



2. LF UK



Advanced examination of brain by magnetic resonance

David Kala

EpiReC

2024

Motivation

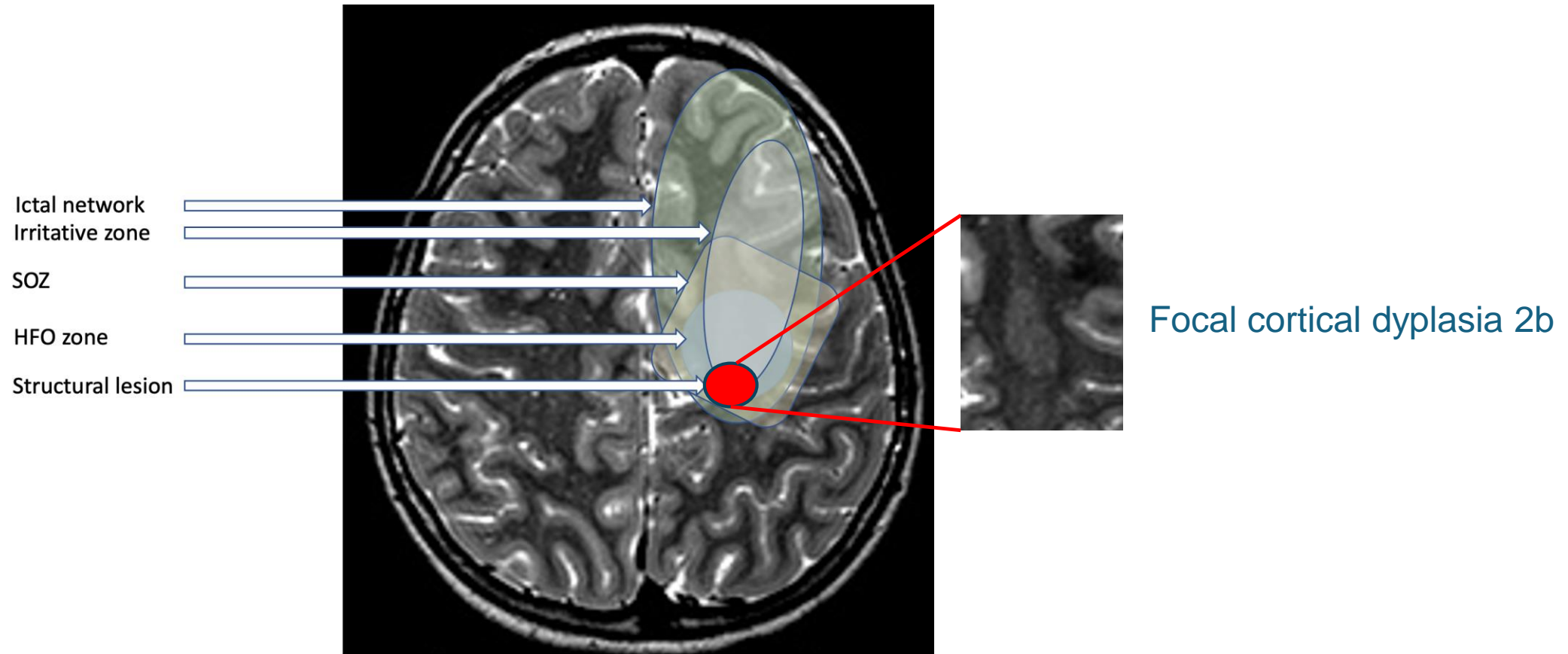
Many pathologies

? Many questions ?
? ?

Motivation

Pharmacoresistant Lesional Epilepsy

Task: Precise delineation of tissue to be resected

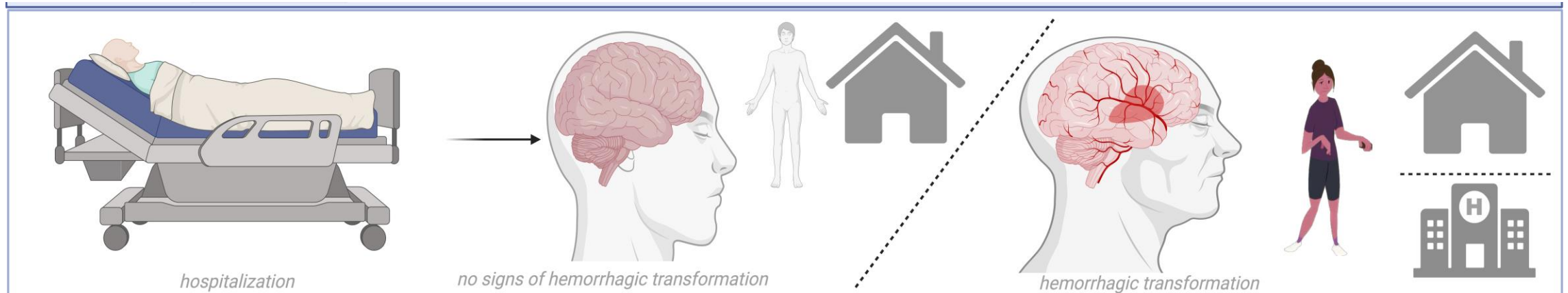


SOZ - seizure onset zone; HFO – high-frequency oscillation

Motivation

Cerebral ischemia

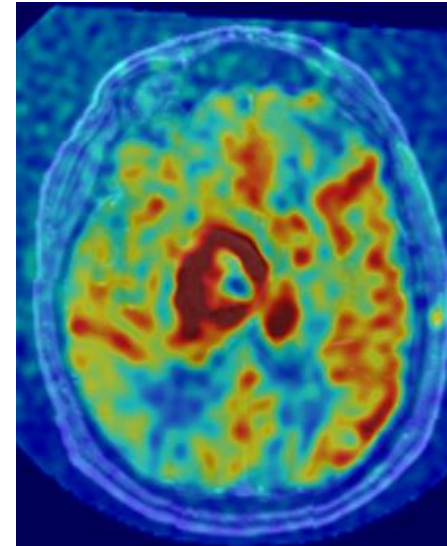
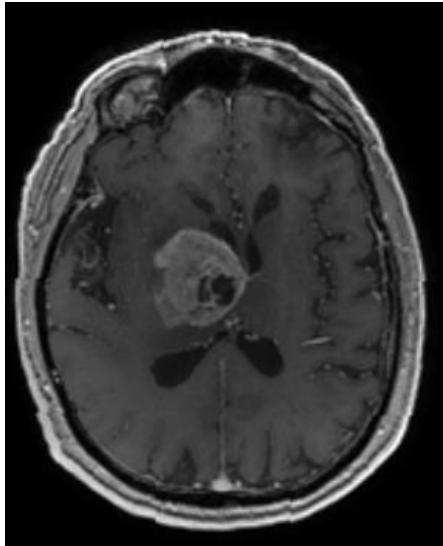
Task: Prediction of haemorrhagic transformation



Motivation

Glioma

Task: Evaluate radiotherapy response

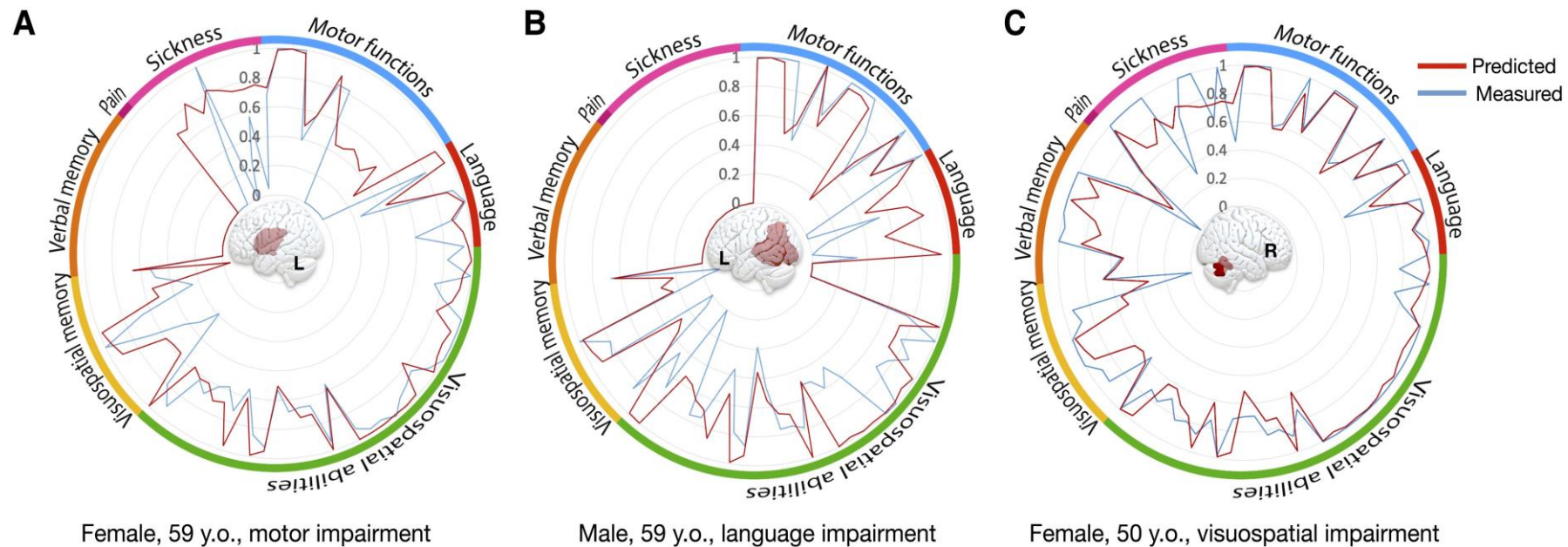


Motivation

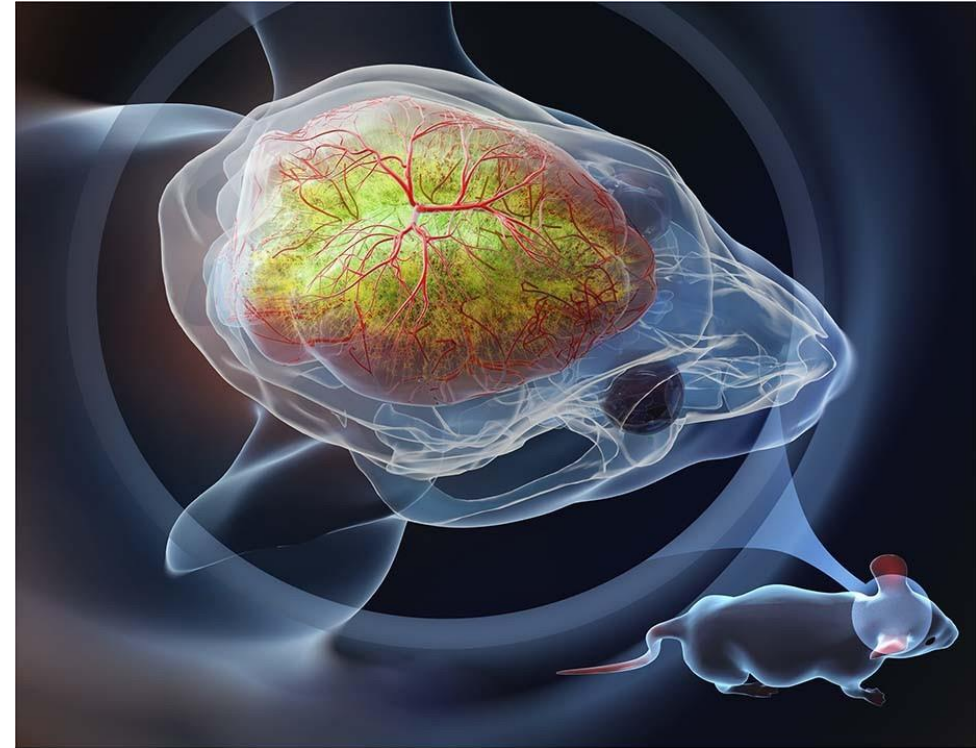
CADASIL

Task: Prediction of disease progression

Personalized Neuropsychological profile predictions



Talozzi et.al. 2023

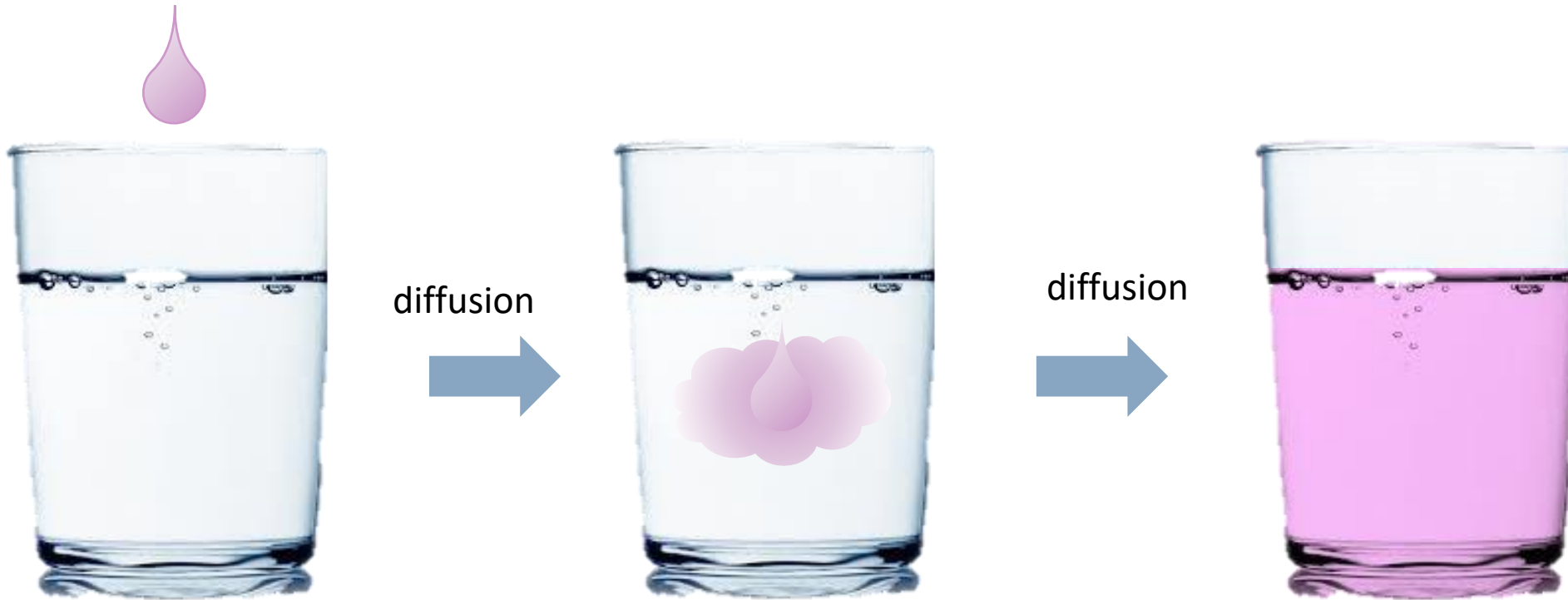


MRI as a non-invasive window to the brain

Imaging of diffusion properties of brain tissue

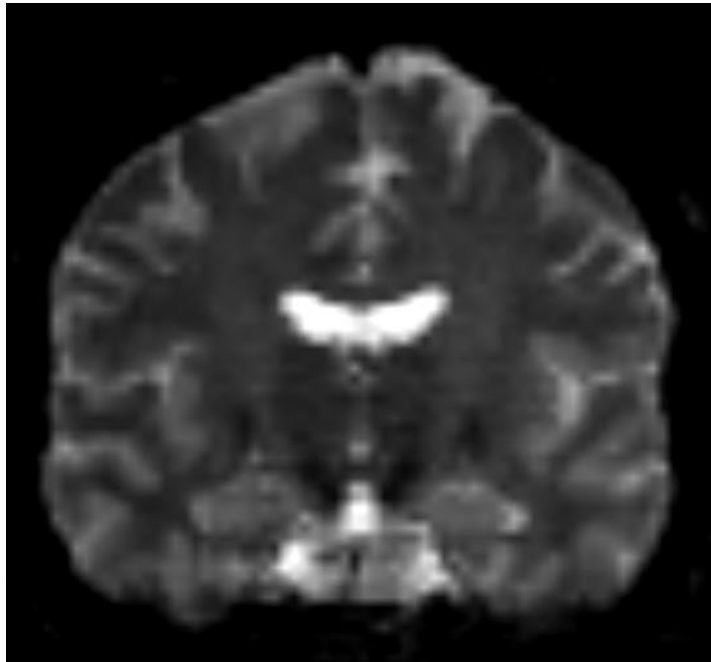
Diffusion

Spontaneous movement of substances through the environment until a uniform concentration is reached

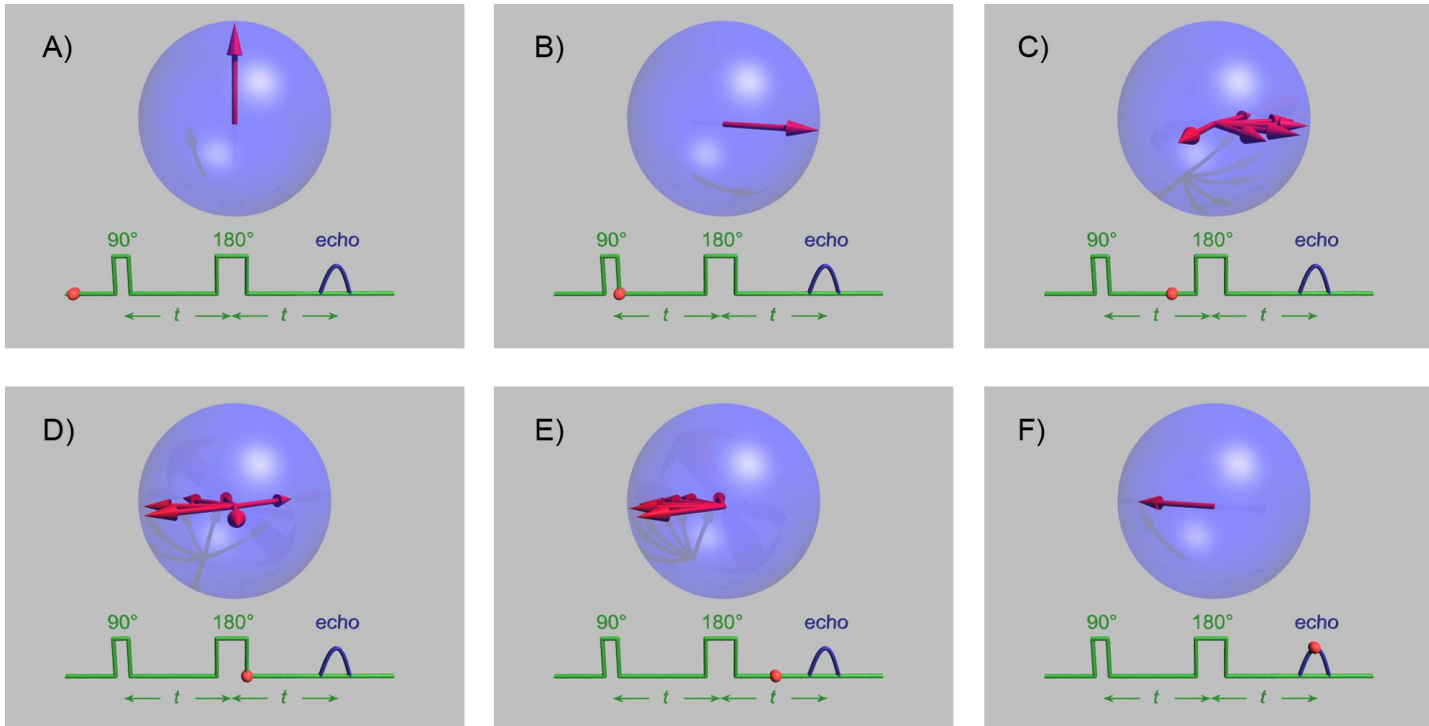


Diffusion in MRI

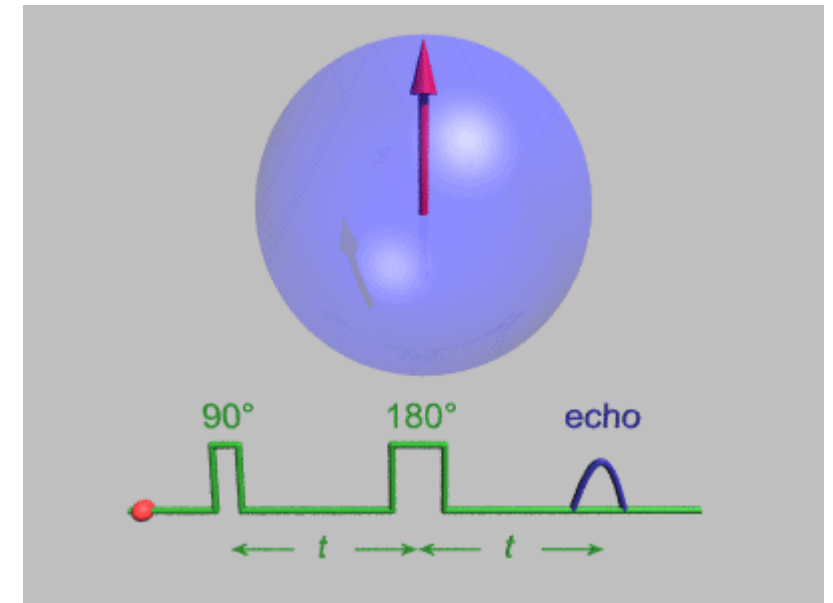
DWI – diffusion weighted image without gradient pulse = b_0



