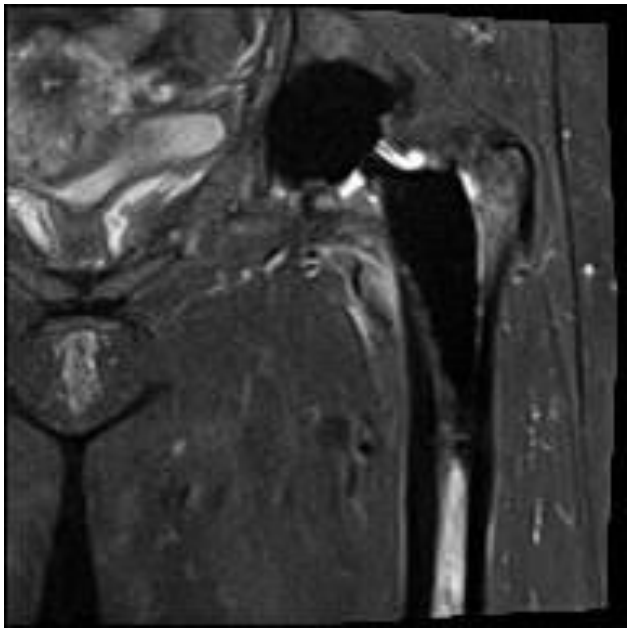
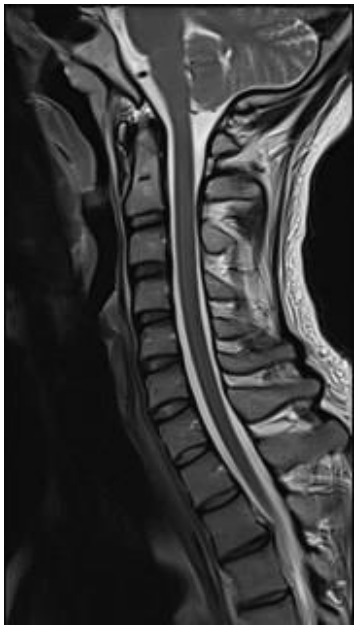
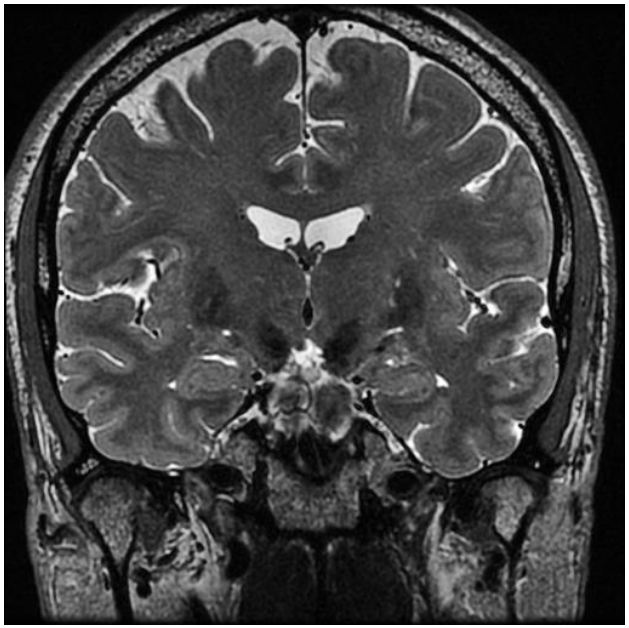
Magnetic Resonance Imaging

F.R.C.R. Physics Lectures

Lawrence Kenning PhD

7.8 Flow-related MR techniques

- Dynamic contrast-enhanced (DCE)
- Perfusion MRI
  - Dynamic susceptibility contrast (DSC)
  - Awareness of arterial spin labelling (ASL)
  - DCE for myocardial perfusion, oncology
- MR angiography (MRA) techniques,
  - Time of flight
  - Contrast-enhanced
  - Phase contrast

Dynamic Contrast Enhanced (DCE) MRI:

- Multiphase contrast enhanced T_1 weighted imaging
- Usually gradient echo based for rapid image acquisition
  - Sometimes with fat-sat (Gradient echo with Dixon fat nulling ideally)
- Image repeatedly at the same locations to observe enhancement and subsequent washout

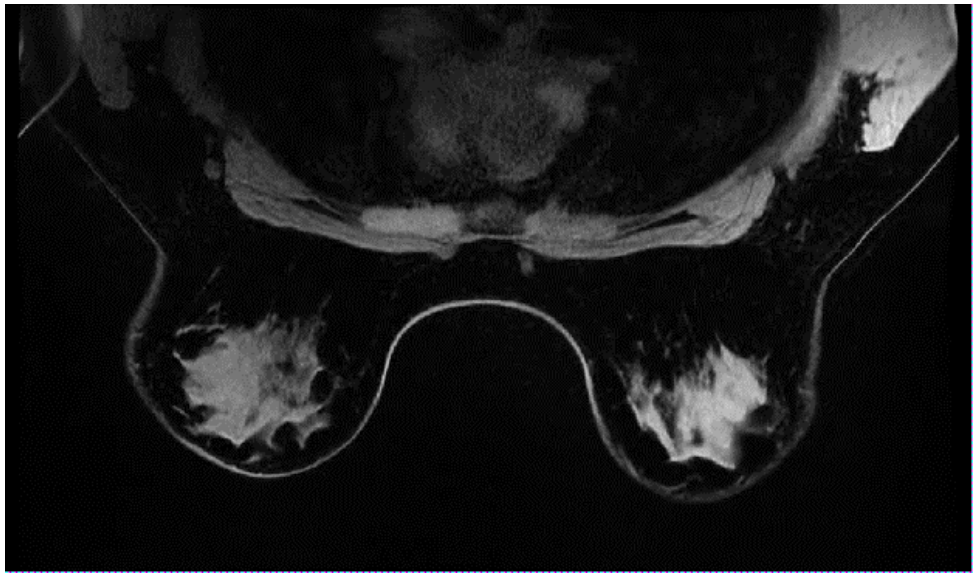


Image Acquisition

- Initial T_1 measurement so signal can be converted to concentration (PK modelling)
  - series of low flip angle images

