CLEARANCE AND FICK'S PRINCIPLE

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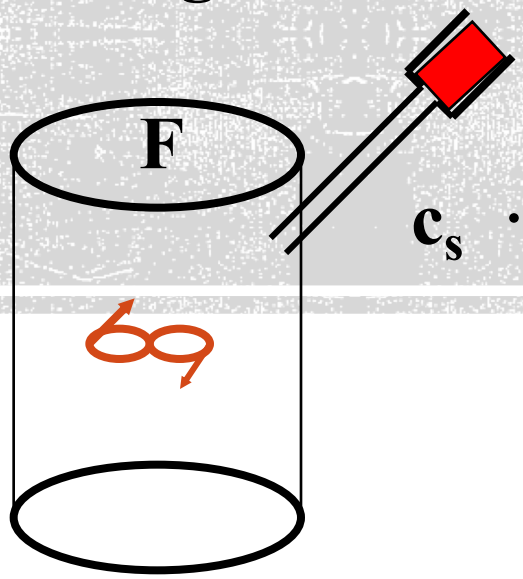
INDICATOR-DILUTION METHODS

Constant Infusion (Stewart principle)

The aim : to measure the flow of an organ or a vessel or a pipeline



[F]= ml/s

$c_s \cdot F_s = j_{in}$ **flux !!!!**

$[c_s]$ = mmol/ml

$[F_s]$ = ml/s

$[j_{in}]$ = mmol/s

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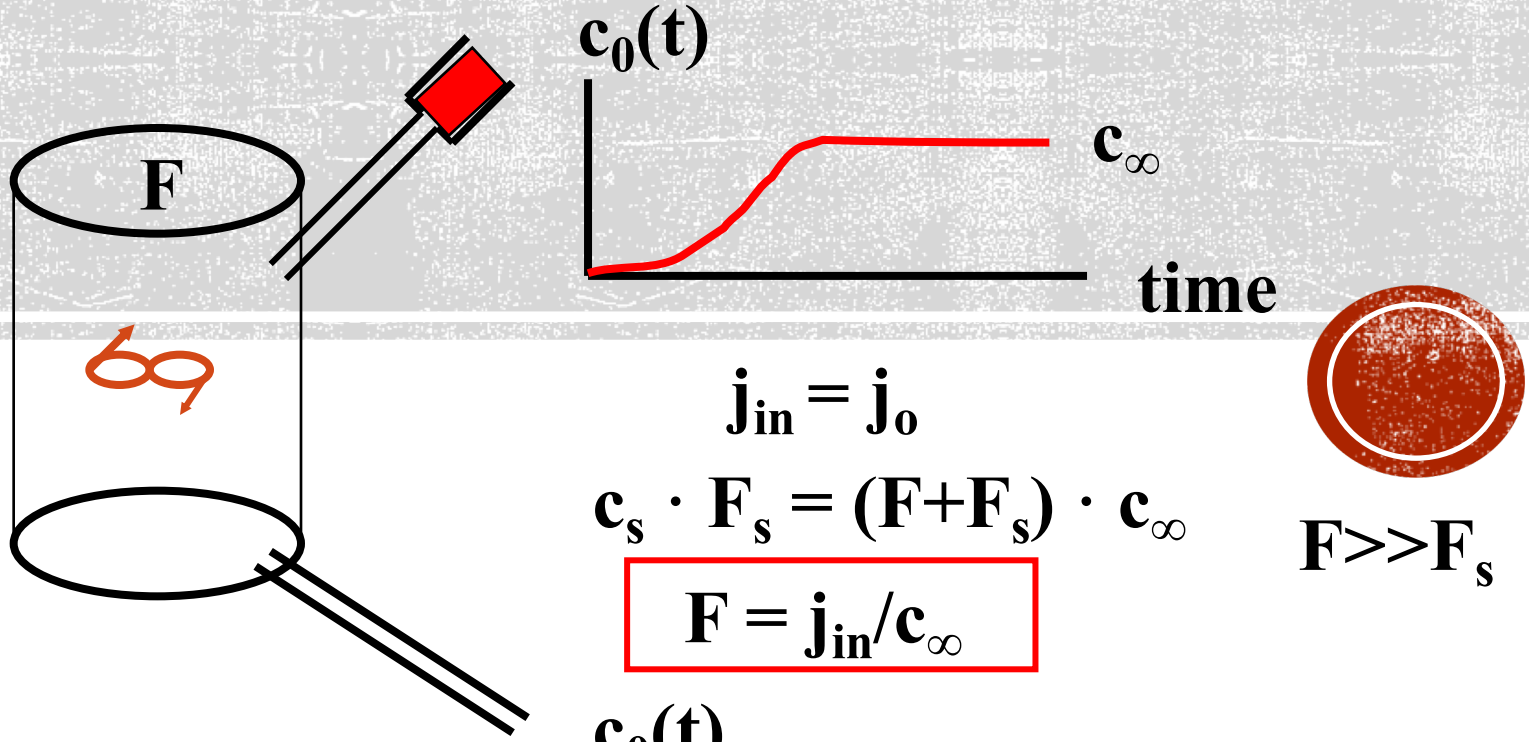
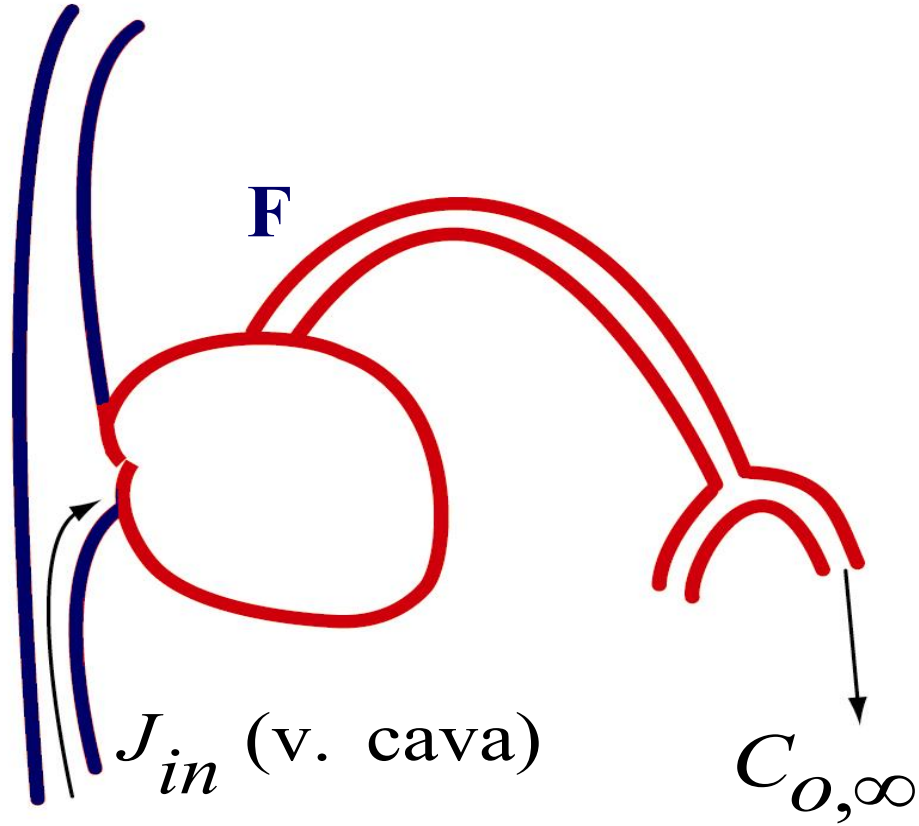


$$j_{in} = j_o$$

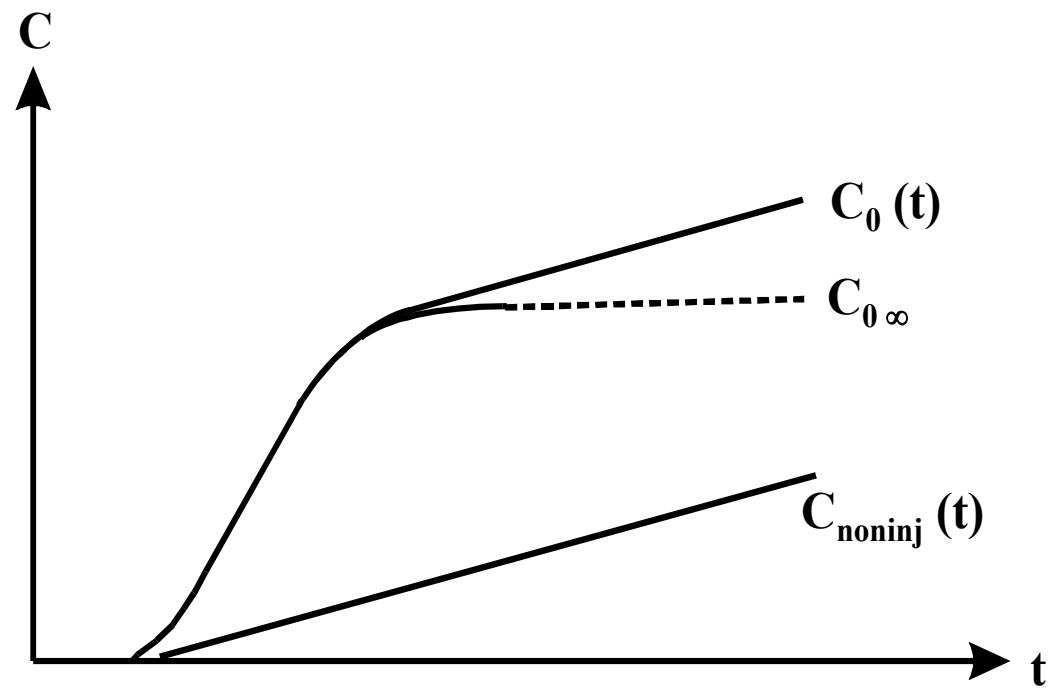
$$c_s \cdot F_s = (F+F_s) \cdot c_\infty$$

$$F = j_{in}/c_\infty$$

$F >> F_s$



Stewarts principle: Continuously infusion in vena cava, and outlet concentration measurement from a peripheral artery.