Diffusion in MRI

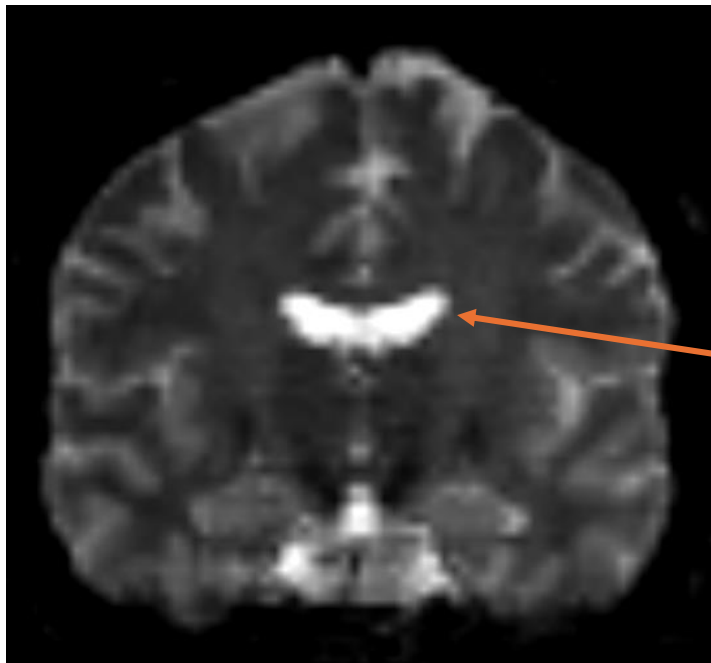


Spin echo MRI



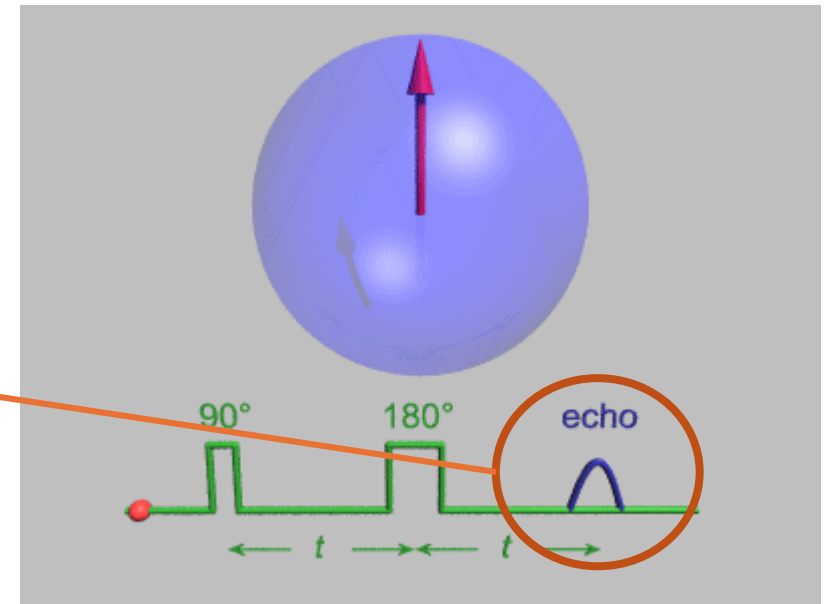
Diffusion in MRI

DWI – diffusion weighted image without gradient pulse = b_0

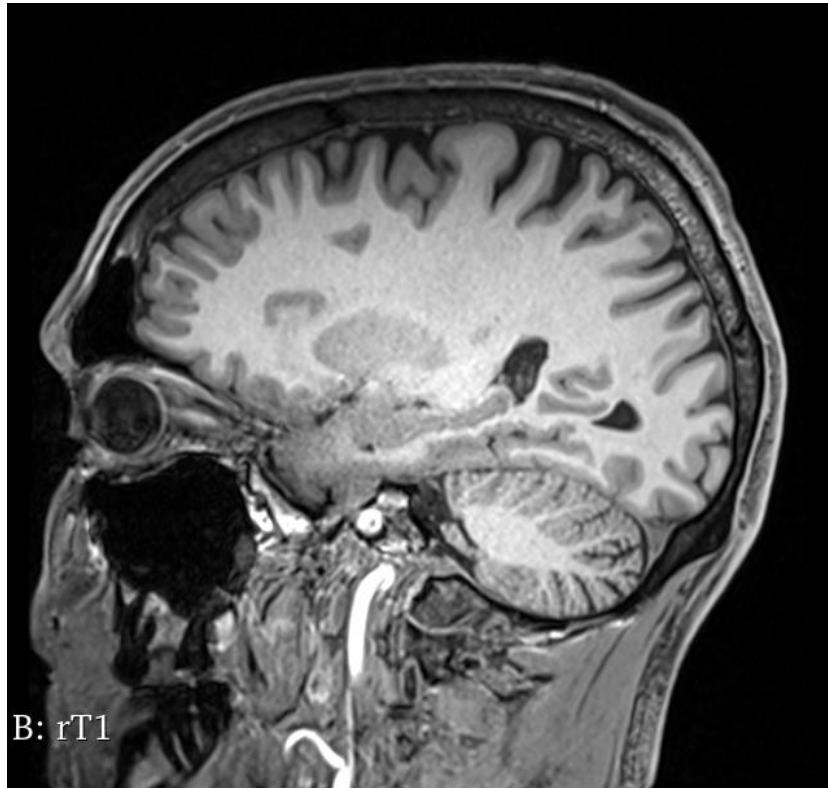


More water = higher signal

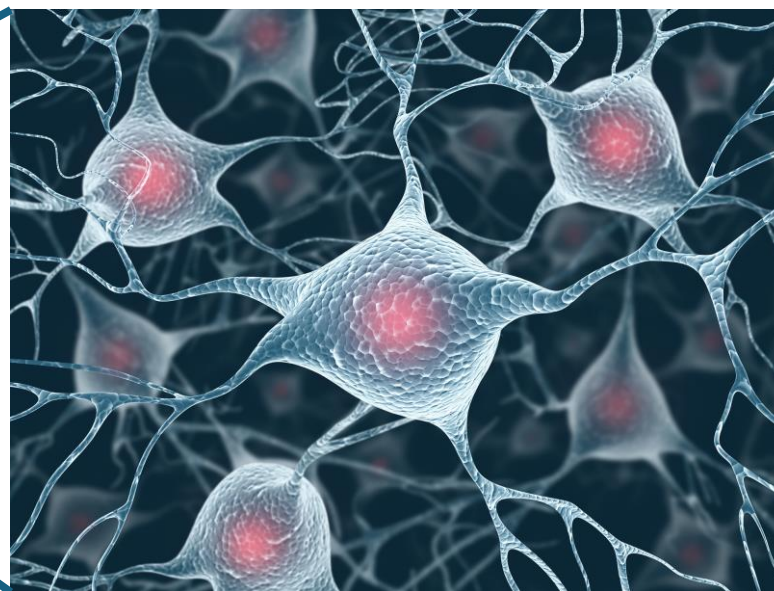
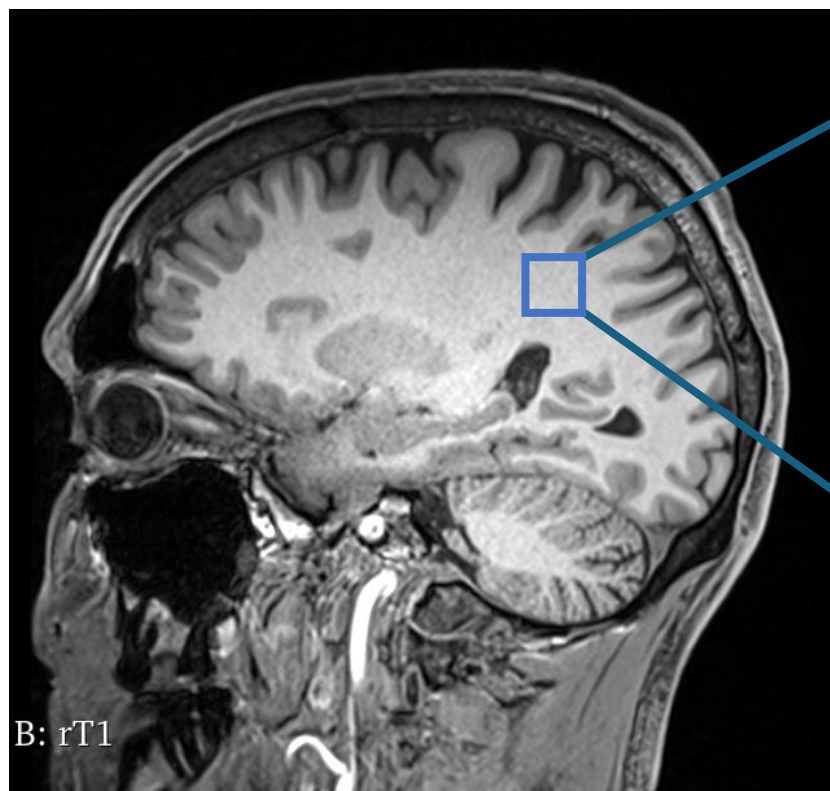
Spin echo MRI



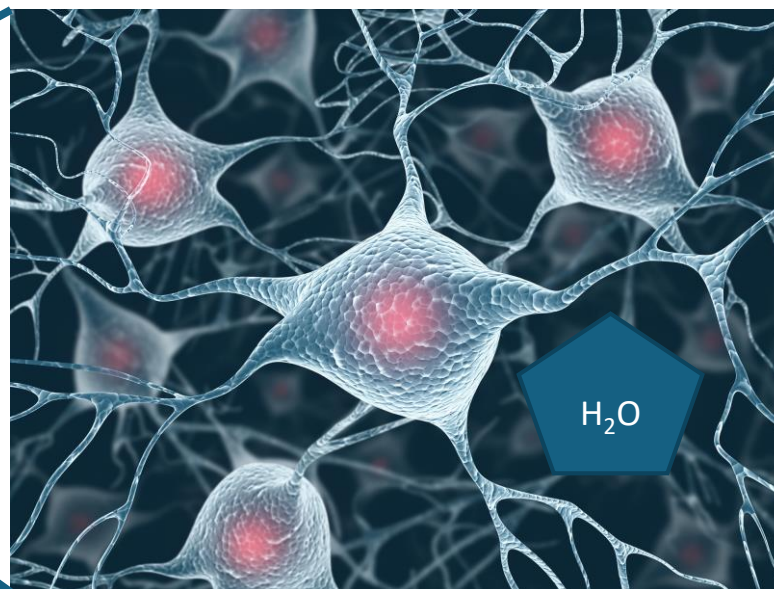
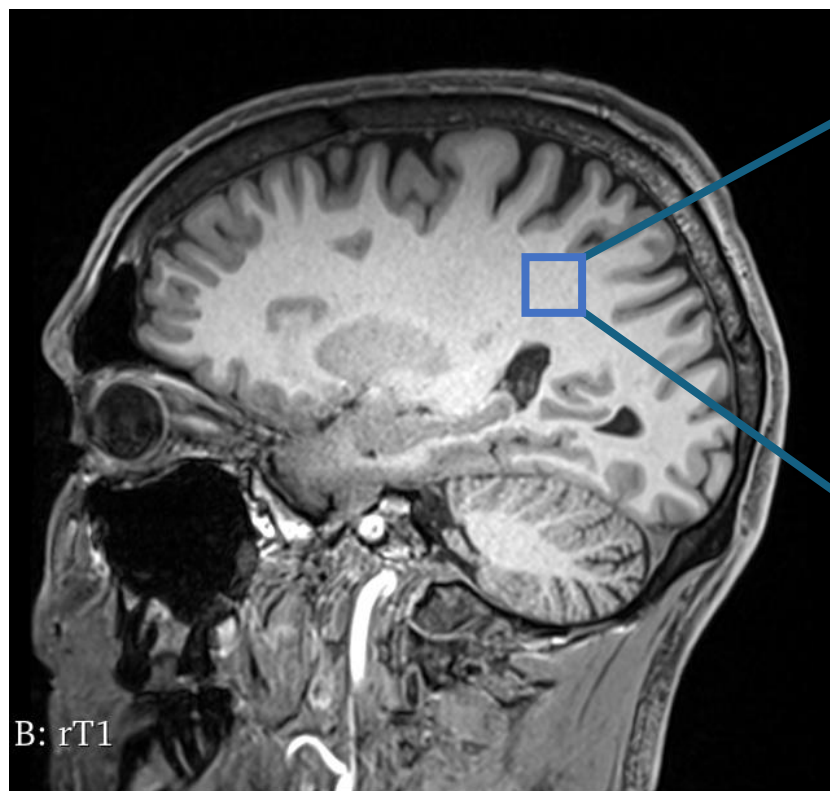
Diffusion in MRI



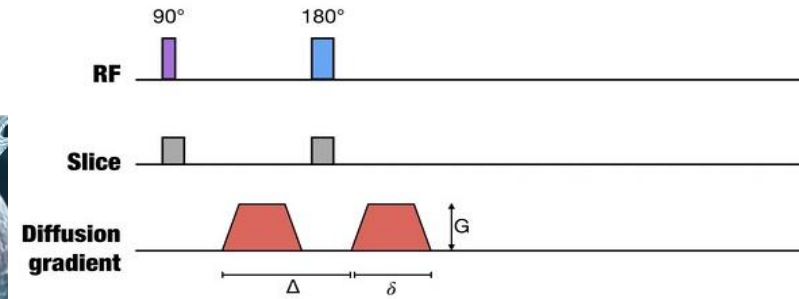
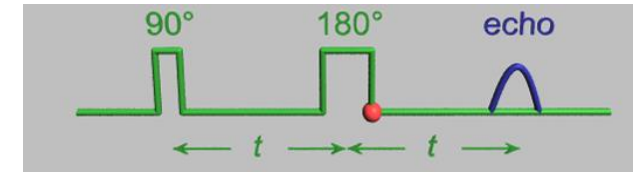
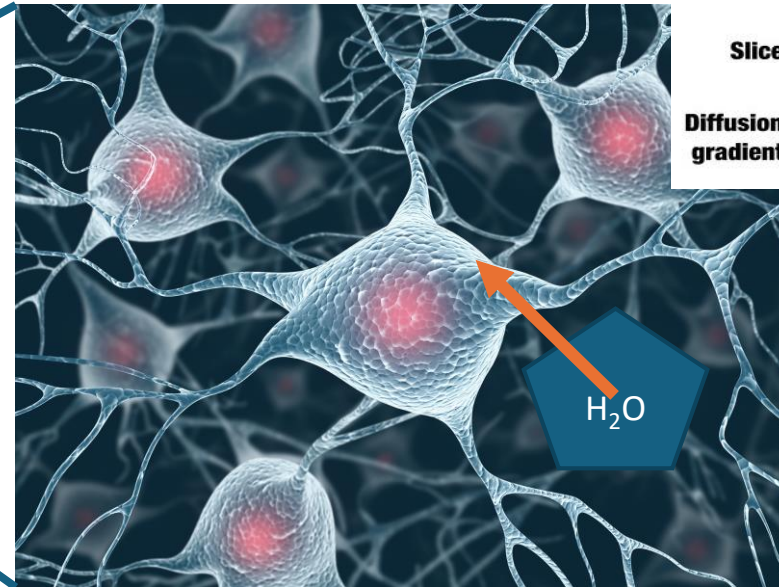
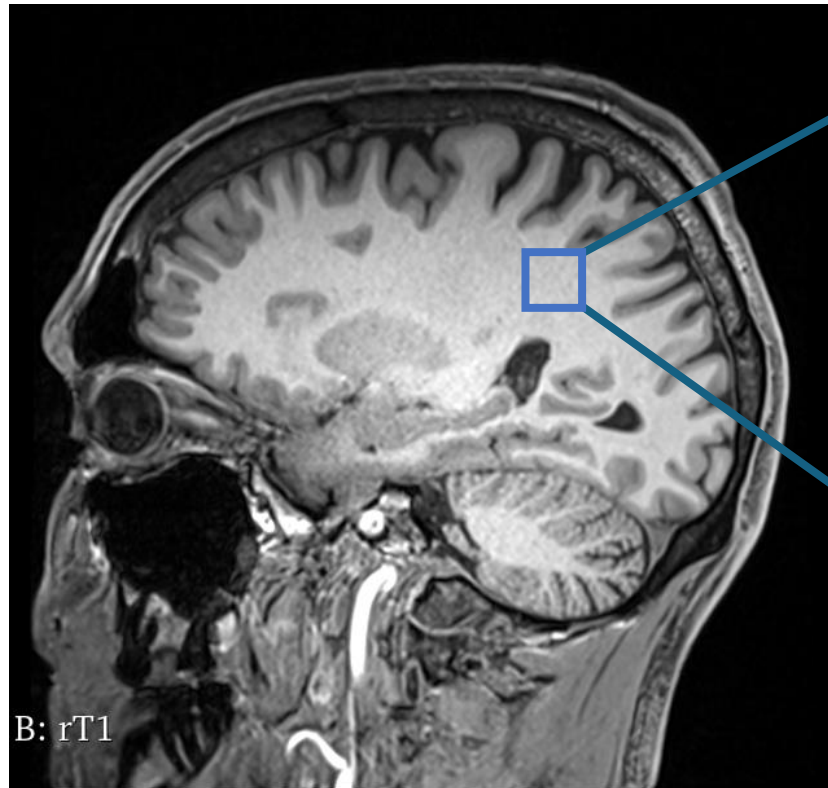
Diffusion in MRI