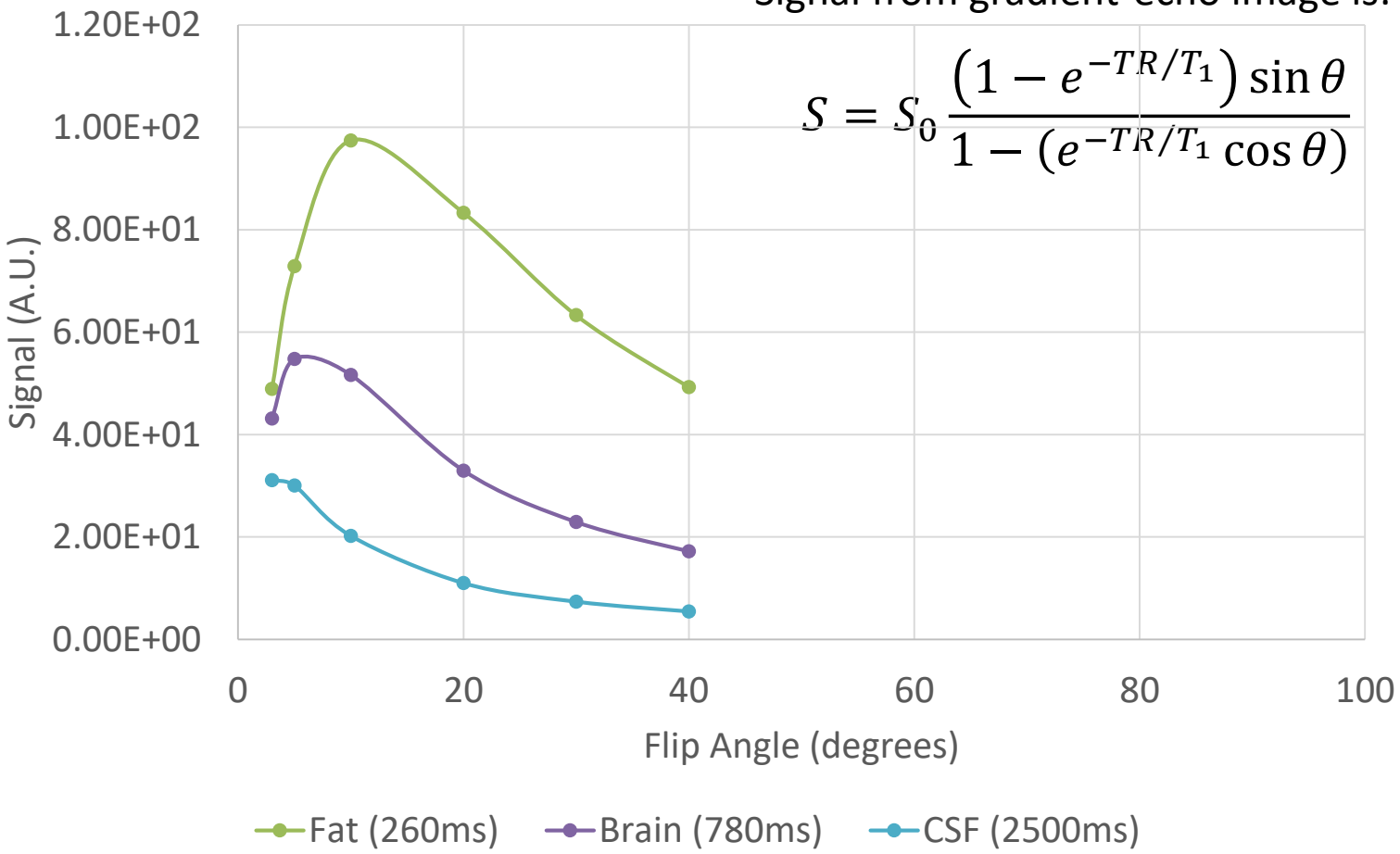
- Repeated T_1 weighted images are collected before, during and after contrast agent injection

- Bolus injection achieved using a power injector followed by saline flush

Variable Flip Angle T_1 Mapping

Signal from gradient-echo image is:

$$S = S_0 \frac{\left(1 - e^{-TR/T_1}\right) \sin\theta}{1 - \left(e^{-TR/T_1} \cos\theta\right)}$$



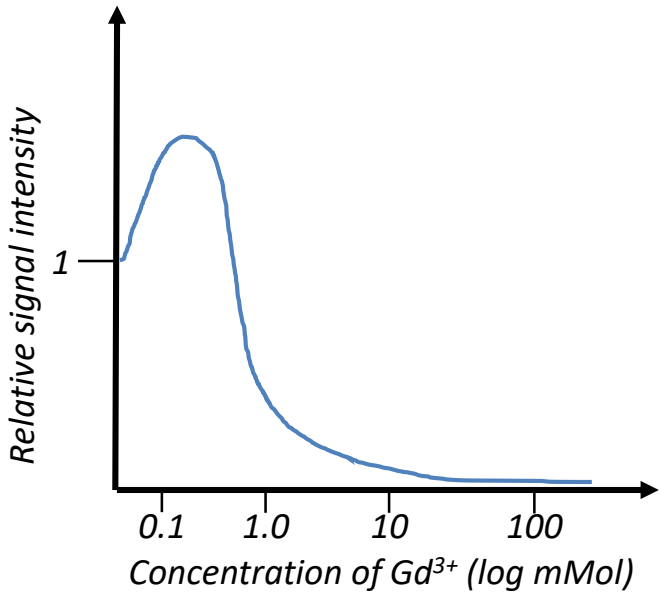
Dynamic contrast-enhanced (DCE)