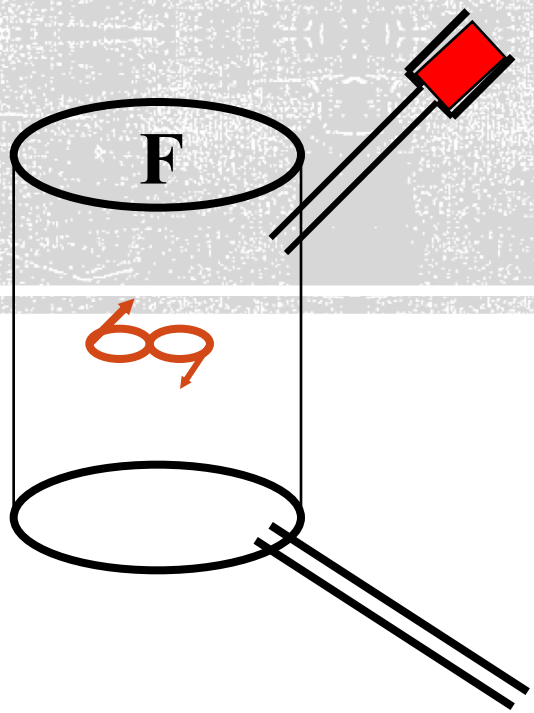


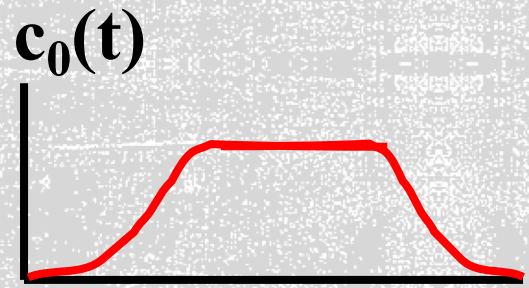
Measurement of concentration at the outlet and the "noninj" side.

BOLUS INJECTION

(Henriques and Hamilton)

The aim : to measure the flow of an organ or a vessel or a pipeline





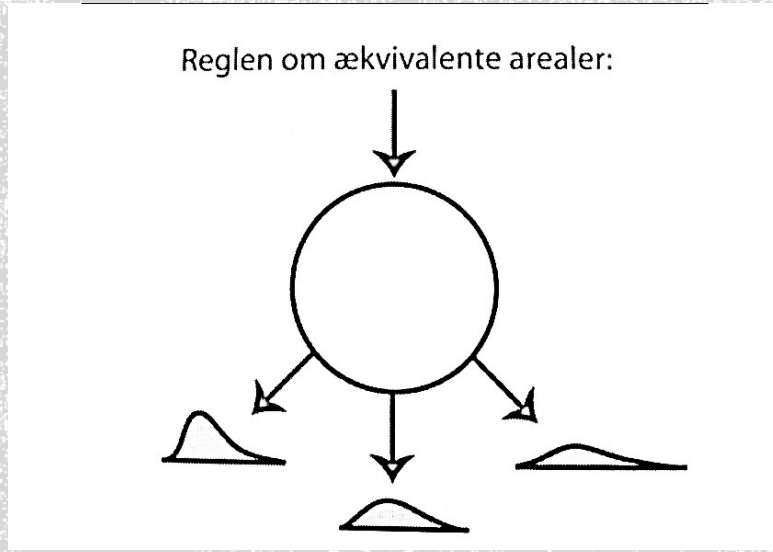
$$\int_0^\infty c_o(t)dt$$

$$F = \frac{Q_o}{\int_0^\infty c_o(t)dt}$$

$$\boxed{F = \frac{dose}{area}}$$

RULE OF EQUIVALENT AREAS

(Sapirstein)



$$F = \frac{dose}{area}$$

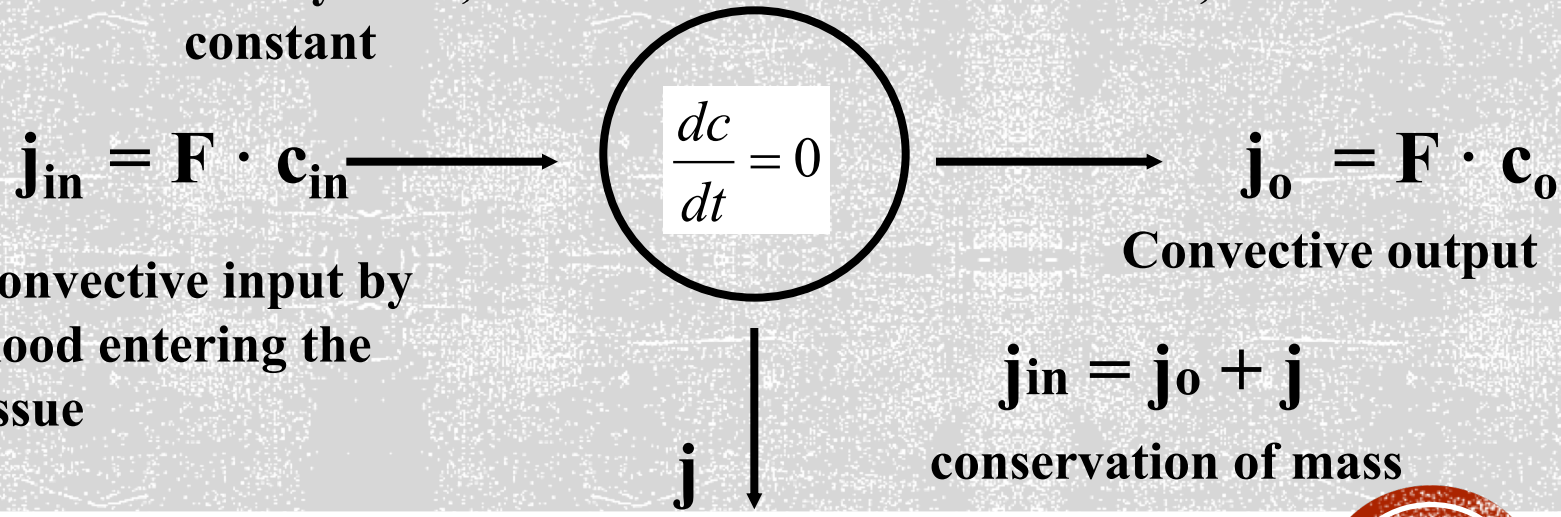
Area is the same no matter where we sample the C_0 curve!

Fick’s principle

The conservation of matter

FICK'S PRINCIPLE

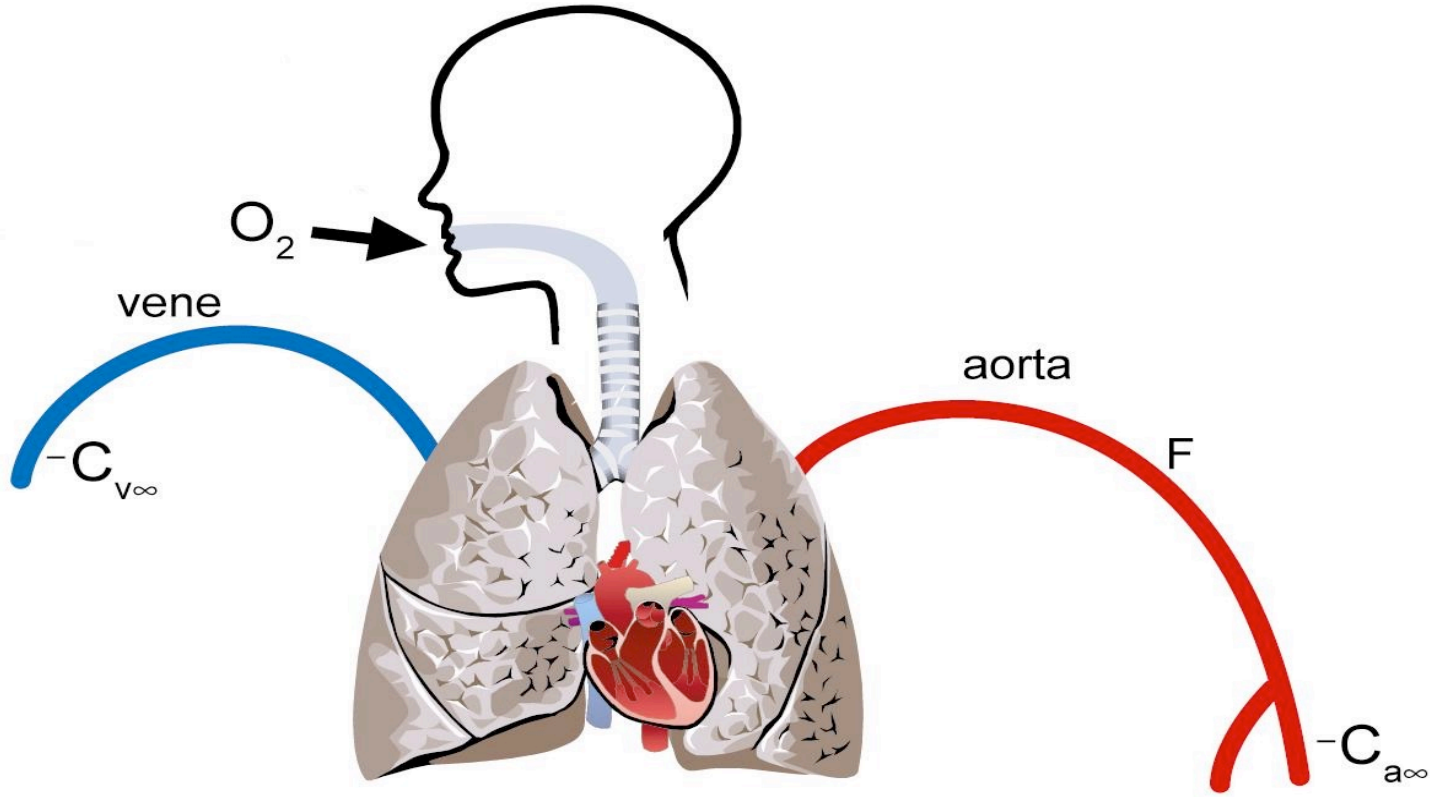
Steady state; Concentration here is constant , fluxes are here constant



