good

Co-registration of scans to standard space

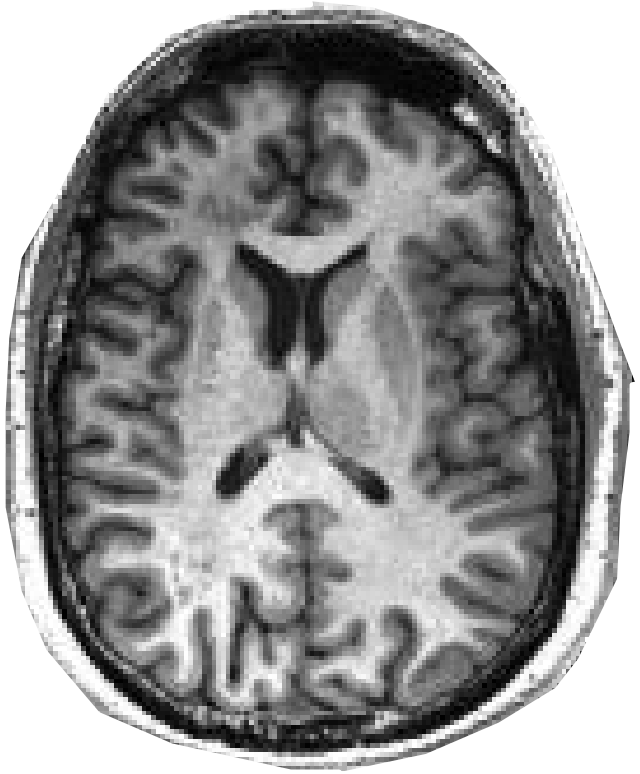


Patient scan

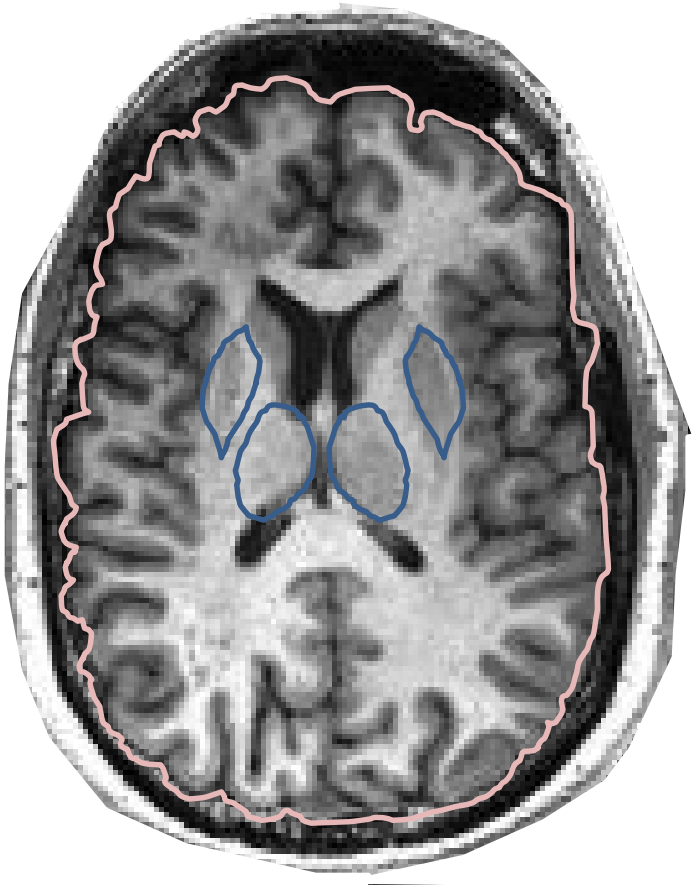


Standard space

Co-registration of scans to standard space

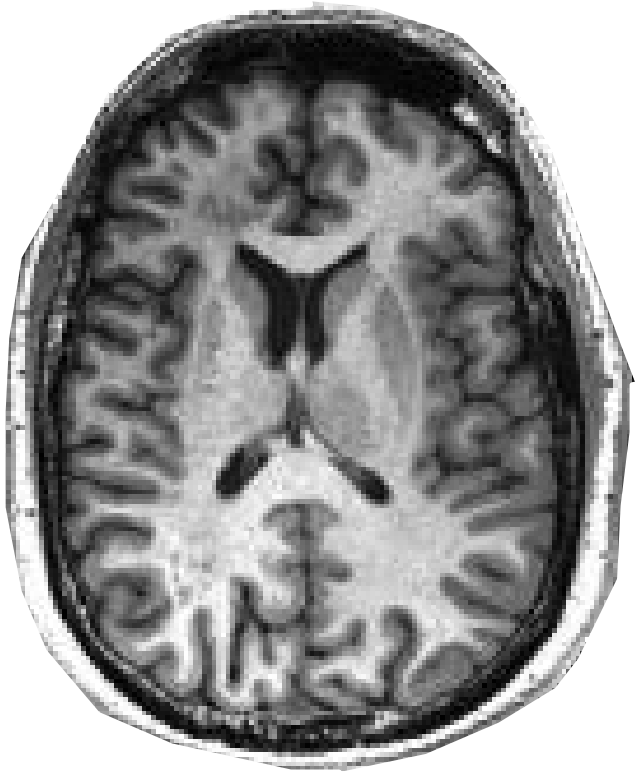


Patient scan

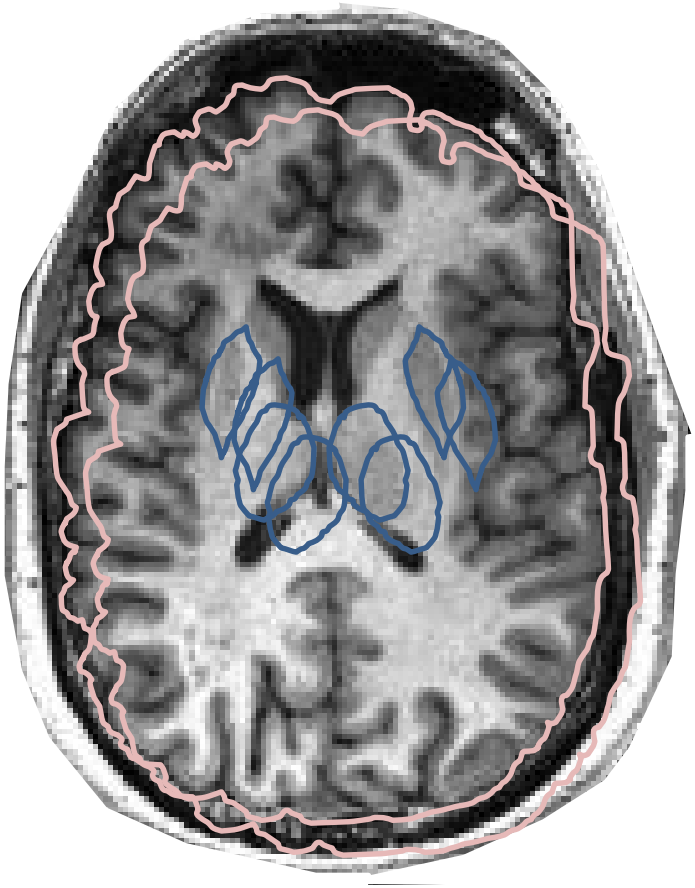


Standard space

Co-registration of scans to standard space

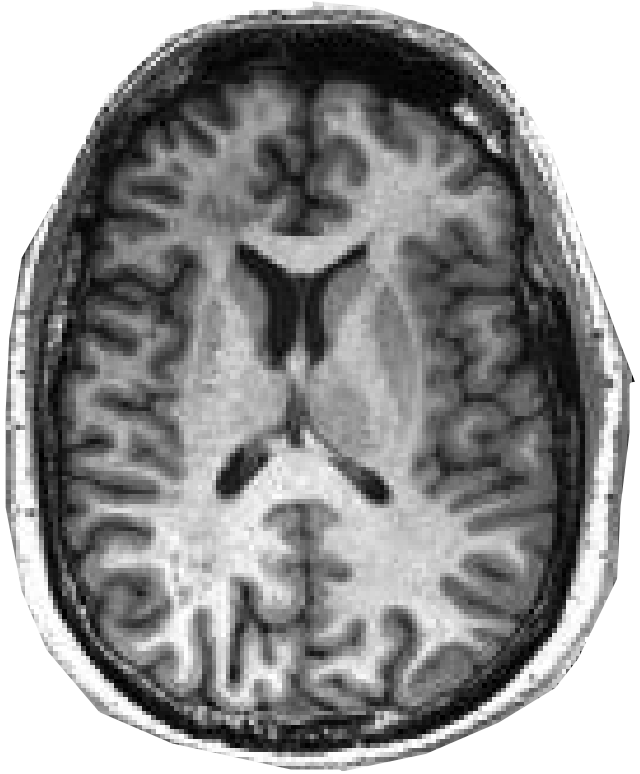


Patient scan

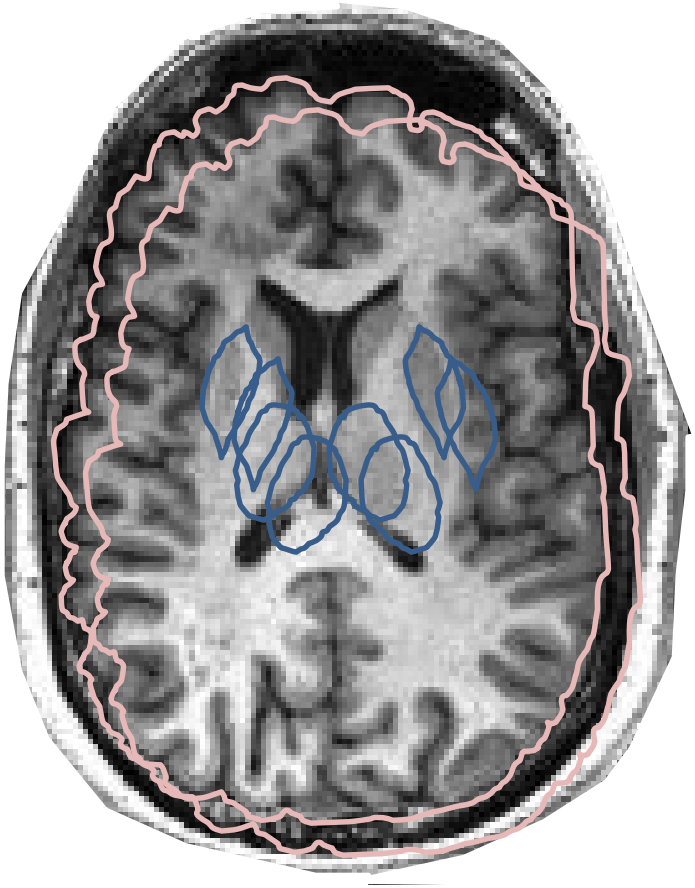


Standard space

Co-registration of scans to standard space

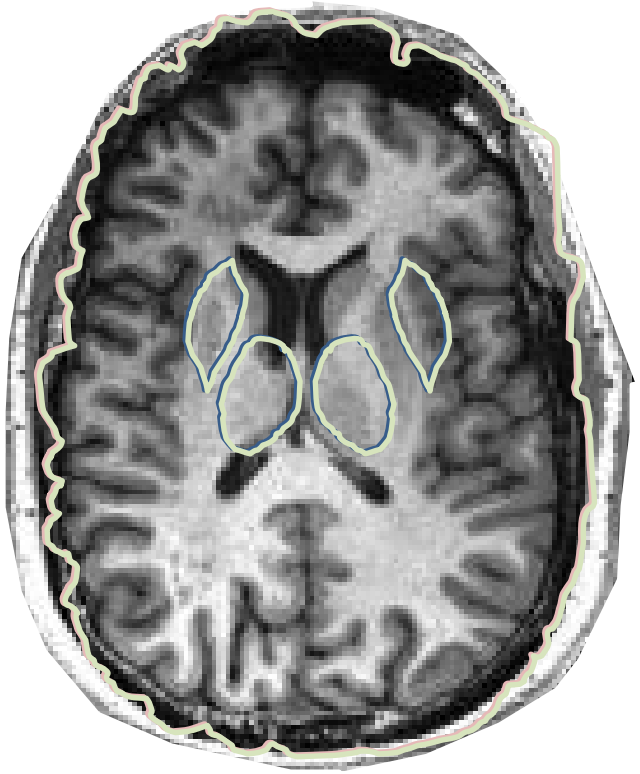


Patient scan

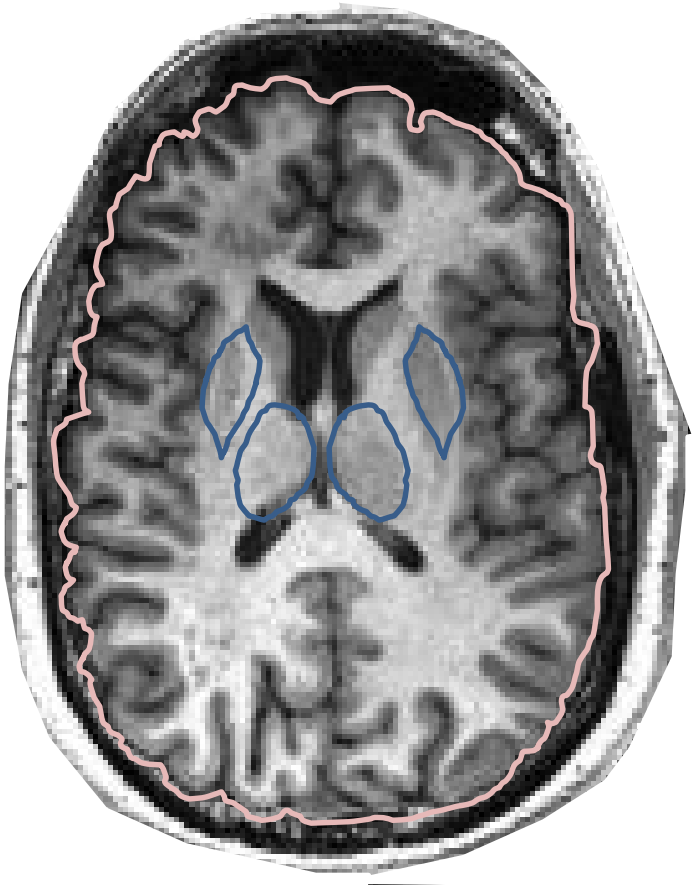