- Gd^{3+} affects both the longitudinal and transverse relaxation rates

$$\frac{1}{T_1} = \frac{1}{T_{10}} + r_1 C \qquad \frac{1}{T_2} = \frac{1}{T_{20}} + r_2 C$$

$T_{1(2)}$ are the reduced relaxation times
$T_{10(20)}$ are the native relaxation times
$r_{1(2)}$ are the contrast agent relaxivities
C is the concentration of contrast

- T_1 shortening effect leads to increase in signal on T_1 weighted image
- T_2 shortening effect leads to decrease in signal on T_2* weighted image
- At high concentration T_2 shortening effect will predominate



Ideal Dynamic Sequence

- Excellent temporal resolution (< 5 secs)
- Volumetric acquisition
- Isotropic spatial resolution (< 1 mm)
- Excellent fat/water suppression
- High sensitivity to contrast agent

Spatial vs. Temporal Resolution

- For a standard T_1 weighted sequence acquisition time for a single slice is:

$$Acquisition\ time = N_y \times TR \times NEX$$

N_y – number of phase encoding steps
TR – repetition time
NEX – number of averages

- Temporal resolution, Δt for multiple slices is therefore:

$$\Delta t = N_y \times TR \times NEX \times N_z$$

N_z – number of slices

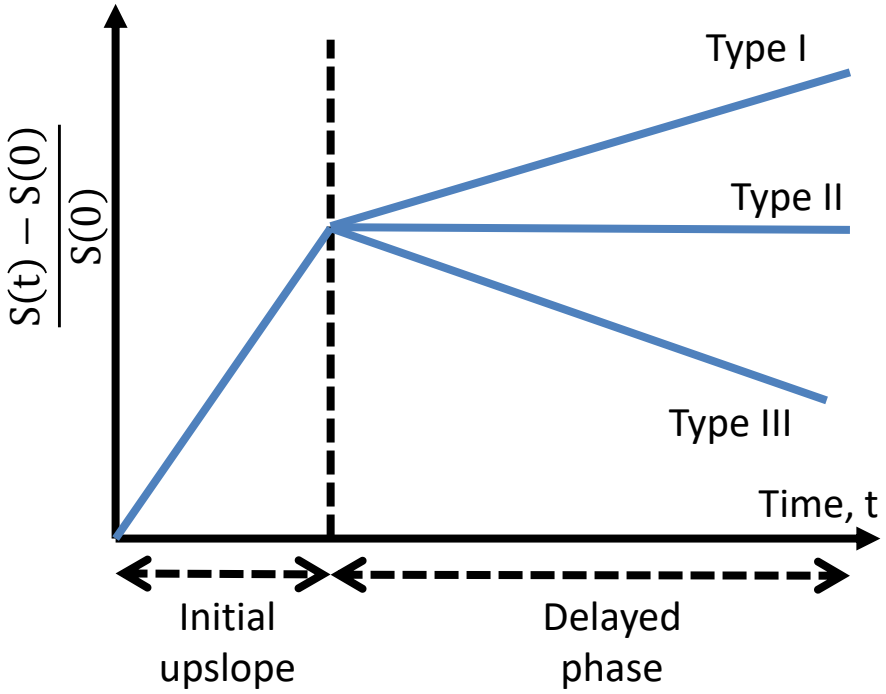
- So for DCE (or any 4D MRI) the acquisition is a trade-off between high temporal or high spatial resolution.
- Prostate – high temporal resolution (~15secs).
- Breast low temporal resolution (45-60 secs)

DCE Image Analysis

- Can analyse DCE data with varying levels of complexity
- Can depend on data available
- Visual inspection
- Empirical analysis
- Pharmacokinetic modelling

Visual Inspection

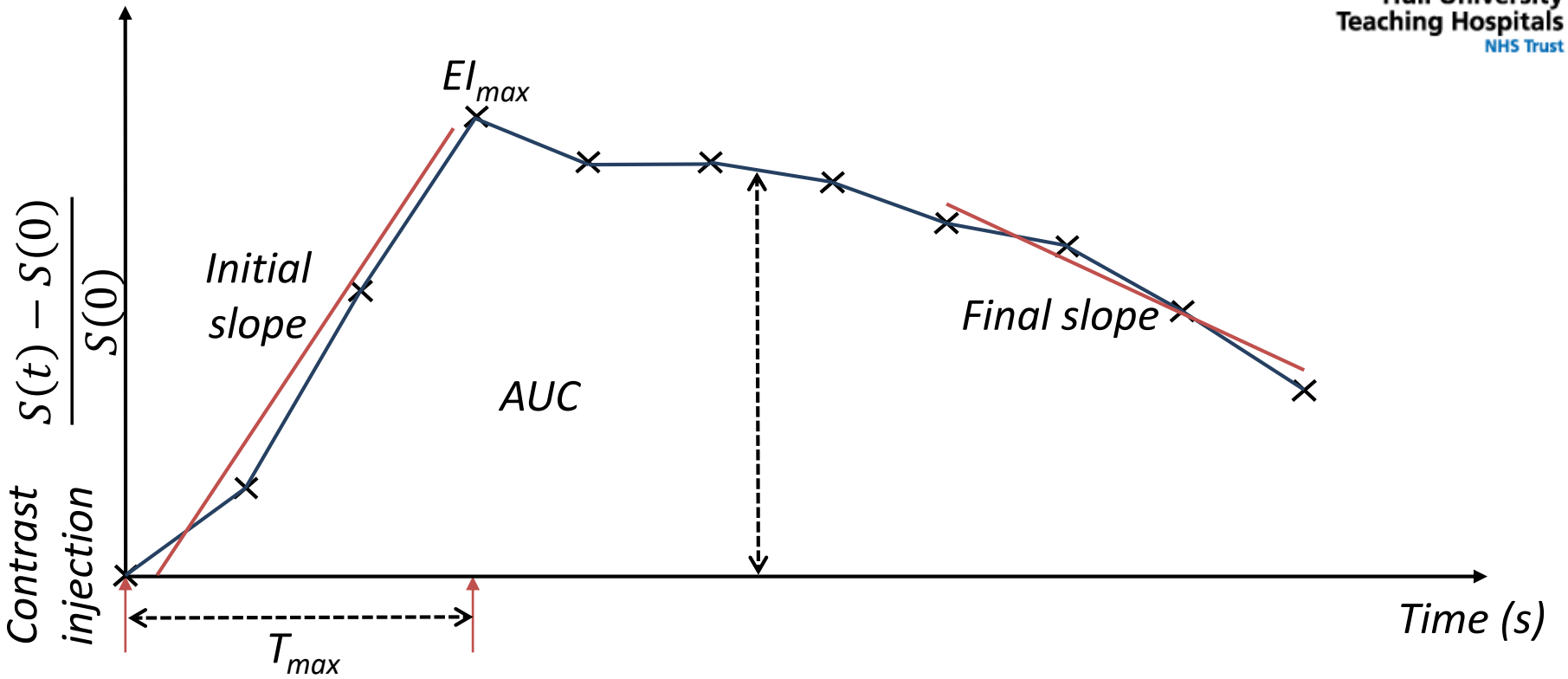
- Type I – progressive enhancement pattern
  - continuous increase in signal
  - considered benign
- Type II curve – plateau pattern
  - initial uptake followed by plateau
  - concerning for malignancy
- Type III curve – washout pattern
  - rapid uptake and then reduction in enhancement
  - strongly suggestive of malignancy