$$F \cdot c_{in} = F \cdot c_o + j$$

$$F = j / (c_{in} - c_o)$$

Fick's principle: cardiac output



$$J_a = J_{O_2} + J_v$$

$$F \cdot C_{a\infty} = J_{O_2} + F \cdot C_{v\infty} \Rightarrow$$

$$F = \frac{J_{O_2}}{C_{a\infty} - C_{v\infty}}$$

CEREBRAL METABOLIC RATE OF OXYGEN $CMRO_2$

- Fick's principle

blood sample

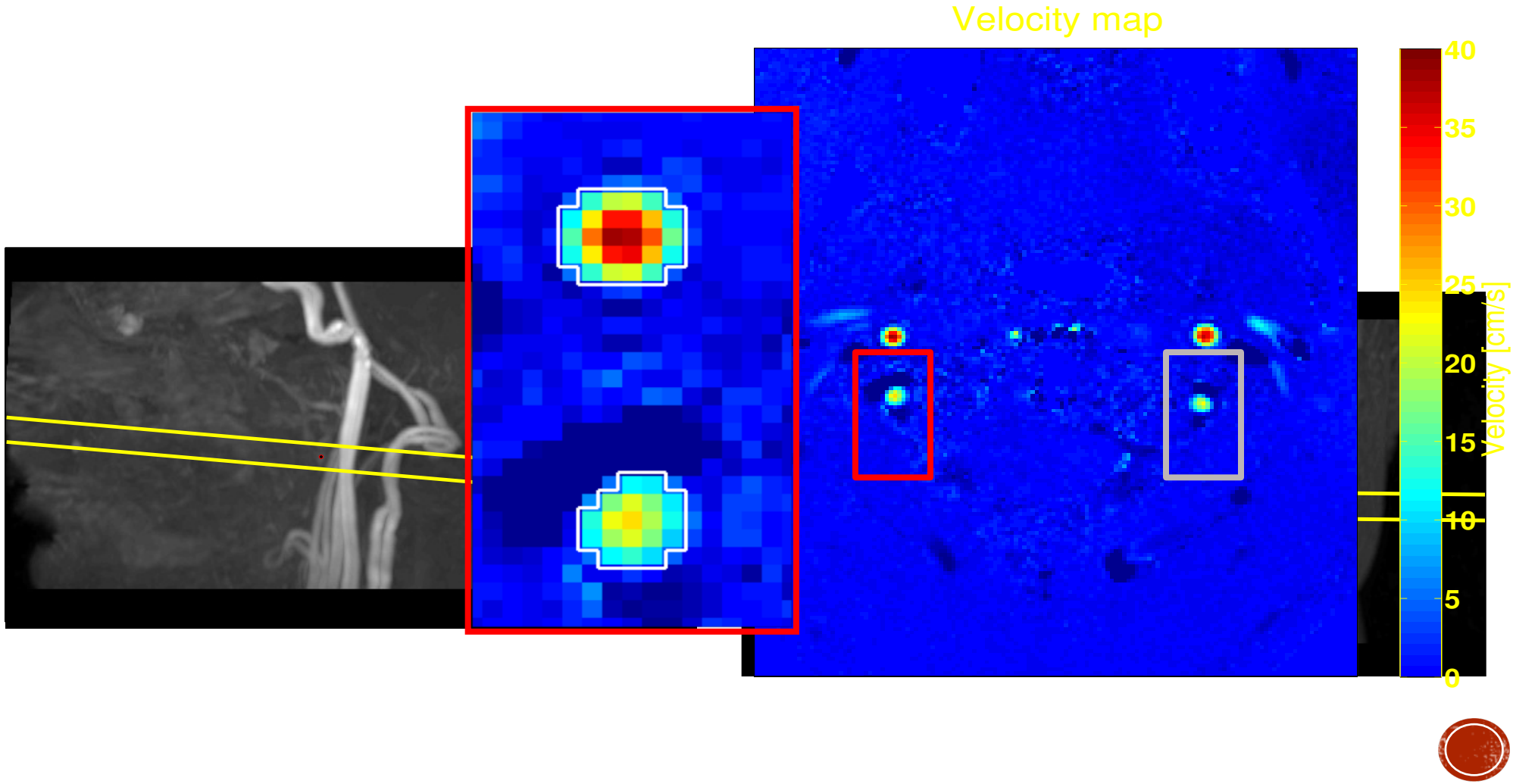
$$CMRO_2 = 4 \bullet [Hgb] \bullet CBF \bullet (S_aO_2 - S_vO_2)$$

MRI phase contrast mapping

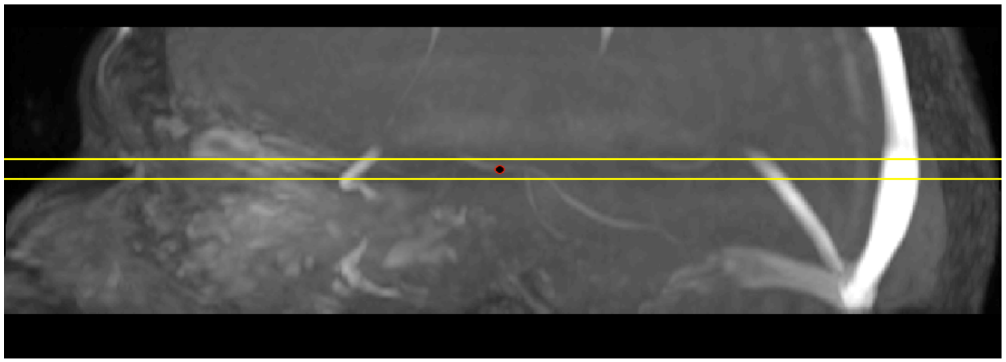
Puls-oximetri (A-cath)

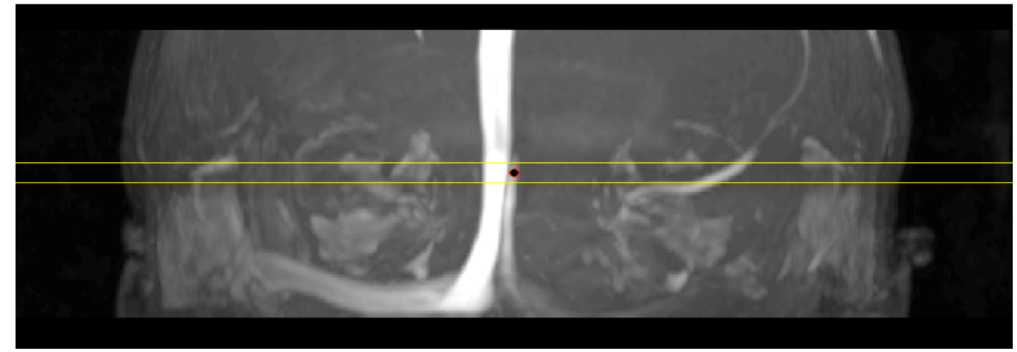
MRI susceptibility-based oximetry from Saggital sinus: venous blood from brain

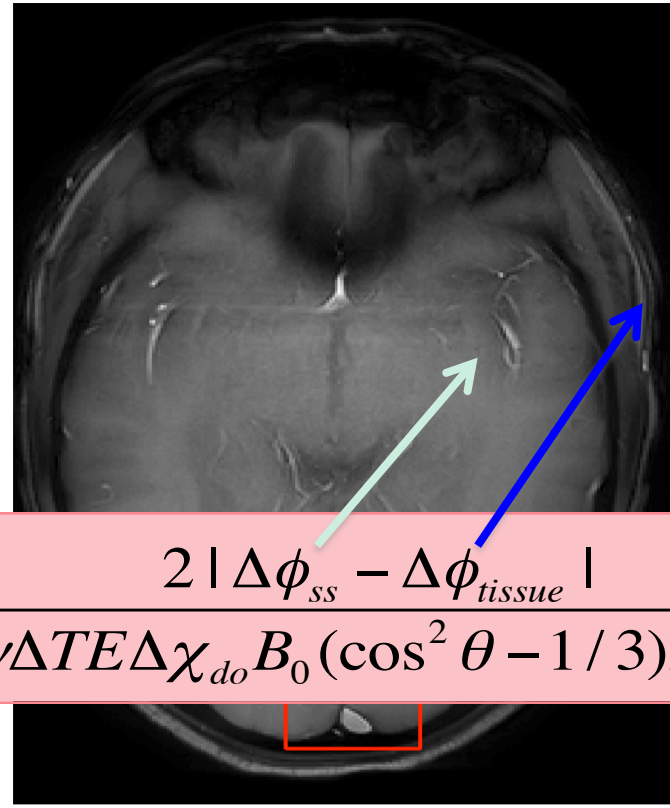
- Velocity through plane (orthogonal the arteries) and Area, thus we get Flow