Diffusion in MRI

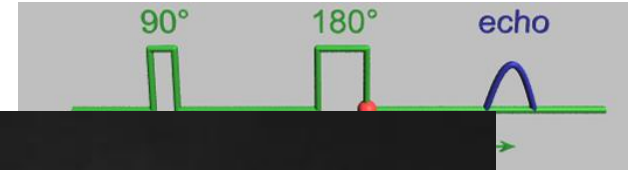
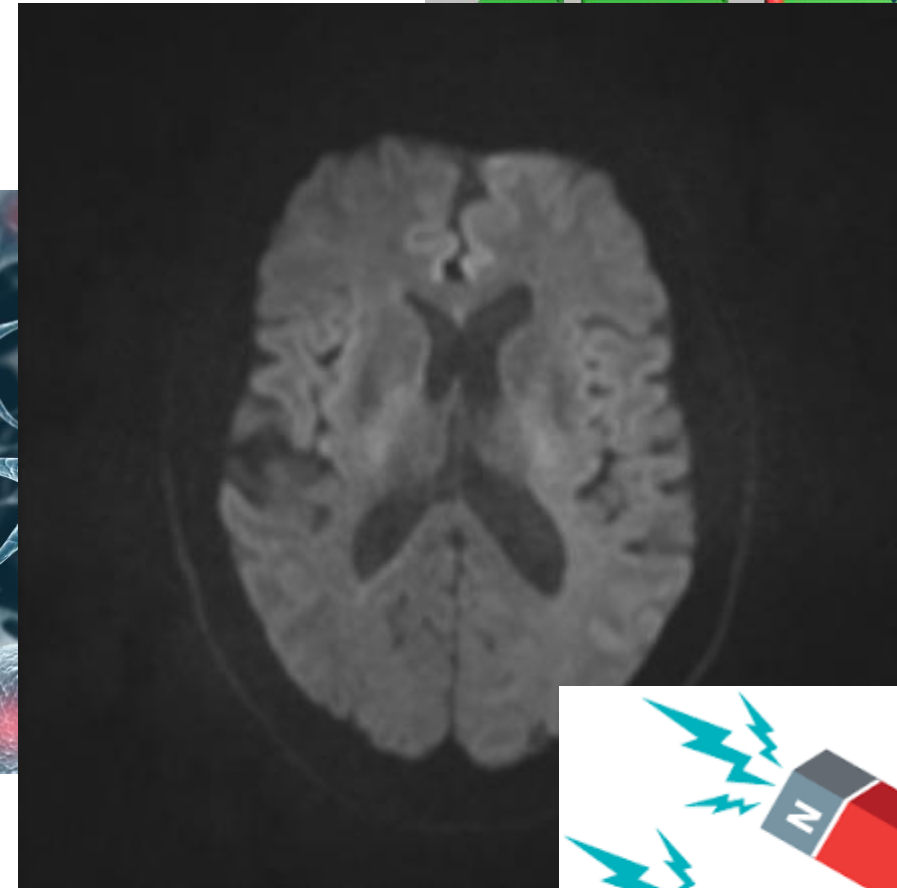
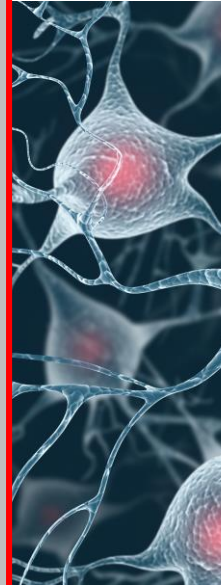
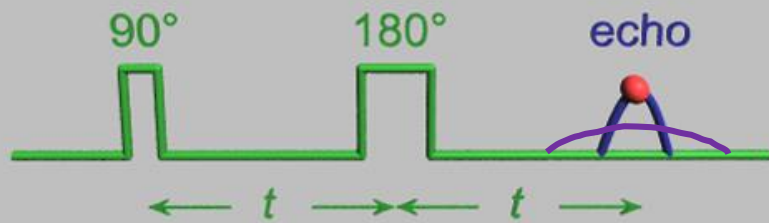
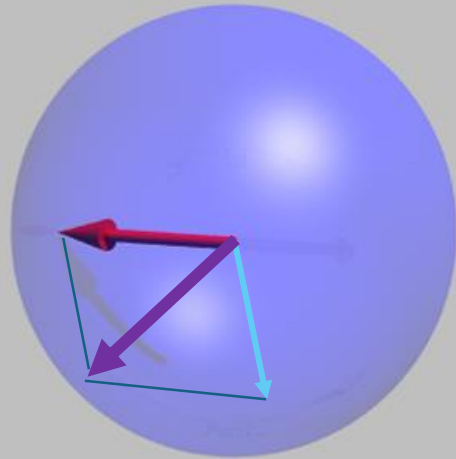


Diffusion in MRI



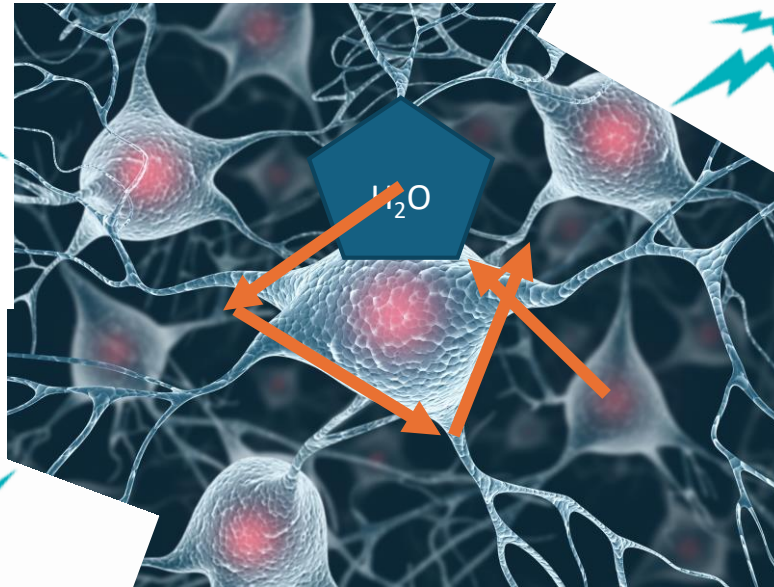
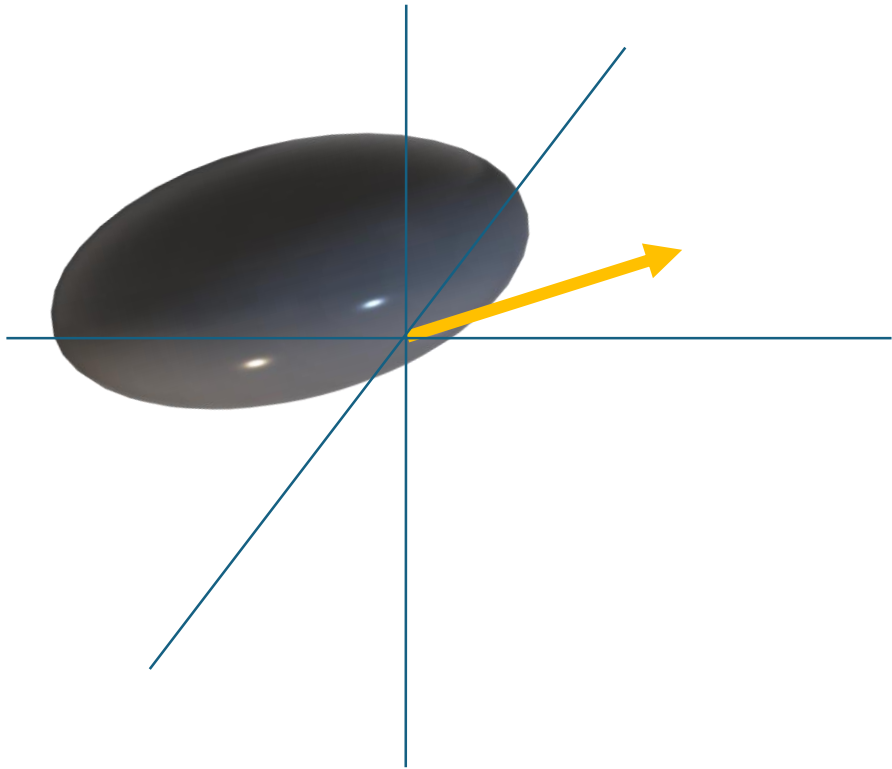
Diffusion in MRI

F)



Diffusion in MRI

Diffusion tensor



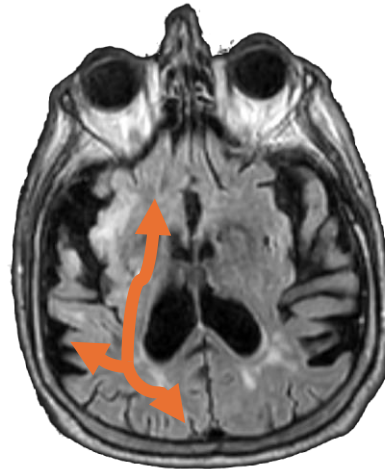
Assessment of tissue diffusion properties

DWI – diffusion weighted image

Isotropic tissue



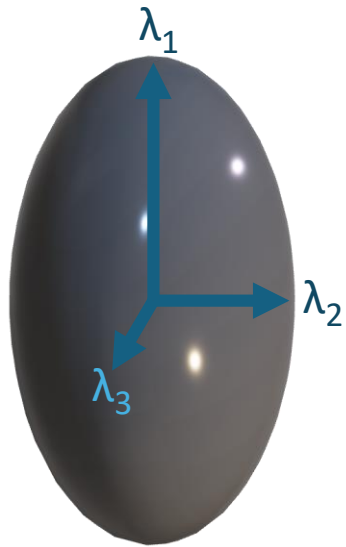
Tissue with dominant direction of diffusion



Assessment of tissue diffusion properties

FA: Fraction anisotropy

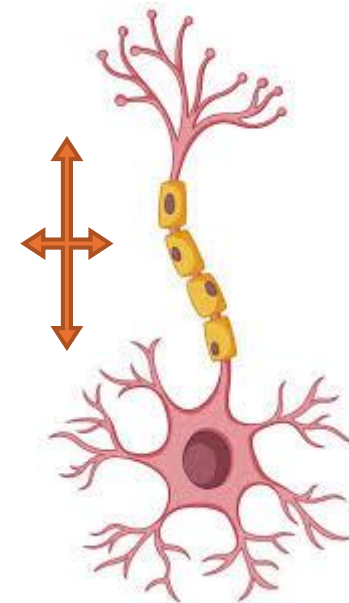
= level of inhomogeneity of diffusion



$$FA = \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}{2 \cdot (\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$



FA = 0
Isotropic tissue

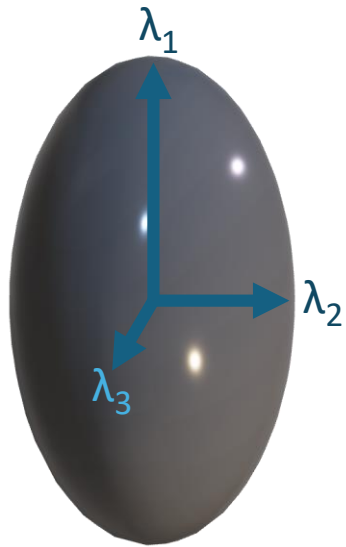


FA \rightarrow 1
Non-isotropic tissue

Assessment of tissue diffusion properties

MD: Mean diffusivity

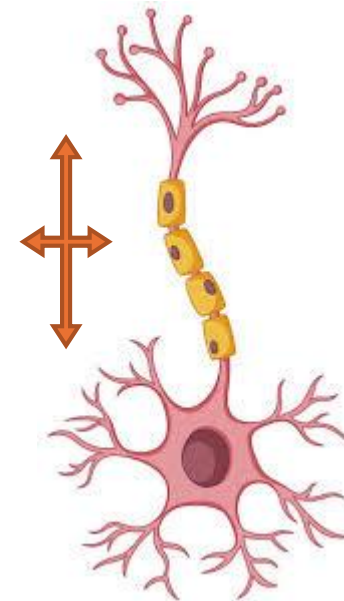
= “strength” of diffusion



$$MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

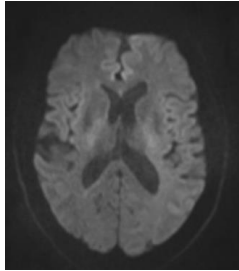


MD >
Faster diffusion



MD <
Slower diffusion

Assessment of tissue diffusion properties



MK: Mean Kurtosis

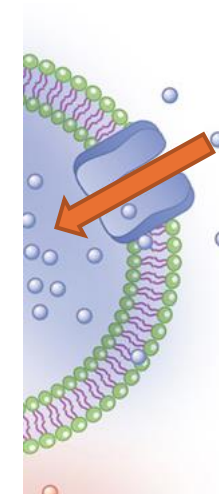
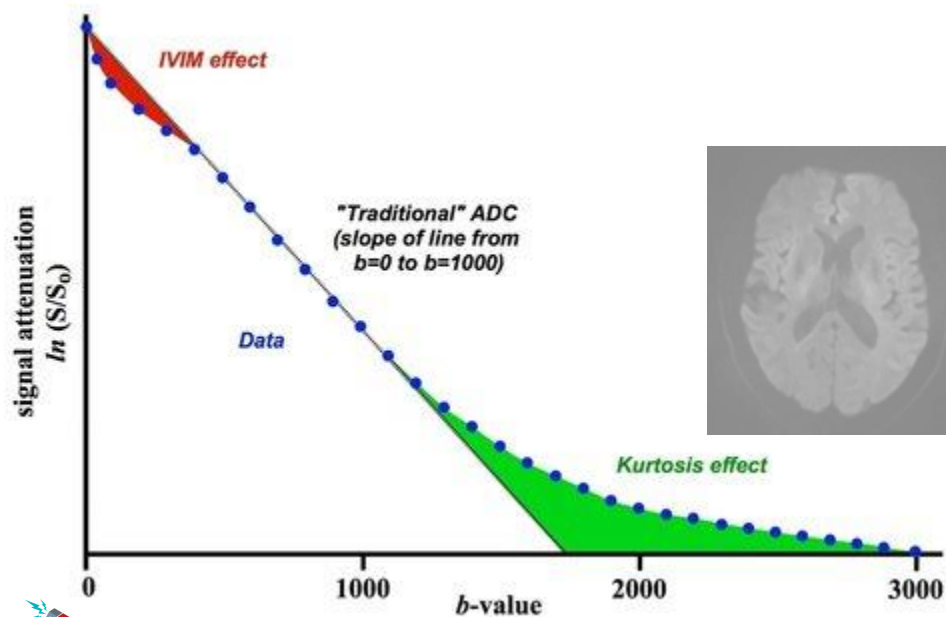
= level of non-linearity

KFA: Kurtosis Anisotropy

= non-homogeneity of kurtosis



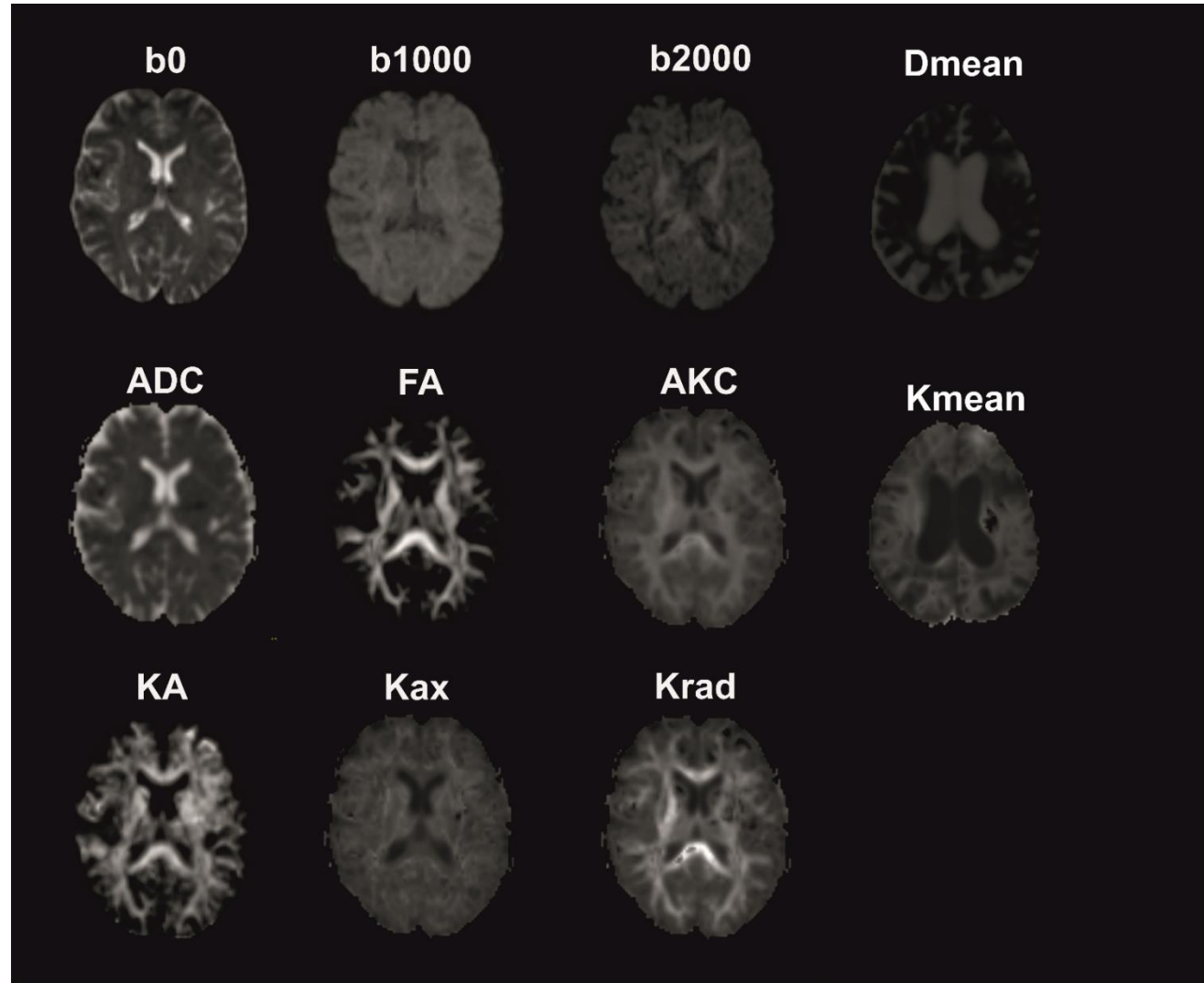
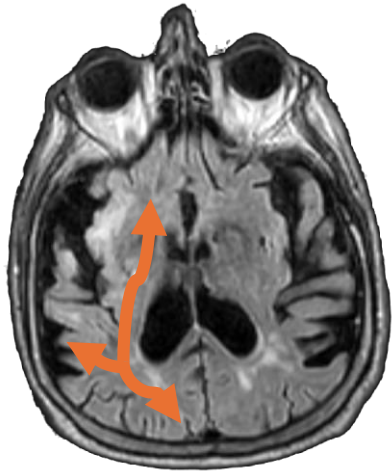
MK \rightarrow 0
Linear diffusion



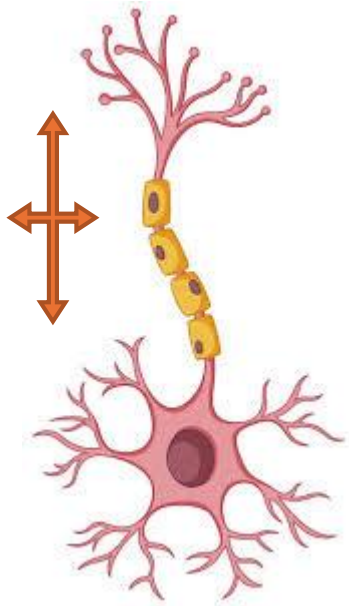
MK $>$ 0
Non-linear diffusion



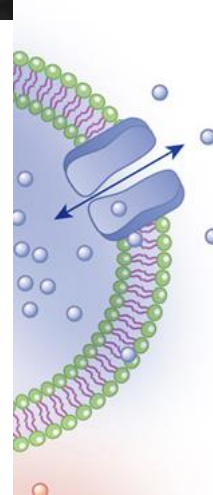
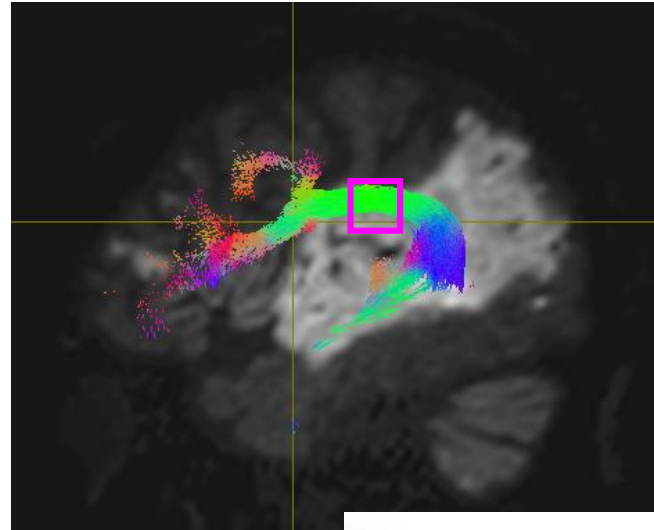
Assessment of tissue diffusion properties