Empirical Analysis

- Many empirical metrics available
  - often related to point of inflexion (maximum enhancement)
- Quick and easy to obtain
- No real physiological meaning
- Probably not comparable across imaging units

Dynamic contrast-enhanced (DCE)



T_{max} – time to maximum enhancement

EI_{max} – relative enhancement at $T_{max,}$

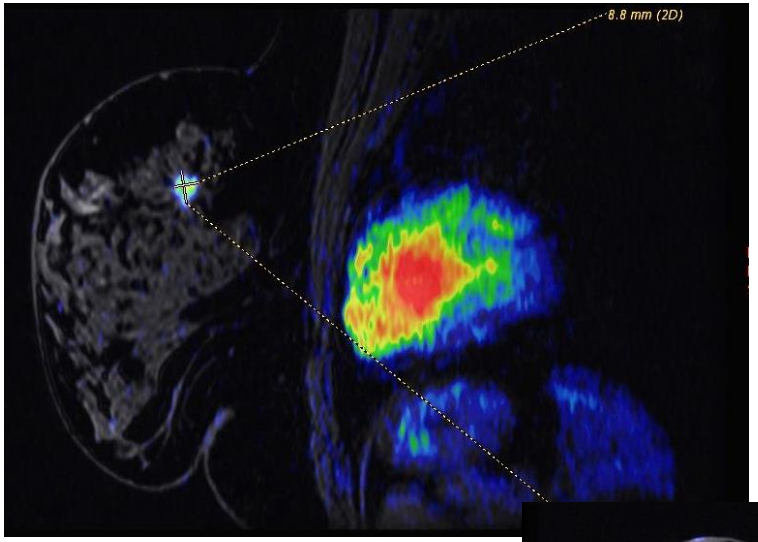
AUC_t – area under the curve (positive enhancement integral)

Initial and *final slope* – rate of change of enhancement per unit time during upslope and washout respectively

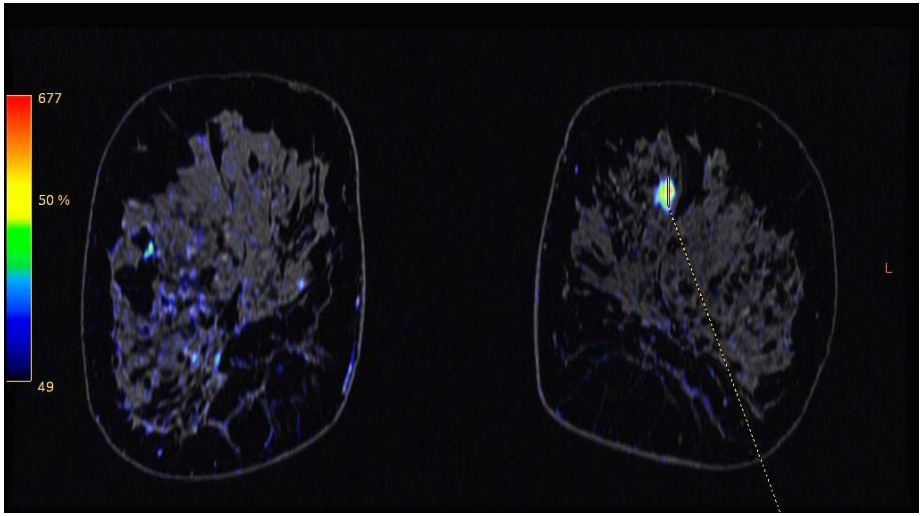
Dynamic contrast-enhanced (DCE) / DCE for oncology

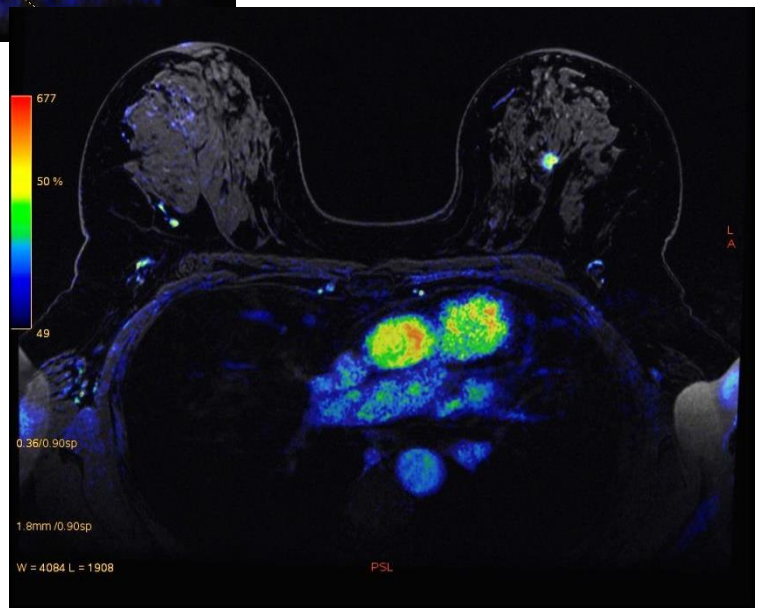
NHS
Hull University Teaching Hospitals
NHS Trust