Standard space

Co-registration of scans to standard space

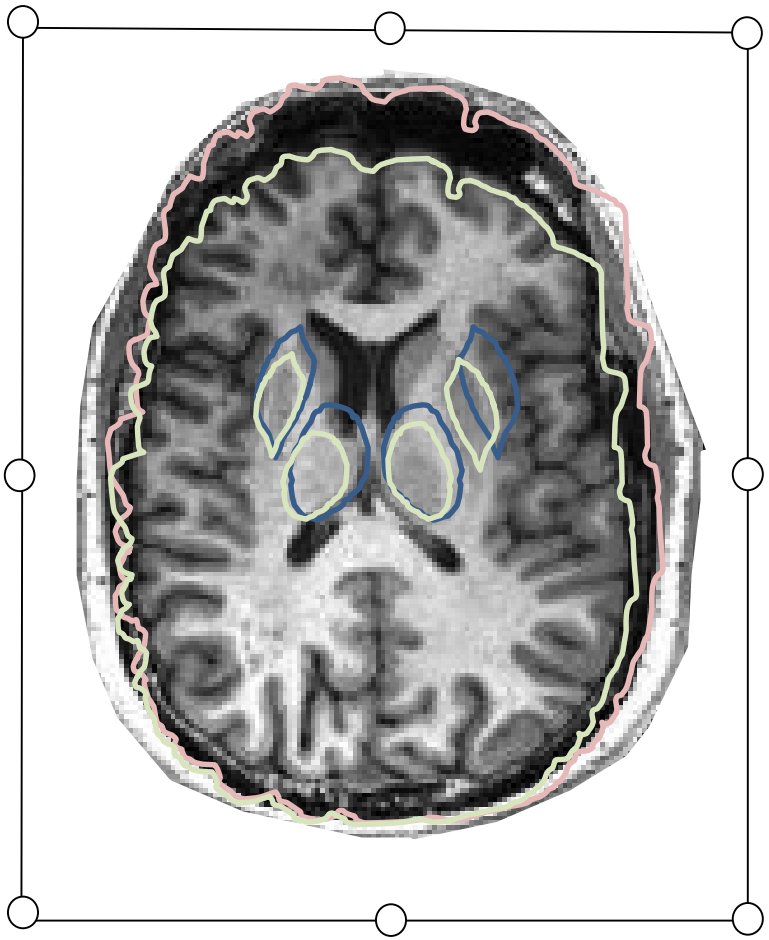


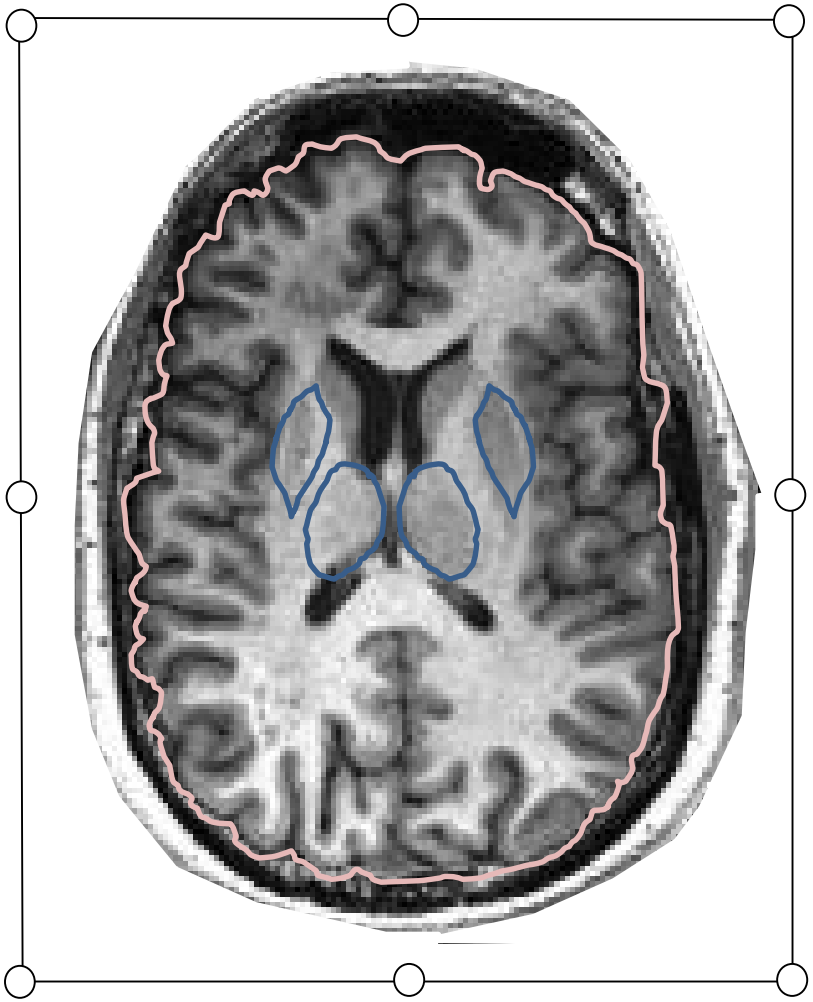
Patient scan



Standard space

Co-registration of scans to standard space

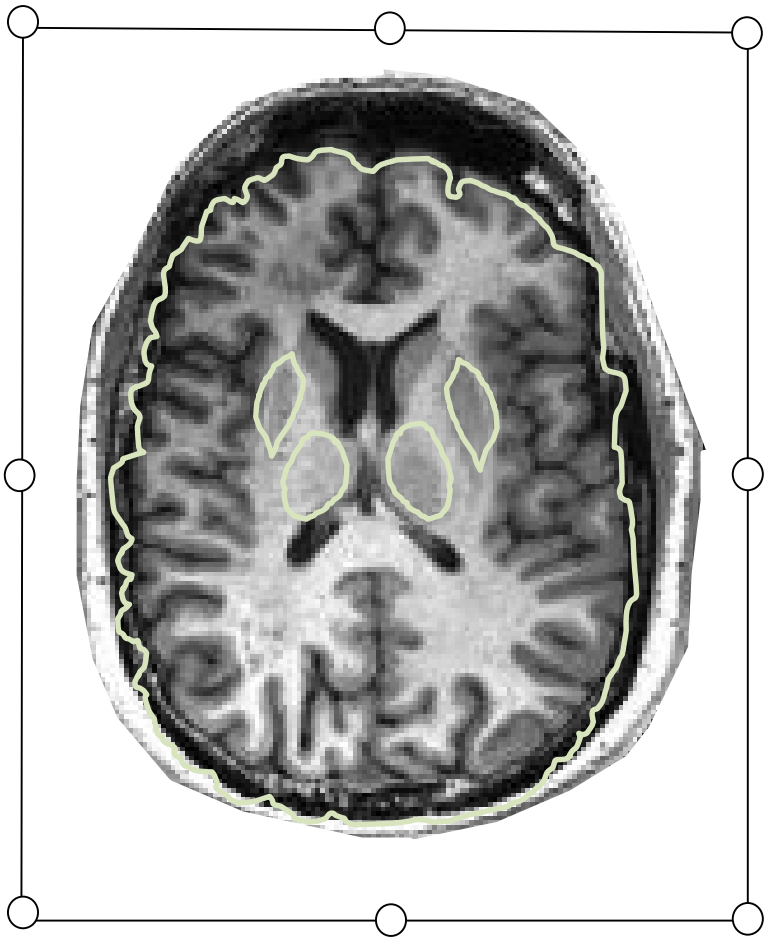




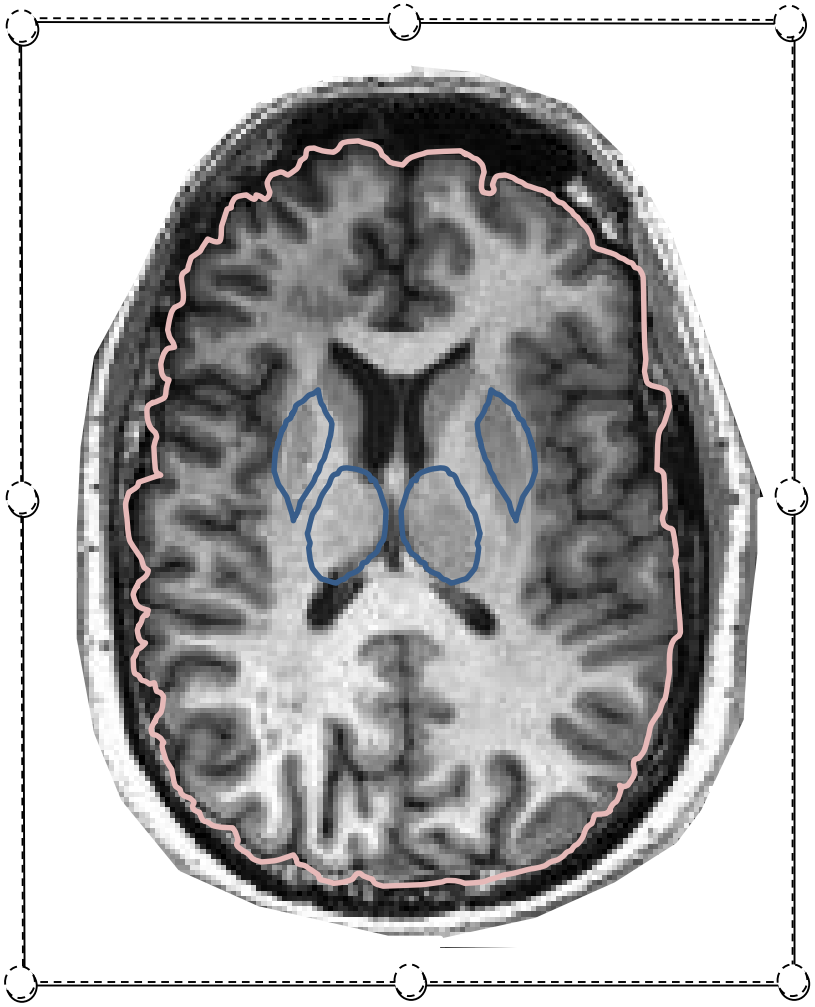
Patient scan

Standard space

Co-registration of scans to standard space

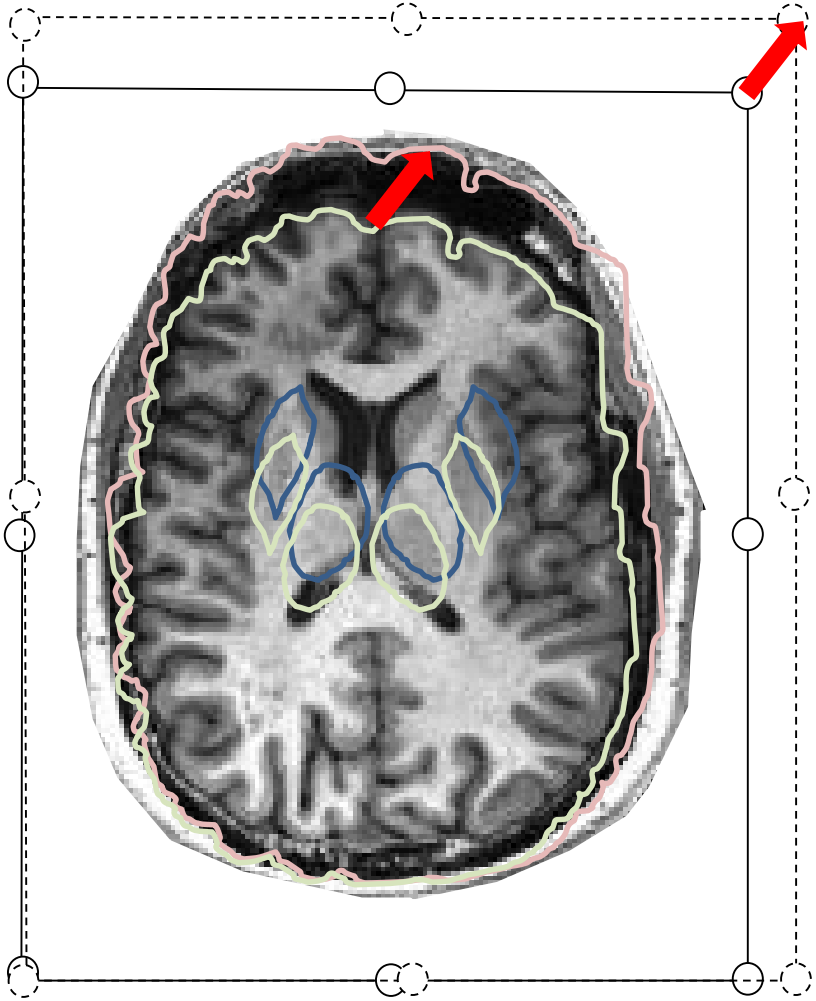


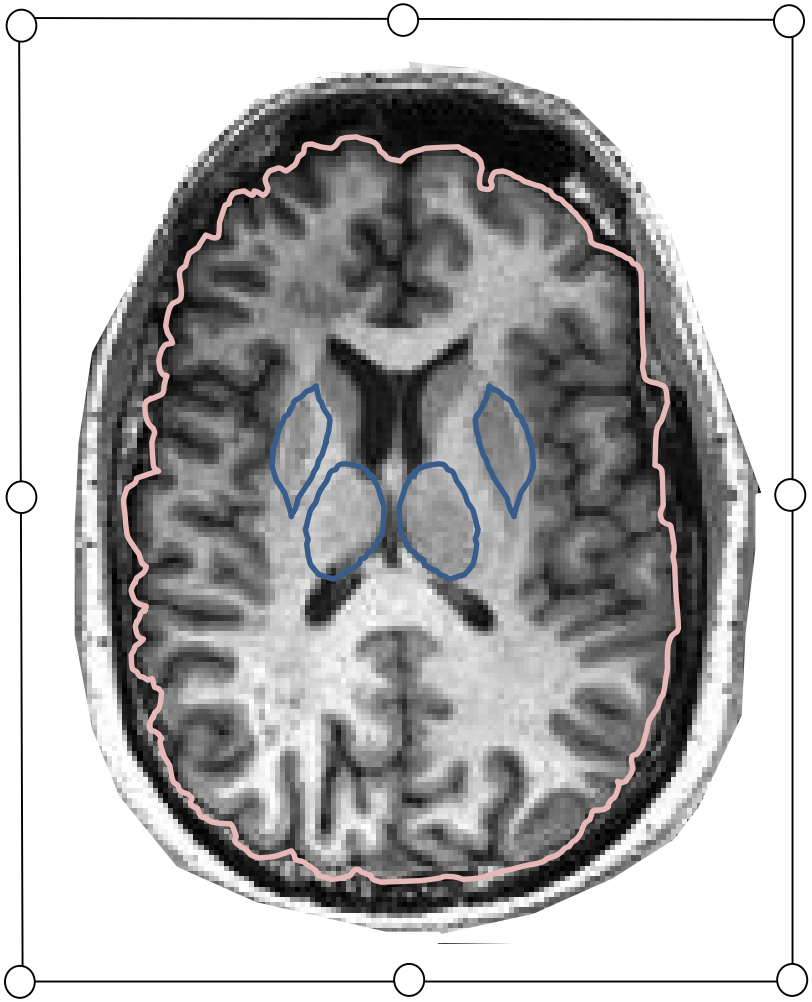
Patient scan



Standard space

Co-registration of scans to standard space

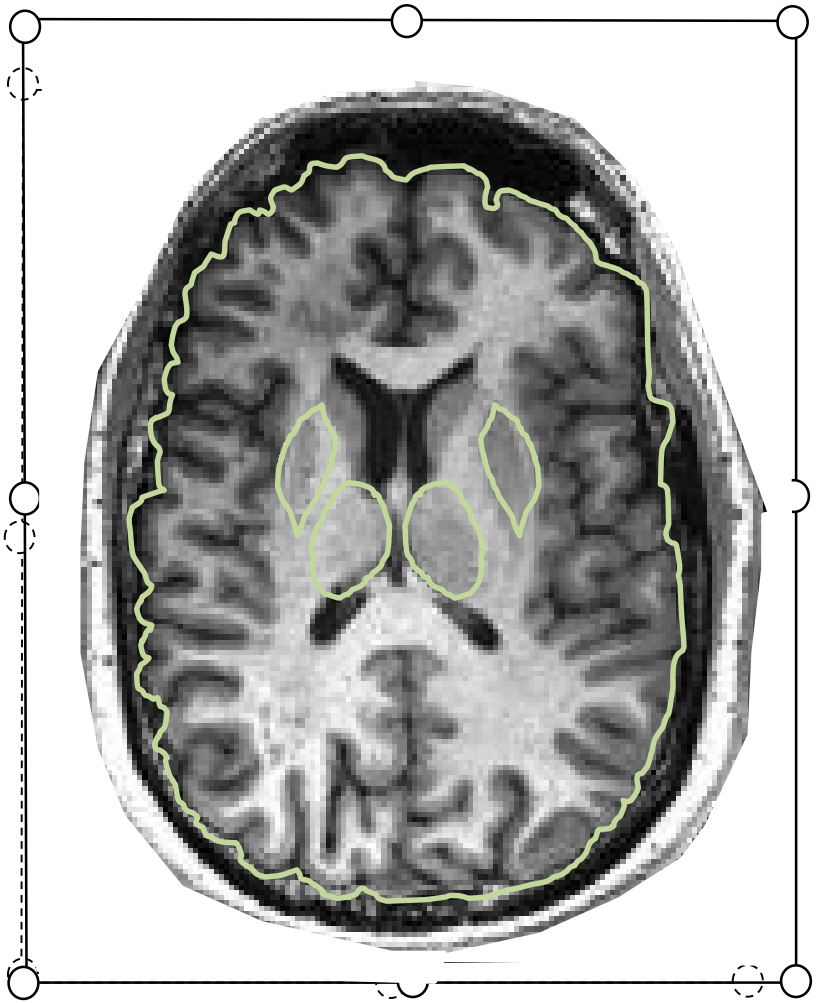


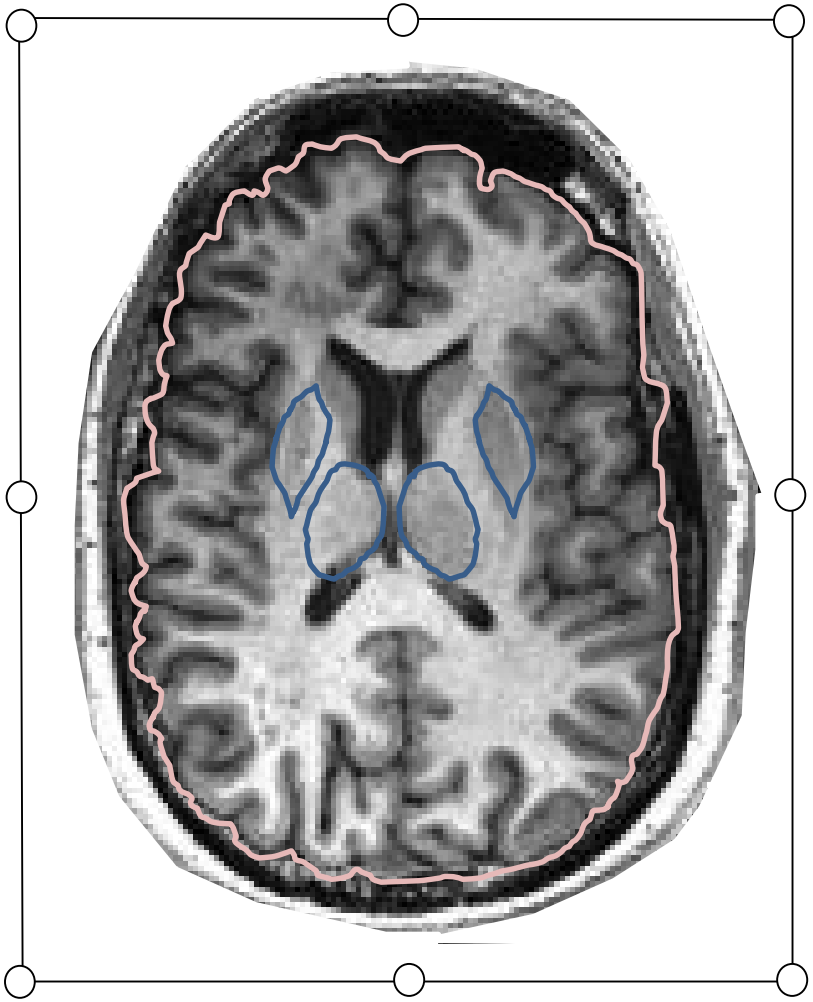