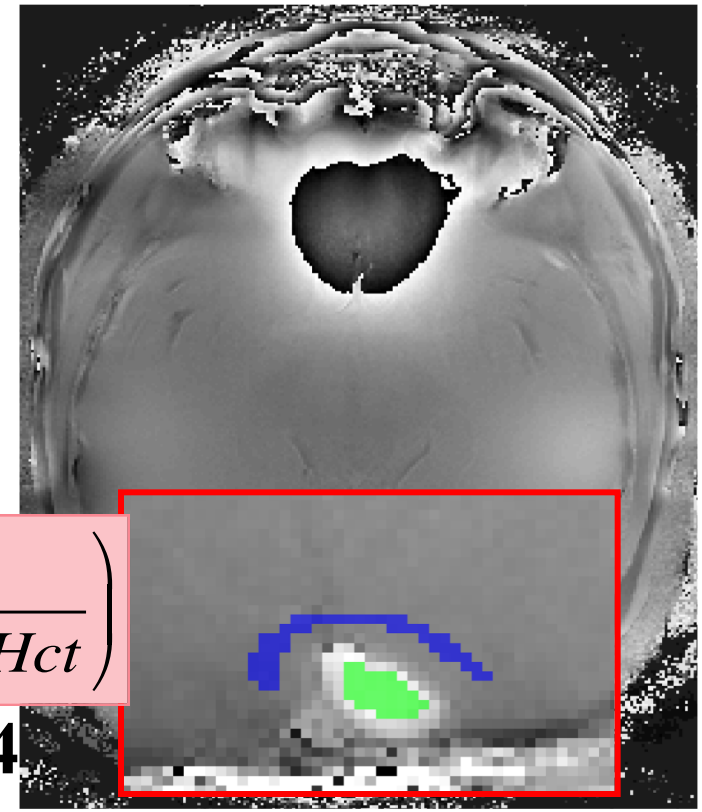


SUSCEPTIBILITY BASED OXIMETRY







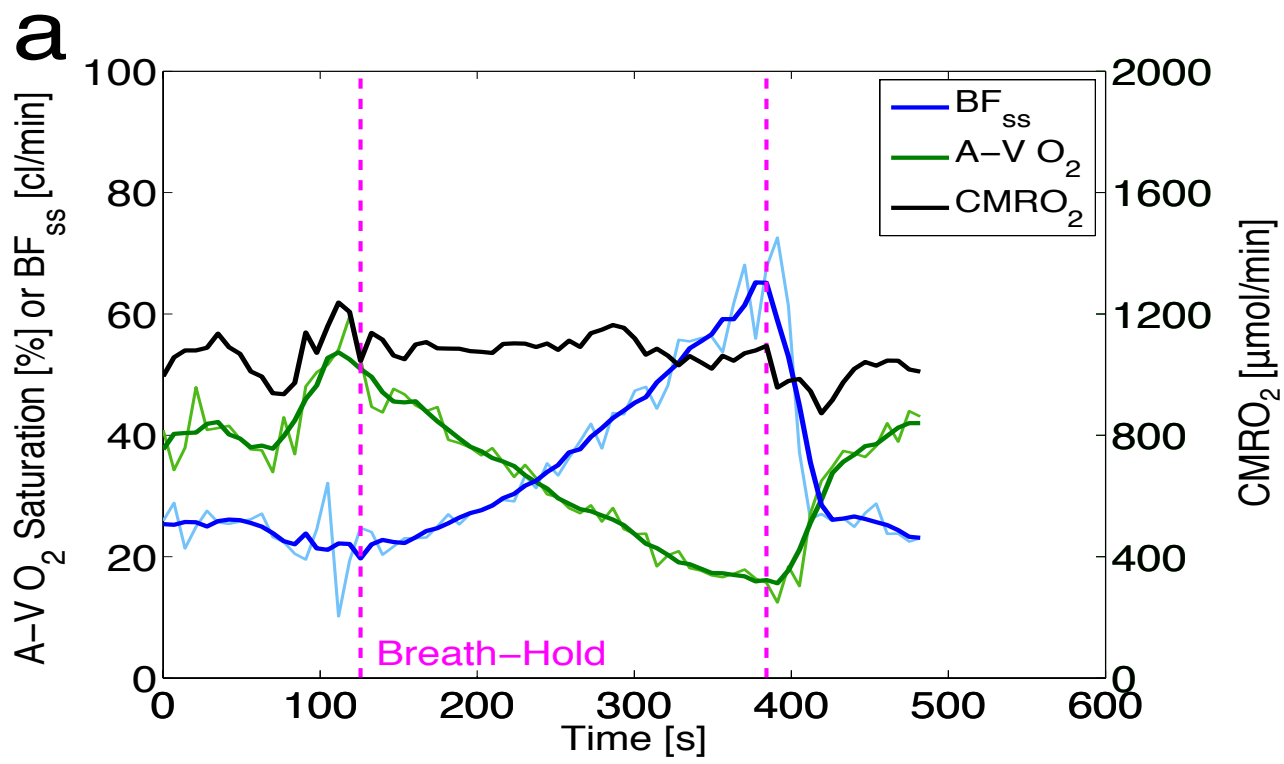


$$SvO_2 = \left(1 - \frac{2\,|\,\Delta\phi_{ss} - \Delta\phi_{tissue}\,|}{\gamma \Delta TE \Delta\chi_{do} B_0 (\cos^2\theta - 1/3) Hct}\right)$$

Breathold: $CMRO_2$

- $CMRO_2 = 4 \cdot [Hgb] \cdot BFss \cdot (S_aO_2 - S_vO_2)$
- Blood-flow i sagittal sinus (BFss)
- Arteriovenous oxygen-difference (A-V O_2)

Vestergaard MB, Larsson HBW. Cerebral metabolism and vascular reactivity during breath-hold and hypoxic challenge in freedivers and healthy controls. J Cereb Blood Flow Metab 2017 .



EXTENDING THE PRINCIPLE OF FICK

The fluxes are not constant, but functions of time

The concentration here is not constant

$j_{in}(t) = F \cdot c_{in}(t)$ → $\frac{dc(t)}{dt}$ → $j_o(t) = F \cdot c_o(t)$

conservation of mass

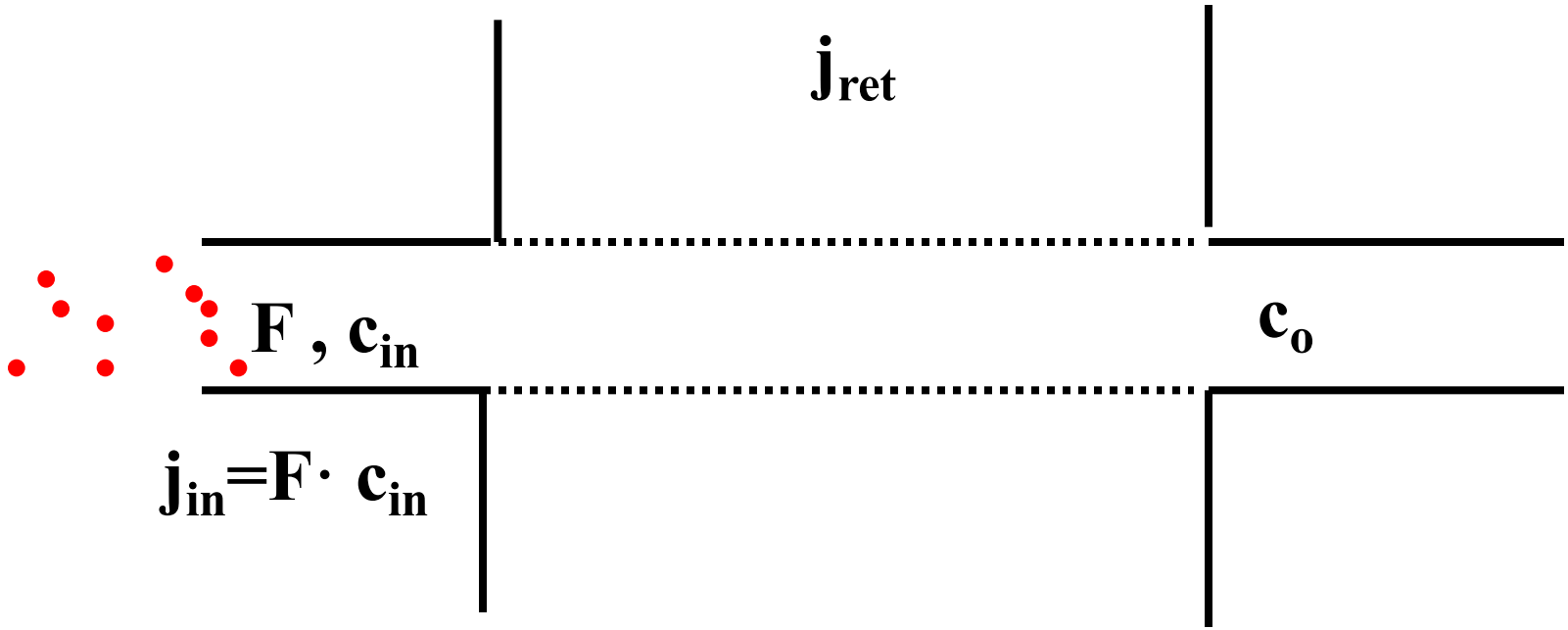
$j_{in}(t) \neq j_o(t) + j(t)$

$$v\frac{dc(t)}{dt} = F \cdot c_{in}(t) - F \cdot c_o(t) - j(t)$$

$j(t) = K_i \cdot c(t)$

$$v\frac{dc(t)}{dt} = F \cdot c_{in}(t) - F \cdot c_o(t) - K_i \cdot c(t)$$

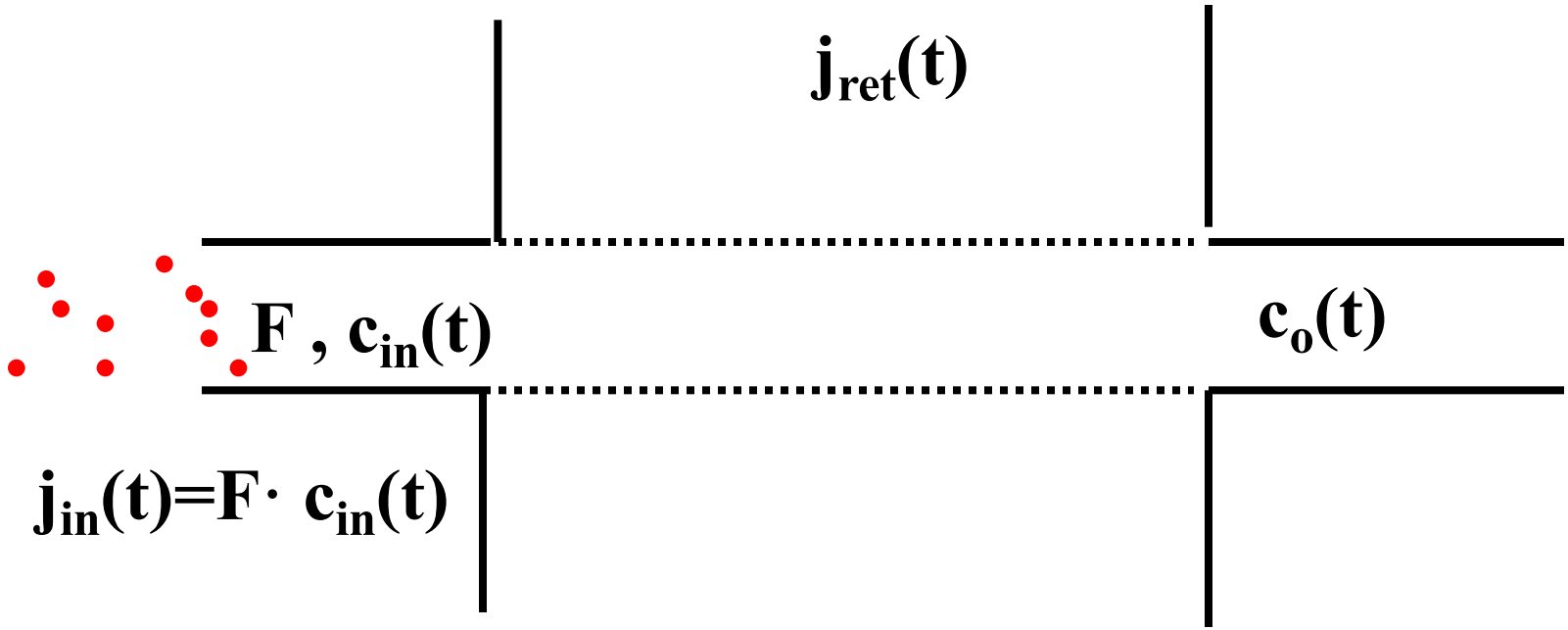
EXTRACTION FRACTION



Extraction: $$E = \frac{j_{ret}}{j_{in}} = \frac{F \cdot c_{in} - F \cdot c_o}{F \cdot c_{in}} = \frac{c_{in} - c_o}{c_{in}}$$