Breast Malignancy

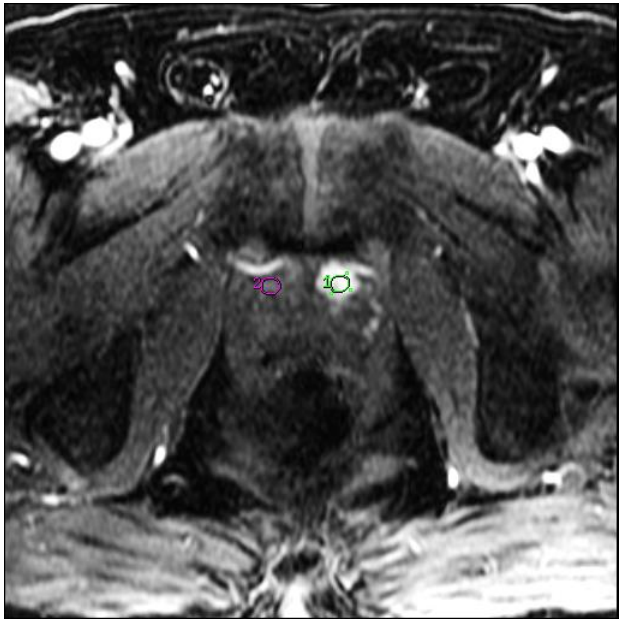


Percentage enhancement curves

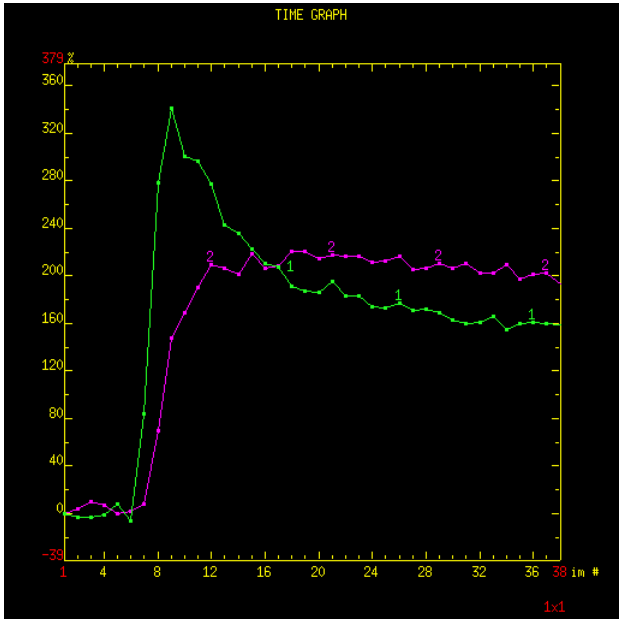




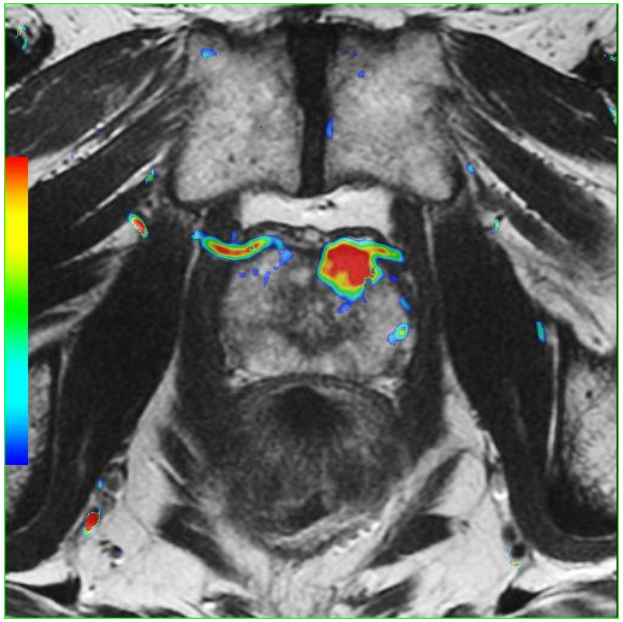
Prostate Malignancy



LAVA-FLEX source data



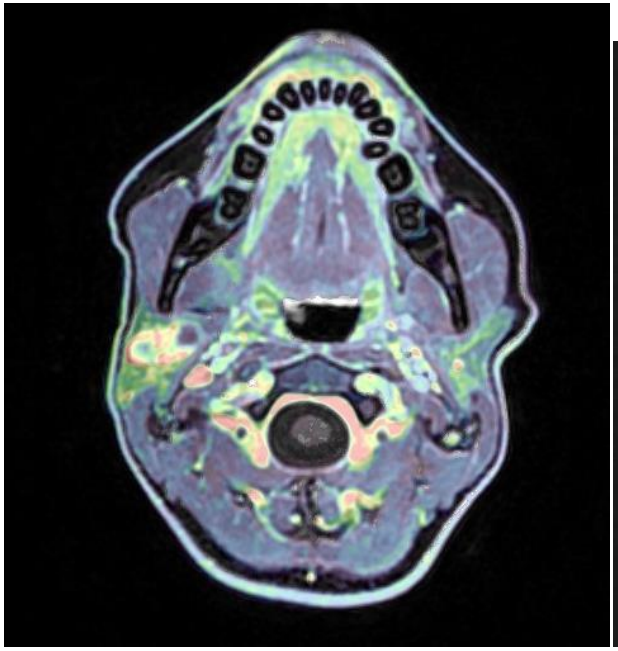
Percentage enhancement curves



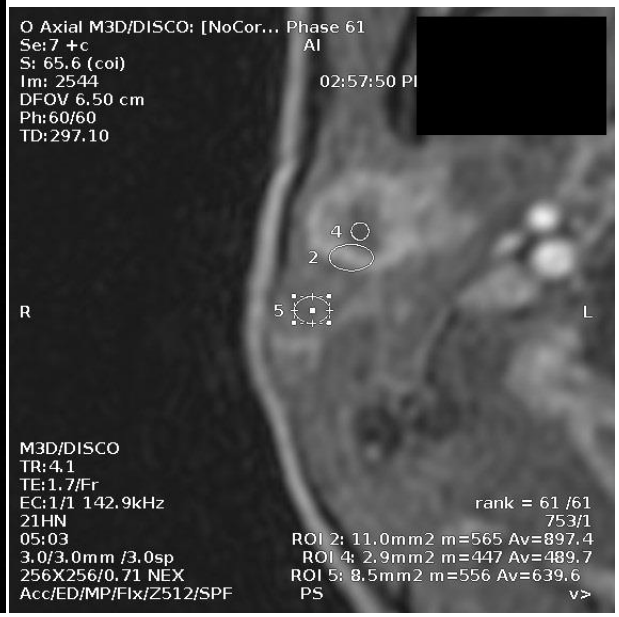