Patient scan

Standard space

Co-registration of scans to standard space

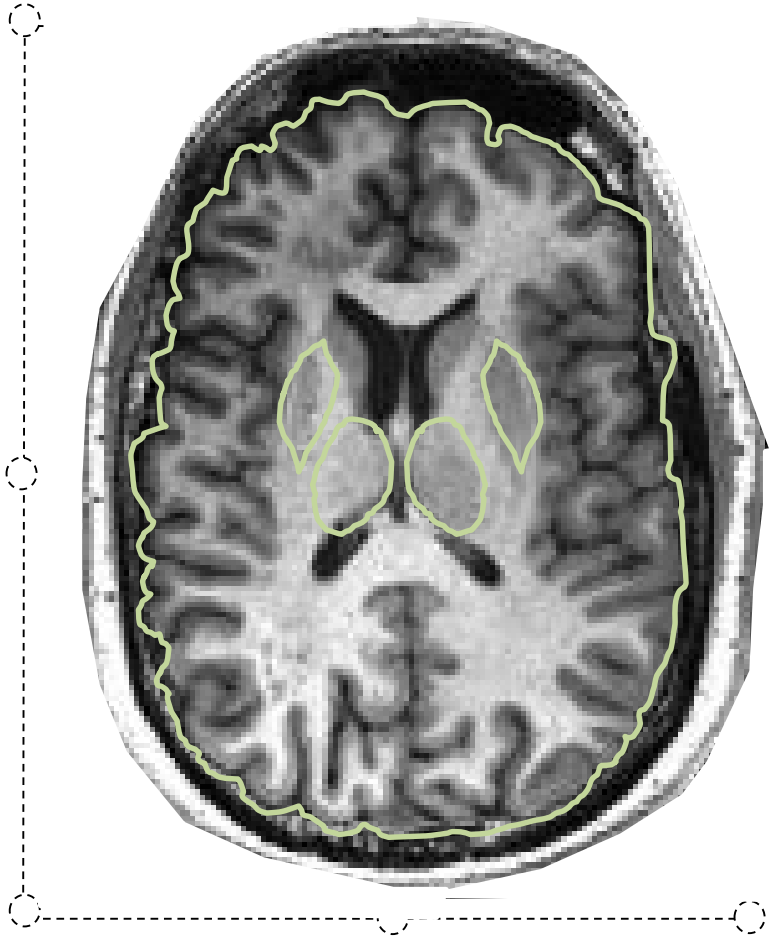




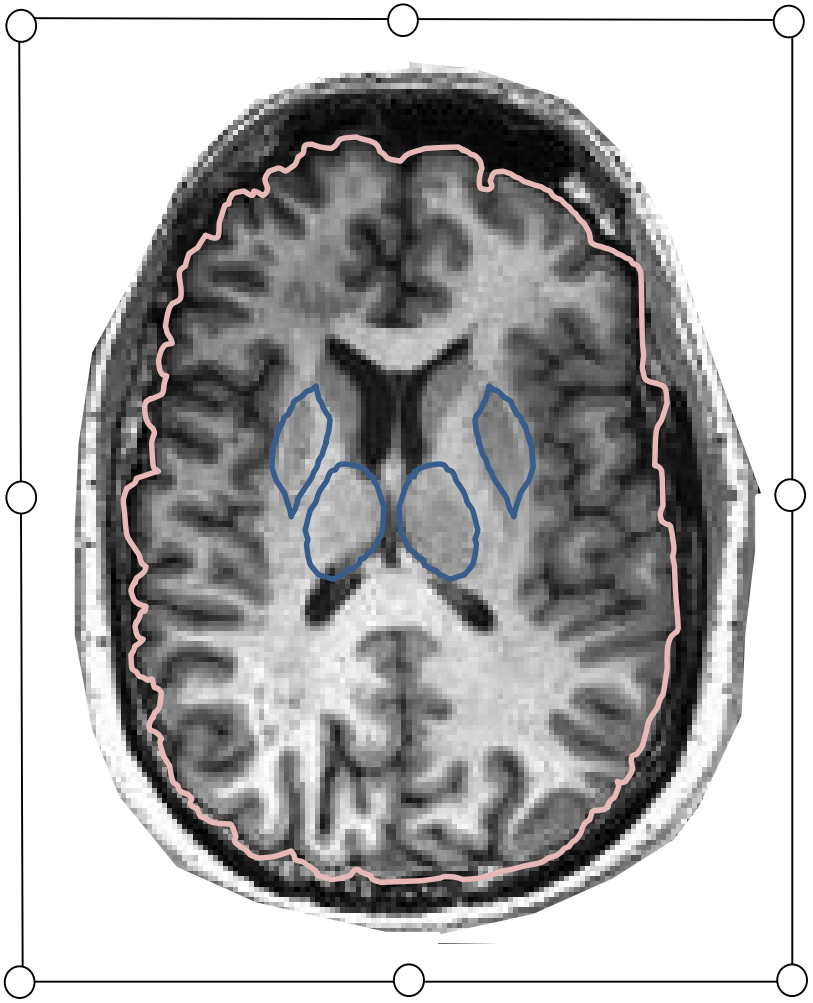
Patient scan

Standard space

Co-registration of scans to standard space

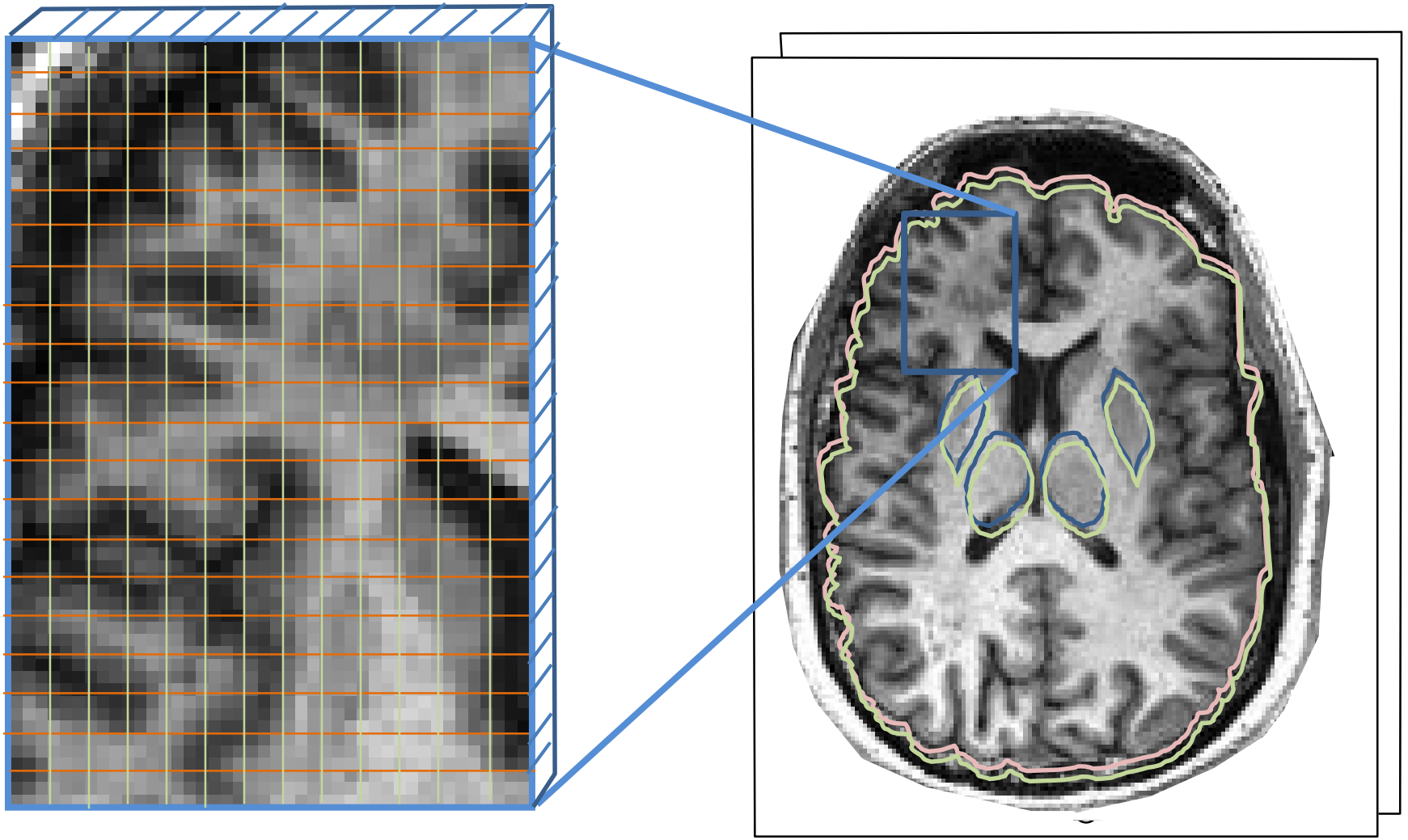


Patient scan



Standard space

Co-registration of scans to standard space

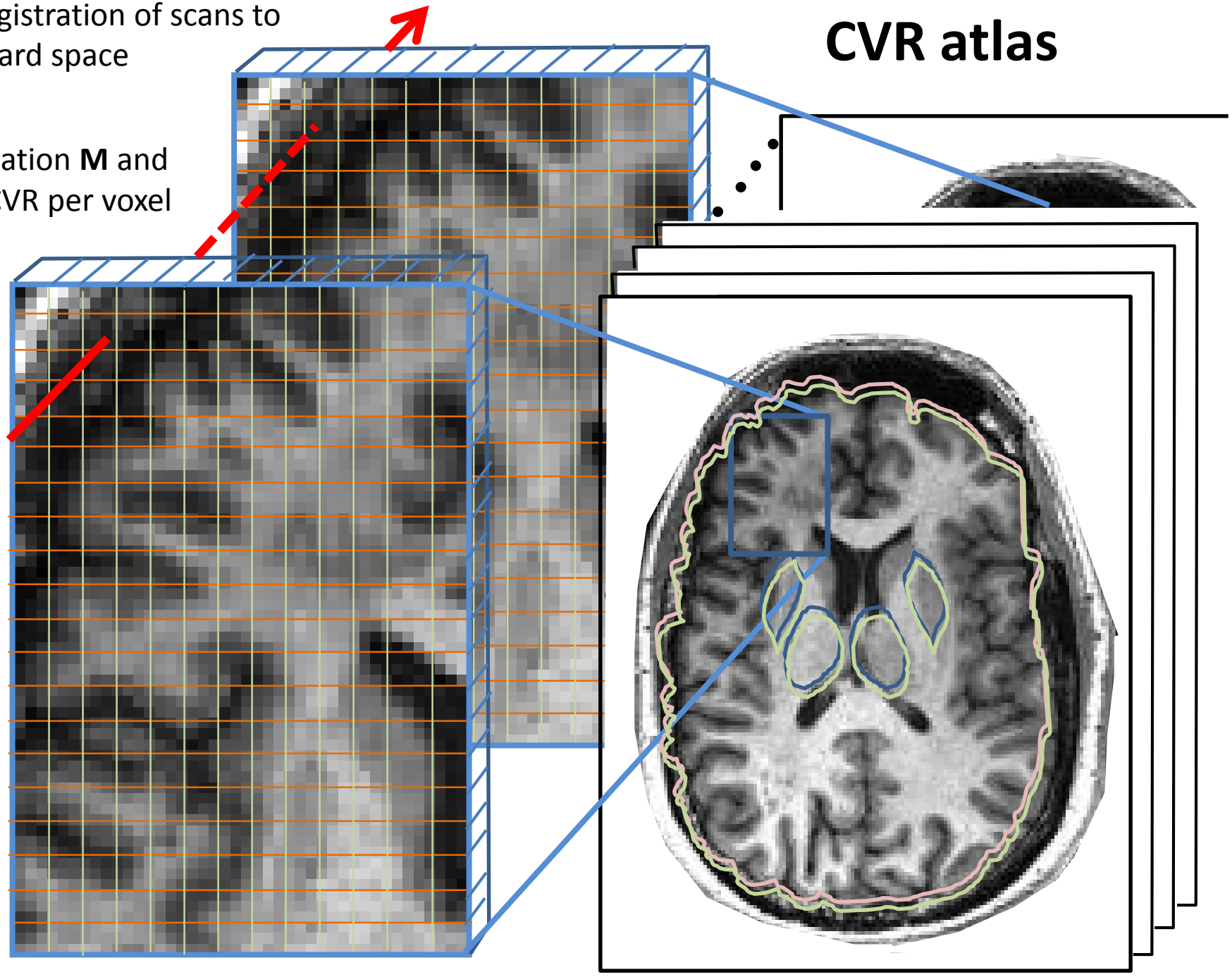


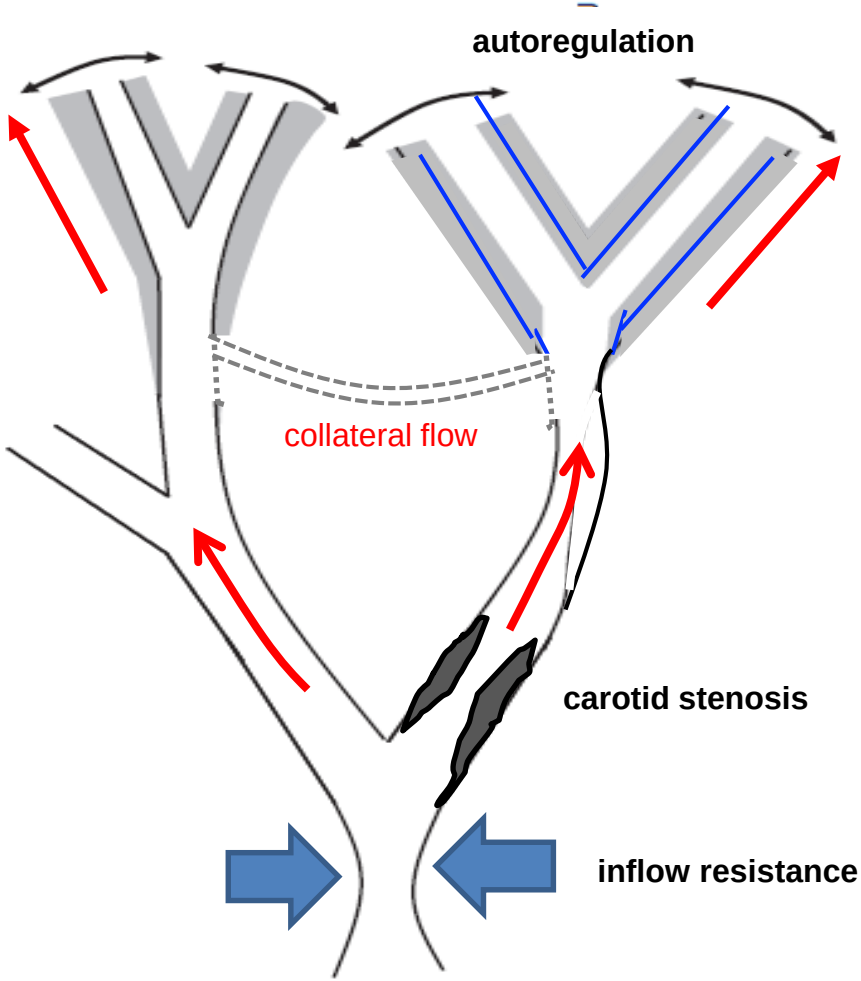
Standard space

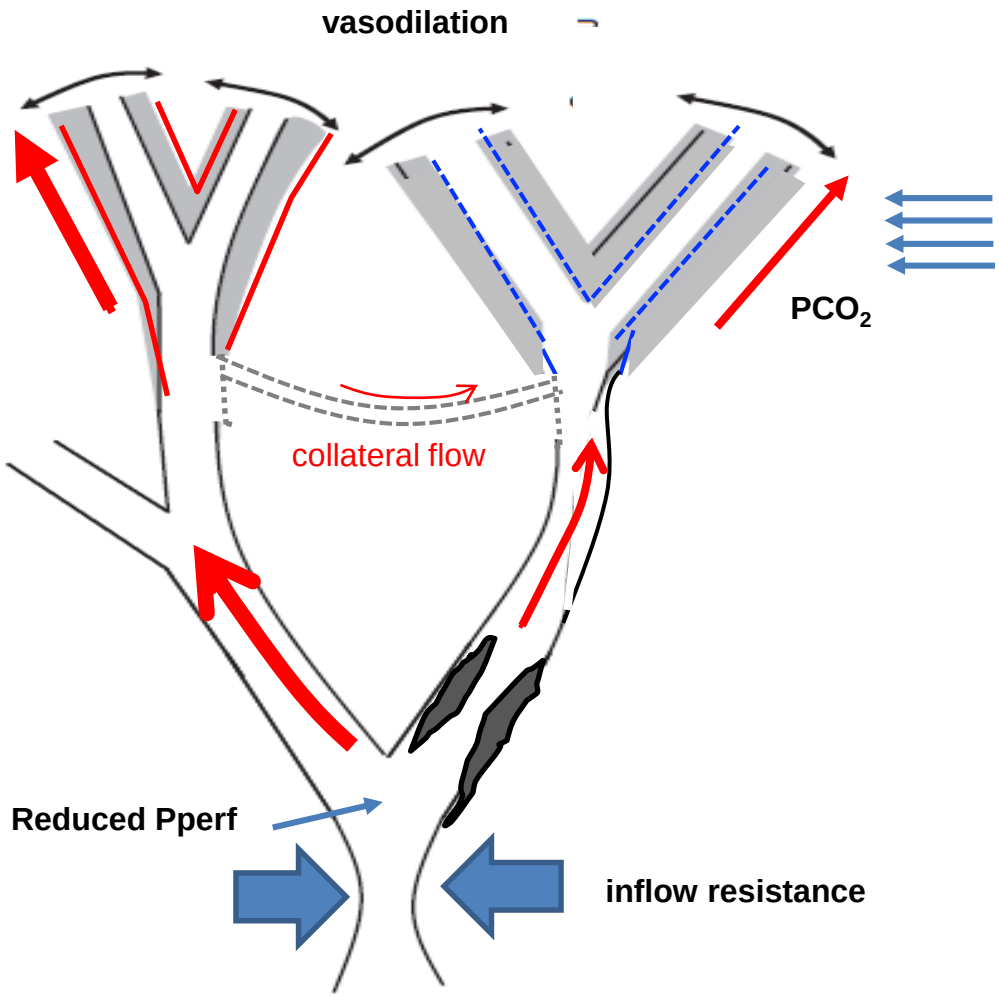
Co-registration of scans to standard space

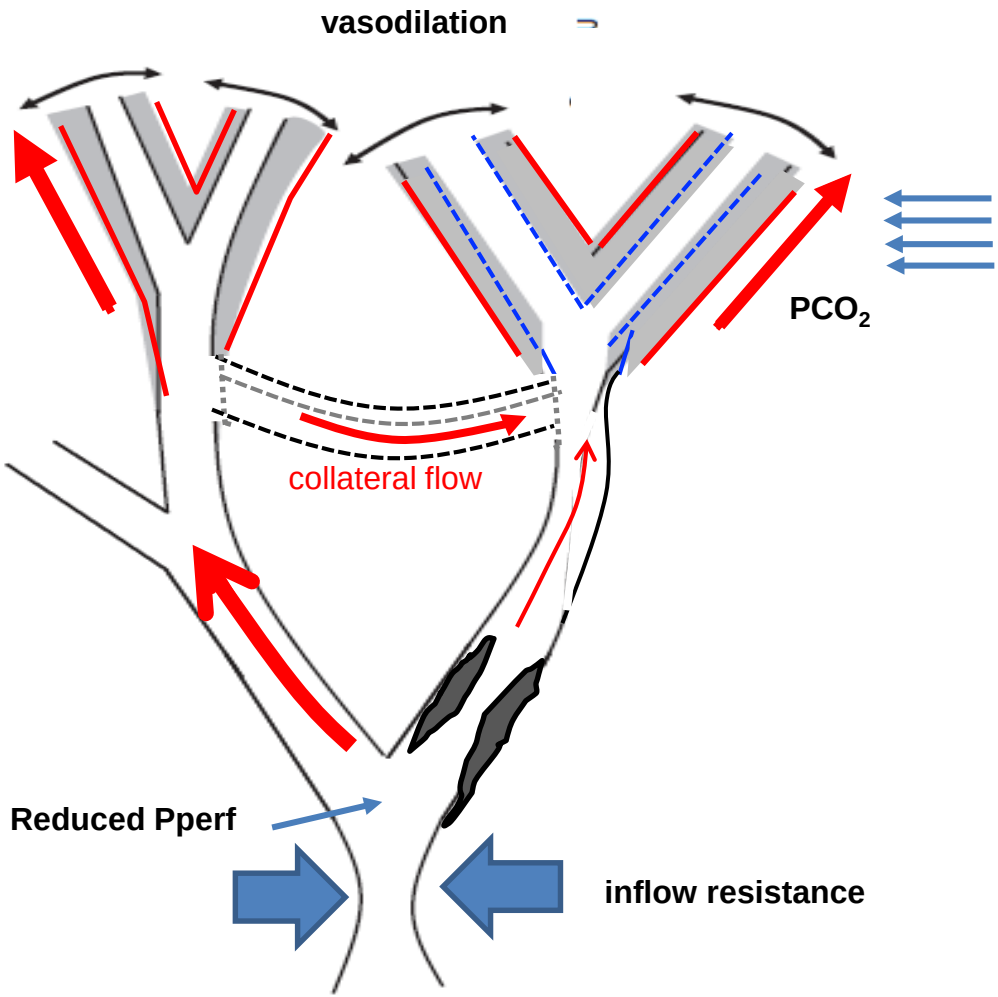
Calculation **M** and σ of CVR per voxel