Assessment of tissue diffusion properties



FA \rightarrow 1
Non-isotropic diffusion



MK $>$ 0
Non-linear diffusion



MD $>$
Fast diffusion

Assessment of tissue diffusion properties

Stroke

- Lesion detection
- Assessment of lesion age
- Evaluation of edema types

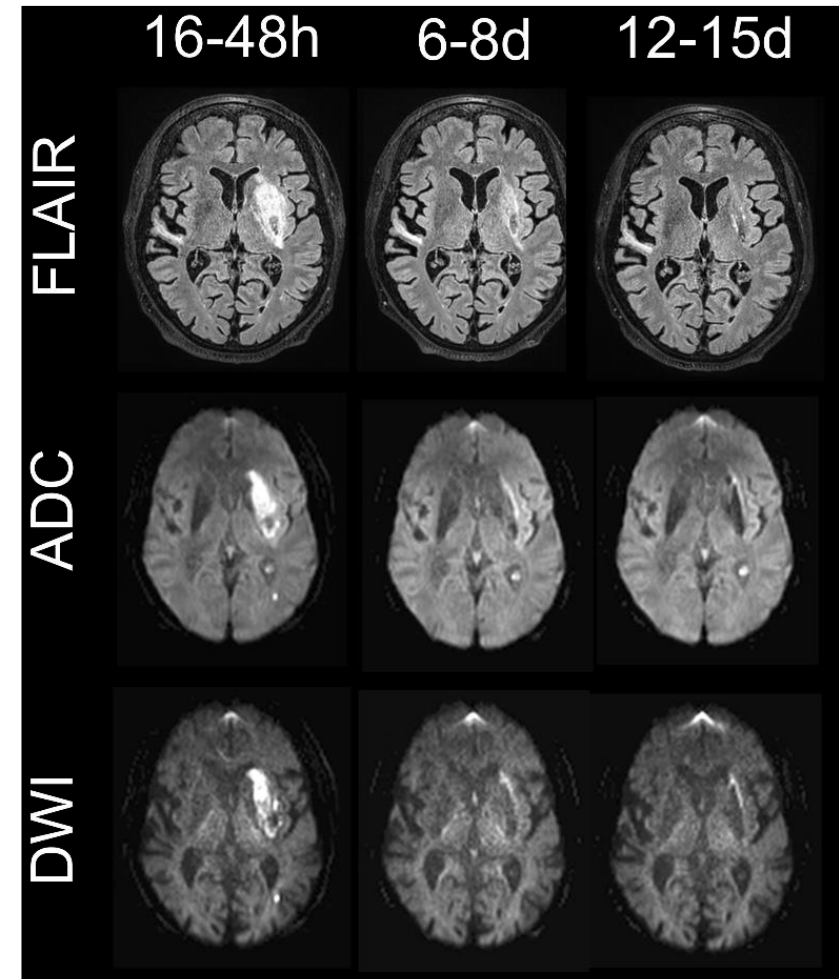


Figure: patient after stroke, time development

Assessment of tissue diffusion properties

Epilepsy

- Pathology detection and delineation
- Assessment of FCD type

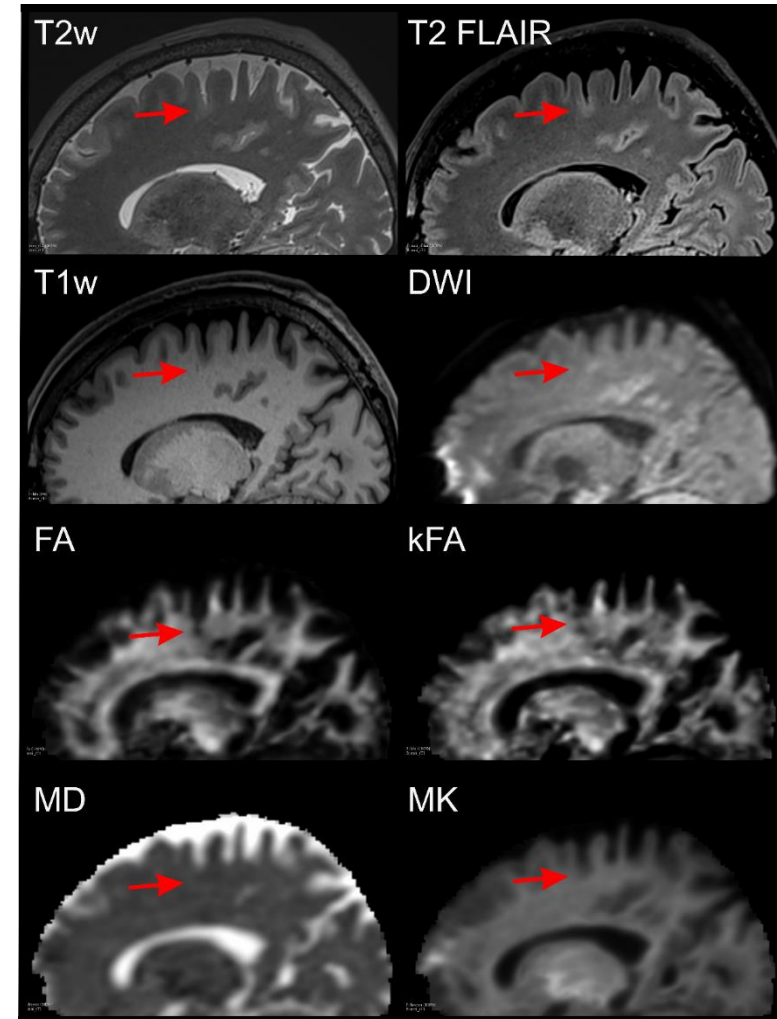
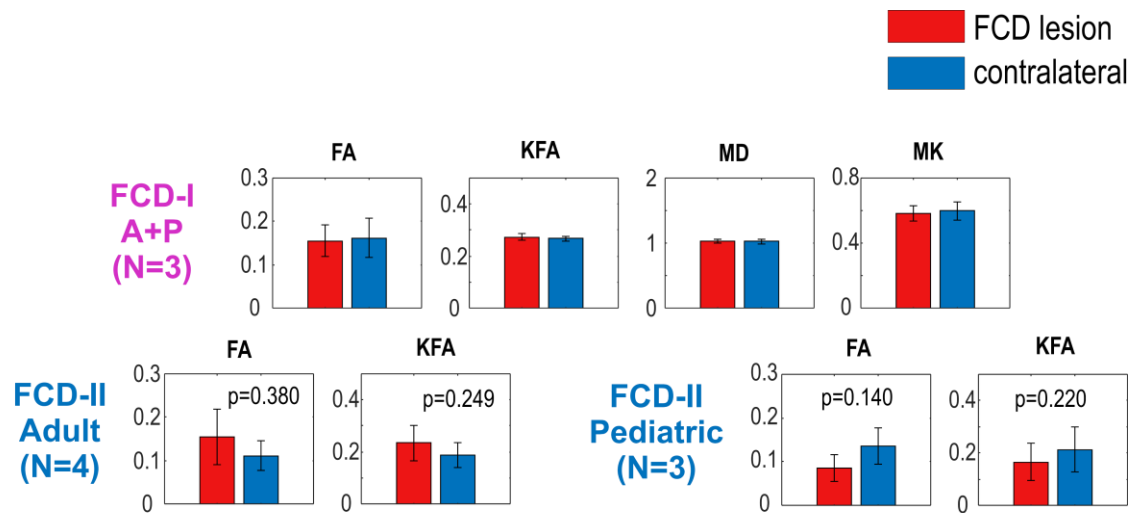


Figure: Patient with FCD type II

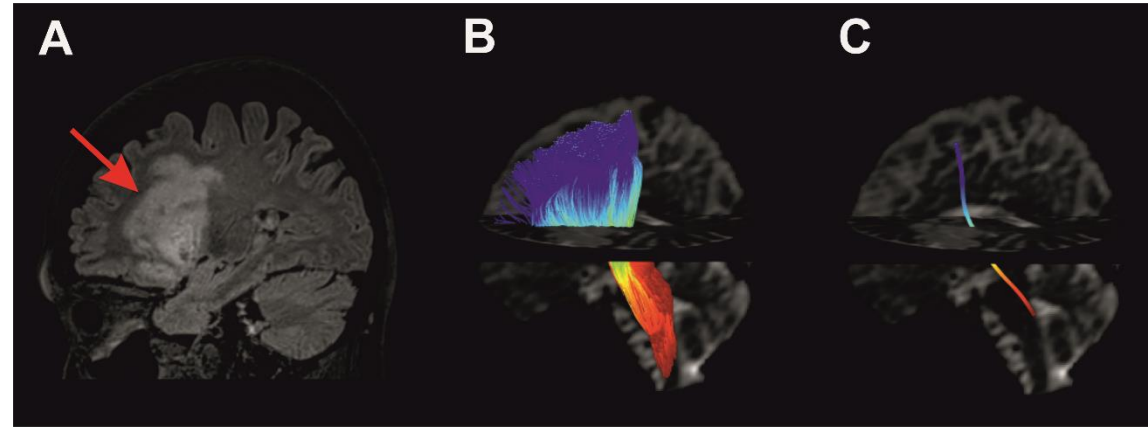


Obrázek. Rozdíl mezi lézí a zdravou tkání je patrný pouze u FCD-II

Neuronal tract detection and along-tract description

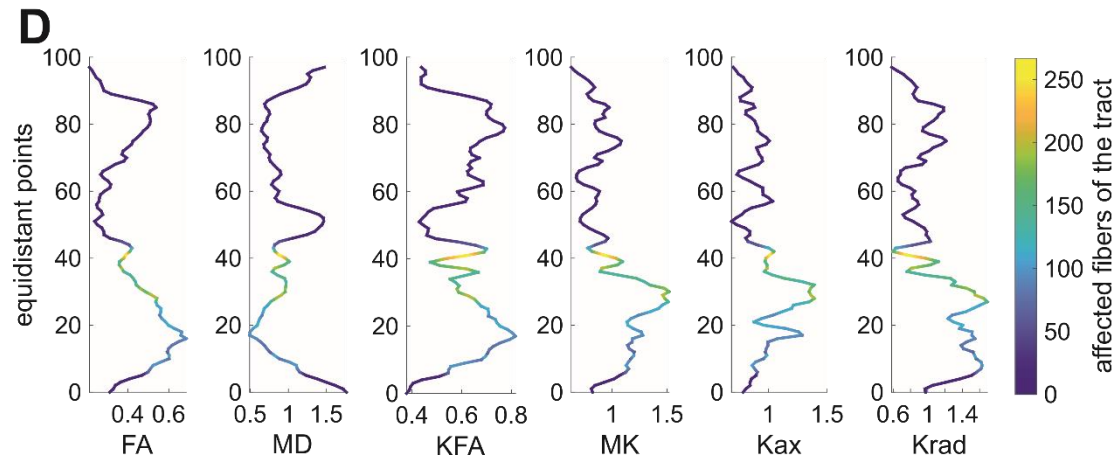
Tractography:

Detection of white matter neuronal tracts based on dominant diffusion



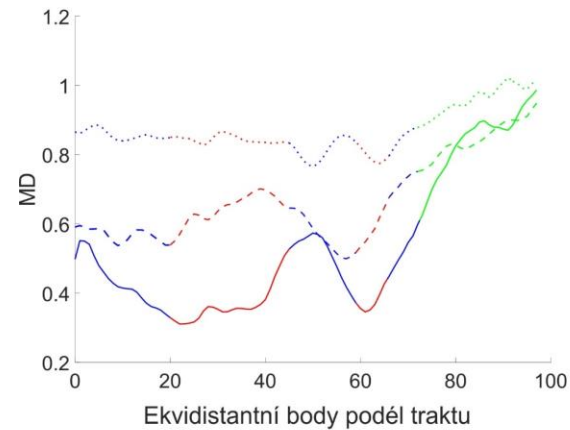
Tractogram

= description of diffusion parameters along neuronal tract

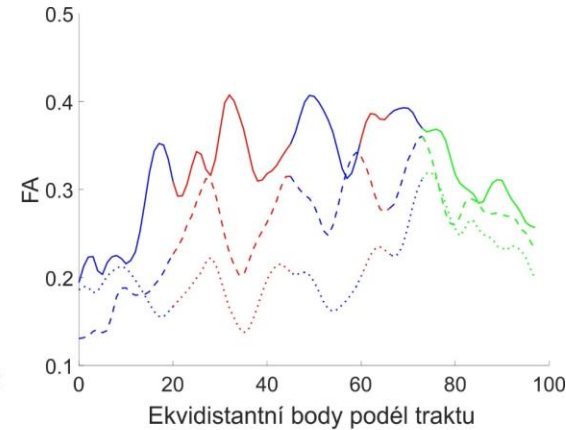


Longitudinal along-tract description

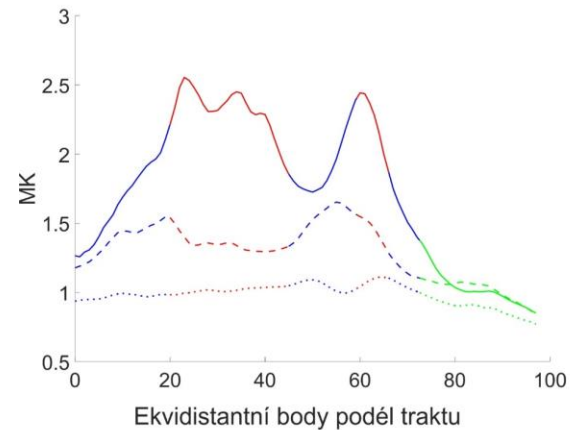
Increase of MD
- (faster difuze)



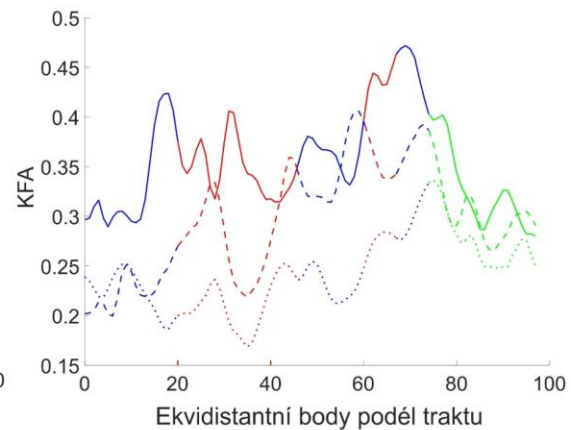
Decrease of FA
- Higher homogeneity of diffusion



Decrease of MK
-increase of linearity



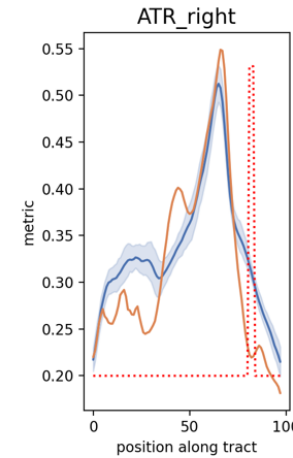
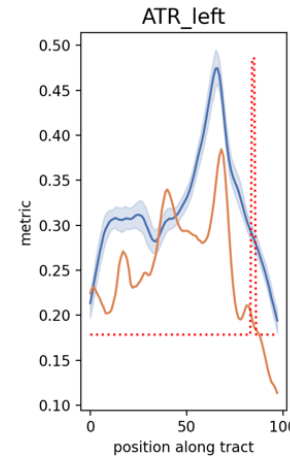
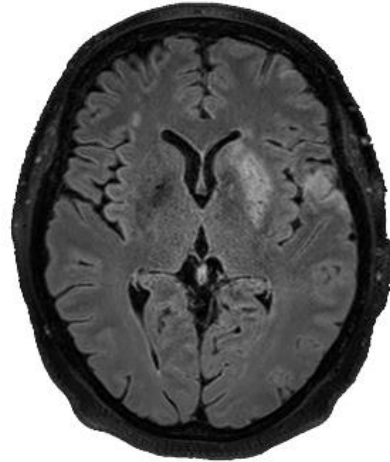
= transition to
vasogenic edema



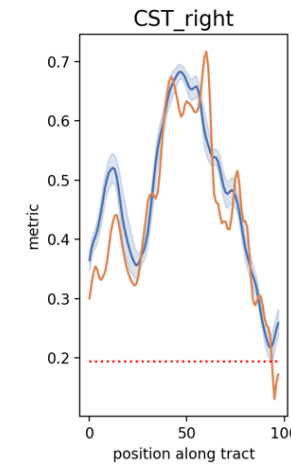
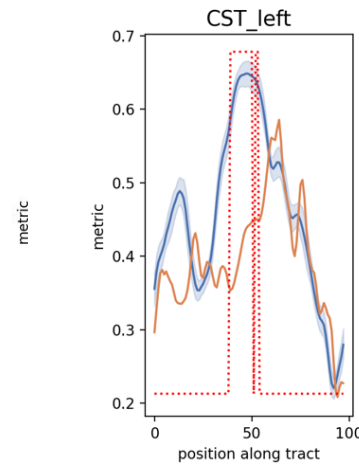
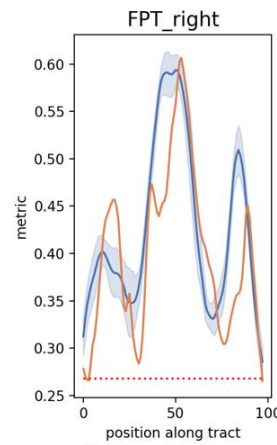
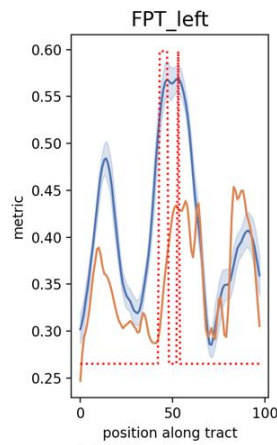
kolokalizace traktu a ischemické léze (%)
■ jádro ■ penumbra ■ mimo lézi
 100 75 25 0

časový odstup od CMP
 — 16-48 hodin - - - 6-8 dní 12-15 dní

Along-tract group comparison



Mean diffusivity
Healthy controls
vs stroke



Fixel-based approach



Contents lists available at ScienceDirect

NeuroImage

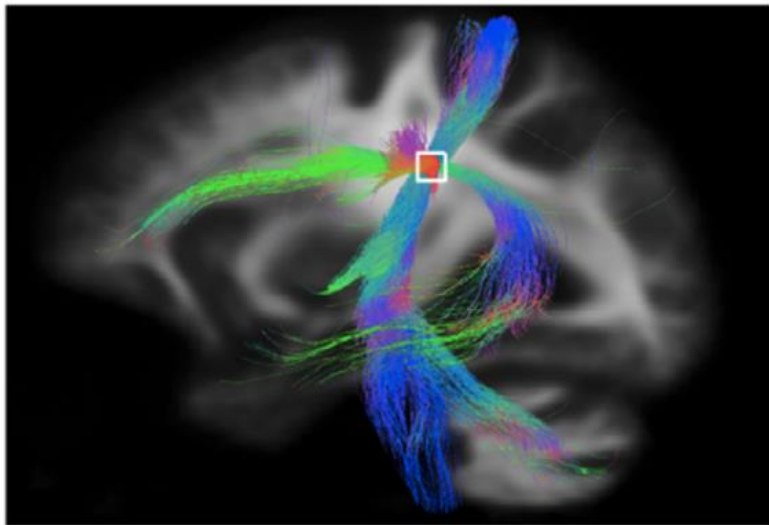
journal homepage: www.elsevier.com/locate/neuroimage



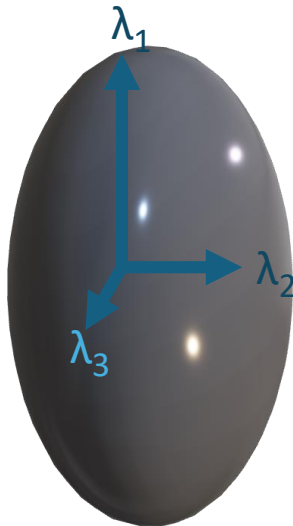
Fixel-based Analysis of Diffusion MRI: Methods, Applications, Challenges and Opportunities