The transmitted fraction = 1-E

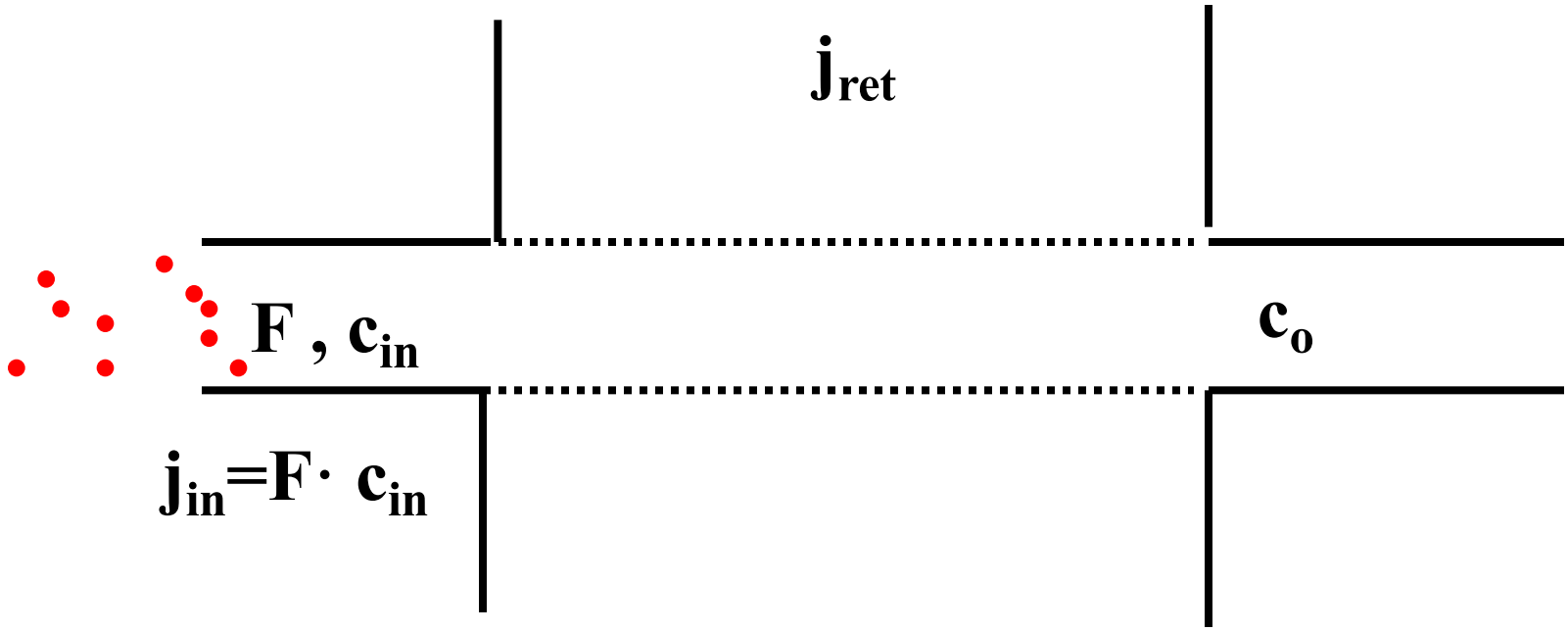
EXTRACTION FRACTION



Extraction: $$E = \frac{j_{ret}(t)}{j_{in}(t)} = \frac{F \cdot c_{in}(t) - F \cdot c_o(t)}{F \cdot c_{in}(t)} = \frac{c_{in}(t) - c_o(t)}{c_{in}(t)}$$

Is E constant?

CLEARANCE

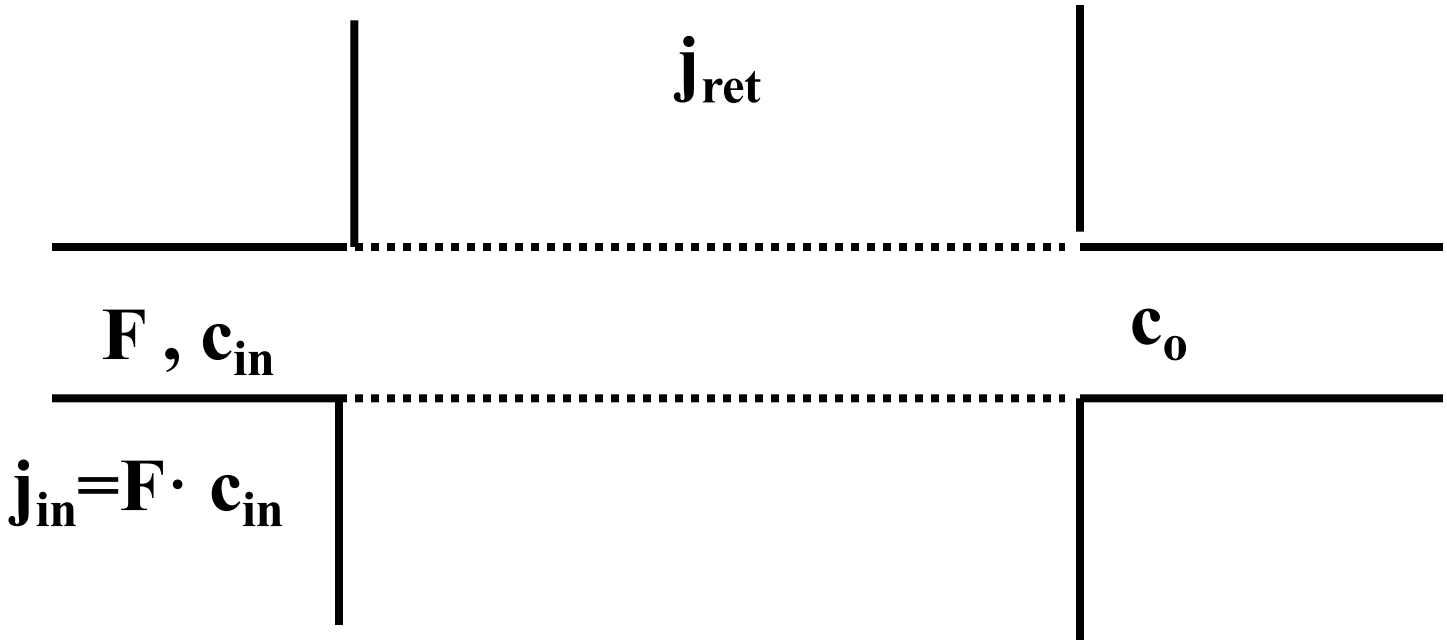


clearance: $Cl = \frac{j_{ret}}{c_{ref}} = \frac{F \cdot c_{in} - F \cdot c_o}{c_{ref}}$ **[Cl] = ml/s**

CLEARANCE

It is a fictive flow: the volume of reference fluid containing the indicator amount taken up or cleared per unit time

CLEARANCE



clearance: $$Cl = \frac{j_{ret}}{c_{ref}} = \frac{j_{ret}}{c_{in}} = \frac{F \cdot c_{in} - F \cdot c_o}{c_{in}} = F \cdot E$$

When E=1, Clearance = Flow

BREAK

EXTRACTION, CRONE-RENKIN, PERMEABILITY

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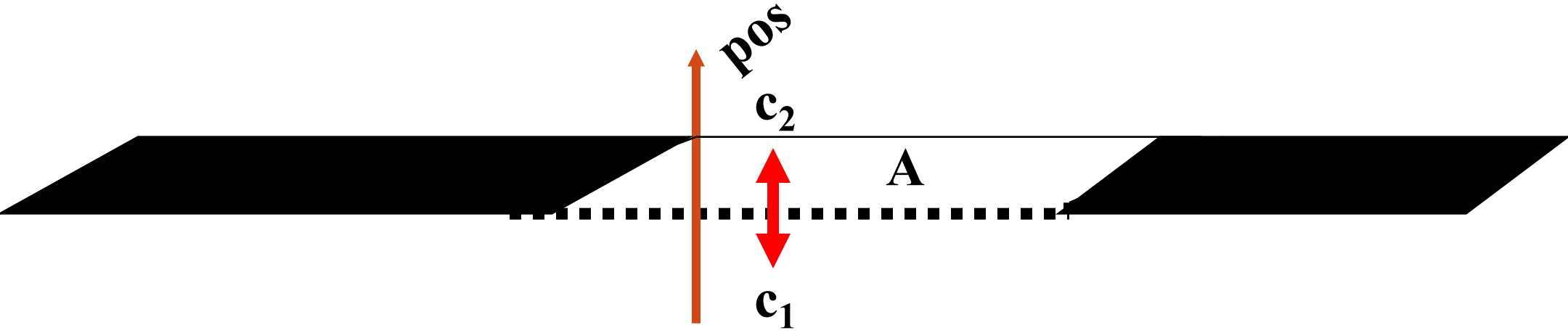
CRONE (1963) & RENKIN (1959) EQUATION

TRANSPORT OVER THE CAPILLARY MEMBRANE

$$c_o = c_{in} \exp(-PS/F)$$

TRANSPORT OVER A MEMBRANE



j ? c_1-c_2

$$J_{1 \rightarrow 2} = PS(c_1 - c_2) \qquad PS = \frac{J_{1 \rightarrow 2}}{c_1 - c_2} \qquad \frac{mmol/min}{mmol/ml}$$

$$[\mathrm{PS}] = ml/min$$

CRONE (1963) & RENKIN (1959) EQUATION

$$c_0 = c_i e^{-\frac{PS}{F}} \Rightarrow \frac{c_o}{c_i} = e^{-\frac{PS}{F}}$$

$$1 - \frac{c_o}{c_i} = 1 - e^{-\frac{PS}{F}} \Rightarrow \frac{c_i - c_o}{c_i} = 1 - e^{-\frac{PS}{F}}$$

$$E = 1 - e^{-\frac{PS}{F}} \wedge Cl = FE \Rightarrow Cl = K_i = F(1 - e^{-\frac{PS}{F}})$$