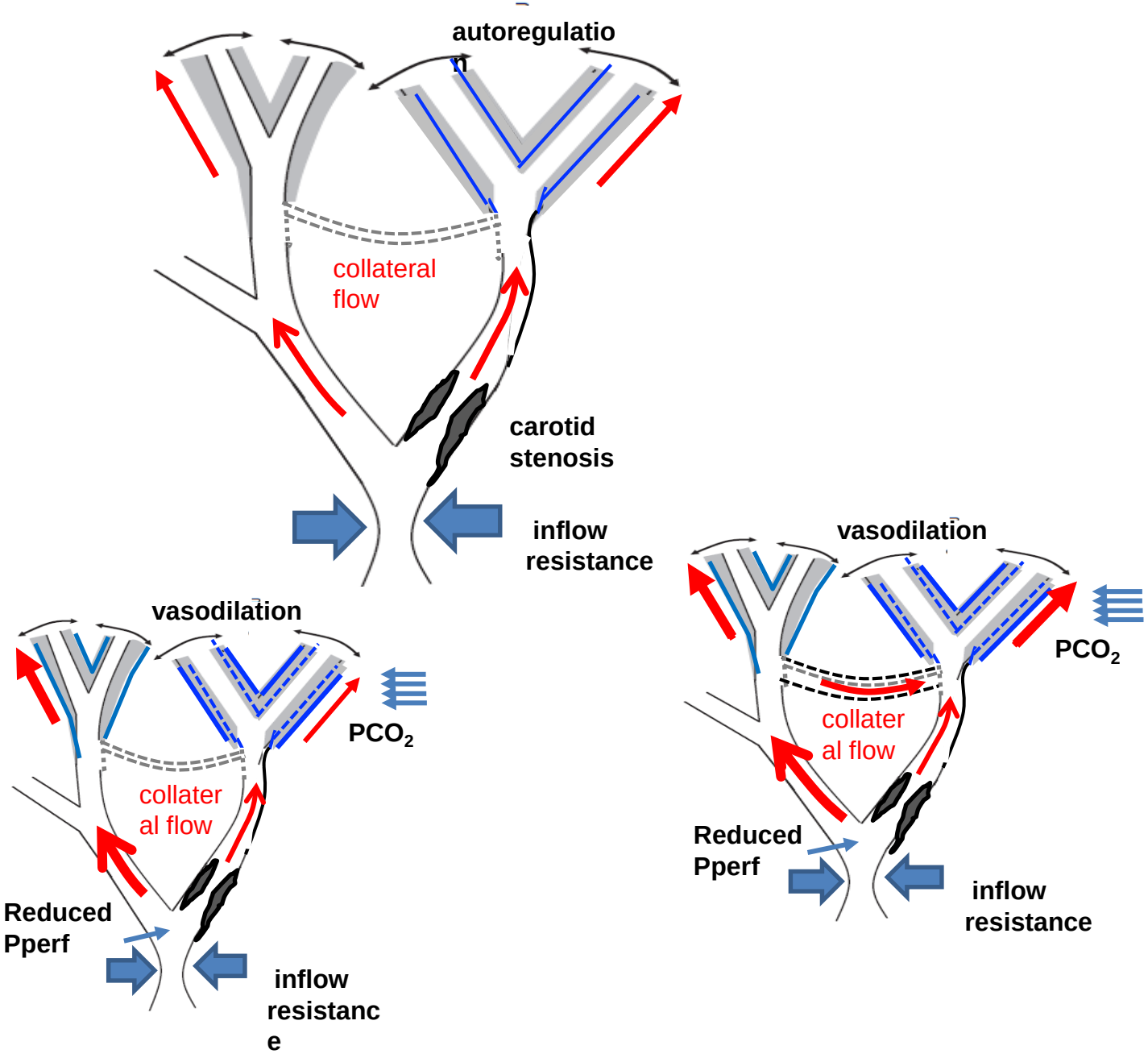
CVR atlas

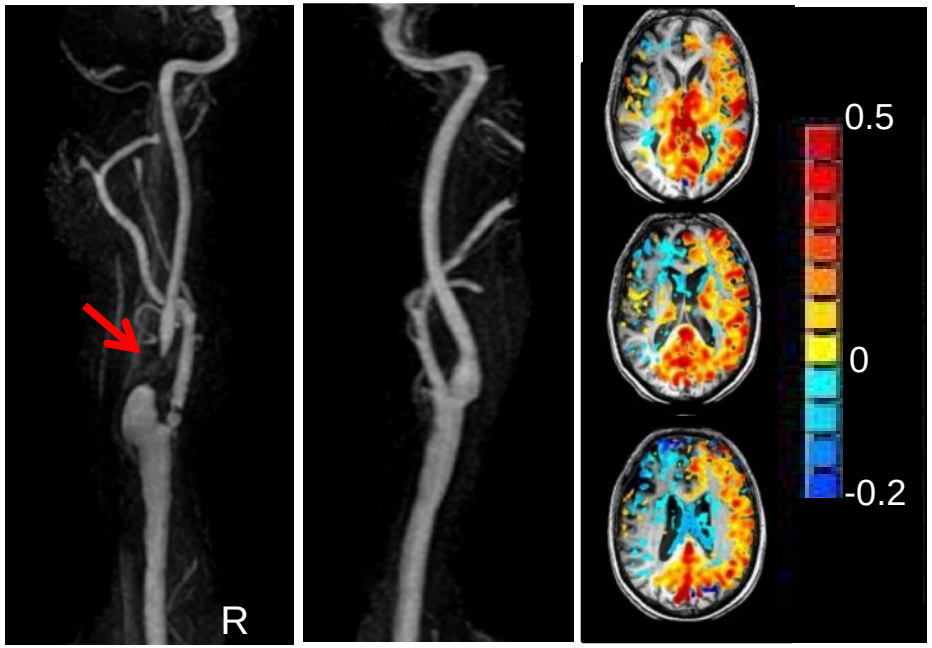


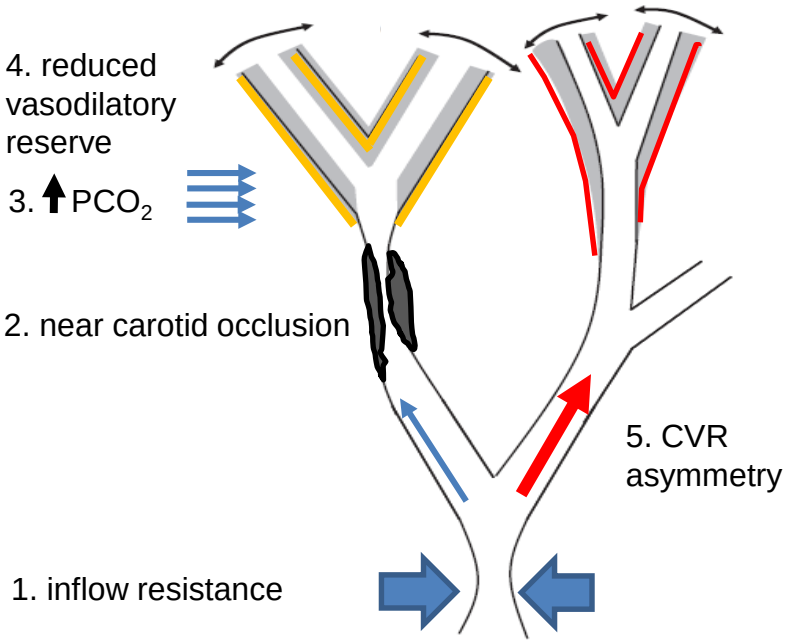

autoregulation
collateral flow
carotid stenosis
inflow resistance

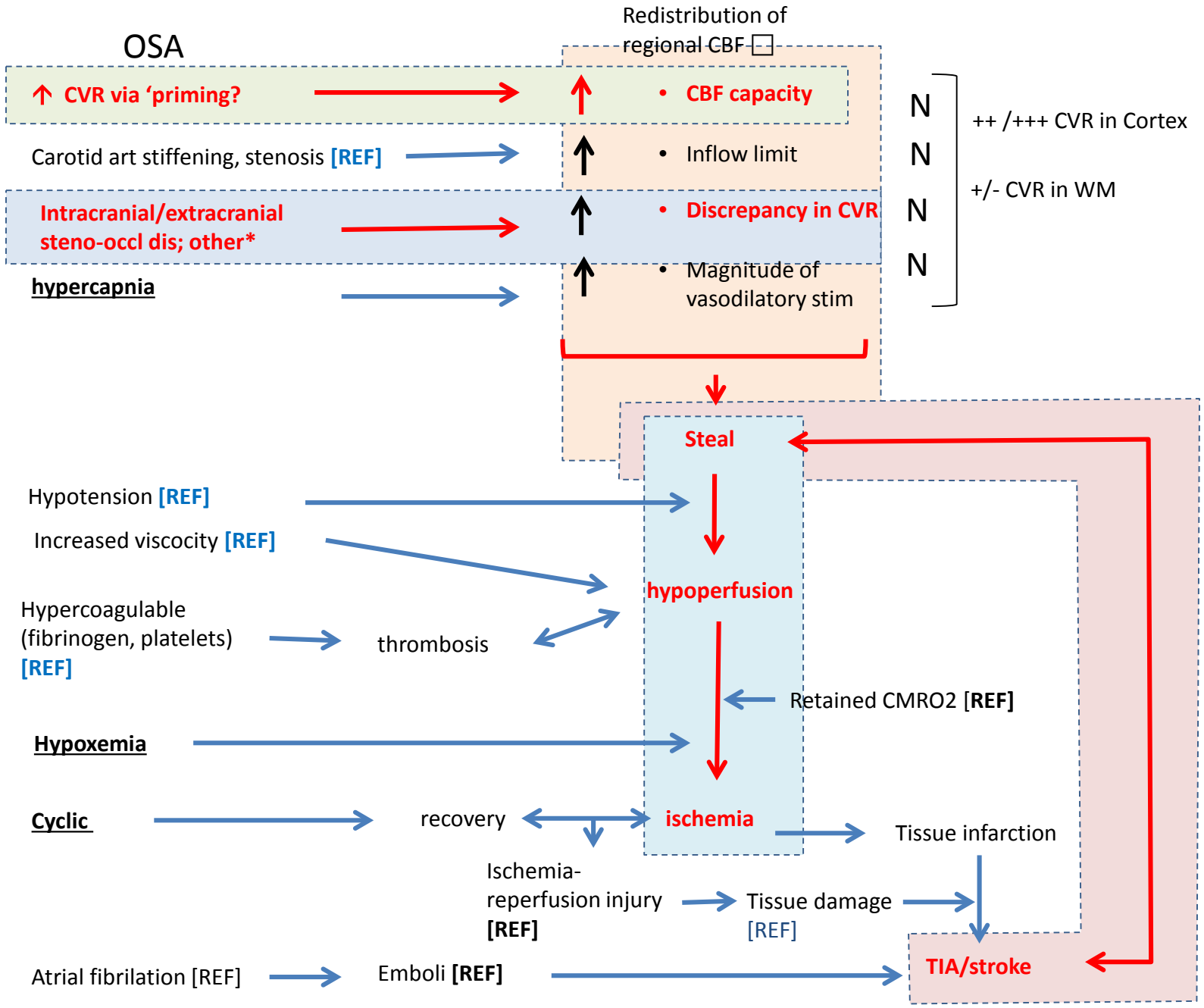

vasodilation
PCO2
collateral flow
Reduced Pperf
inflow resistance


vasodilation
PCO2
collateral flow
Reduced Pperf
inflow resistance


autoregulatio
n
collateral
flow
carotid
stenosis
inflow
resistance
vasodilation
PCO2
collater
al flow
Reduced
Pperf
inflow
resistanc
e
vasodilation
PCO2
collater
al flow
Reduced
Pperf
inflow
resistance


R
0.5
0
-0.2


4. reduced vasodilatory reserve
3. ↑PCO2
2. near carotid occlusion
5. CVR asymmetry
1. inflow resistance


OSA
Redistribution of regional CBF
↑ CVR via 'priming?
• CBF capacity
Carotid art stiffening, stenosis [REF]
• Inflow limit
Intracranial/extracranial steno-occl dis; other*
• Discrepancy in CVR
hypercapnia
• Magnitude of vasodilatory stim
N
N
N
N
++ /+++ CVR in Cortex
+/- CVR in WM
Steal
Hypotension [REF]
Increased viscocity [REF]
hypoperfusion
Hypercoagulable (fibrinogen, platelets) [REF]
thrombosis
Retained CMRO2 [REF]
Hypoxemia
Cyclic
recovery
ischemia
Tissue infarction
Ischemia-reperfusion injury [REF]
Tissue damage [REF]
Atrial fibrilation [REF]
Emboli [REF]
TIA/stroke

CVR: a Brain stress test

1) How does it work?

Model; the heart stress test

Applied to brain

2) Making it clinical

Size: matters

Variability of stimulus: -> variability of CVR result

Normalize for anatomical location

Optimize resolution of test-test changes

3) Clinical implications:

True test of hemodynamic significance

Research tool → individualized Dx → research tool:

Test of efficacy of intervention

CREST 2?

Implication 1

Assessing risk for stroke:

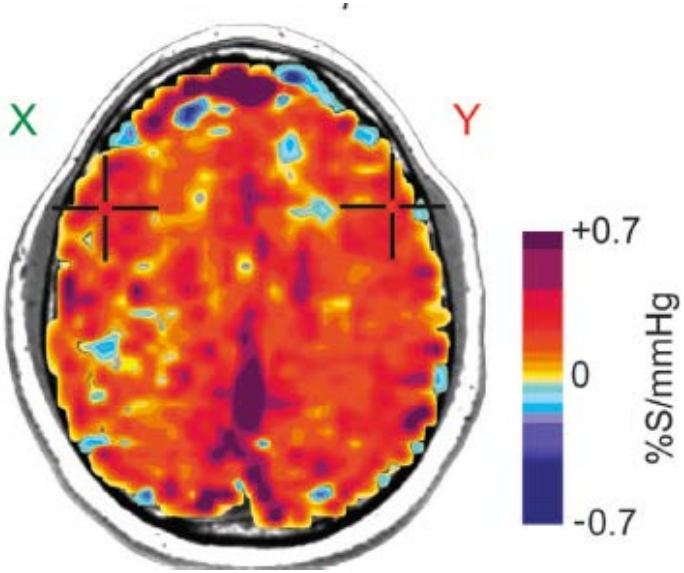
need a functional test: a trial of recruitment of collateral blood flow*

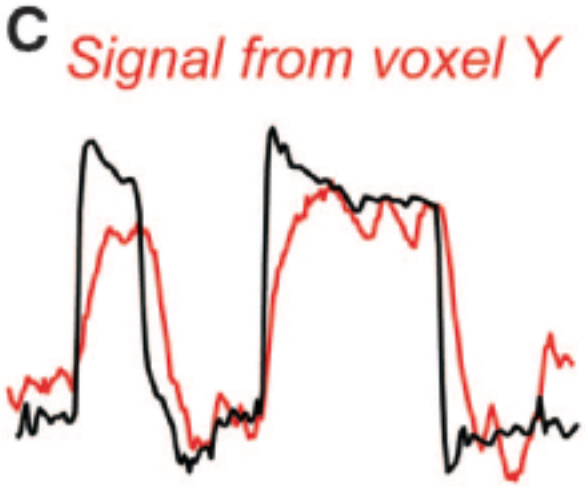
*MRA is just an anatomical test

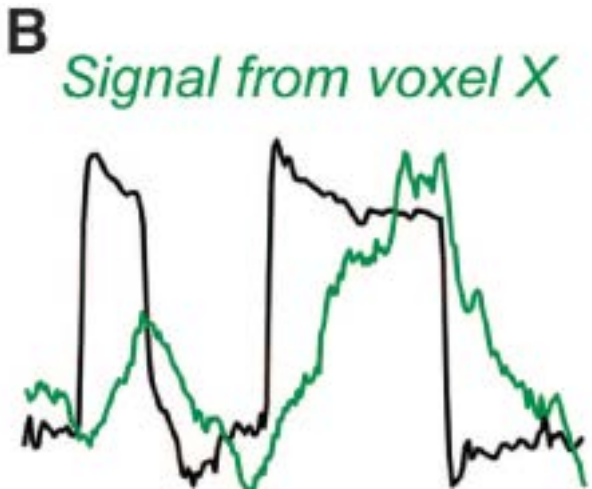
amplitude of response

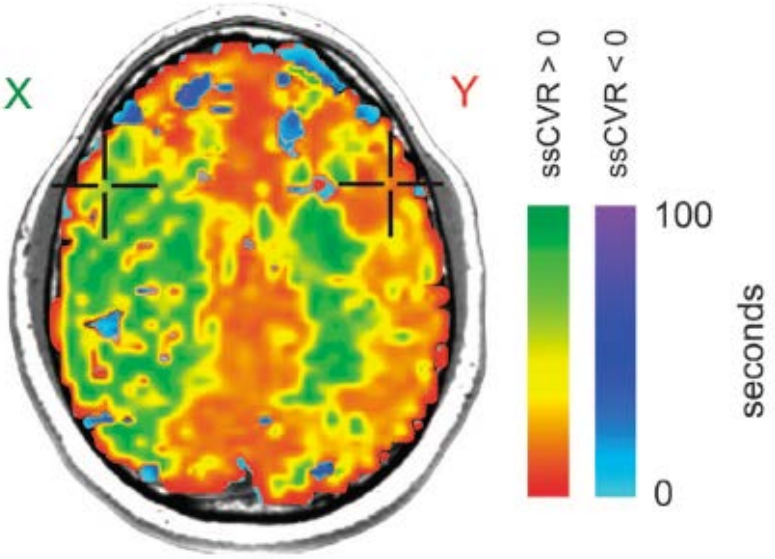
Vs.

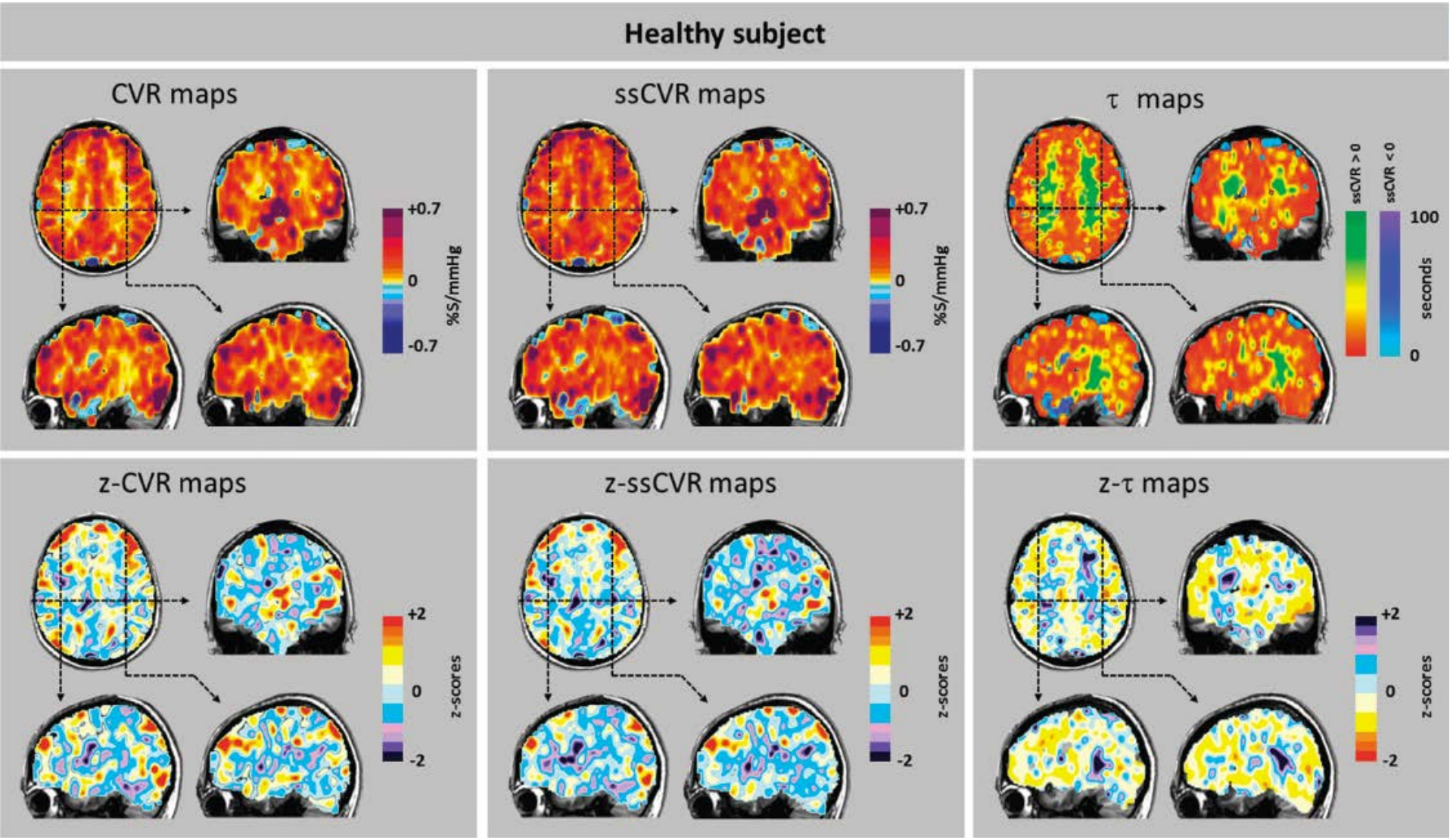
speed of response


X
Y
+0.7
0
-0.7
%S/mmHg

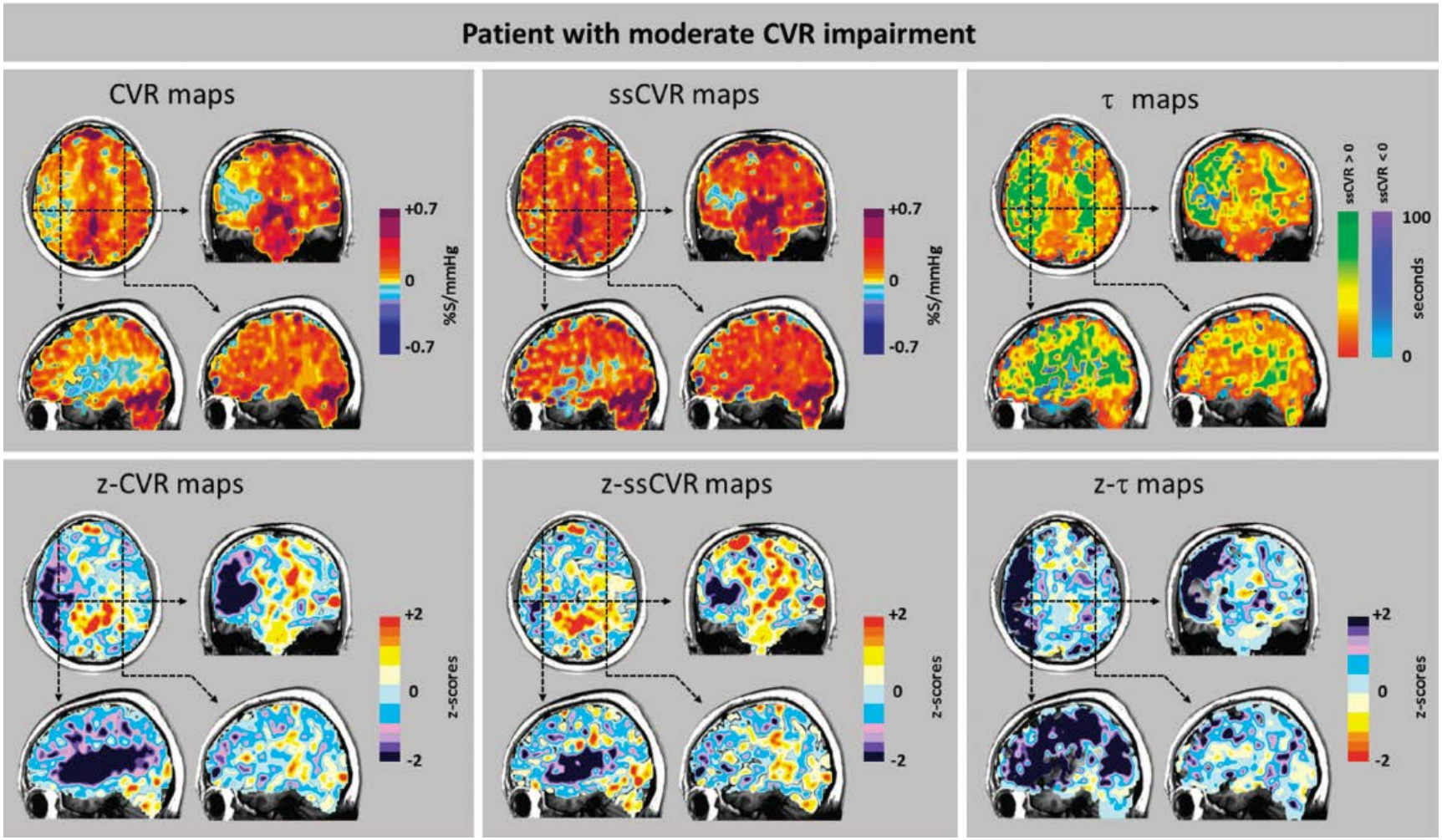

C
Signal from voxel Y


B
Signal from voxel X


X
Y
ssCVR > 0
ssCVR < 0
100
0
seconds



Poublanc J. et al JCBFM 2015

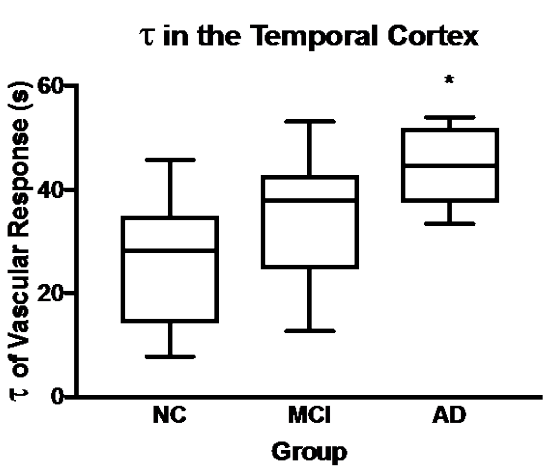


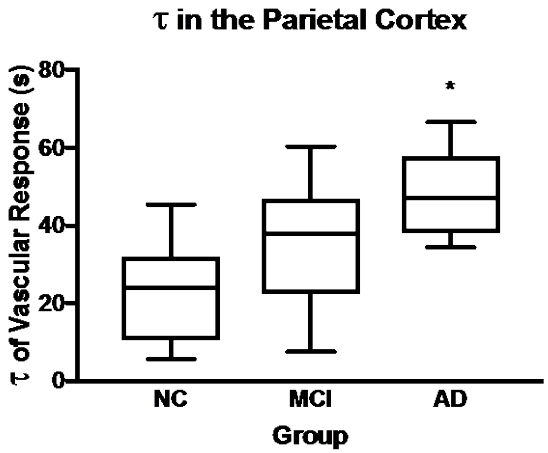
Poublanc J. et al JCBFM 2015

30 elderly subjects (mean age = 69), NC (n=13), MCI (n=11) or AD (n=6)