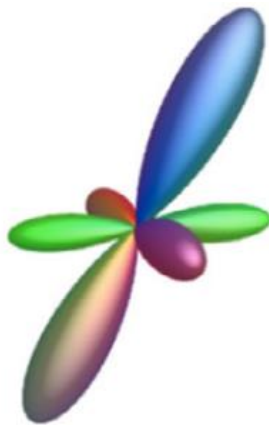
Thijs Dhollander^{a,*}, Adam Clemente^{b,f}, Mervyn Singh^{c,f}, Frederique Boonstra^d, Oren Civier^e, Juan Dominguez Duque^e, Natalia Egorova^{b,g}, Peter Enticott^c, Ian Fuelscher^c, Sanuji Gajamange^h, Sila Genc^{a,i}, Elie Gottlieb^g, Christian Hyde^c, Phoebe Imms^b, Claire Kelly^{a,j}, Melissa Kirkovski^c, Scott Kolbe^d, Xiaoyun Liang^{b,g,j}, Atul Malhotra^{k,l,m}, Remika Mito^g, Govinda Poudel^b, Tim J. Silk^{a,c,n}, David N. Vaughan^{g,o}, Julien Zanin^p, David Raffelt^g, Karen Caeyenberghs^c



Diffusion tensor



Fibre orientation distribution

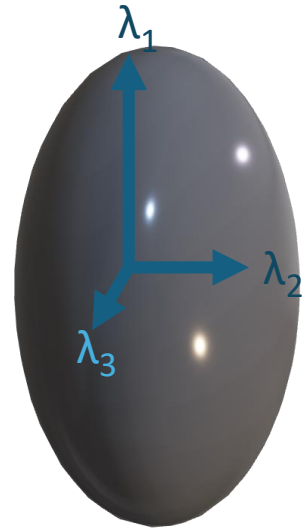


Fixel-based approach

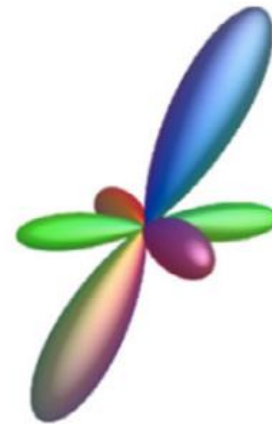
additional characteristics of diffusion

Mean diffusivity
Mean Kurtosis
Fraction anisotropy
Kurtosis anisotropy

Diffusion tensor

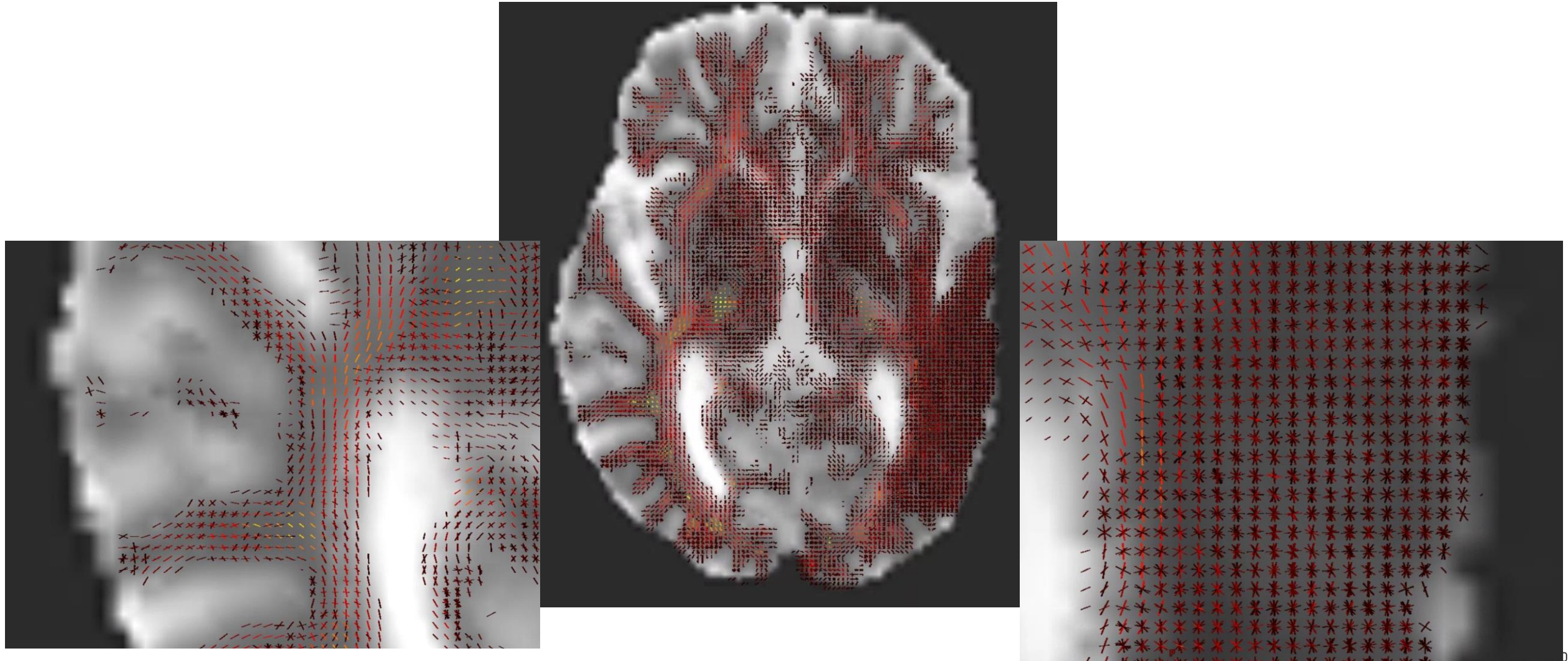


Fibre orientation
distribution



Fiber density
Fibre-bundle cross-section

Fixel-based comparison



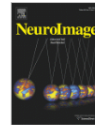
Fixel-based comparison with healthy template

= Statistical comparison in fixel space
avoid voxel-wise registration to template space





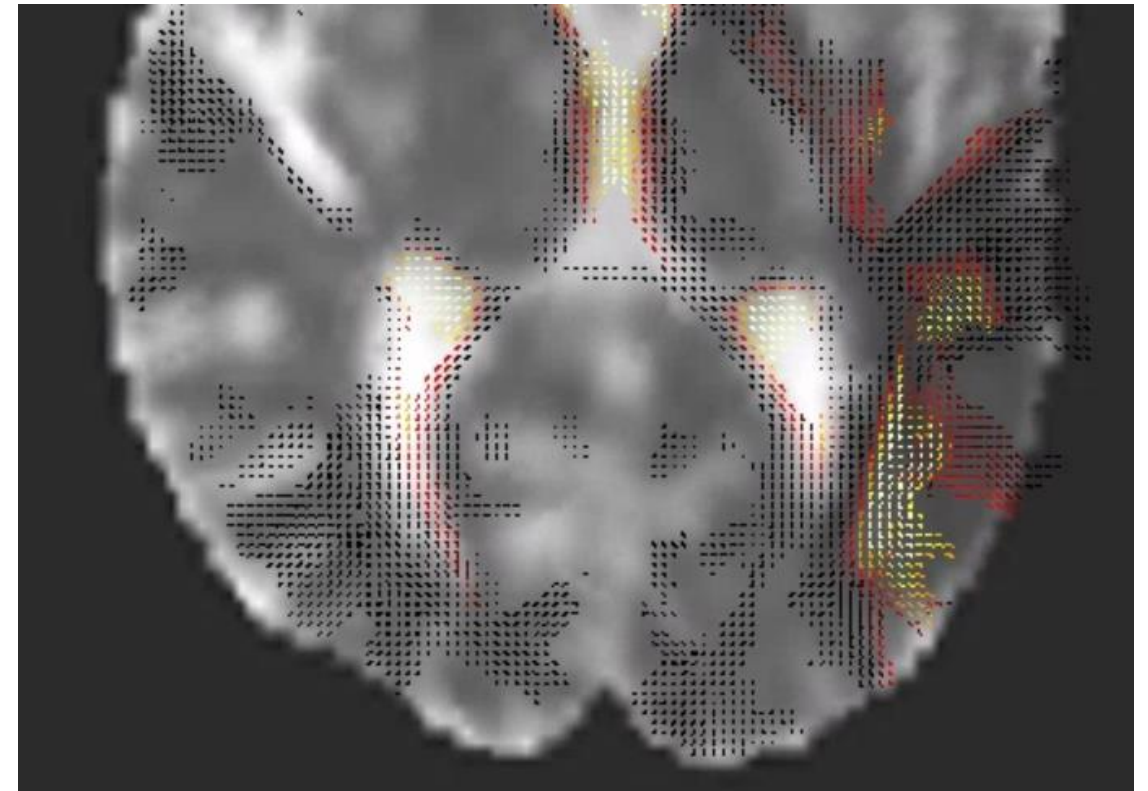
NeuroImage

Volume 56, Issue 3, 1 June 2011, Pages 1171-1180



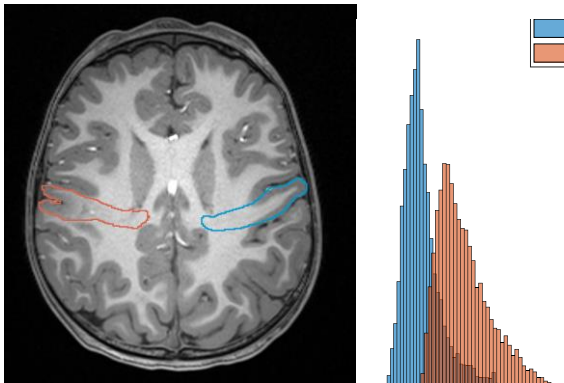
Symmetric diffeomorphic registration of fibre orientation distributions

David Raffelt^{a,b}  , J-Donald Tournier^{c,d}, Jurgen Fripp^a, Stuart Crozier^b, Alan Connelly^{c,d},
Olivier Salvado^a

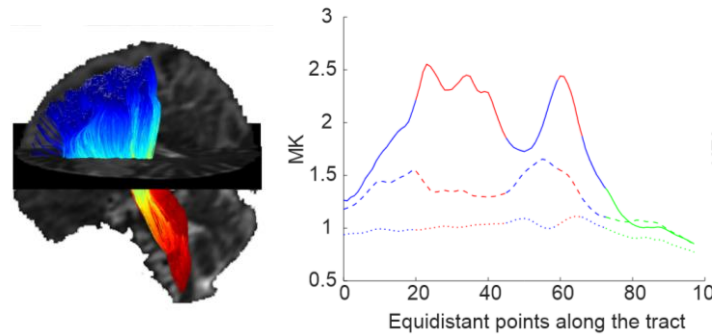


Description of brain diffusion properties

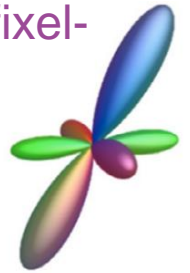
Individual / group
description of ROIs



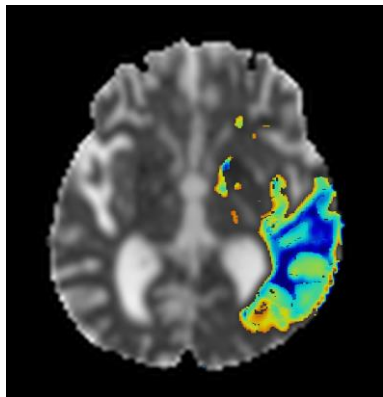
Description of diffusion
along neuronal tracts



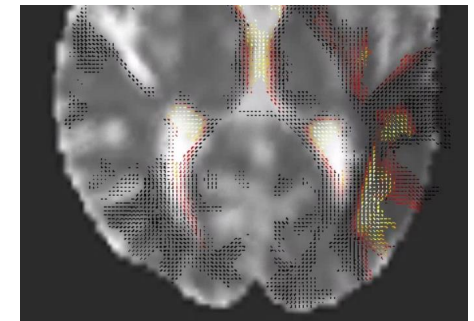
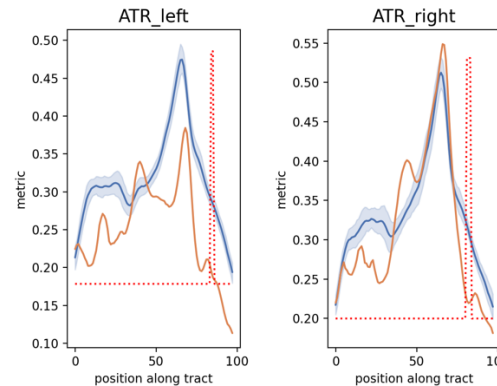
Description and group
comparison in fixel-
space



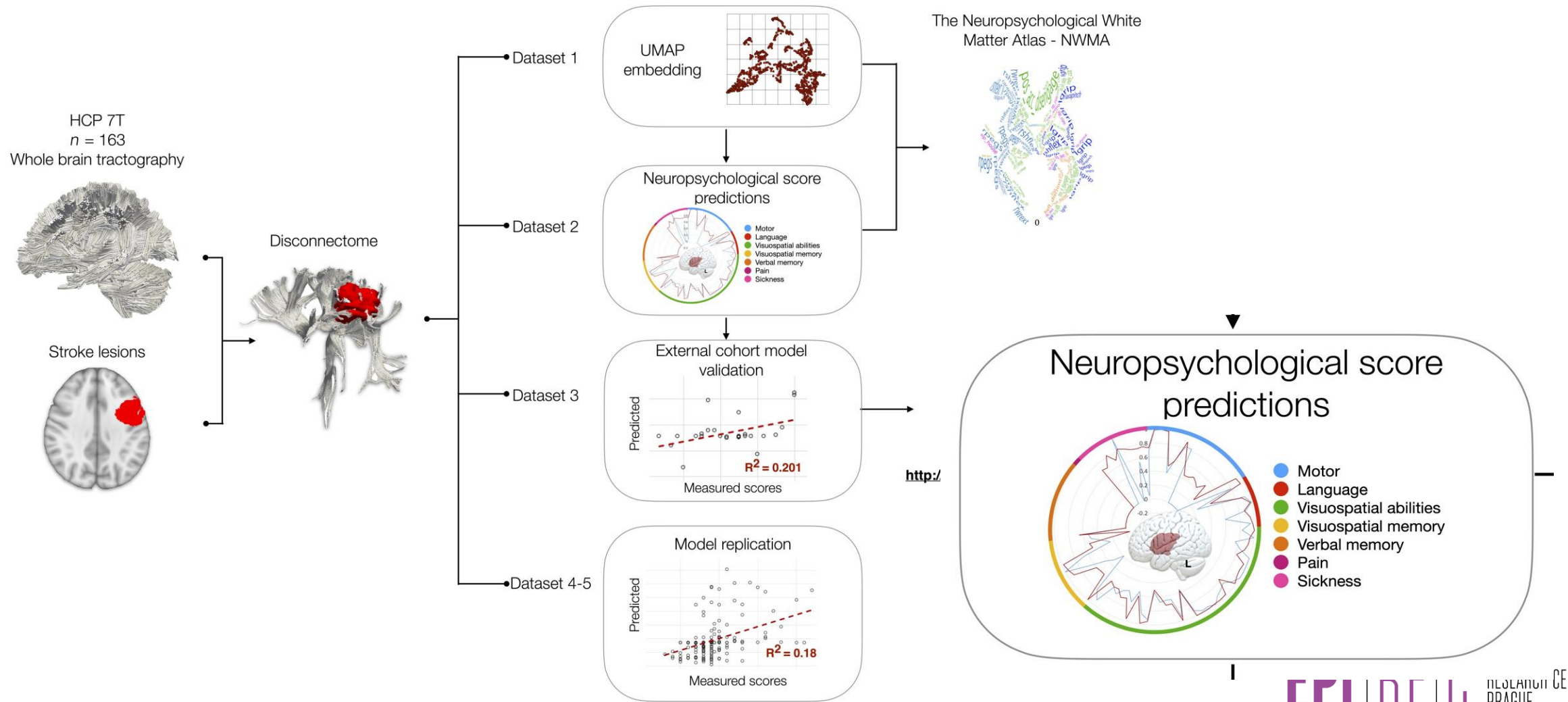
Detection of anomalies



Intersubject comparison



Disconnectome - Prediction of pathology impact



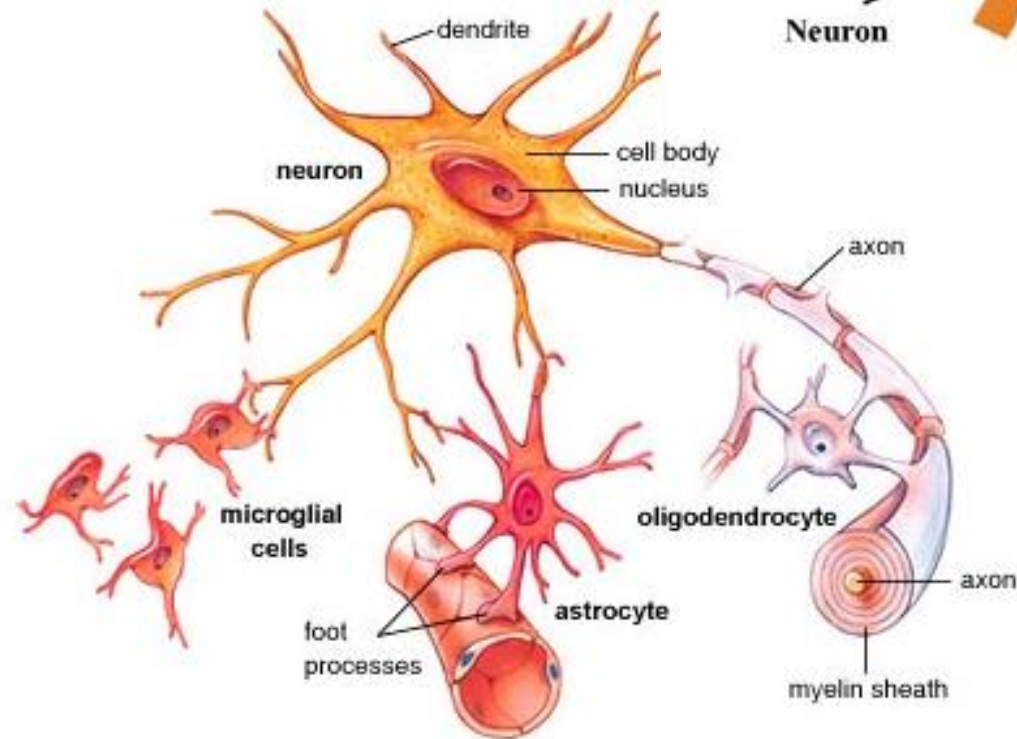
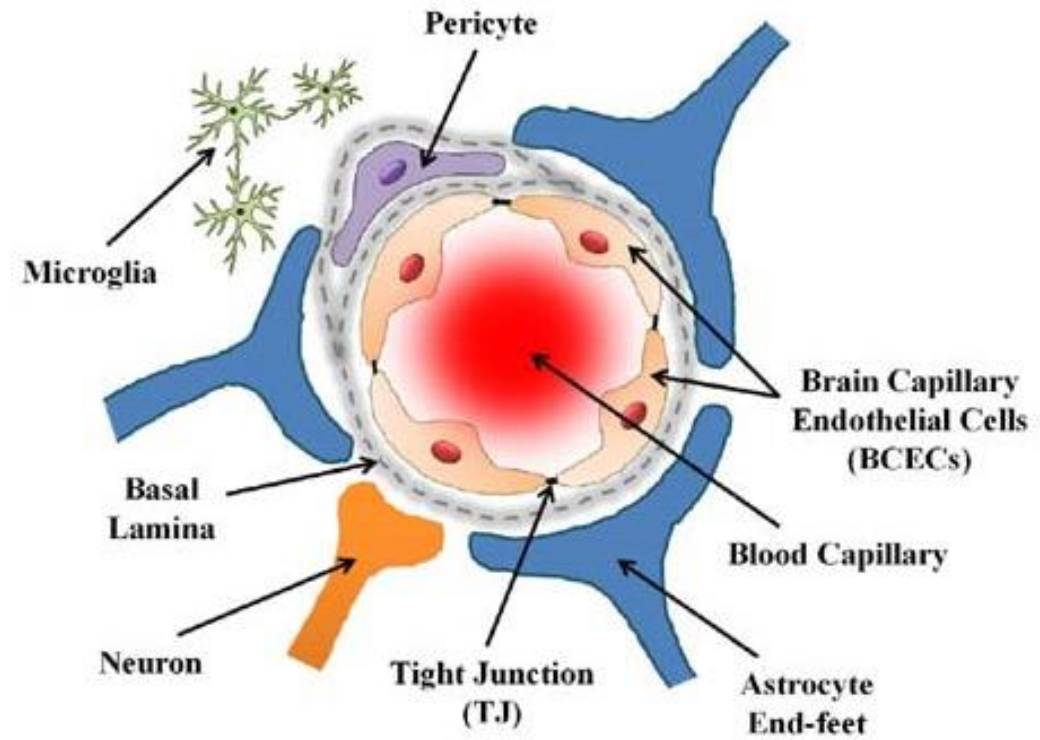
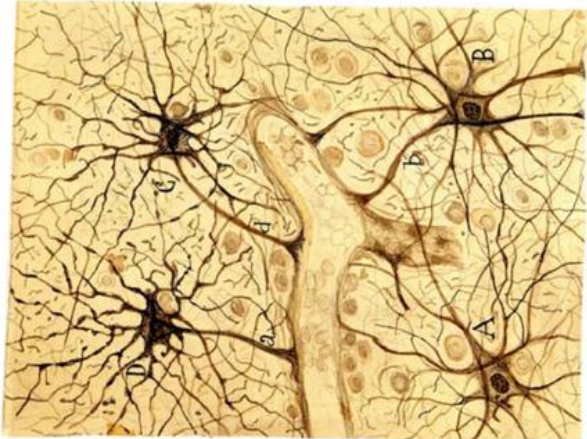
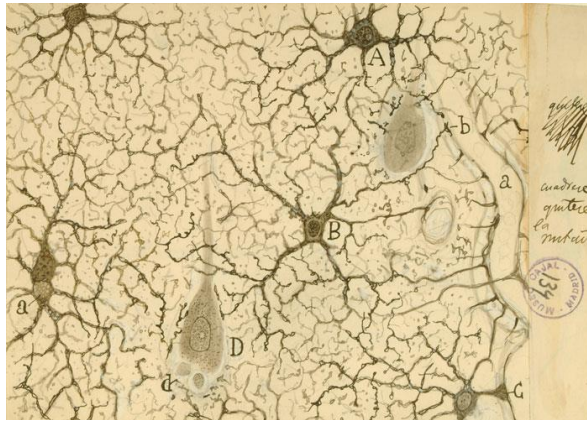
Evaluation of blood-brain barrier integrity