ACCUMULATION OF TRACER IN TISSUE CAN BE FLOW LIMITED OR DIFFUSION LIMITED

Flow limited : $PS >> F \rightarrow PS/F$ **is large**

$E = 1 - \exp(-PS/F)$ $E \rightarrow 1$ **for** $PS/F \rightarrow \infty$

$$Cl = F\,E \rightarrow F$$

ACCUMULATION OF TRACER IN TISSUE CAN BE FLOW LIMITED OR DIFFUSION LIMITED

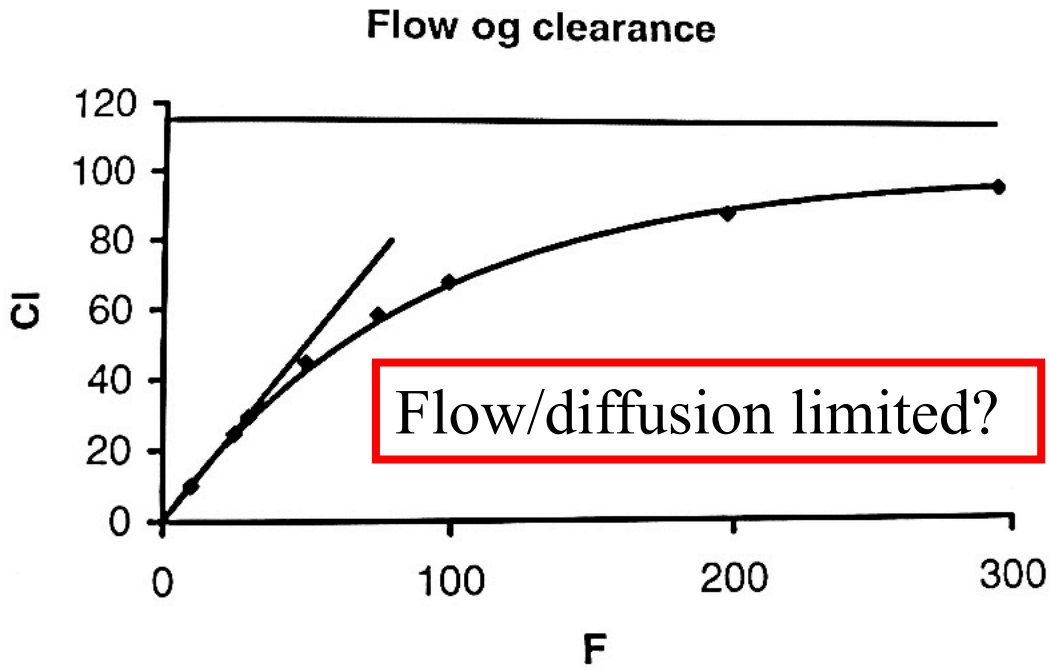
Diffusion limited : $PS \ll F \rightarrow PS/F$ small

$E = 1 - \exp(-PS/F)$ $\quad E \rightarrow 0$ for $PS/F \rightarrow 0$

$E = 1 - \exp(-PS/F) \approx 1 - (1-PS/F) = PS/F$

$Cl = F\,E \rightarrow PS$

FLOW AND CLEARANCE



E=0.90 (at rest)

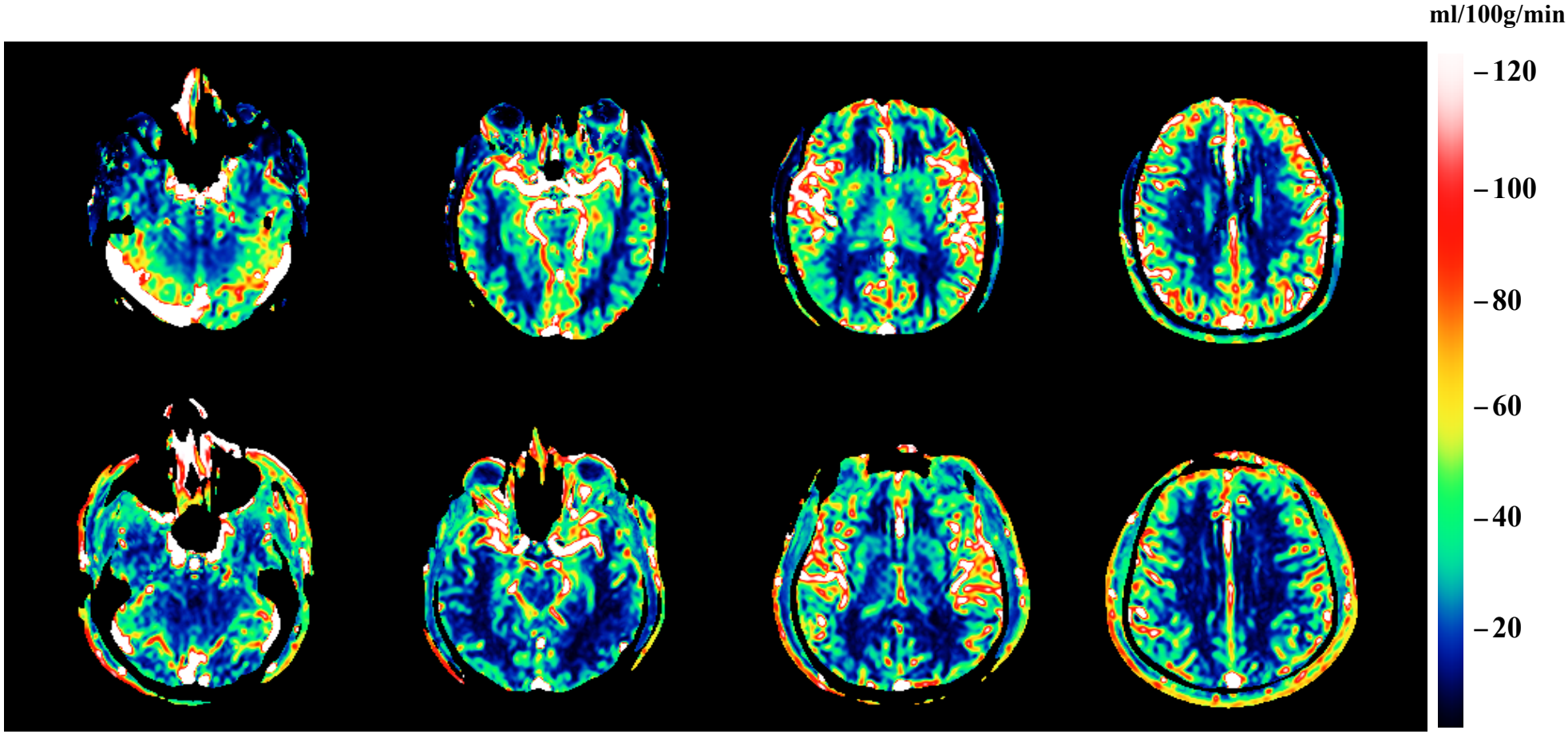
→ Flow limited tracer

Resting F = 50 ml/100g/min

$$E = 1 - e^{\frac{-PS}{F}} \Rightarrow 0.90 = 1 - e^{\frac{-PS}{50}}$$

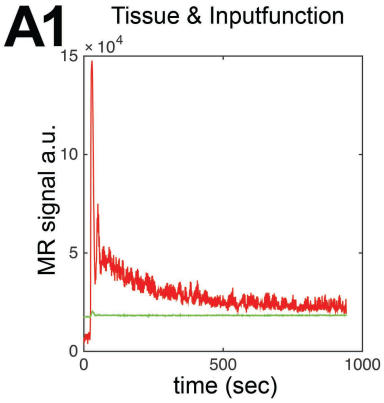
$$PS = -\ln(0.1)\ 50 \frac{\text{ml}}{100\text{g min}} = 115 \frac{\text{ml}}{100\text{g min}}$$

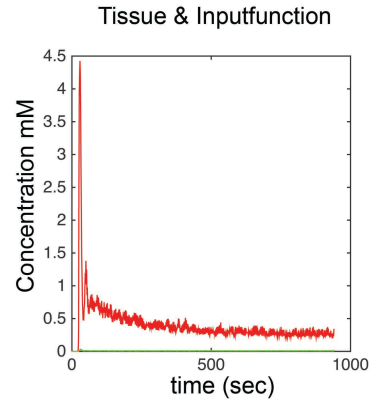
Examples of CBF maps



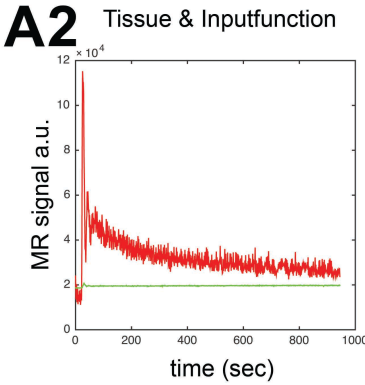
We found perfusion value for ROI's to be
62 ml/100g/min in gray matter and
21 ml/100g/min in white matter
in 7 patients with acute optic neuritis.

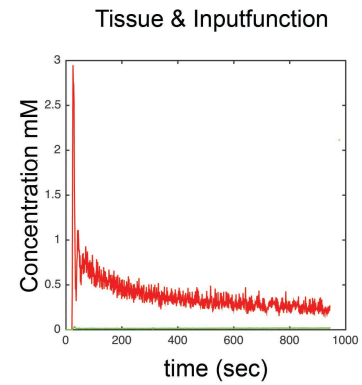
A1



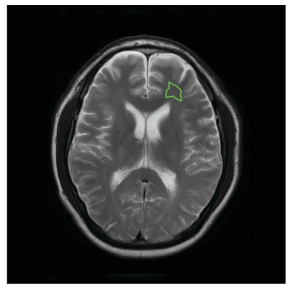


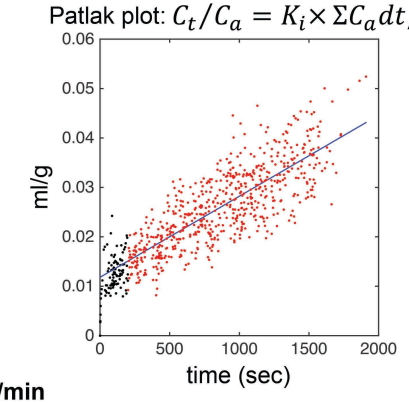
A2





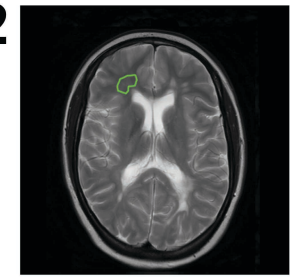
B1

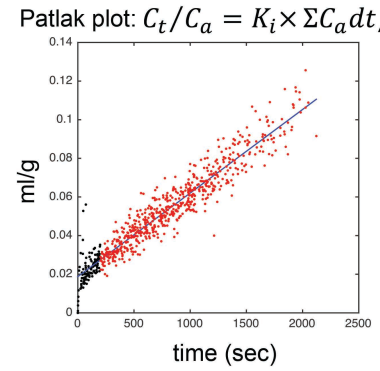




Ki = 0.0984 ml/100g/min
SD of Ki = 0.0029 ml/100g/min
Intercept: λ = 1.18 ml/100g; SD λ = 0.047ml/100g
pixels-tissue = 142