Segmentation via Freesurfer)

Region	Group	Mean (s)	SD
Temp.	NC	26.4	11.5
	MCI	34.2	12.9
	AD	44.5	7.8
Parietal	NC	23.7	12.9
	MCI	34.3	16.5
	AD	48.3	11.6

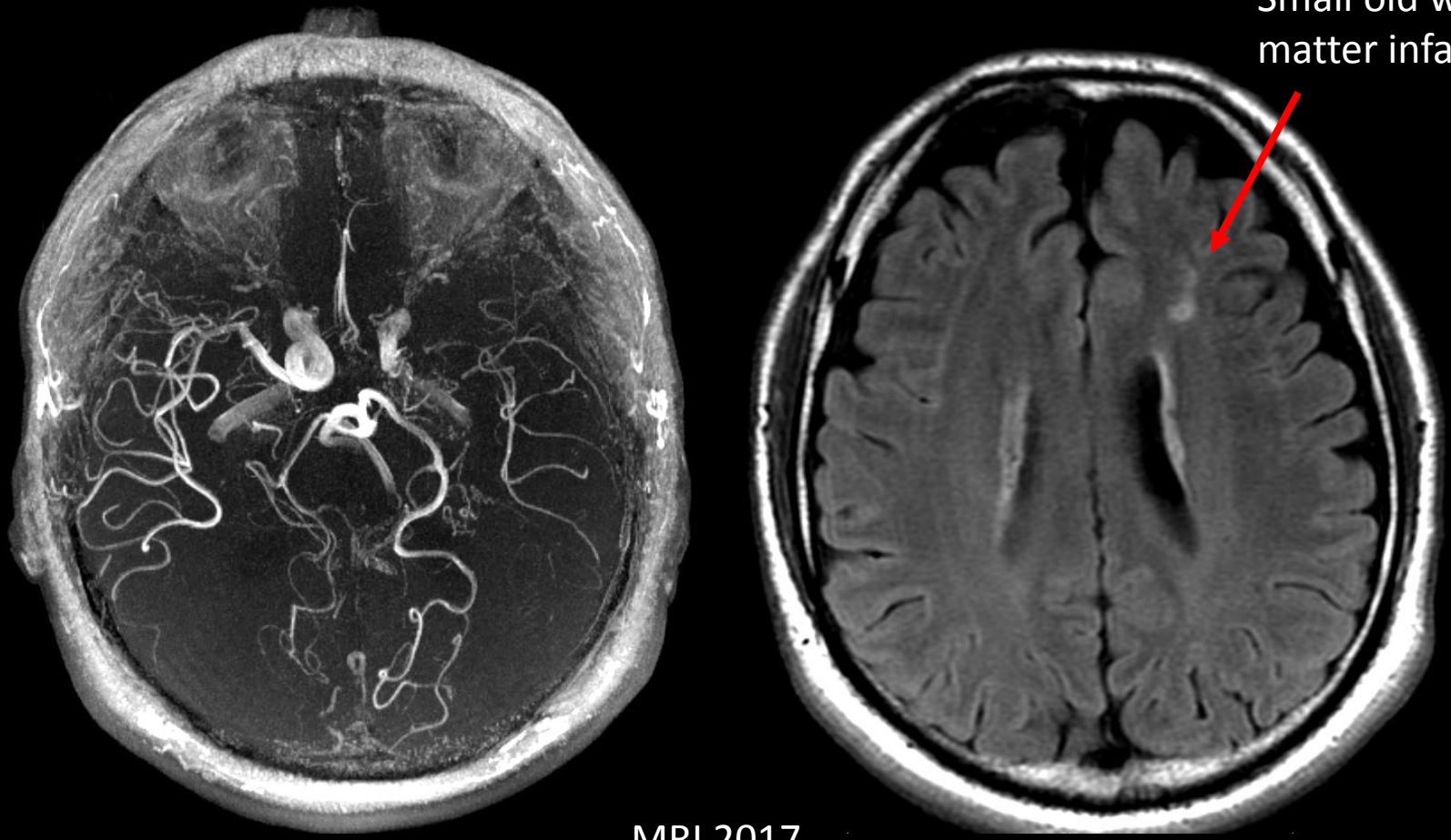




Conclusion:

AD is associated with a progressive slowing of the cerebrovascular response: a potential biomarker?

37 M with MM dis
PHx: IVH 13 y ago
c/o intermittent hemisensory symptoms and headaches.



MRI 2017

- This MRA shows high grade stenosis of:
  - Distal left ICA
  - Proximal left MCA
  - Proximal left ACA
  - Proximal right ACA
- Dilated left PCA

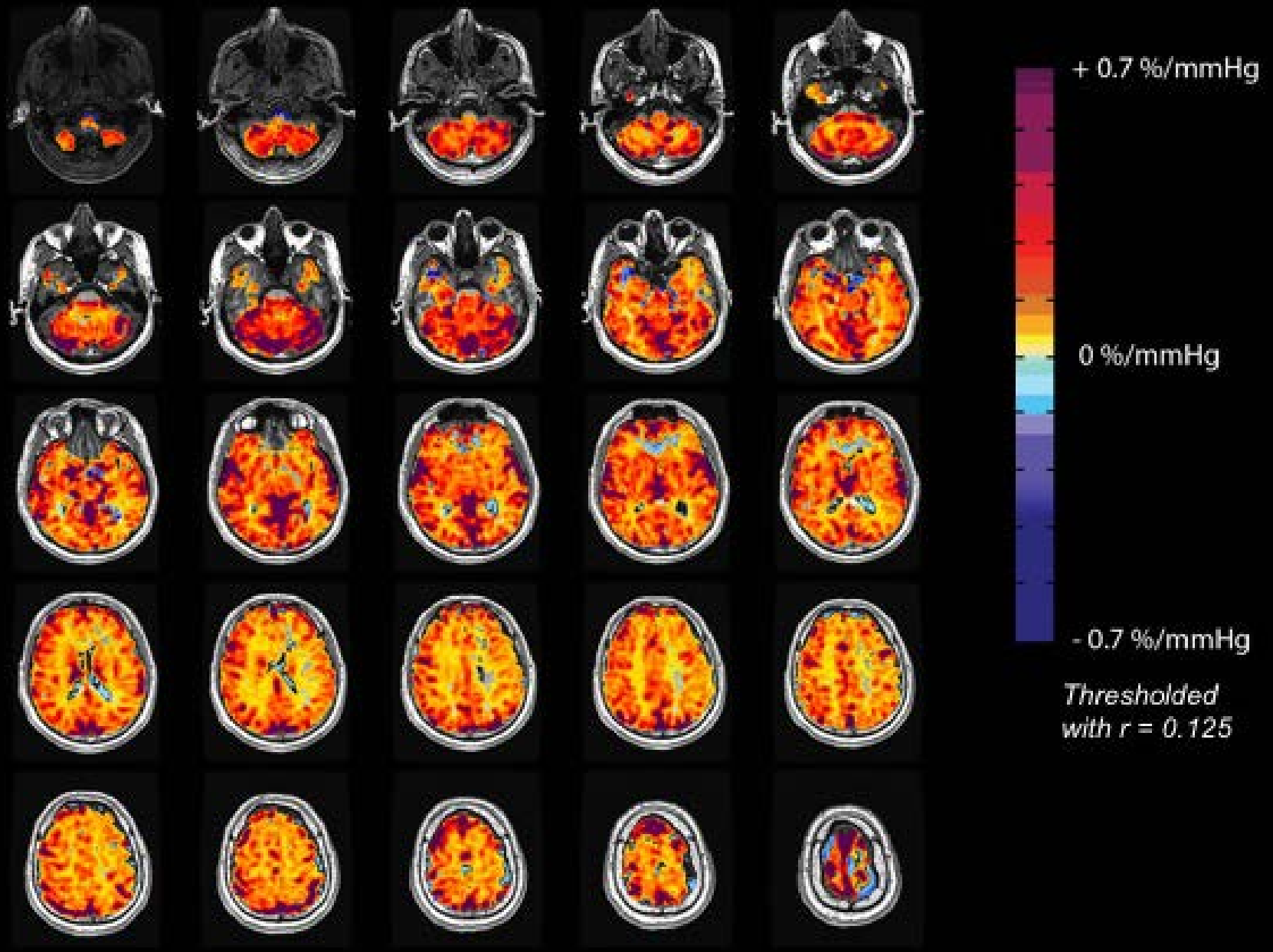
MRA 2015

MRA 2017

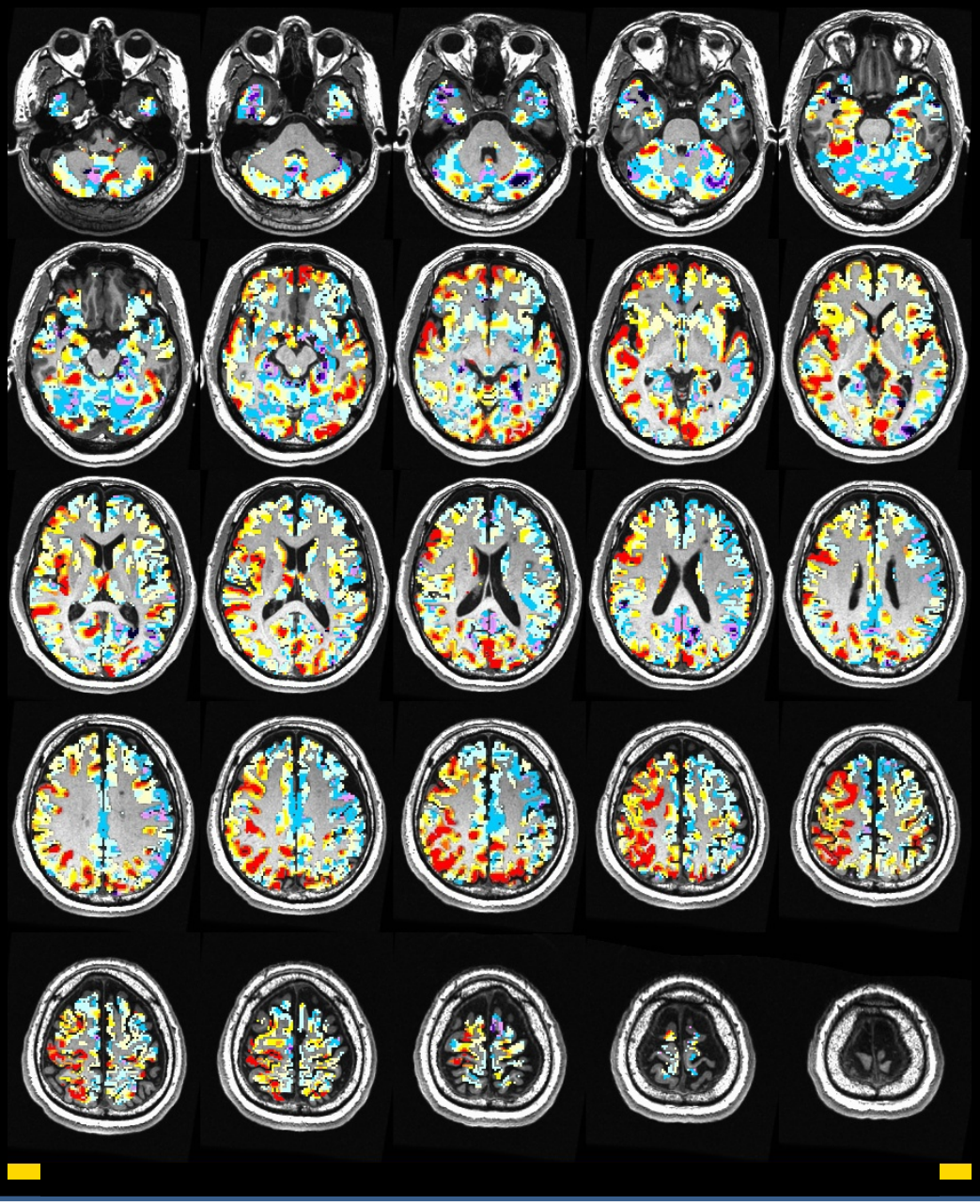
How effective are this patient’s collaterals?

Will he benefit from pre-op revascularization surgery?