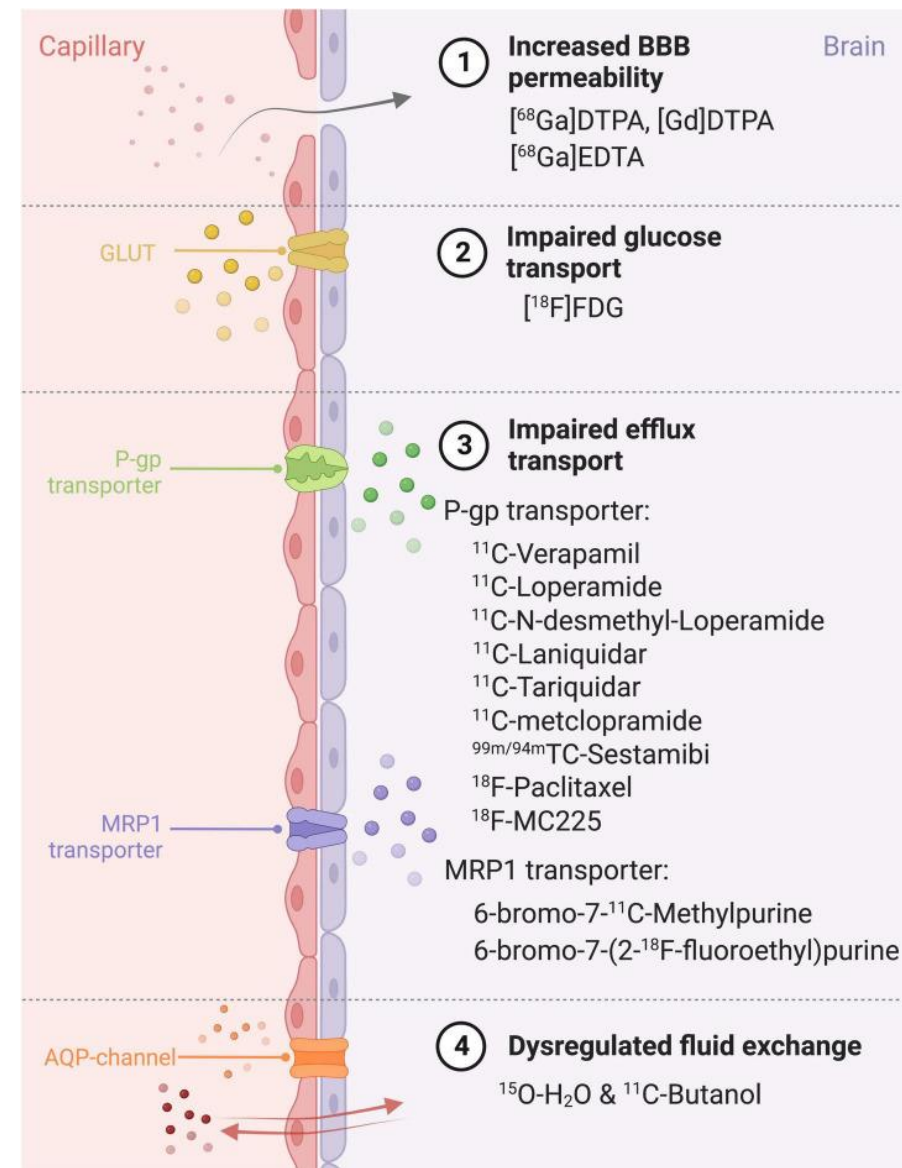
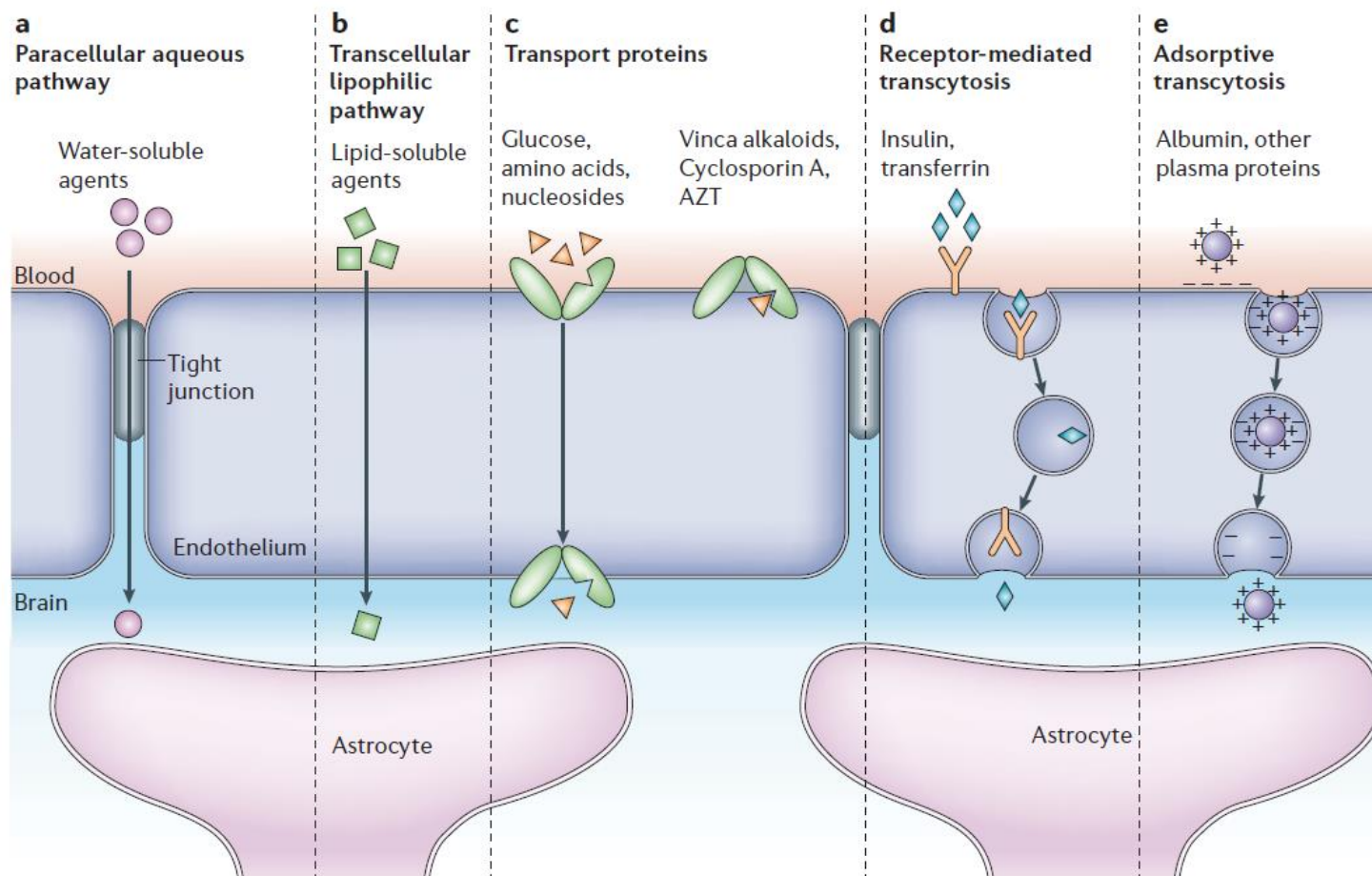
Paul Ehrlich - original concept of BBB. 1878



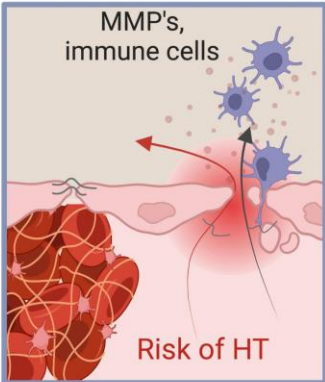
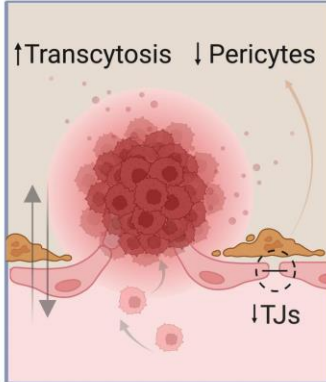
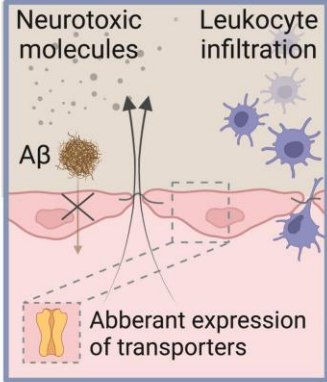
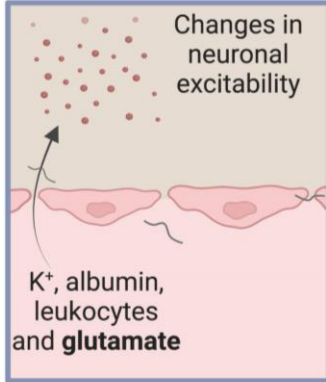
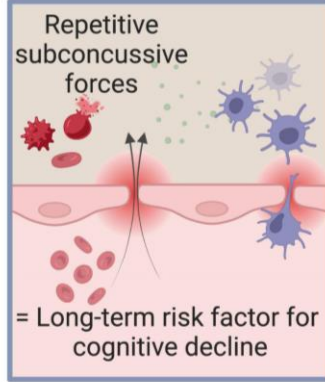
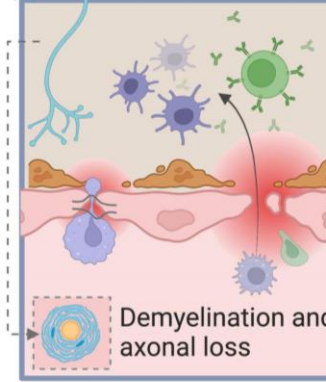
Structure of BBB



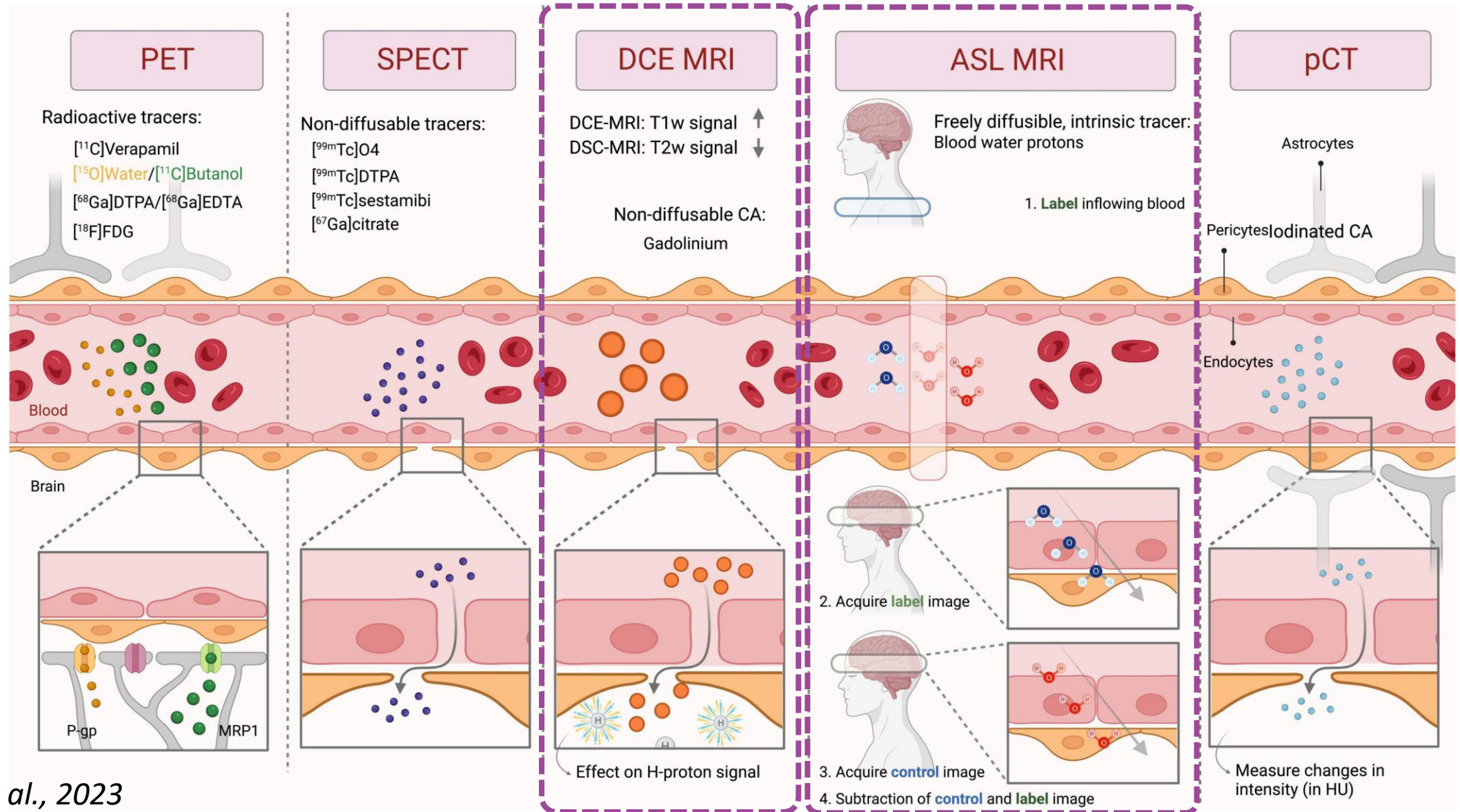
Transport across BBB



Diagnostic value of blood-brain barrier imaging

Disease:	Stroke	Cancer	AD	Epilepsy	TBI	MS
Cause:	Ischemia, hypoperfusion	Tumor disrupts BBB integrity	Unknown	TBI, ischemia, inflammation	Head injury (e.g. repetitive subconcussive forces)	Focal inflammation
Consequence:	 <p>MMP's, immune cells Risk of HT</p>	 <p>↑Transcytosis ↓Pericytes ↓TJs</p>	 <p>Neurotoxic molecules Leukocyte infiltration Aβ Aberrant expression of transporters</p>	 <p>Changes in neuronal excitability K⁺, albumin, leukocytes and glutamate</p>	 <p>Repetitive subconcussive forces = Long-term risk factor for cognitive decline</p>	 <p>Demyelination and axonal loss</p>
Potential role of BBB imaging:	MRI, CT: Thrombolysis after 4.5h time window	MRI, PET: Improvement of drug delivery	MRI, PET: Biomarker of cognitive impairment	MRI, PET, SPECT: New therapeutic targets	MRI, CT: comorbidities associated with TBI	MRI: Disease diagnosis and monitoring

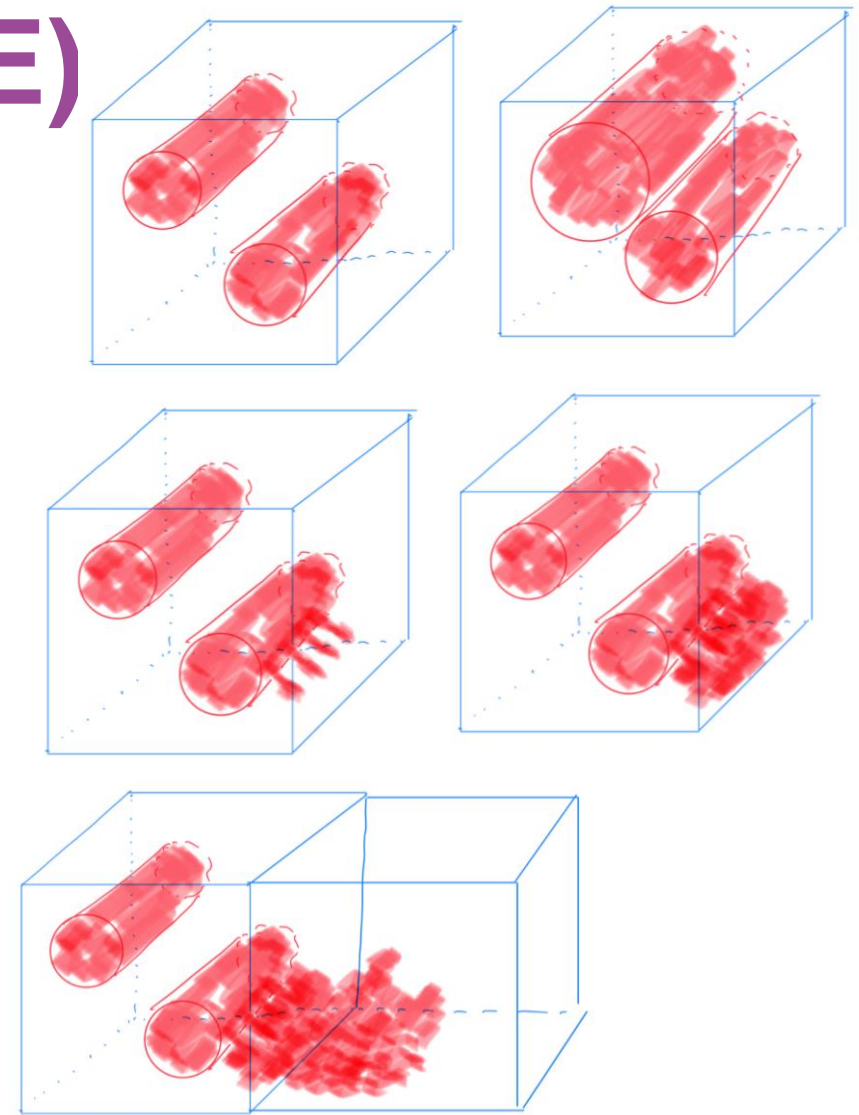
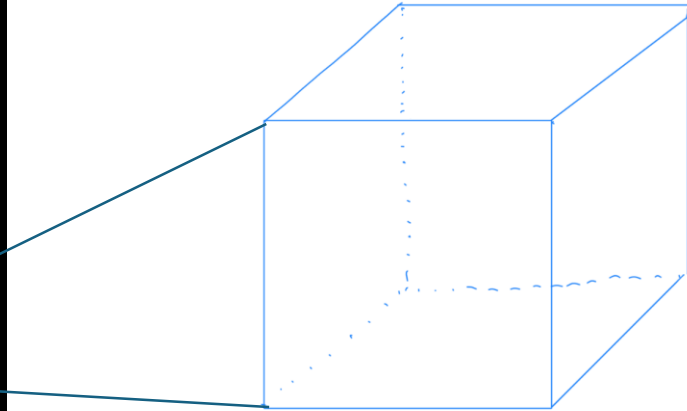
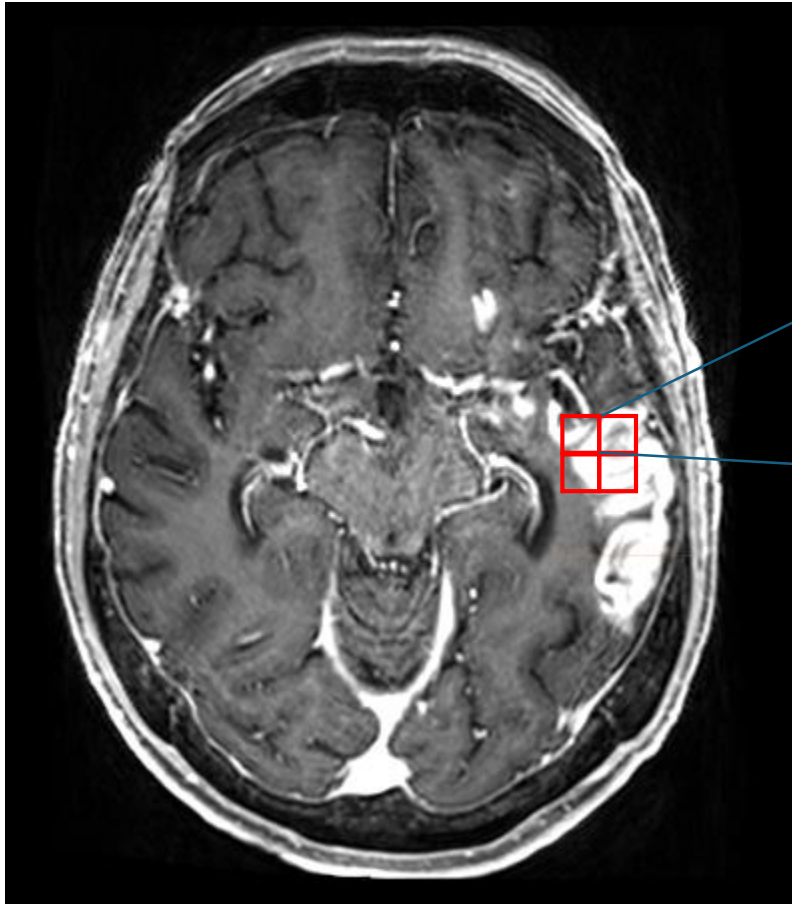
Methods for BBB imaging