Positive integral enhancement map overlaid onto T2 FSE

Dynamic contrast-enhanced (DCE) / DCE for oncology

Hull University Teaching Hospitals NHS Trust



Enhancement integral enhancement map overlaid onto T1 LAVA-FLEX +C



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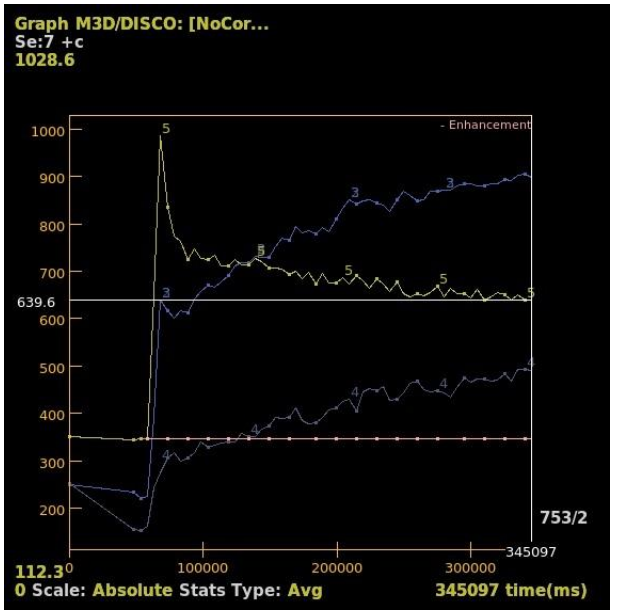
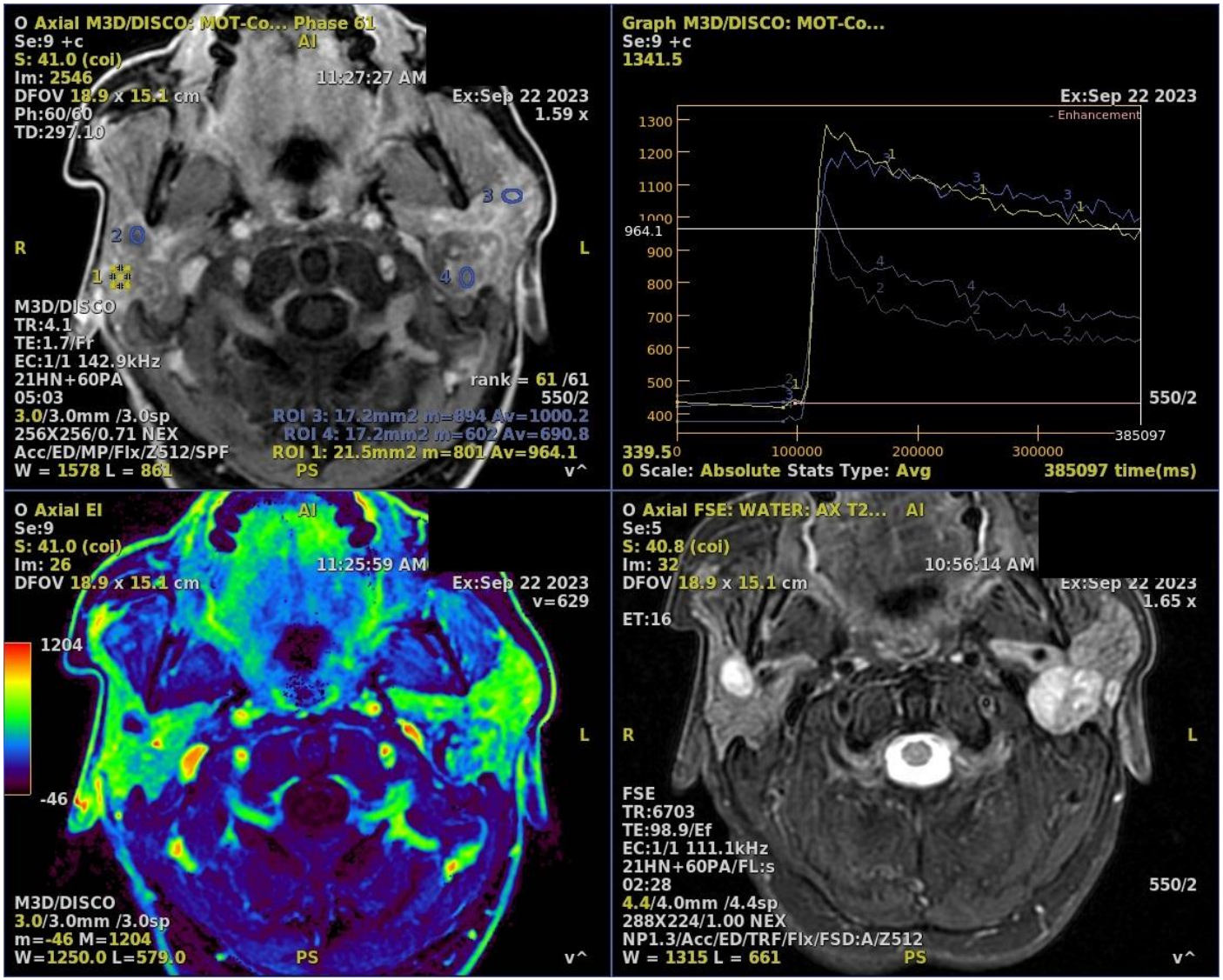