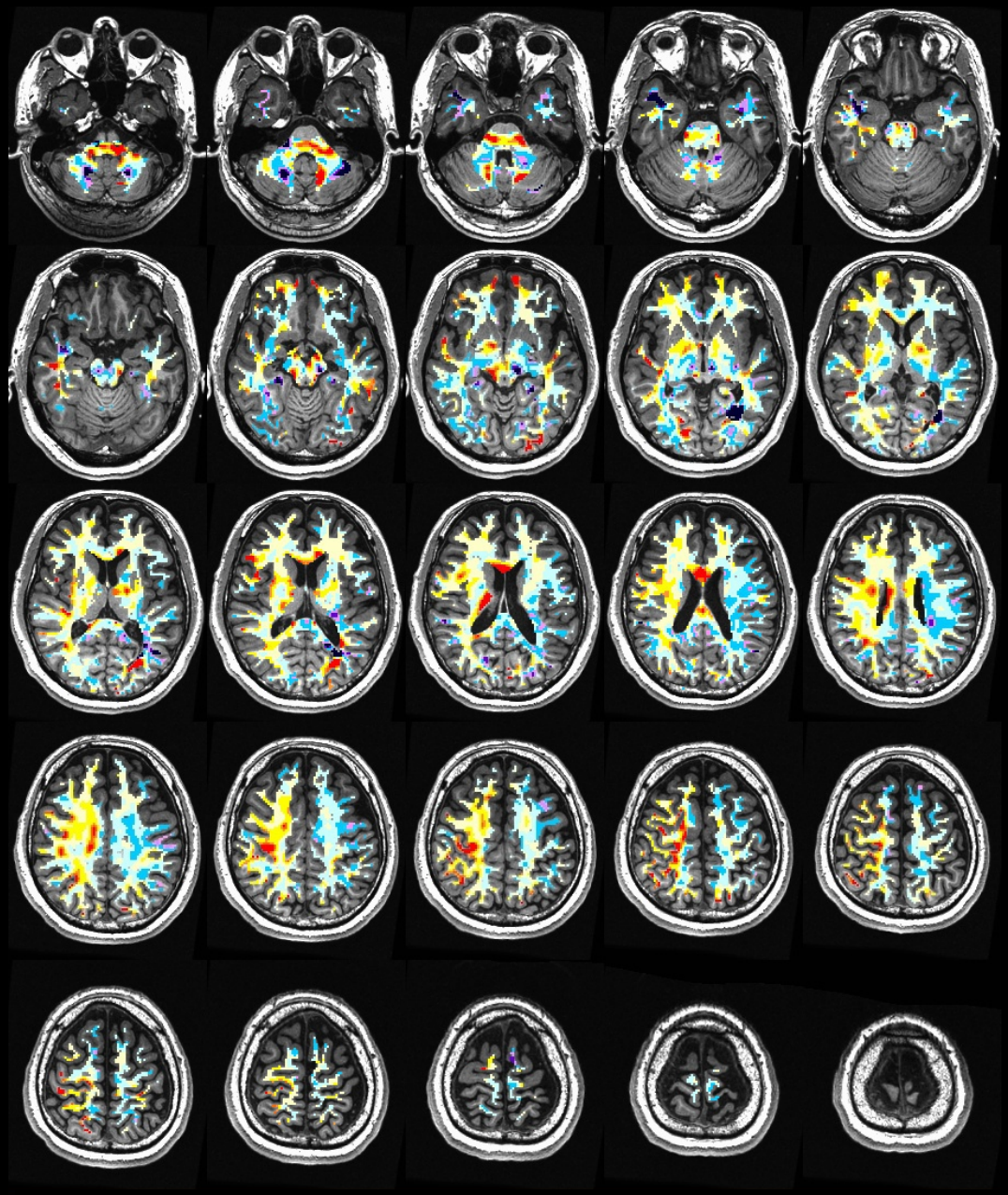
CVR Study



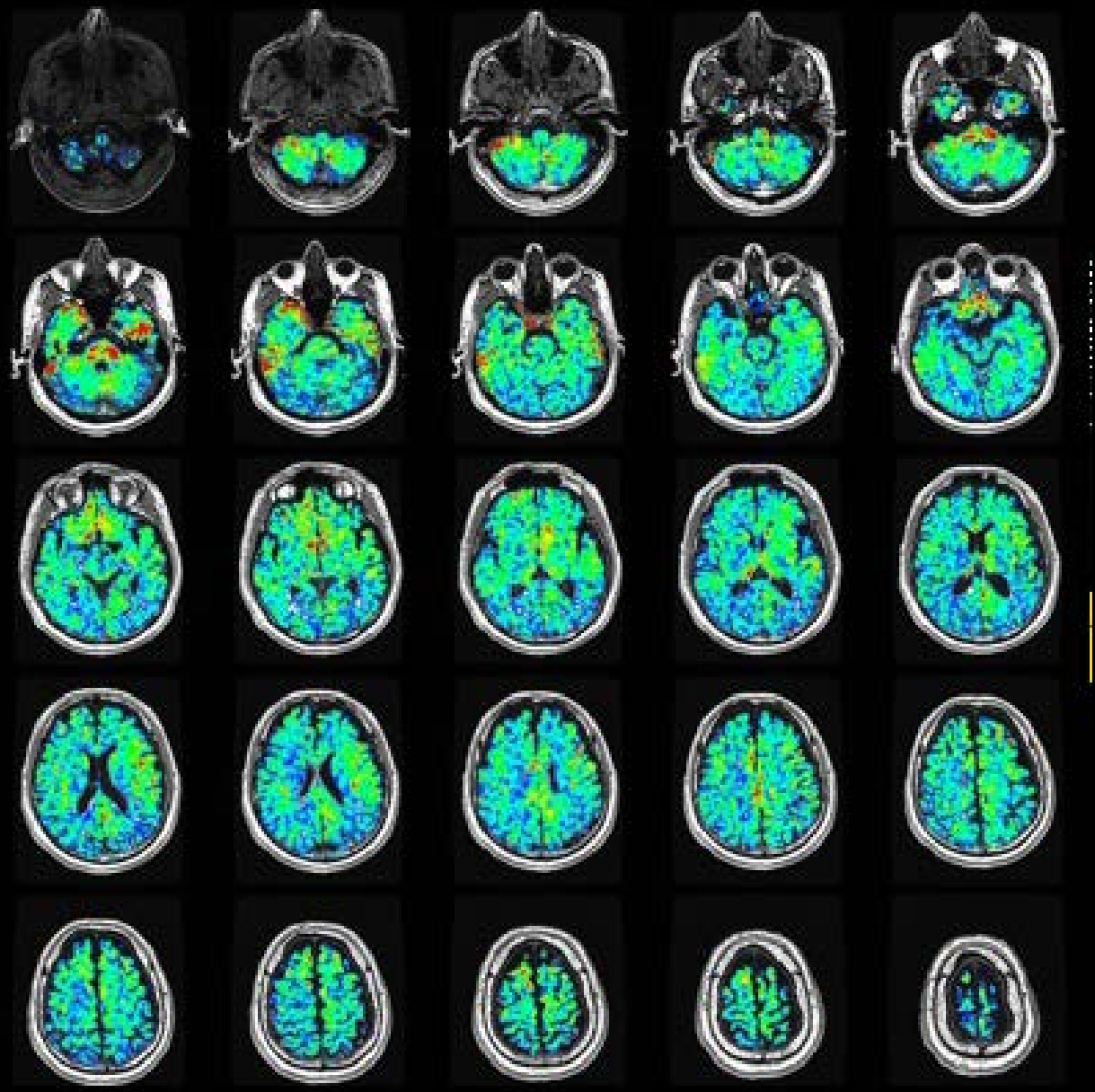
Z map CVR– Gray Matter



Z map CVR – White Matter



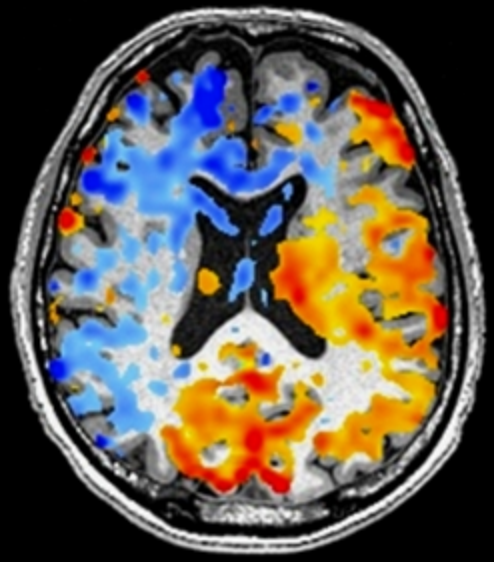
ASL



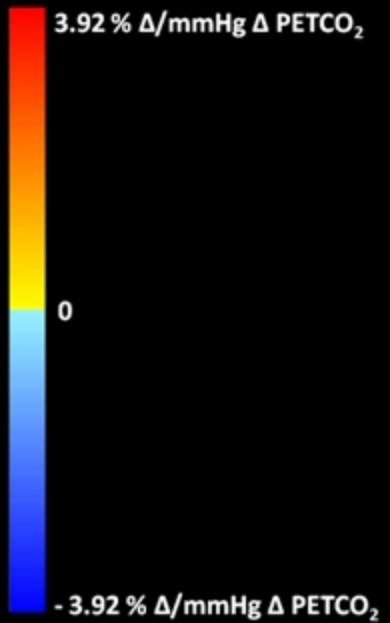
revascularization vs. reperfusion

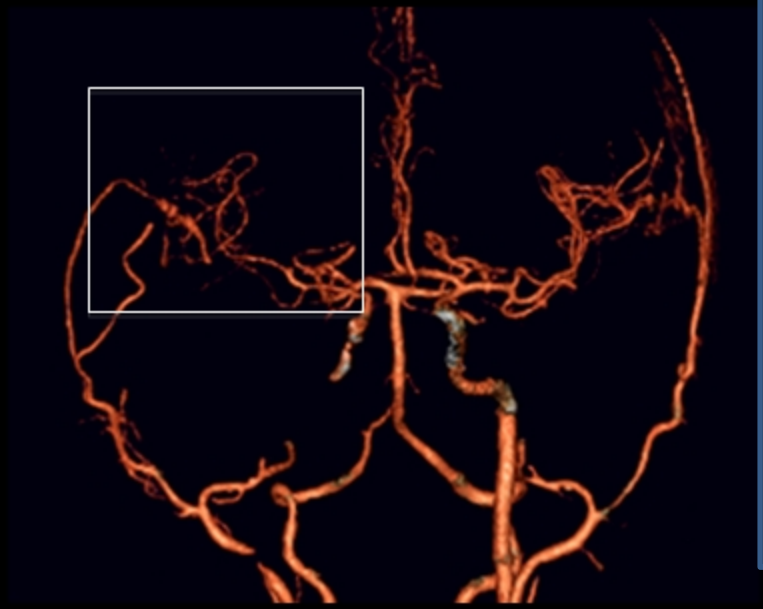
A

Initial CTA – R ICA Occlusion



Initial BOLD CVR Study

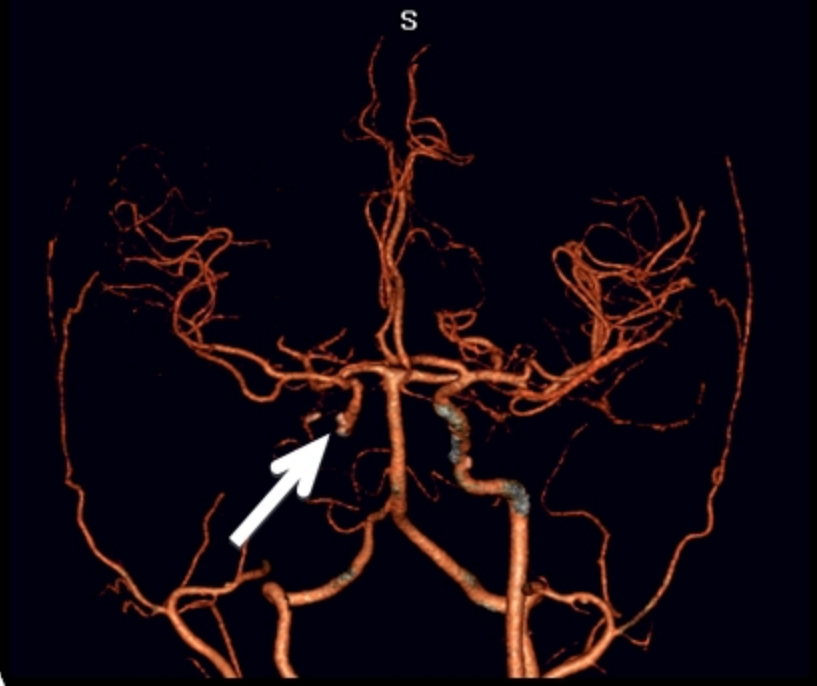




B

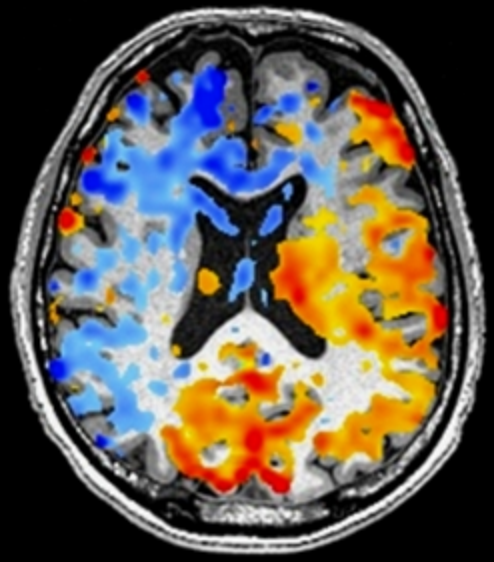
CTA Post R side EC – IC Bypass

Follow Up BOLD CVR Study
(3 months after discharge)

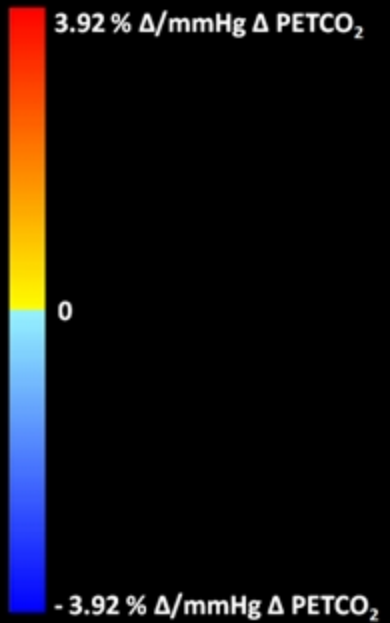


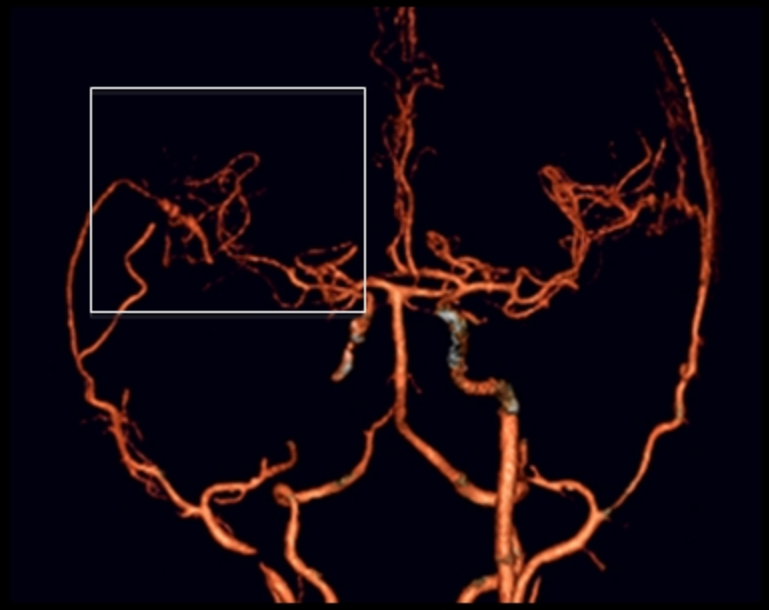
A

Initial CTA – R ICA Occlusion



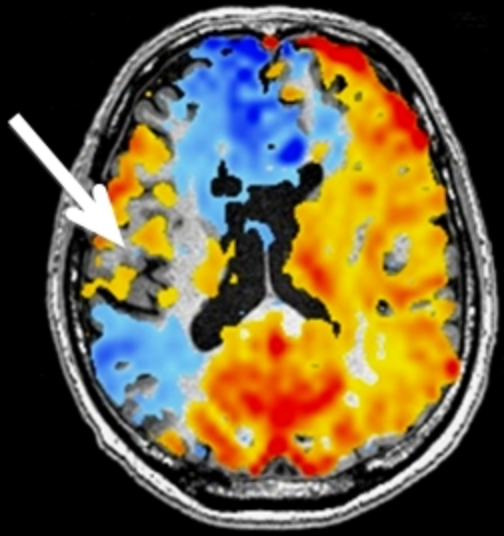
Initial BOLD CVR Study





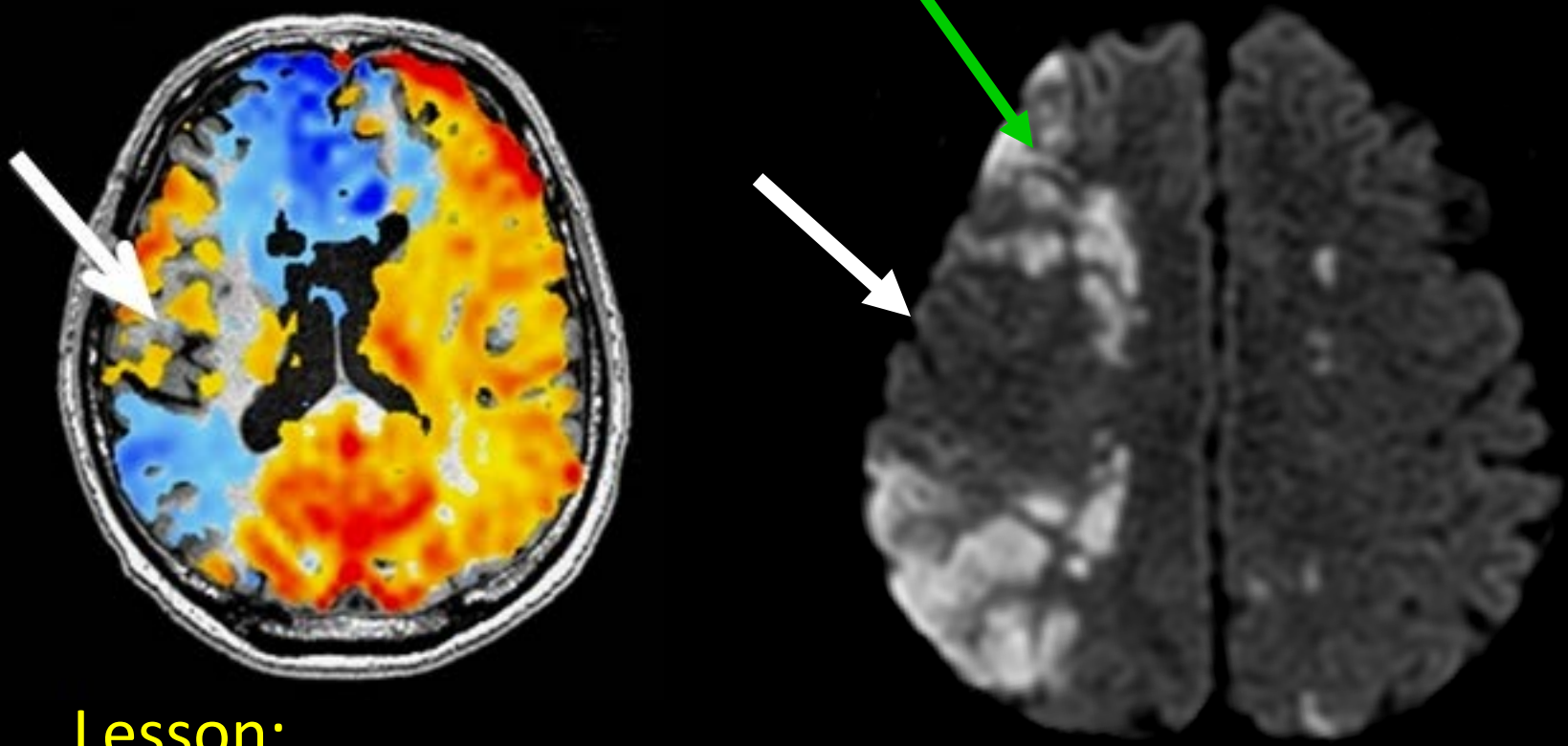
B

CTA Post R side EC – IC Bypass



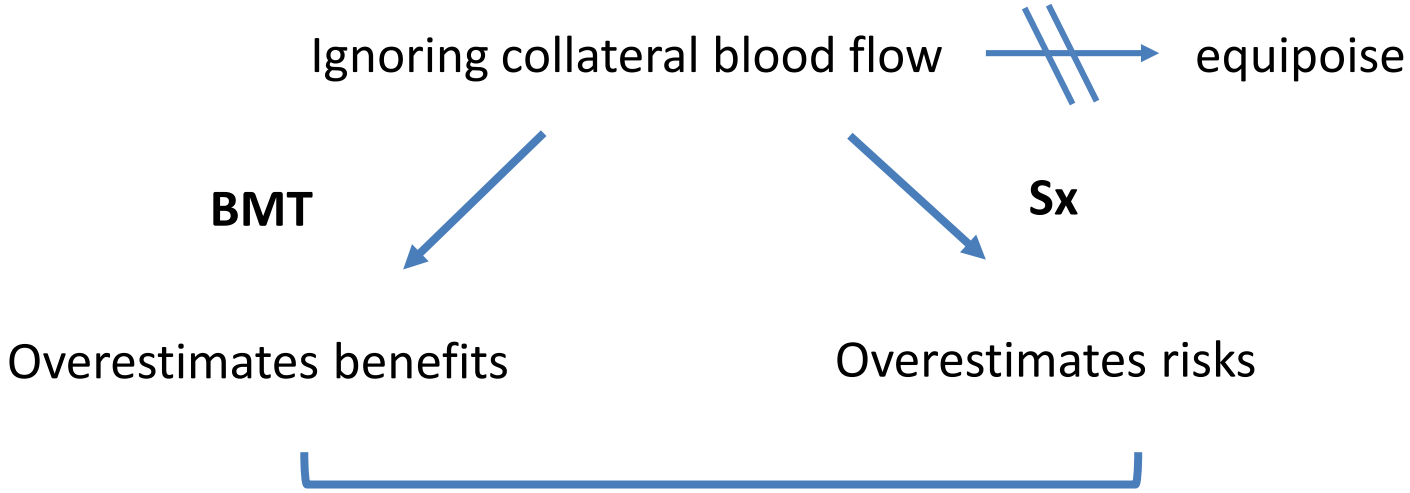
Follow Up BOLD CVR Study
(3 months after discharge)

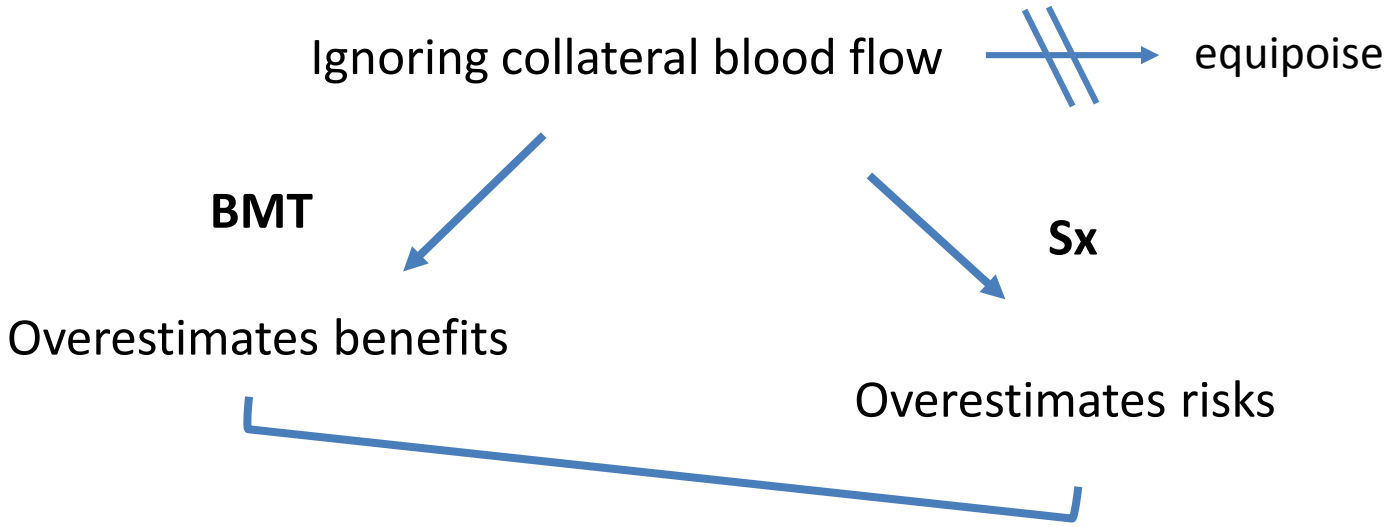
White increased signal from stroke areas



Lesson:

Revascularization is not the intervention.
Reperfusion is.


Ignoring collateral blood flow
equipoise
BMT
Sx
Overestimates benefits
Overestimates risks


Ignoring collateral blood flow
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CVR: a Brain stress test

1) How does it work?