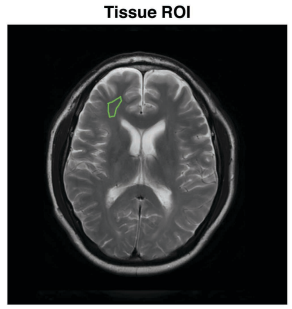
B2

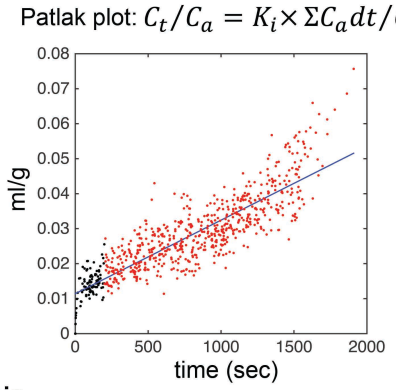




Ki = 0.260 ml/100g/min
SD of Ki = 0.0036 ml/100g/min
Intercept: λ = 1.88 ml/100g; SD λ = 0.058 ml/100g
pixels-tissue = 208

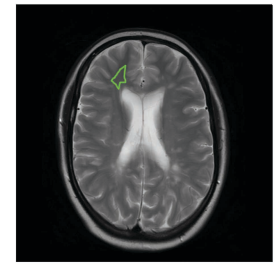
C1

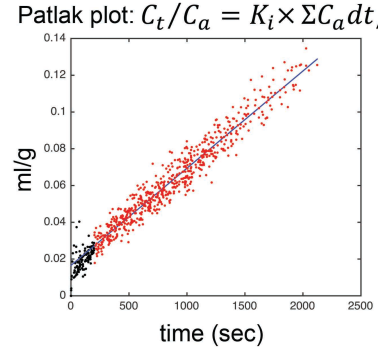




Ki = 0.126 ml/100g/min
SD of Ki = 0.0034 ml/100g/min
Intercept: λ = 1.14 ml/100g; SD λ = 0.055 ml/100g
pixels-tissue = 129

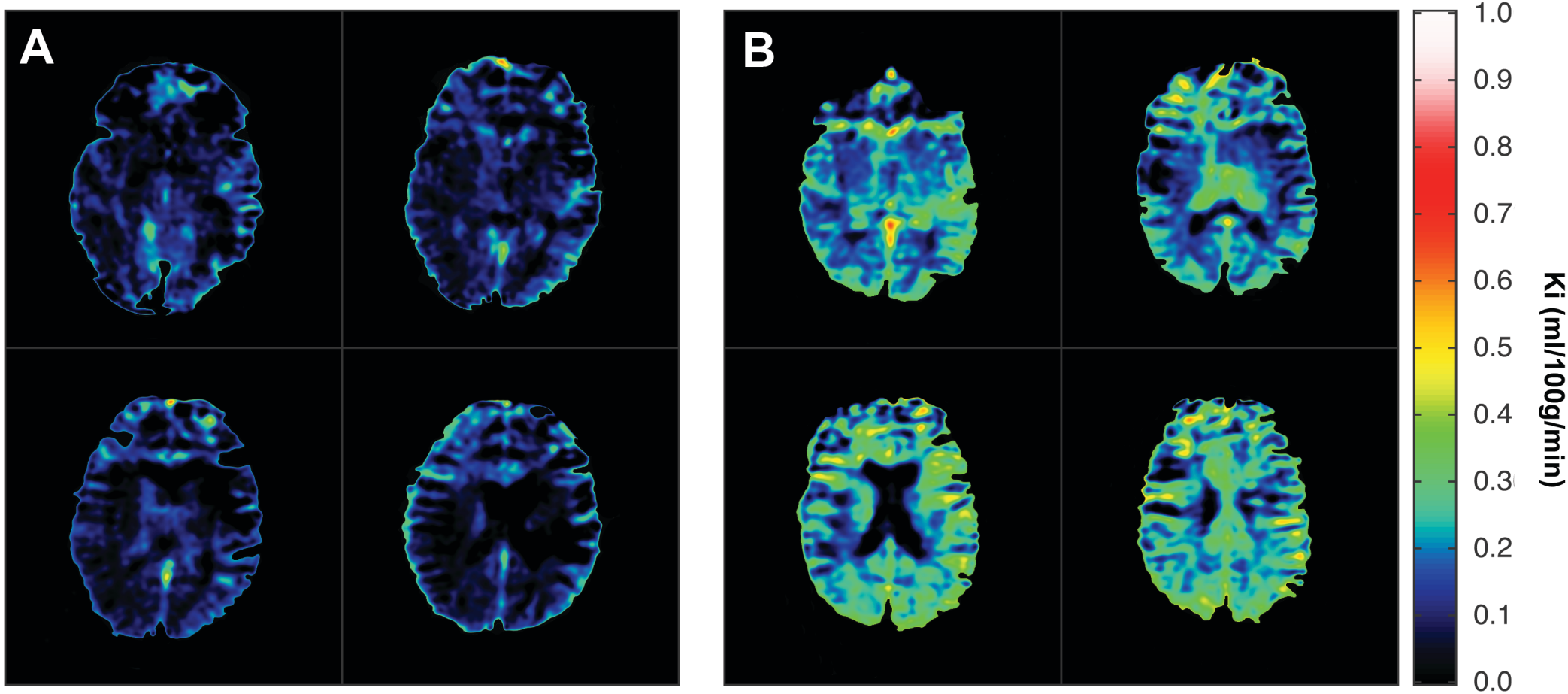
C2

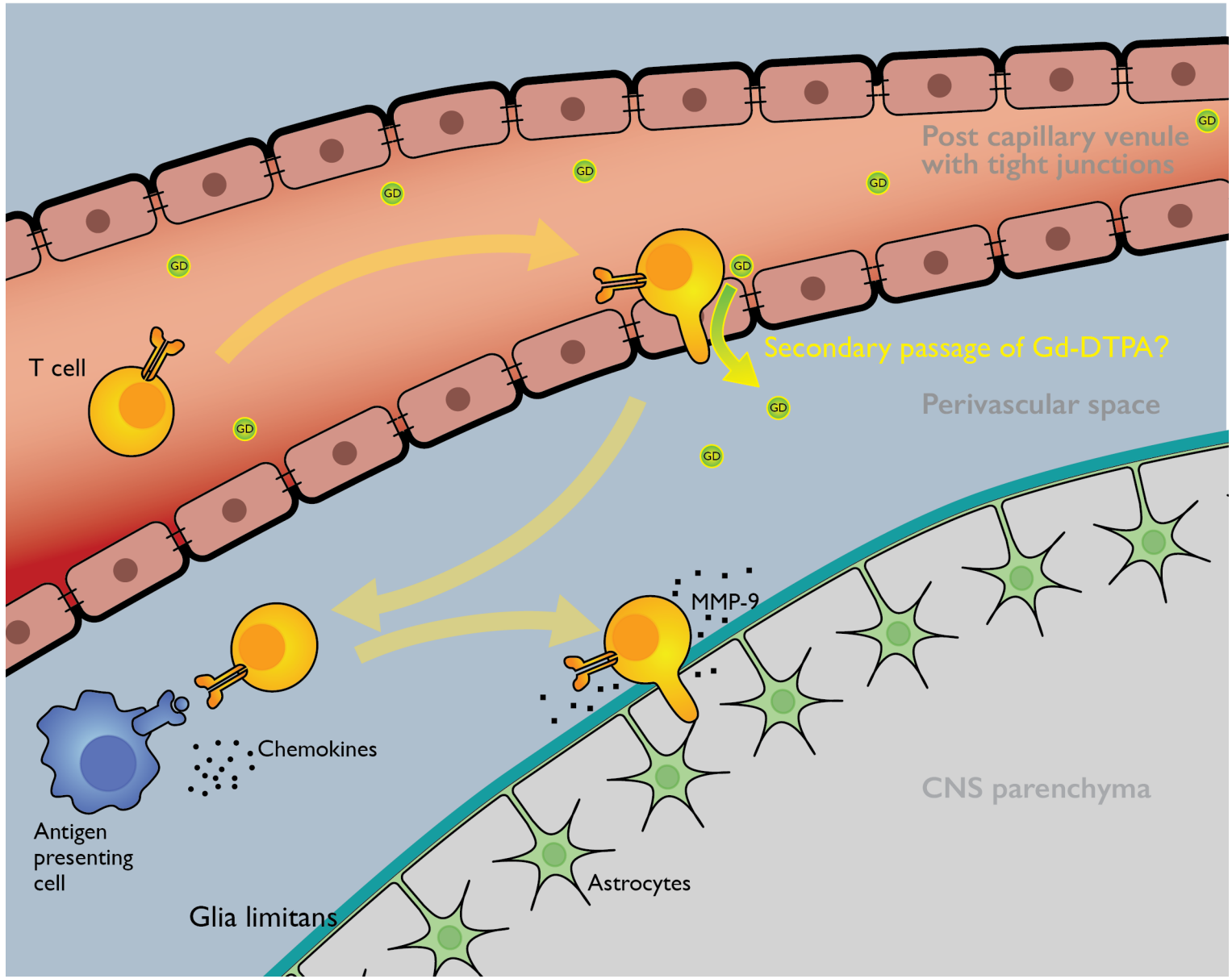




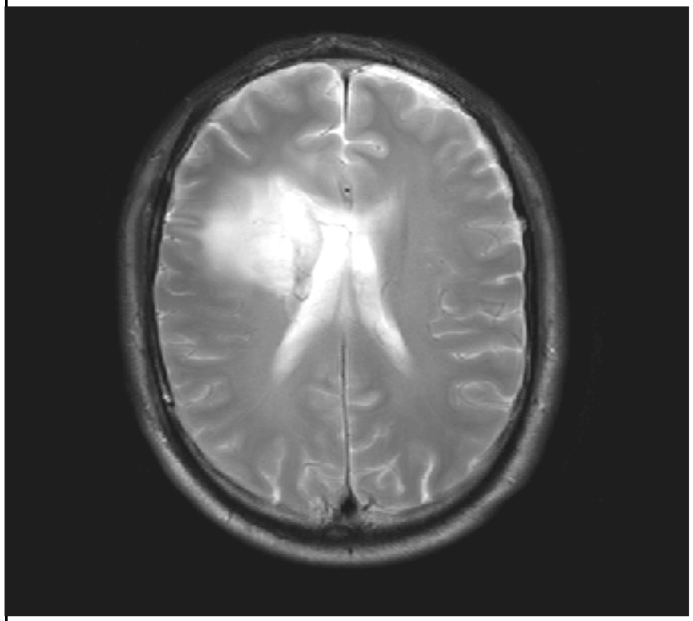
Ki = 0.317 ml/100g/min
SD of Ki = 0.0032 ml/100g/min
Intercept: λ = 1.66 ml/100g; SD λ = 0.052 ml/100g
pixels-tissue = 147