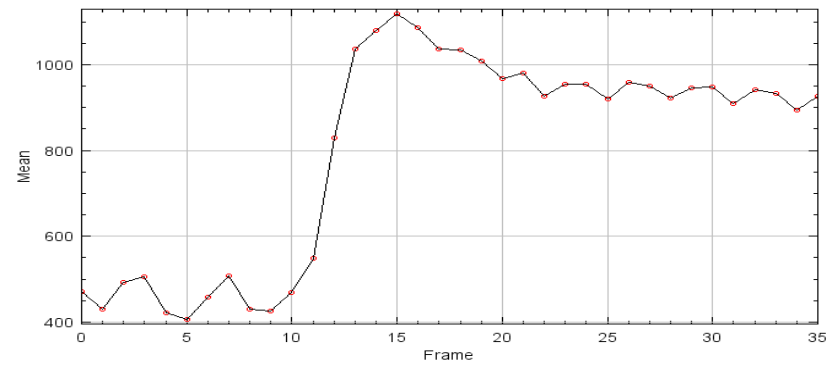
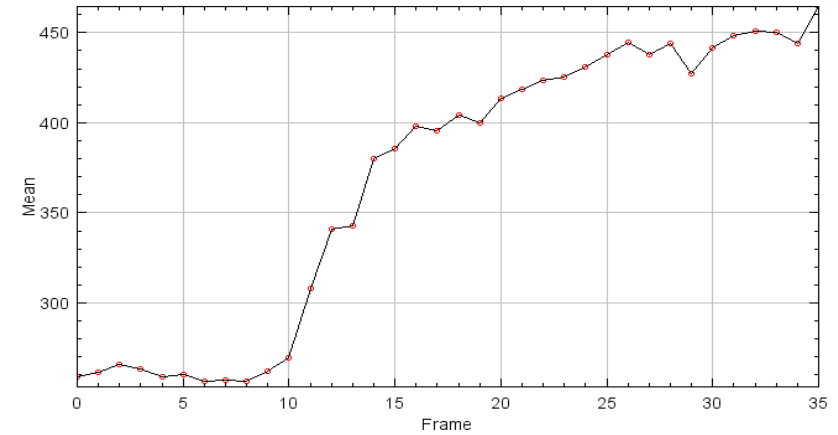
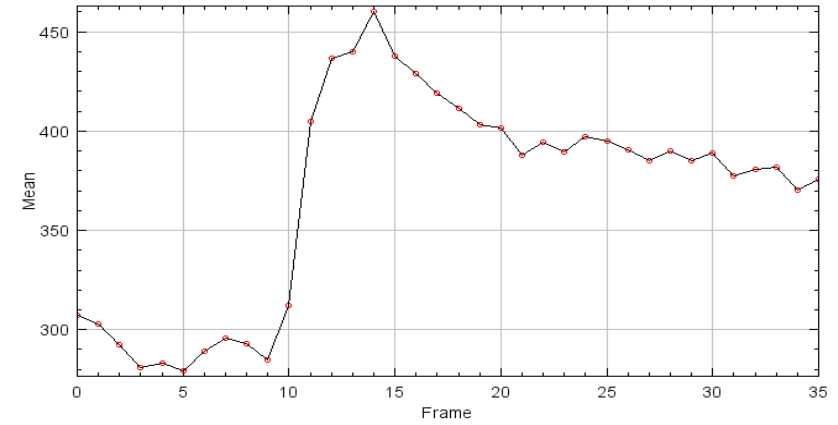
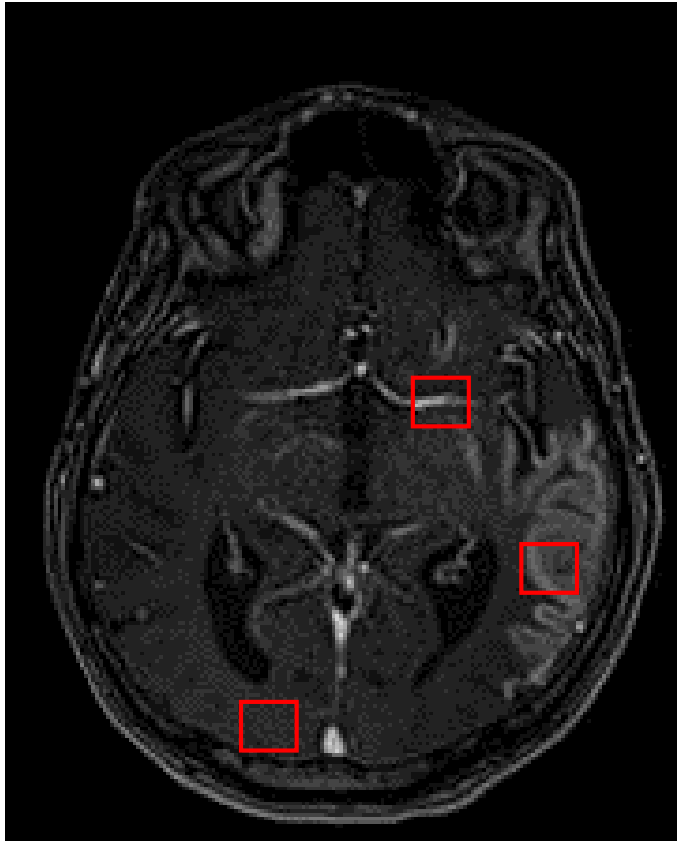
MRI methods to evaluate BBB

- **Dynamic Contrast Enhancement (DCE)**
 - Time lapsed acquisition of MRI data during and after controlled injection of a bolus of gadolinium-based contrast agent
- **BBB ASL – multi-TE ASL**
 - Endogenous contrast – magnetization of water molecules of the blood
 - difference in transverse relaxation time (T2) which is longer for blood water molecules (~275 ms at 3T) than for water molecules in the brain tissue (~99 ms at 3T)

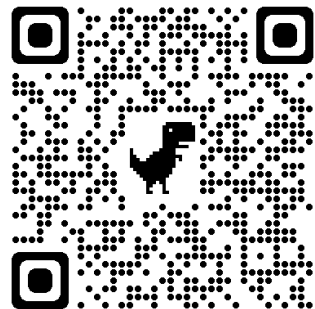
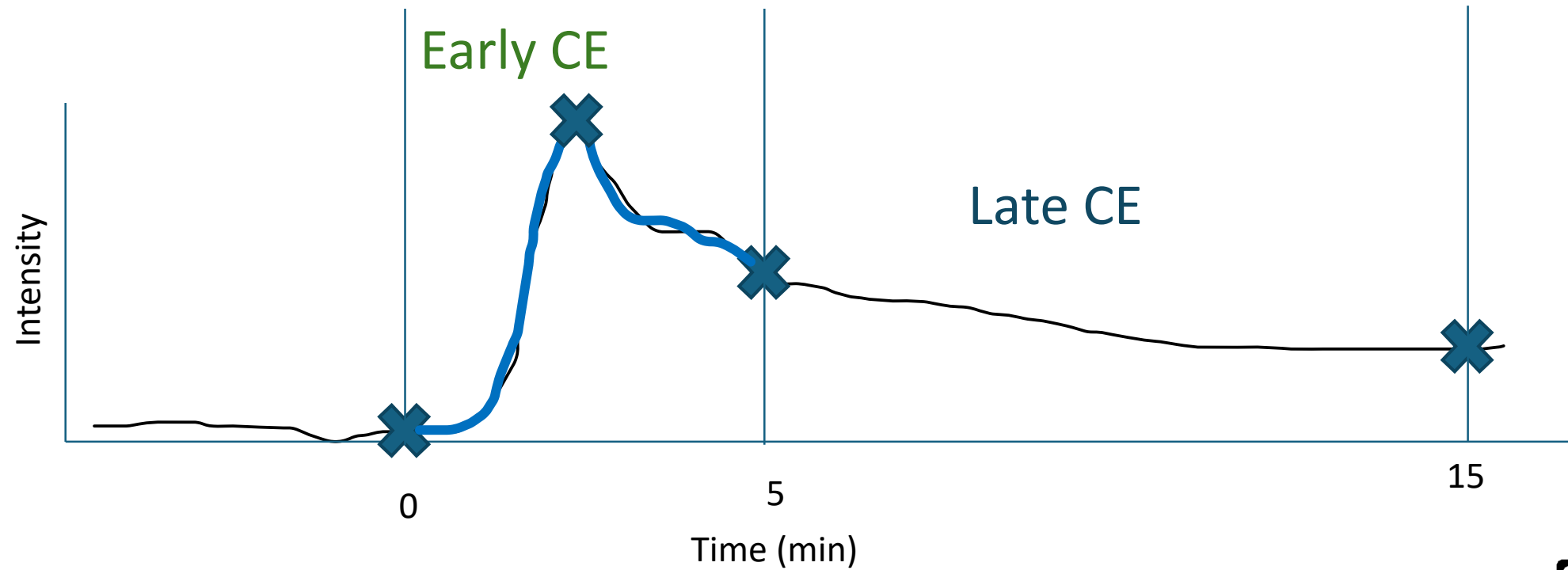
Contrast Enhancement (CE)



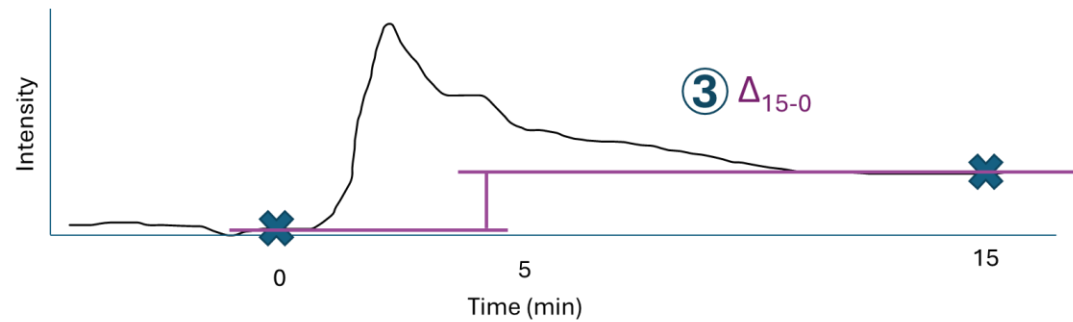
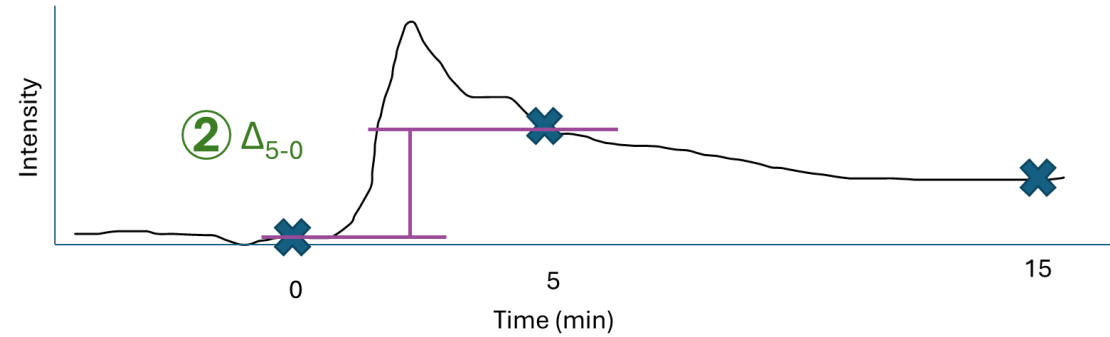
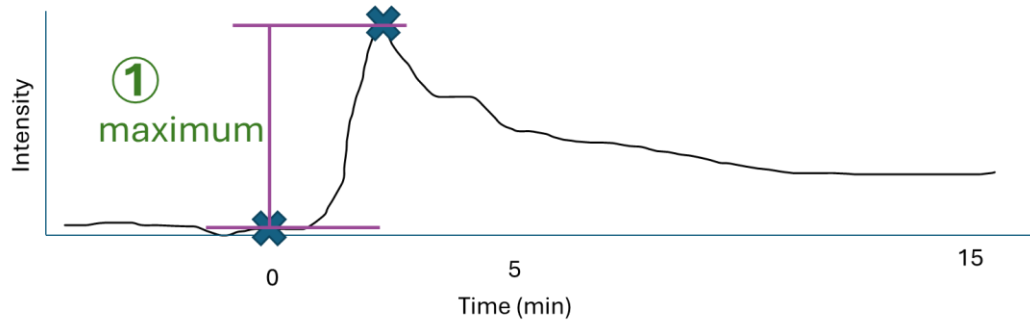
Dynamic Contrast Enhancement (DCE)



Time intensity curve (TIC)

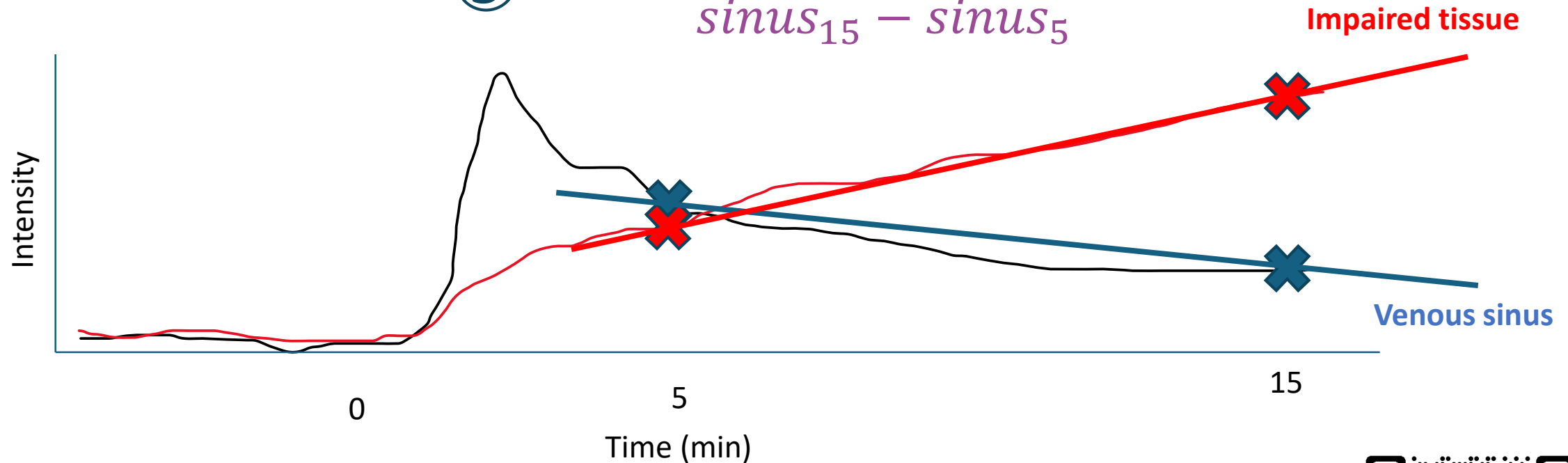


Parameters of TIC – change between timepoints



Parameters of TIC - normalized permeability index (NPI)

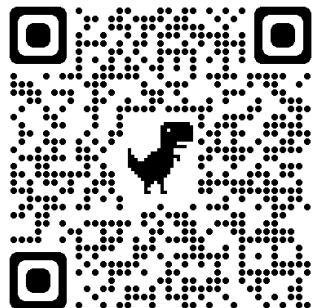
$$\textcircled{5} \text{NPI} = \frac{\textit{tissue}_{15} - \textit{tissue}_5}{\textit{sinus}_{15} - \textit{sinus}_5}$$



NPI < 0 – cumulation of CA

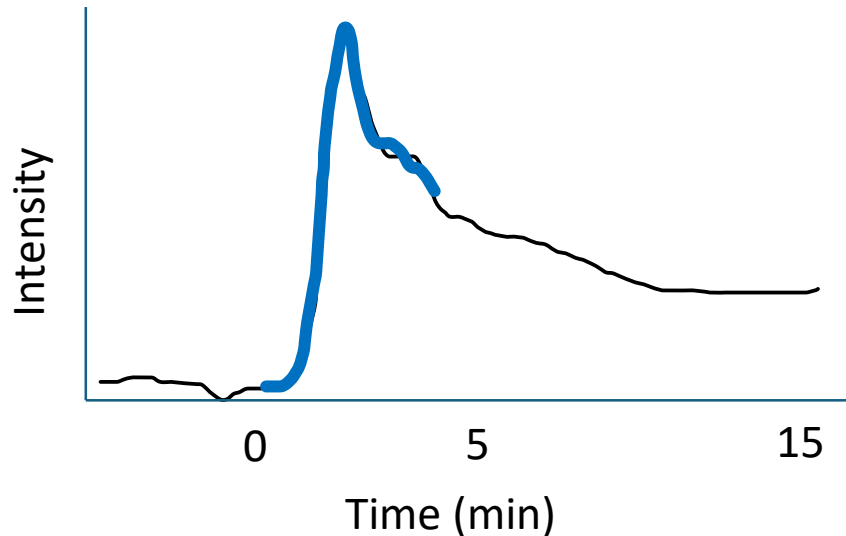
$0 < \text{NPI} < 1$ – tissue clearance of CA is slower than blood's

$\text{NPI} > 1$ – tissue clearance of CA is faster than blood's



Pharmacokinetic models

Mathematic compartment model describes dynamic of fast increase and decrease of TIC