Model; the heart stress test

Applied to brain

2) Making it clinical

Size: matters

Variability of stimulus: -> variability of CVR result

Normalize for anatomical location

Optimize resolution of test-test changes

3) Clinical implications:

True test of hemodynamic significance

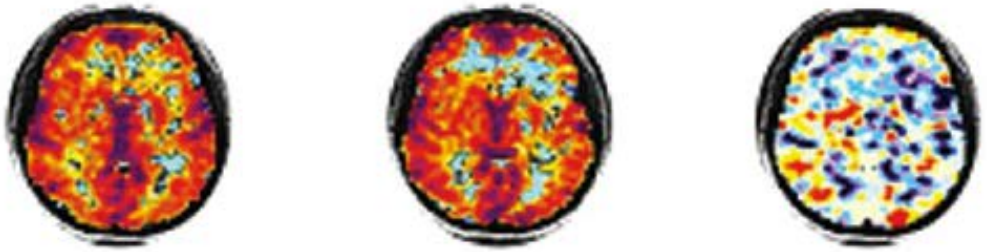
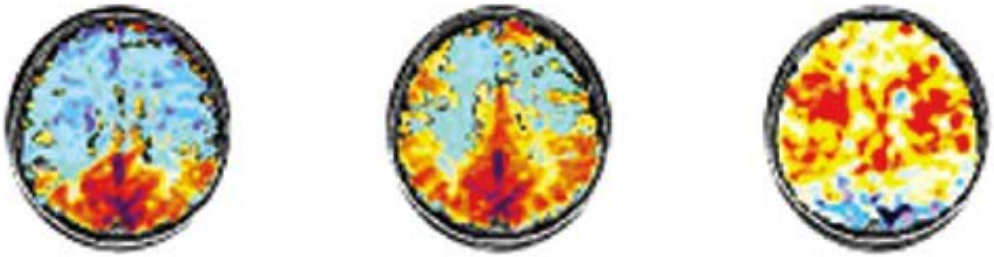
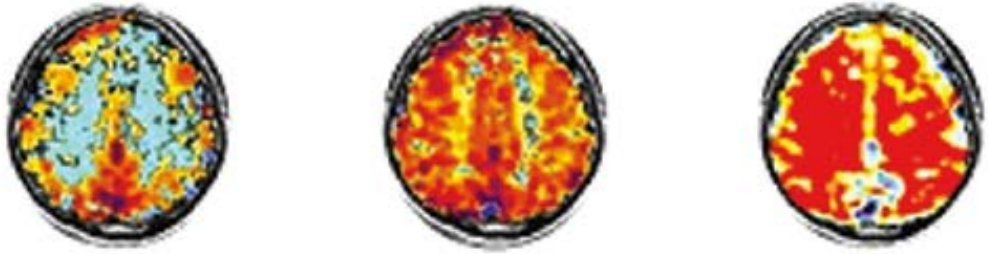
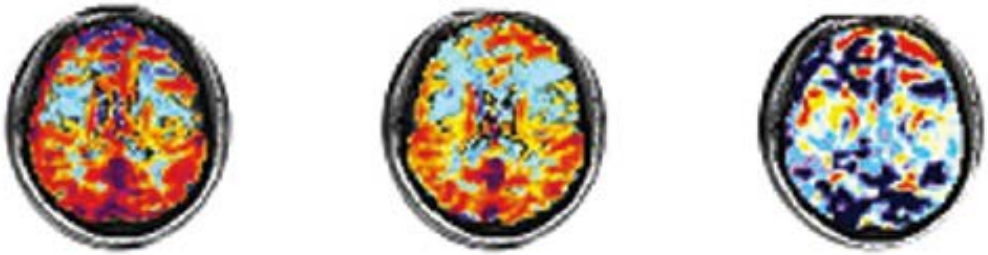
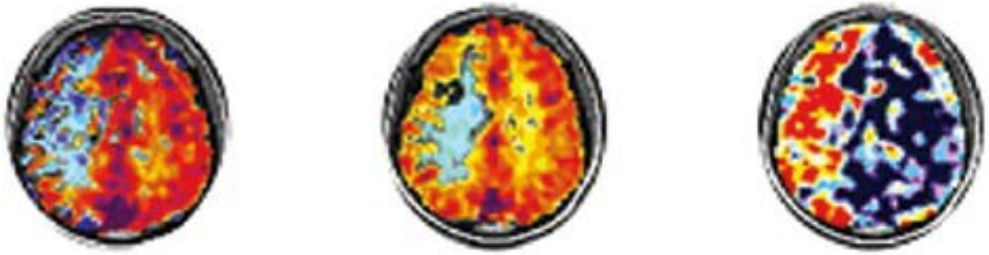
Research tool → individualized Dx → **DB** research tool

Test of efficacy of intervention

4) Self sufficient research program


THORNHILL
MEDICAL
INSPIRING INNOVATION
VELUT
ARBOR
ÆVO

Implications for control trials

55	L-ICA occlusion, R-ICA stenosis	1.5	No	
16	Moya Moya	6	Yes	
53	L-ICA stenosis	4	Yes	
26	Moya Moya	8	No	
63	R-ICA occlusion	3	Yes	

CVR study xxxx-

(Report condensed to provide example of analysis)

49 years old

Reason for referral:
Moyamoya type phenotype
Stroke TIAs

History of present illness:
Right ACA strokes 4 months previous and 1 month previous t study
1 week history of left arm shaking, with left lower and upper extremity weakness

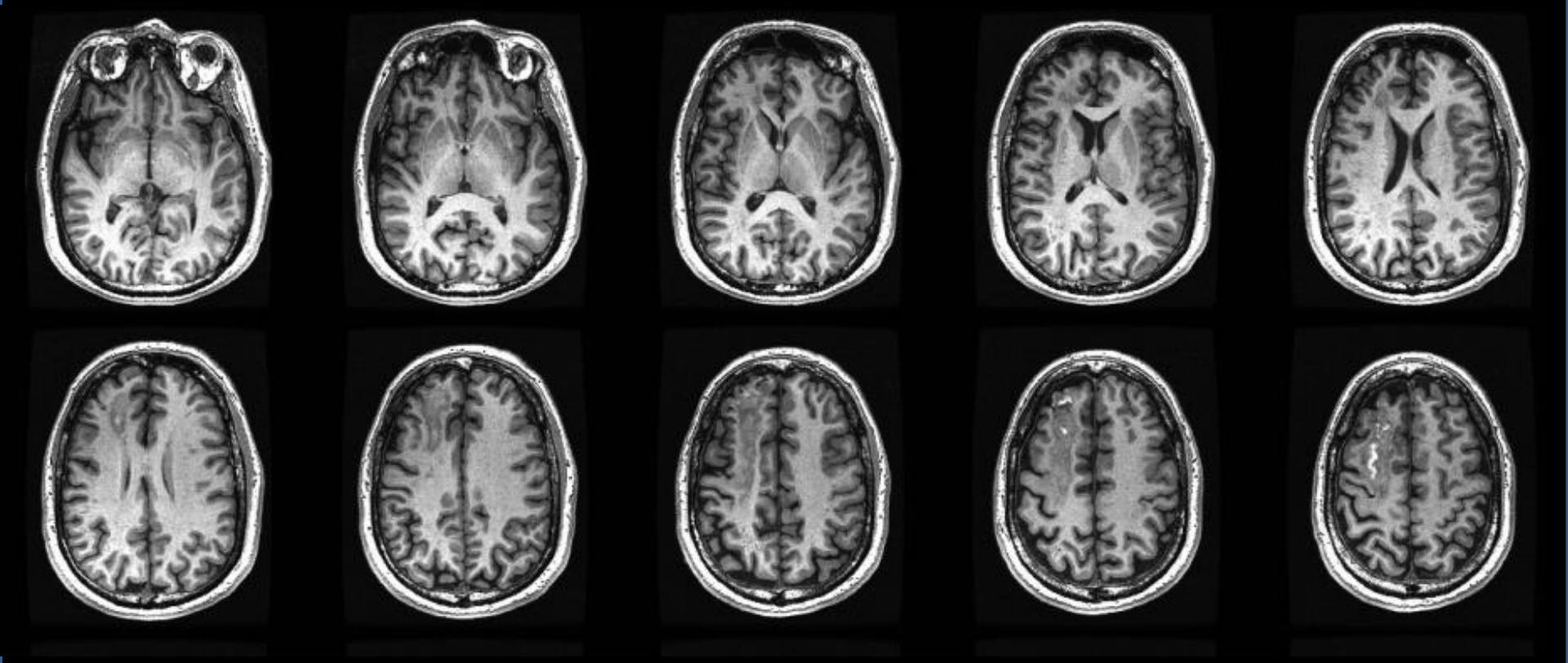
Past medical and surgical history:

- Hypertension
- Diabetes mellitus type 2

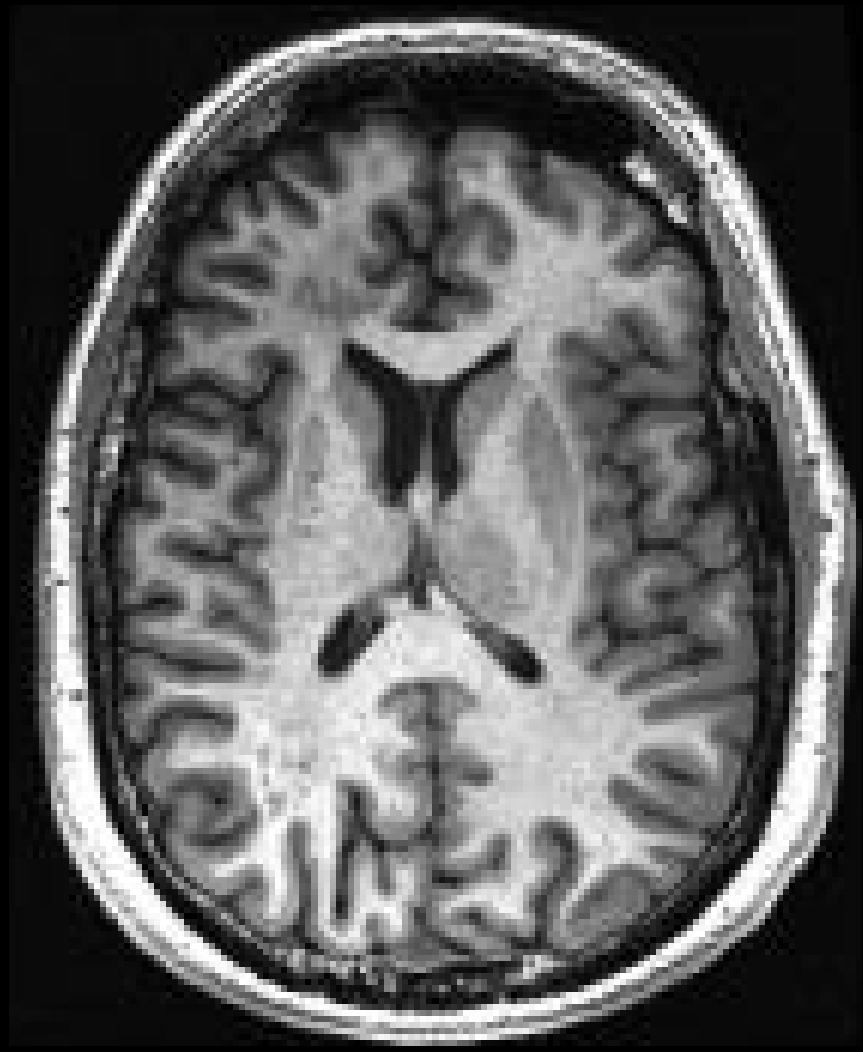
Respiract type: Gen III
Stimulus Protocol: STEP (resting pCO_2 + 10 mmHg) + RAMP
Resting pCO2: 35mmHg
Past CVRs: None