REGIONAL K_I MAPS; ONE WITH AND ONE WITHOUT MULTIPLE SCLEROSIS

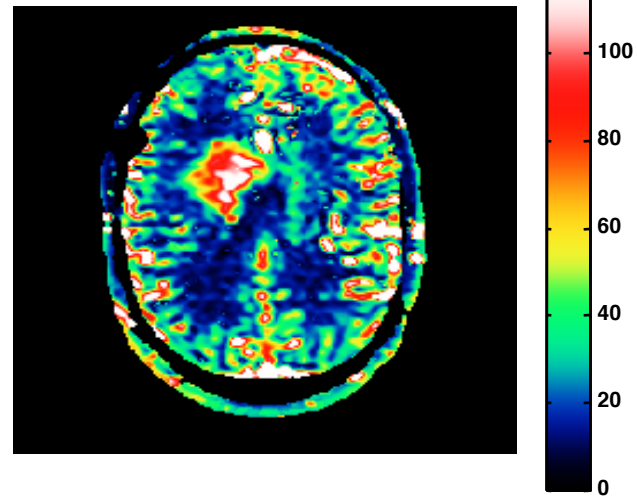



Post capillary venule
with tight junctions
GD
T cell
Secondary passage of Gd-DTPA?
Perivascular space
MMP-9
Chemokines
CNS parenchyma
Antigen
presenting
cell
Astrocytes
Glia limitans

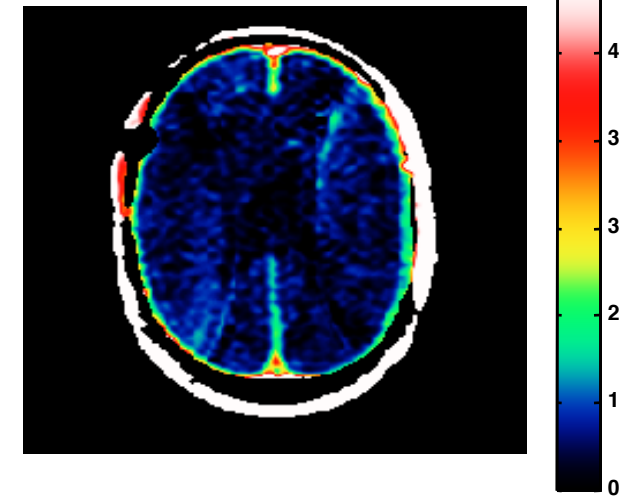
Anatomy, T2w



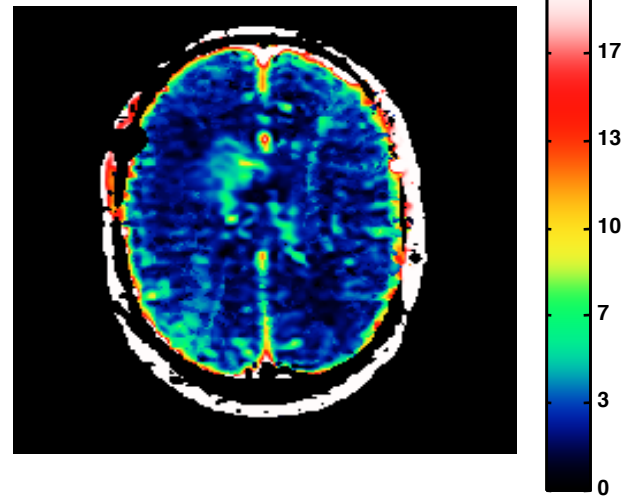
F (ml/100g/min)



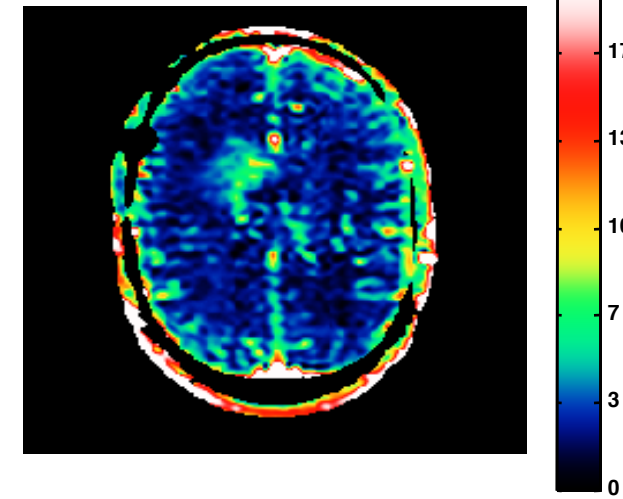
K_i (ml/100g/min)



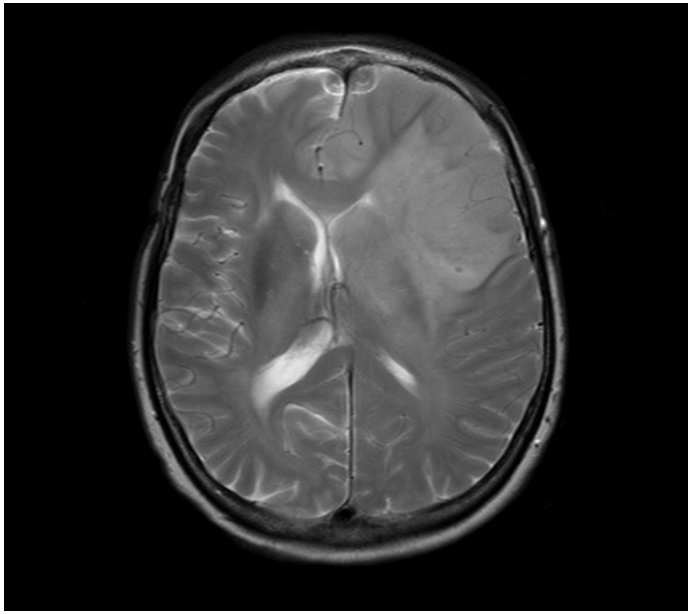
V_d (ml/100g)



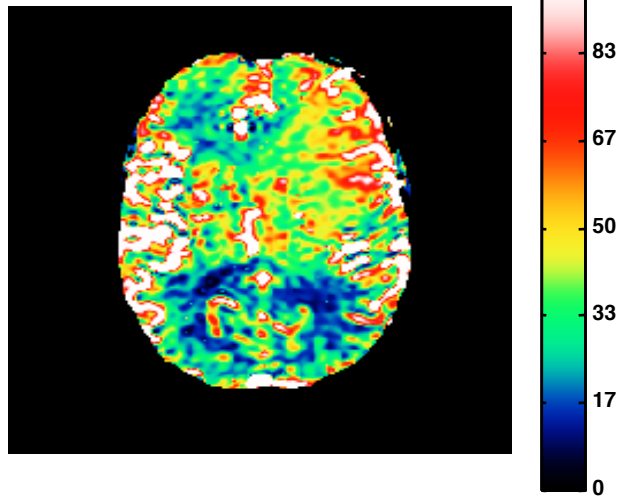
V_b (ml/100g)



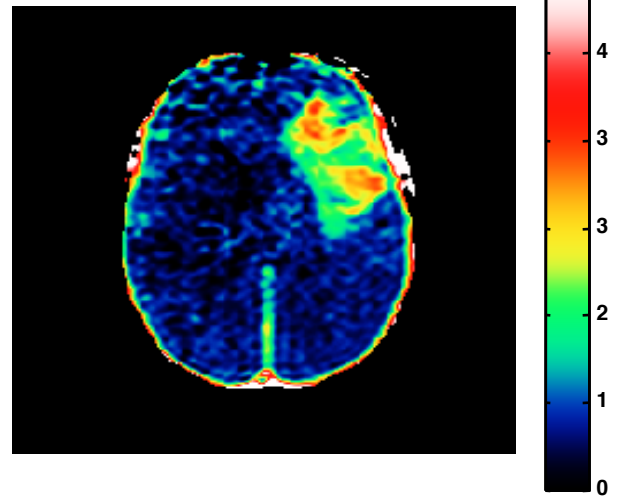
Anatomy, T2w



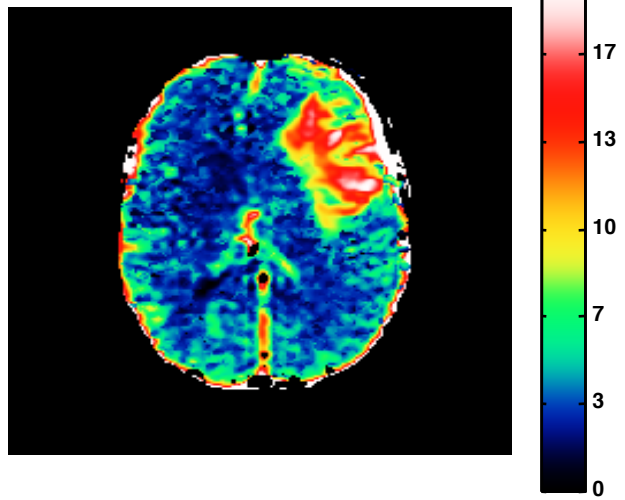
F (ml/100g/min)



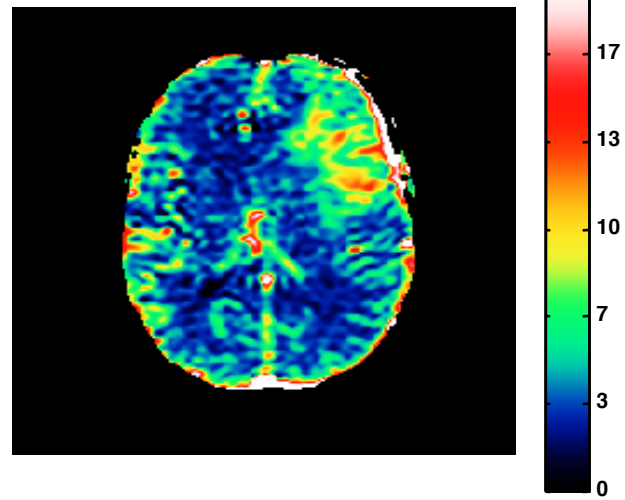
K_i (ml/100g/min)



V_d (ml/100g)



V_b (ml/100g)



BREAK