Enhancement curves

Dynamic contrast-enhanced (DCE) / DCE for oncology



DCE for myocardial perfusion

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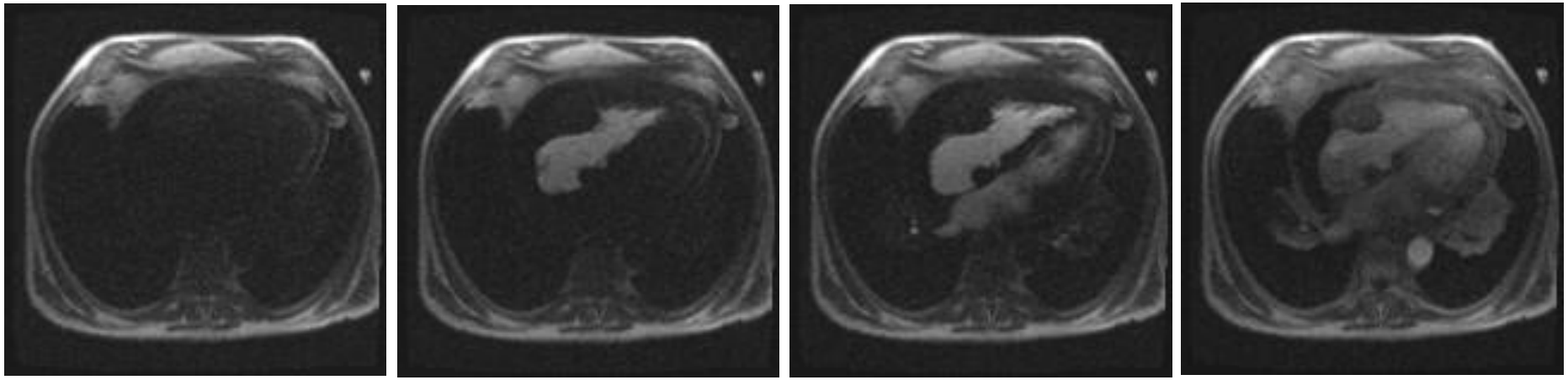
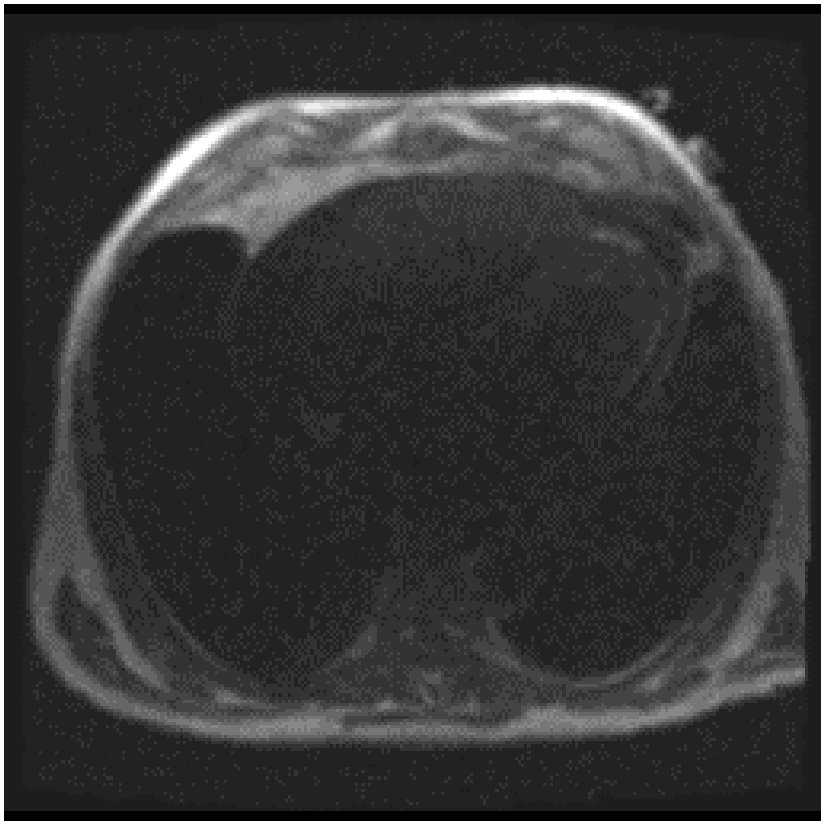
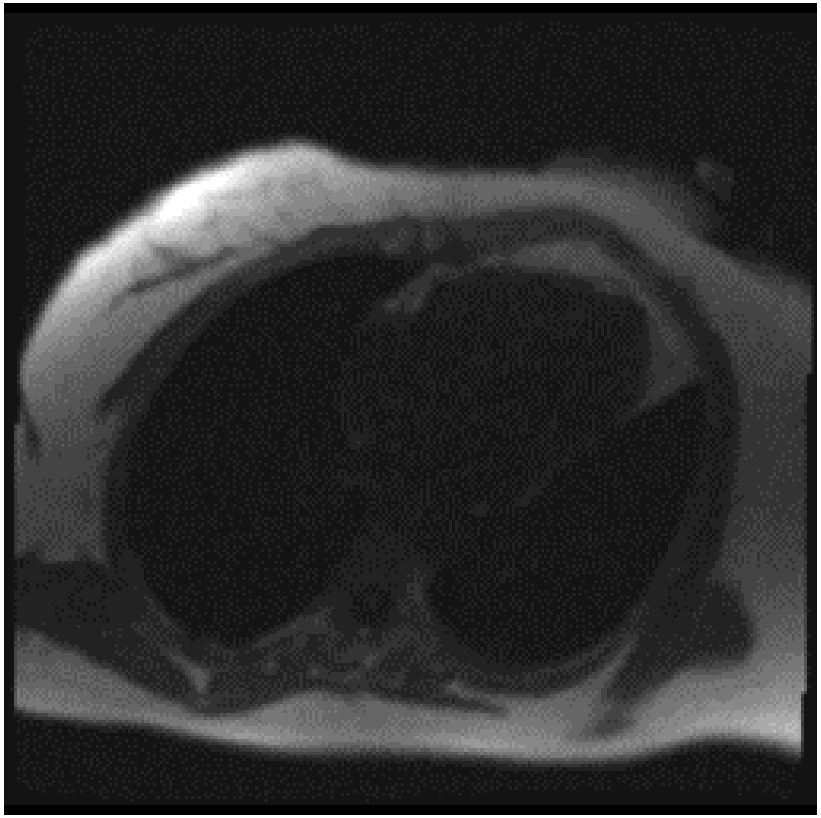
Dynamic contrast enhanced perfusion CMR tracks and displays the first passage of an injected contrast agent bolus through the heart.