Mikulis Lab, University Health Network,
Toronto, Canada

SPGR



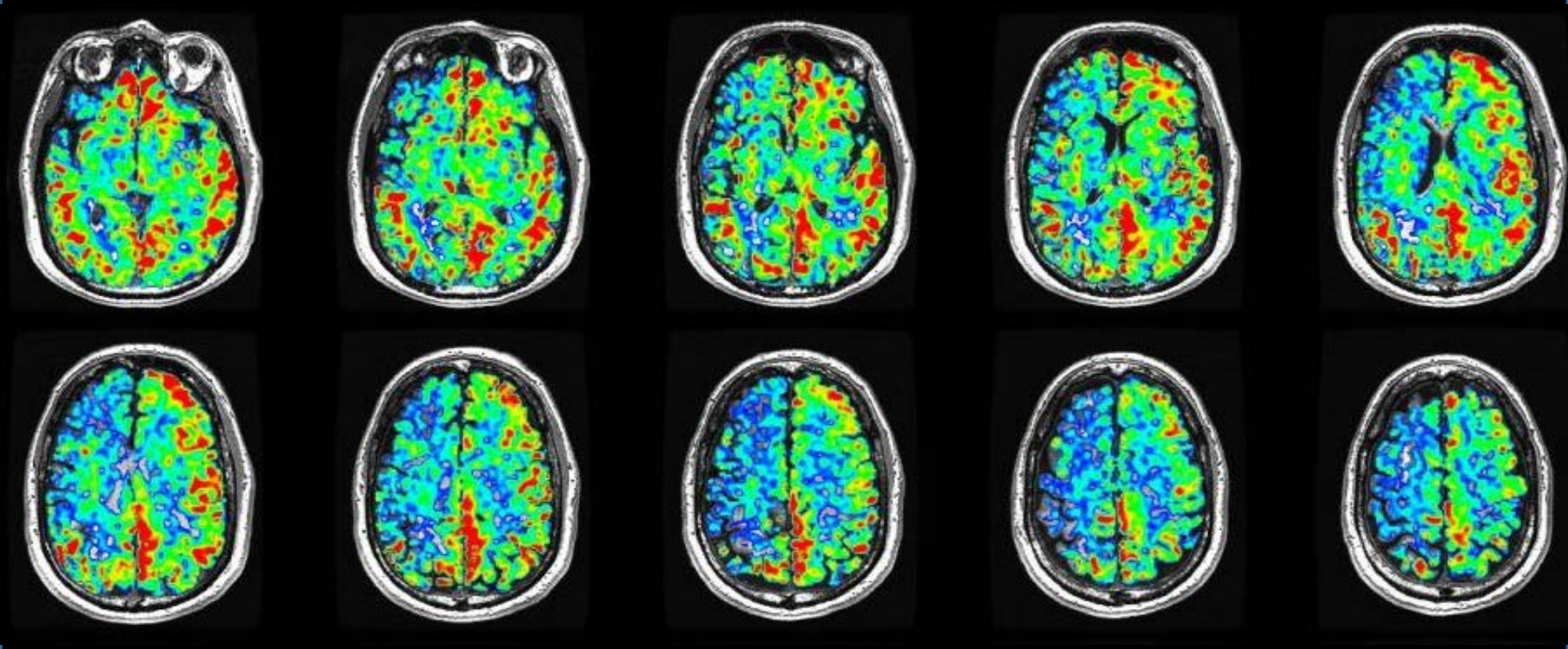
SPGR

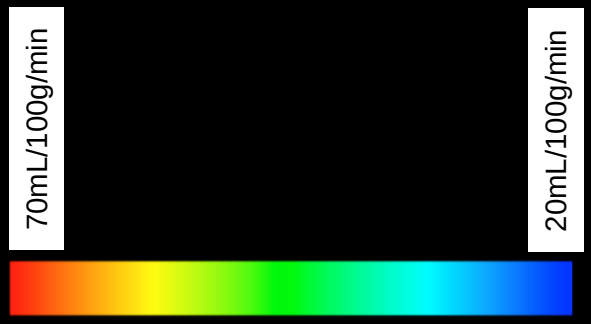


SPGR

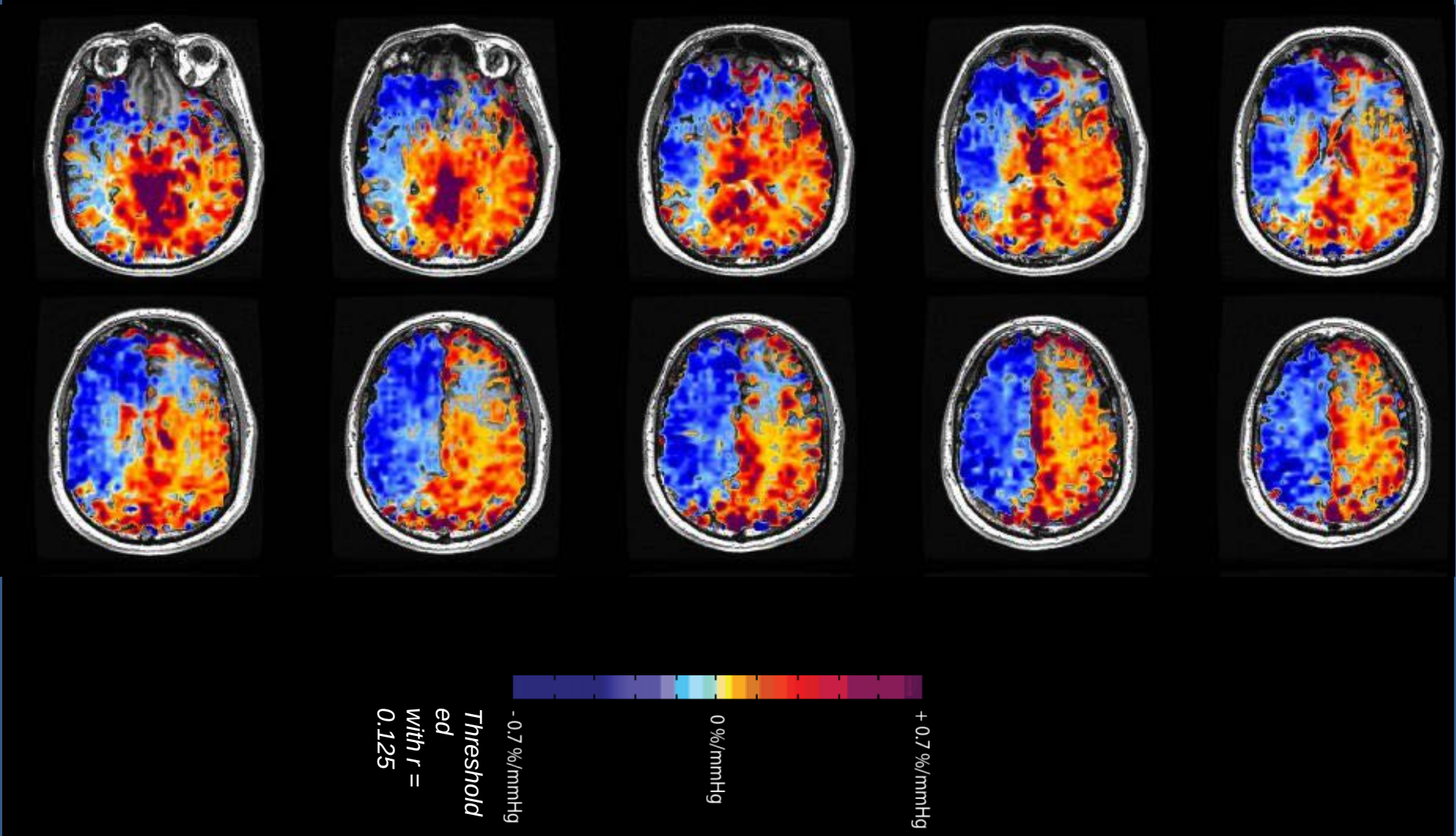
3D-COW

CBF using 3D-ASL

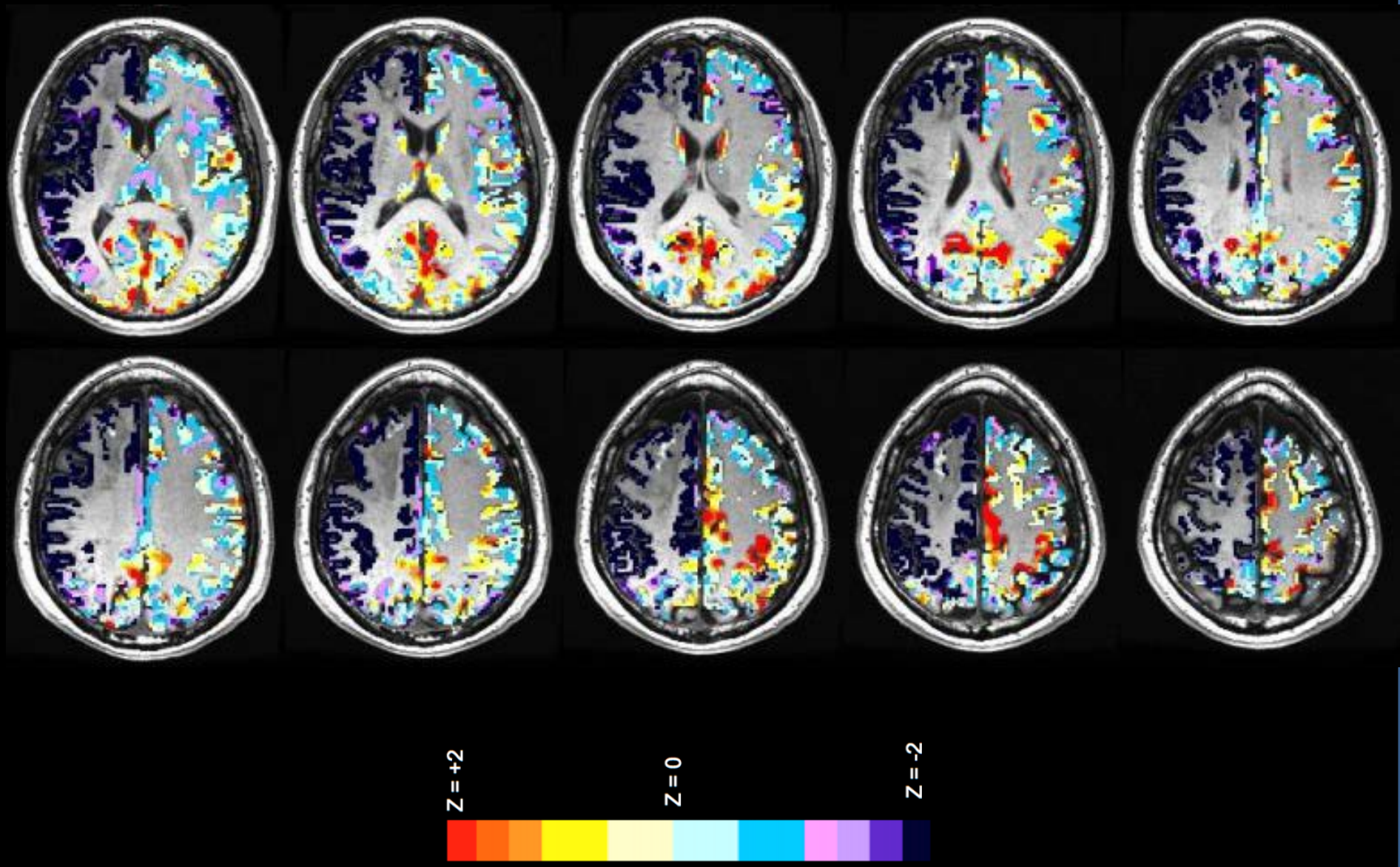




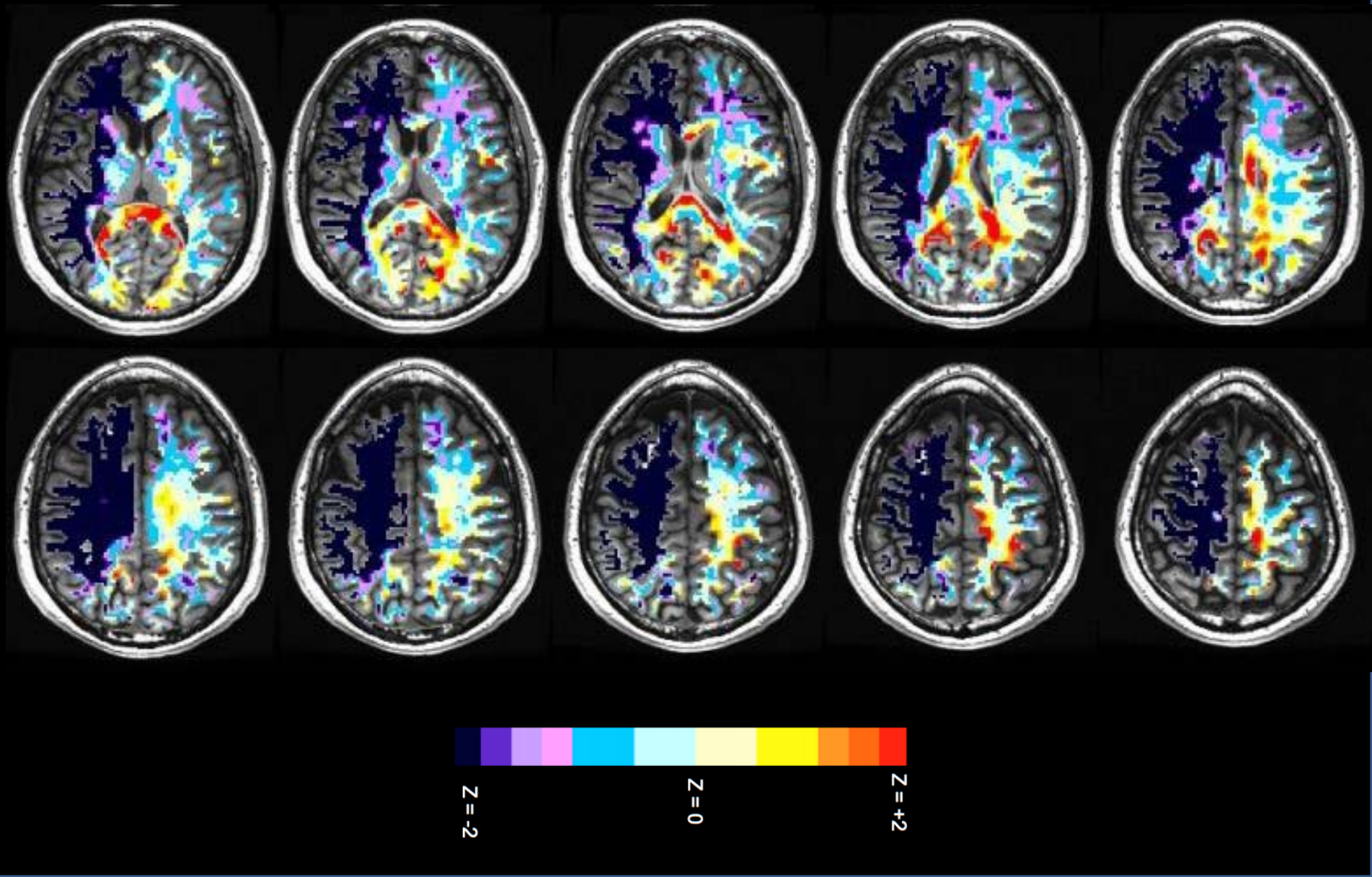
CVR Ramp (Resting + 10)

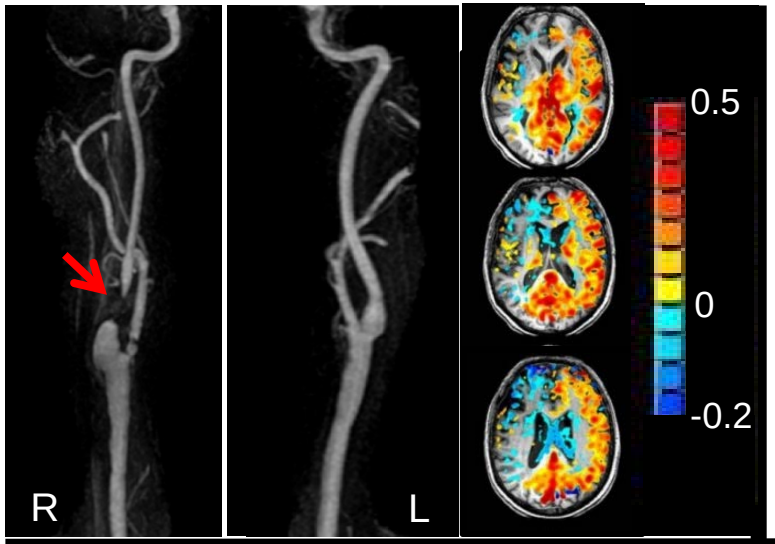


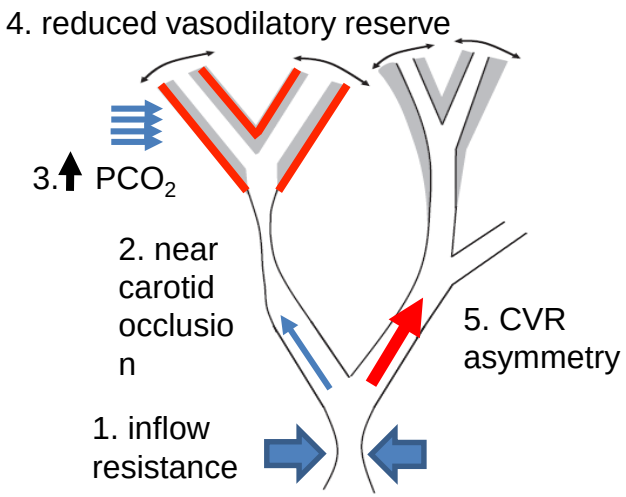
Zmap CVR-Ramp+10 (grey matter)

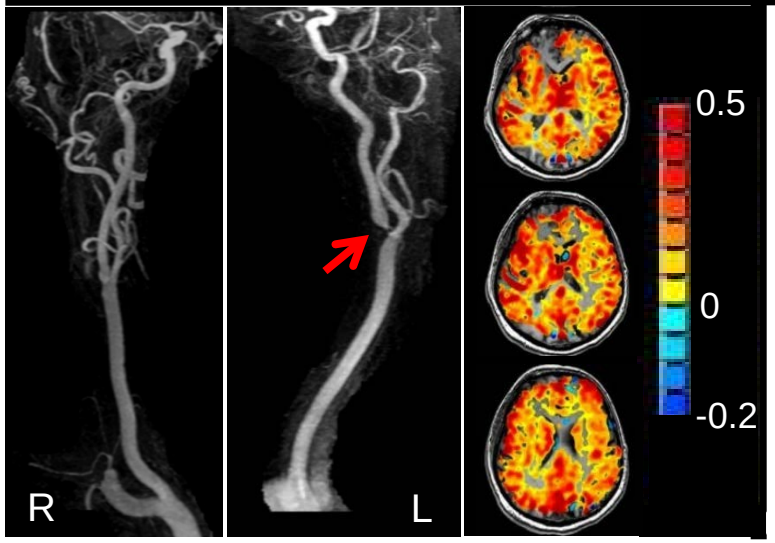


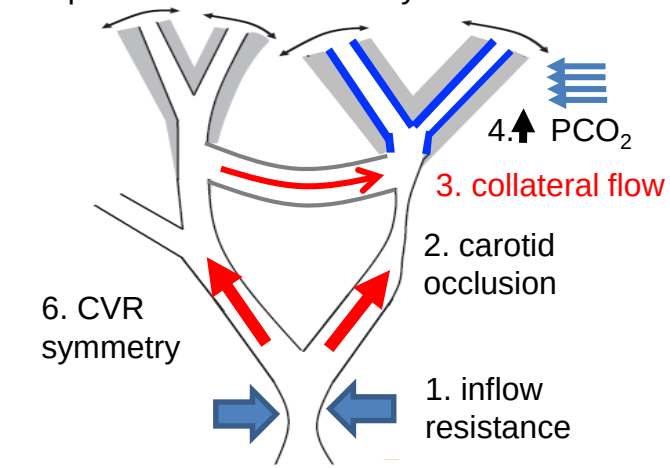
Zmap CVR-Ramp+10 (white matter)




R
L
0.5
0
-0.2


4. reduced vasodilatory reserve
3. ↑ PCO2
2. near carotid occlusion
5. CVR asymmetry
1. inflow resistance


R
L
0.5
0
-0.2

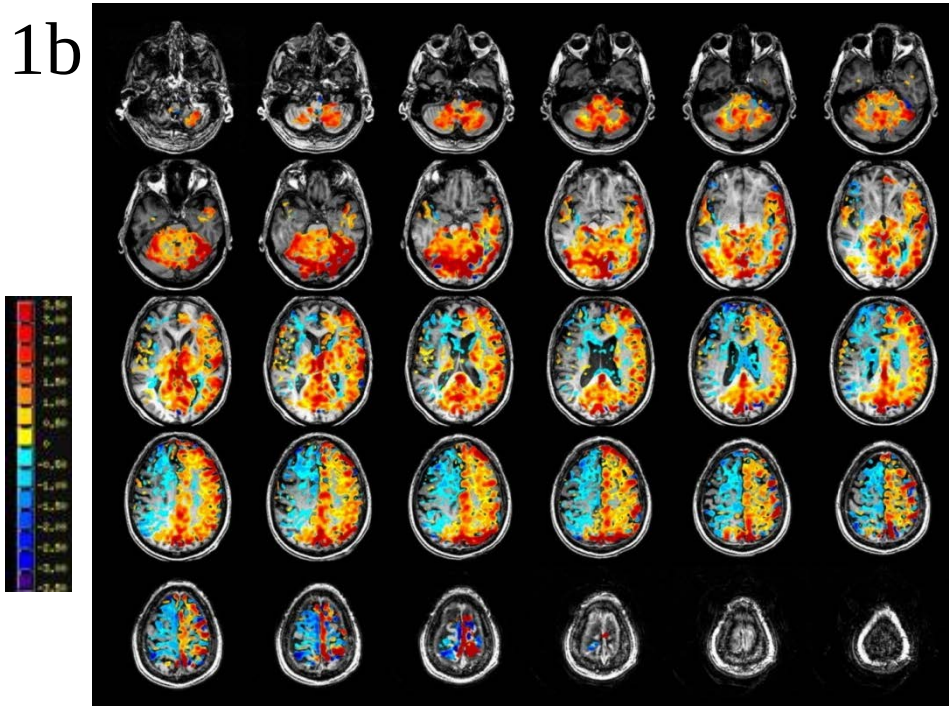

5. equal bilateral vasodilatory reserve
4. ↑ PCO2
3. collateral flow
2. carotid occlusion
6. CVR symmetry
1. inflow resistance

1a

right

left

1b

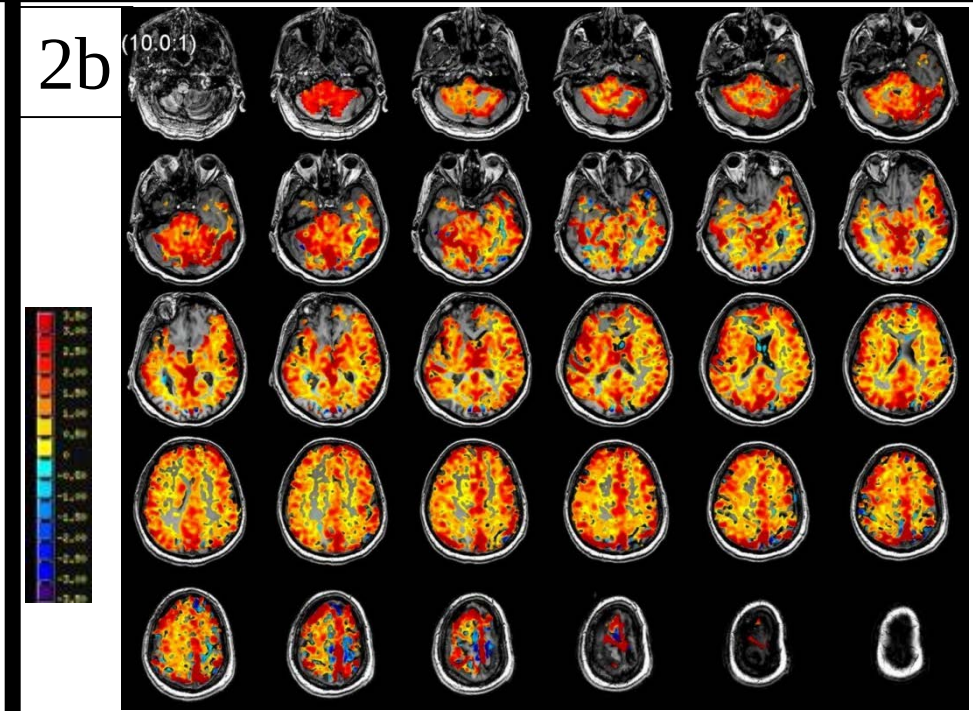


2a

right

left

2b



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Test of efficacy of intervention

CREST 2?

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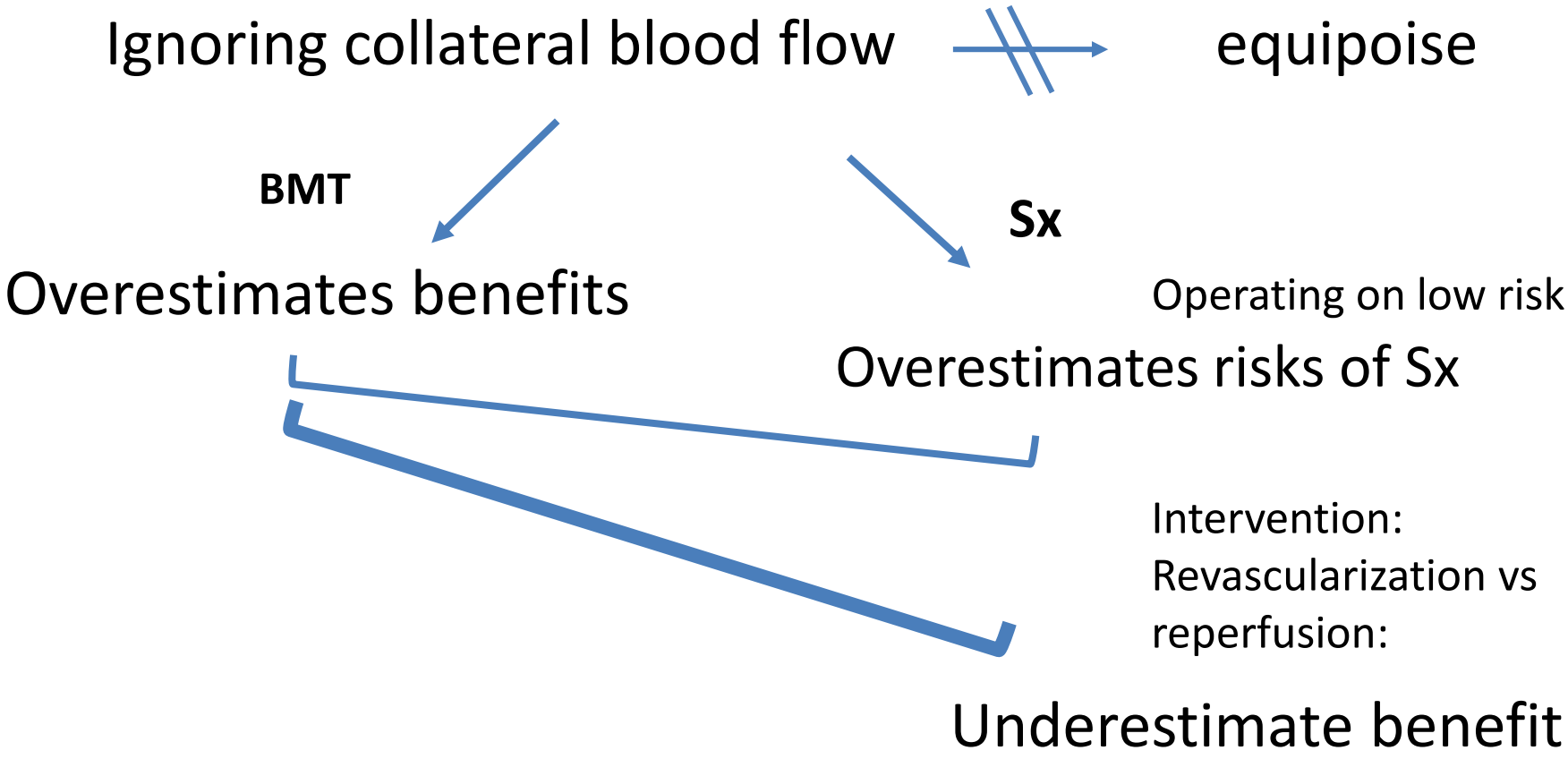

Implications:

This will skew the outcome of CREST 2 & H