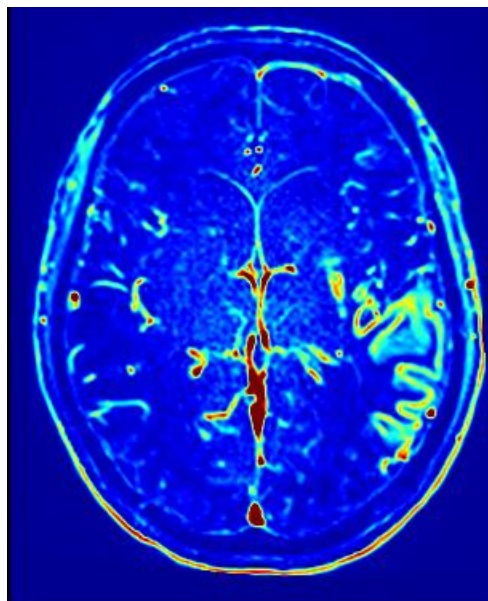


$$C_t(t) = K^{trans} \int_0^t C_p(\tau) e^{-(K^{trans}/v_e)(t-\tau)} d\tau$$

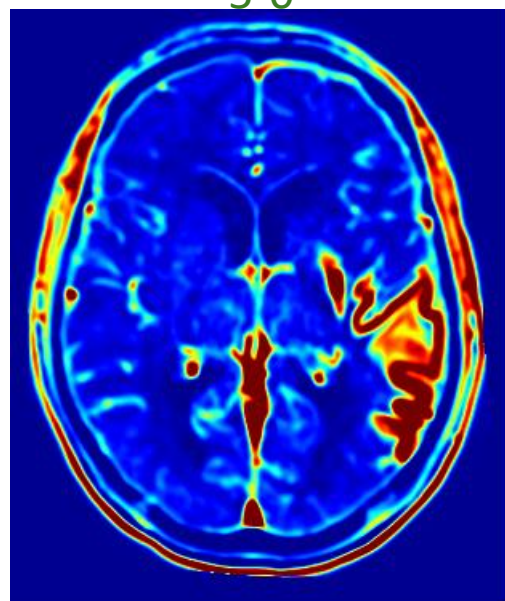
- ⑥ K^{trans} = **transfer constant** (min^{-1}) and describes the balance between permeability and blood flow



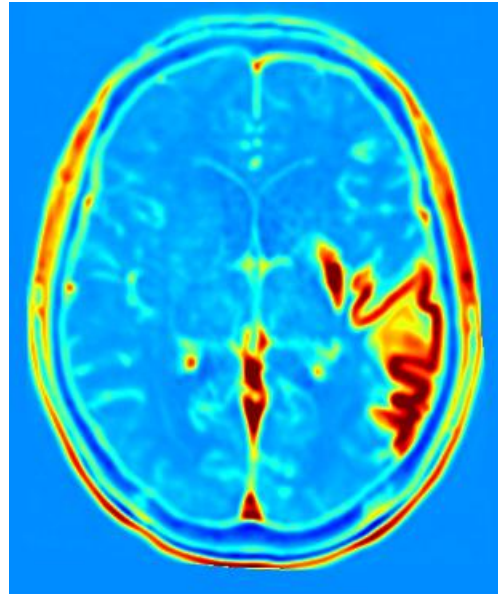
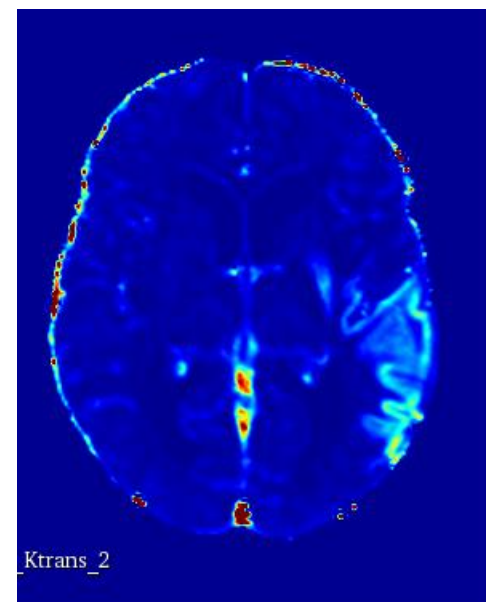
maximum



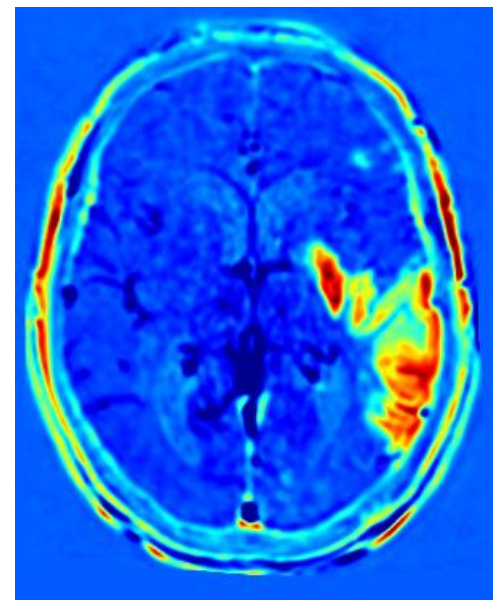
Δ_{5-0}



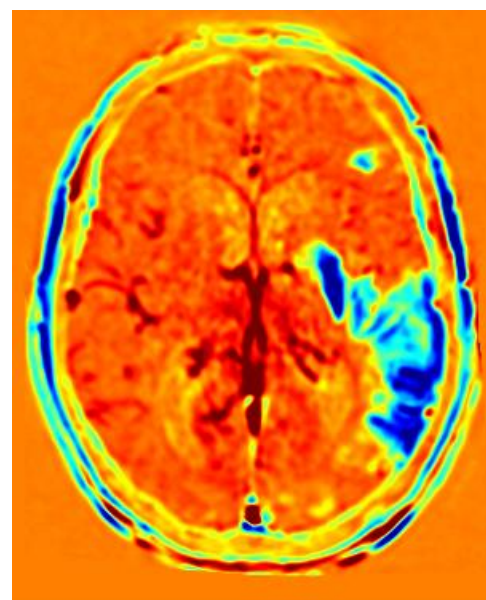
Ktrans



Δ_{15-0}



Δ_{15-5}



NPI

Kala et al. 2023



Parameters of TIC

① maximum

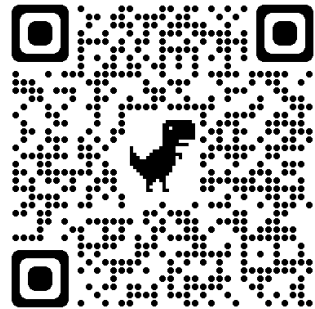
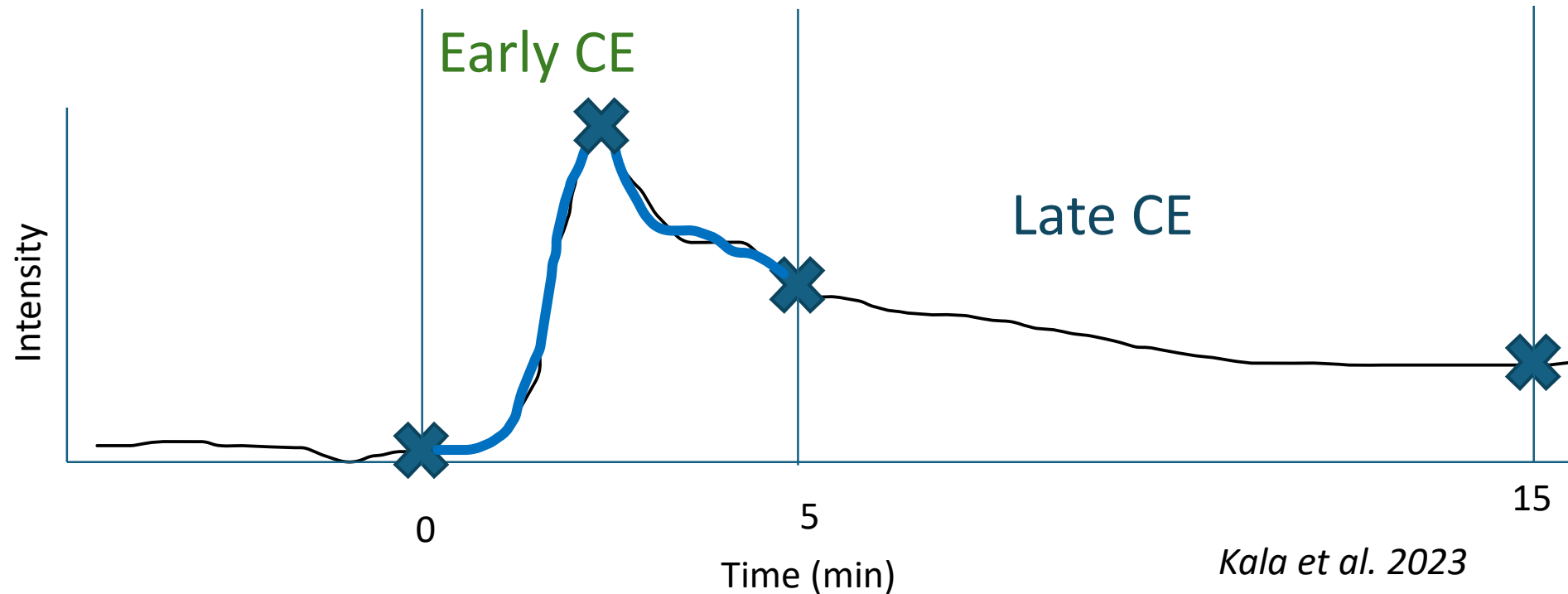
② Δ_{5-0}

⑥ Ktrans

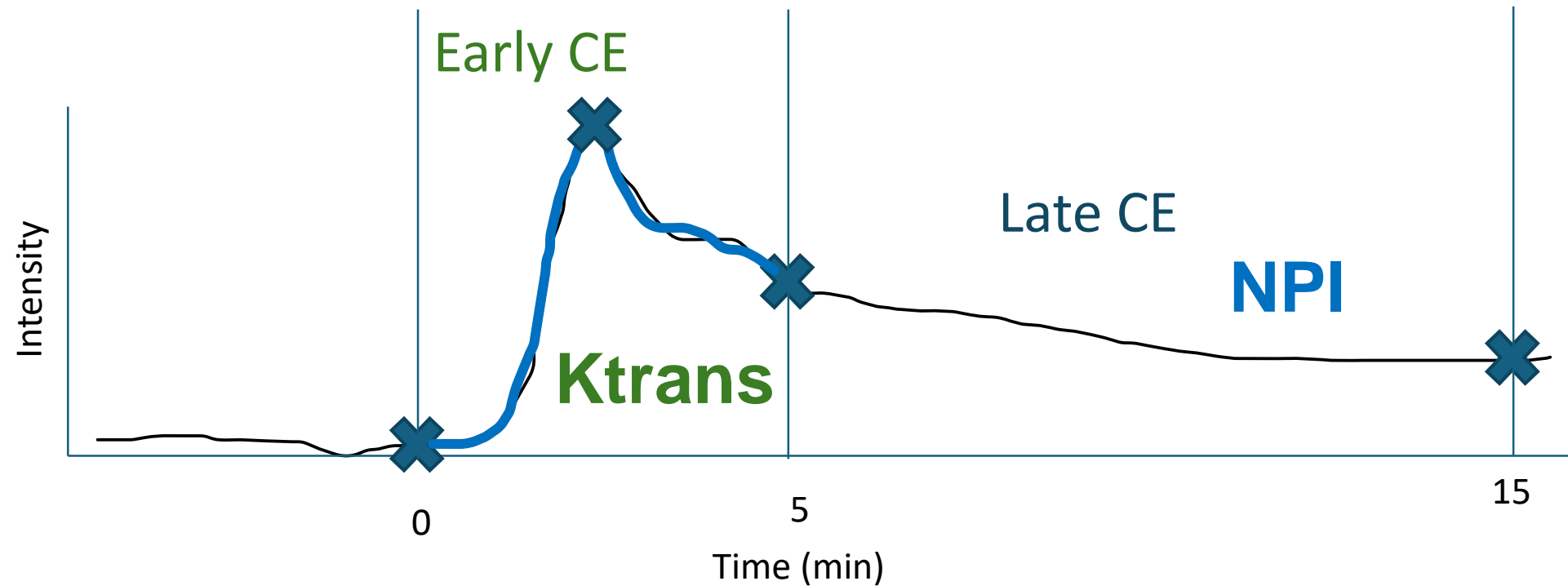
④ Δ_{15-5}

③ Δ_{15-0}

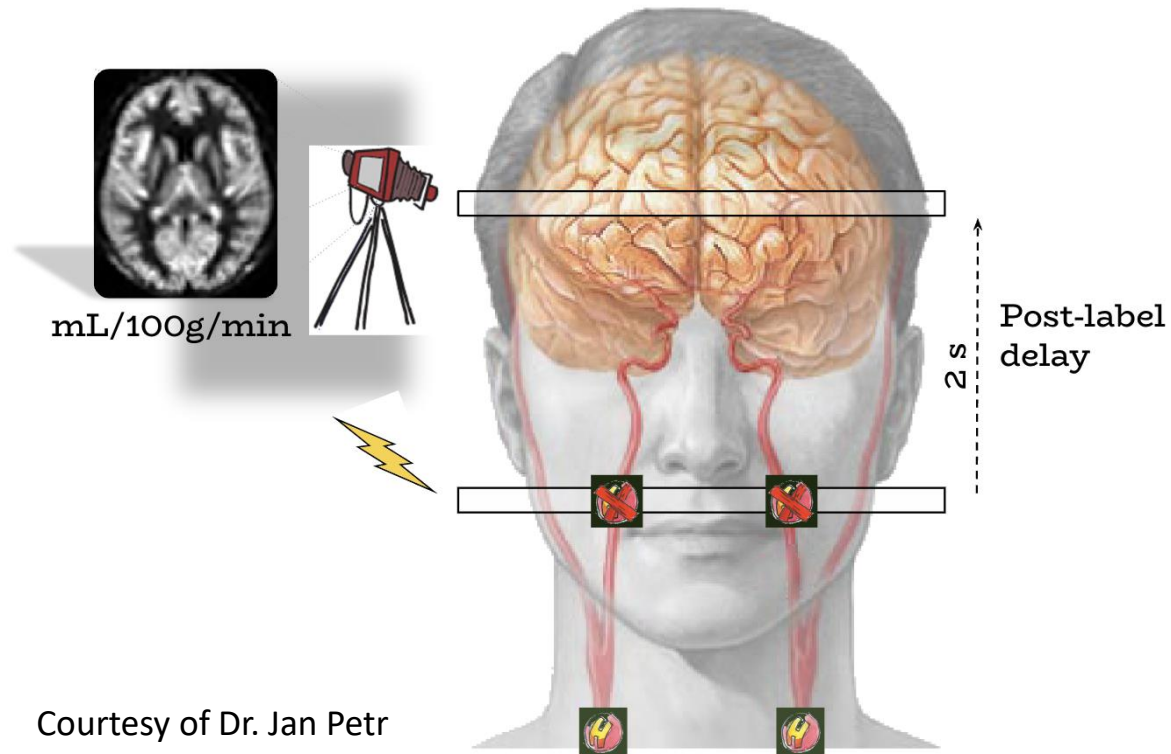
⑤ NPI



Recommended parameters of TIC



Multi-TE ASL for BBB imaging



+

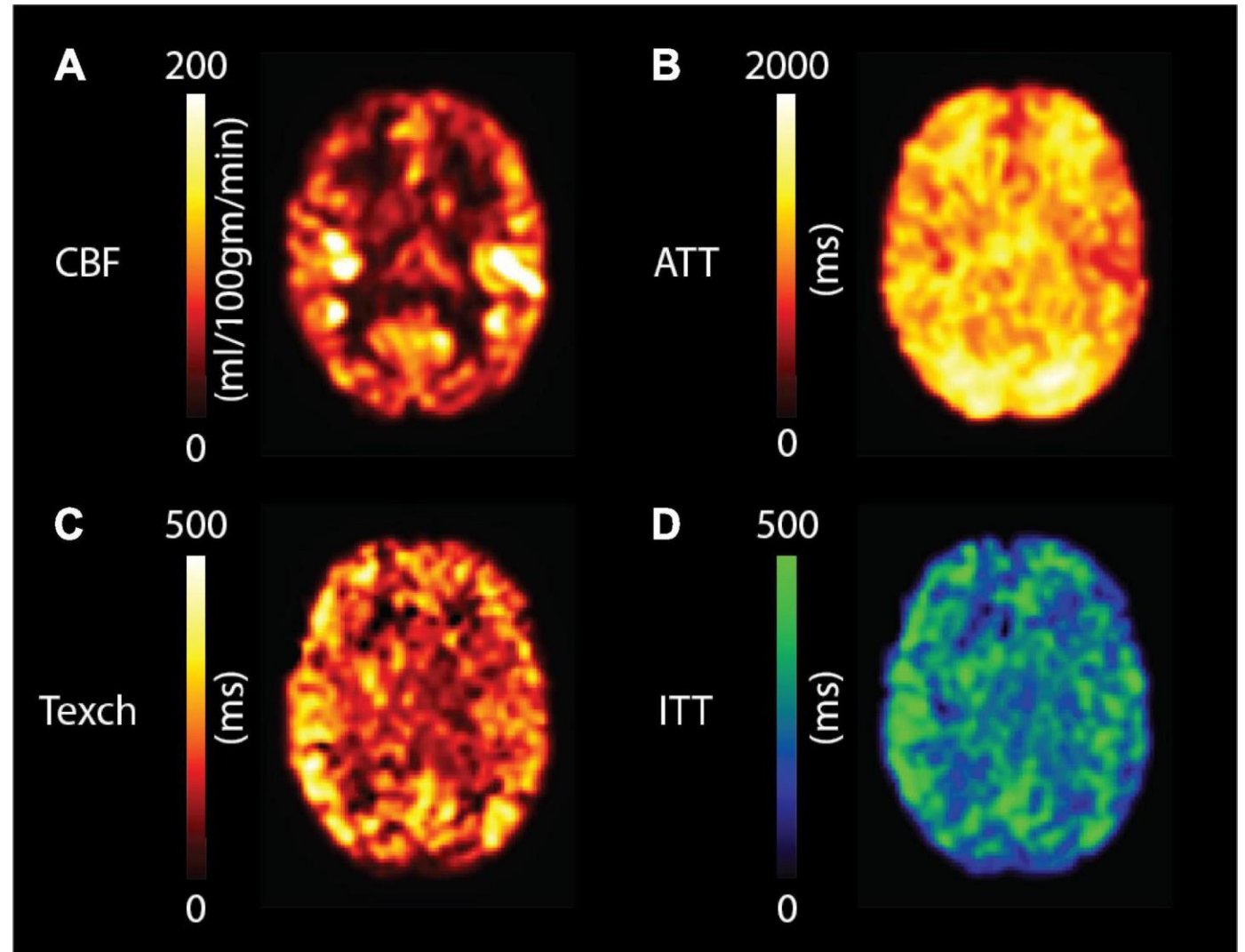
Refocusing pulses which allow signal compartmentalization

- difference in transverse relaxation time (T_2) which is longer for blood water molecules (~ 275 ms at 3T) than for water molecules in the brain tissue (~ 99 ms at 3T)
- Per-voxel subtraction to quantify water exchange rate

Courtesy of Dr. Jan Petr

BBB ASL

- **CBF** - cerebral blood flow
- **ATT** - arterial transit time
- **Texch** - exchange time
- **ITT** - intravoxel transit time



Neuroimaging team

- Jakub Otáhal
- Martin Kynčl
- David Kala
- Jan Šanda
- Yeva Prysiazhniuk
- Lukáš Michal
- Pavlína Pokošová
- Bruno Jurášek
- Jan Svoboda
- Zuzana Holubová
- Nora Profanotvá
- Šárka Danačíková
- Radek Janča
- Adéla Faridová
- Jan Brhel
- Veronika Borovcová
- Jan Daněk

Internal collaboration EpiReC:

- Petr Marusič
- Pavel Kršek
- Aleš Tomek
- Anna Olšerová
- Vlasta Šulc
- Petr Jánský
- Martin Kudr
- Petr Ježdík