- pre-contrast arrival
- contrast arrival in the right ventricle
- contrast arrival in the left ventricle (LV)
- contrast arrival in the myocardium



DCE for myocardial perfusion





Pharmacokinetic Modelling

- Models how contrast agent distributes in the body
- Model is independent of imaging conditions
  - field strength
- Simplest model has one tissue and one vascular compartment
- Model applicability is dependent on image acquisition details
  - temporal resolution
  - overall sampling time

Dynamic contrast-enhanced (DCE)

Sampling Rate \ Acquisition Time	Short (<60 s)	Intermediate (60-600 s)	Long (>600 s)
High (1-3 s)	$v_p\ F_t$ *First pass model*	$v_p\ F_t\ PS$	$v_p\ F_t\ PS\ v_e$ *Comprehensive model*
Intermediate		$v_p\ PS$ *Patlak model*	$v_p\ PS\ v_e$ *Extended Kety model*
Low (30-60 s)			$K^{trans}\ v_e$ *Tofts model*

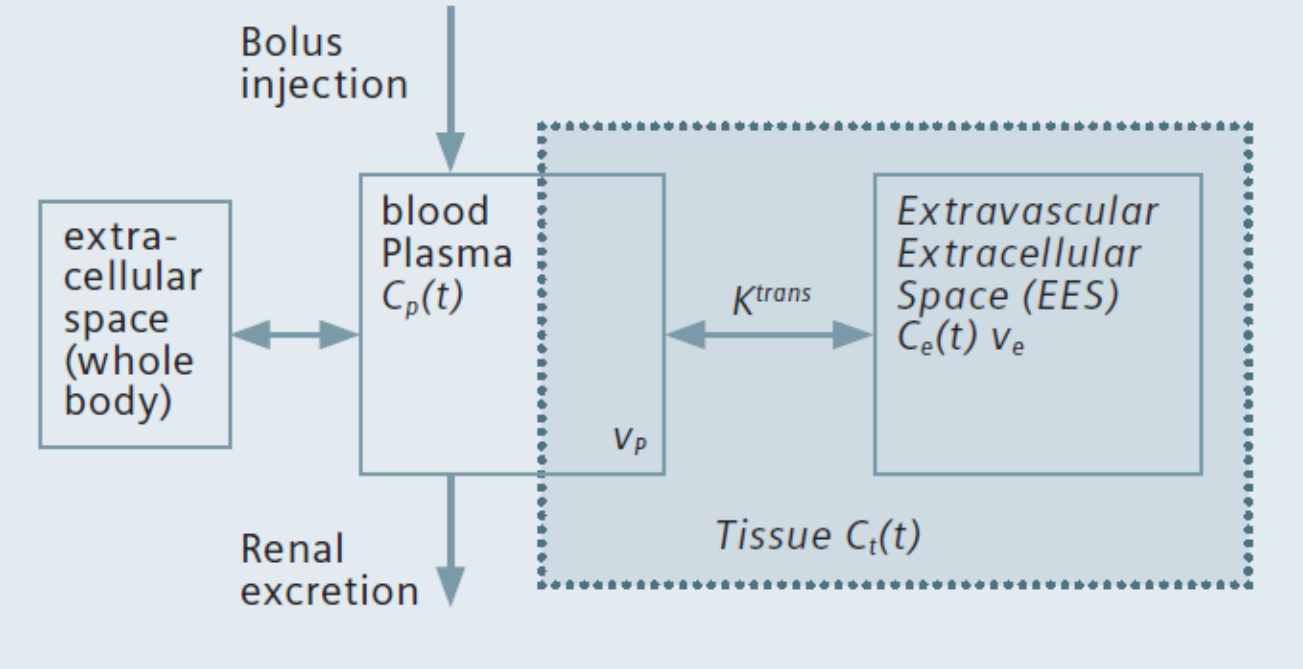
v_p – fractional volume of blood tissue in plasma, F_t – flow rate in tissue

PS – permeability surface area product, K^{trans} – transfer constant

v_e – fractional volume of extravascular extracellular space

Compartmental Models

- Simplest model has one tissue and one vascular compartment
  - so called 'Tofts model' (equivalent to Kety model)



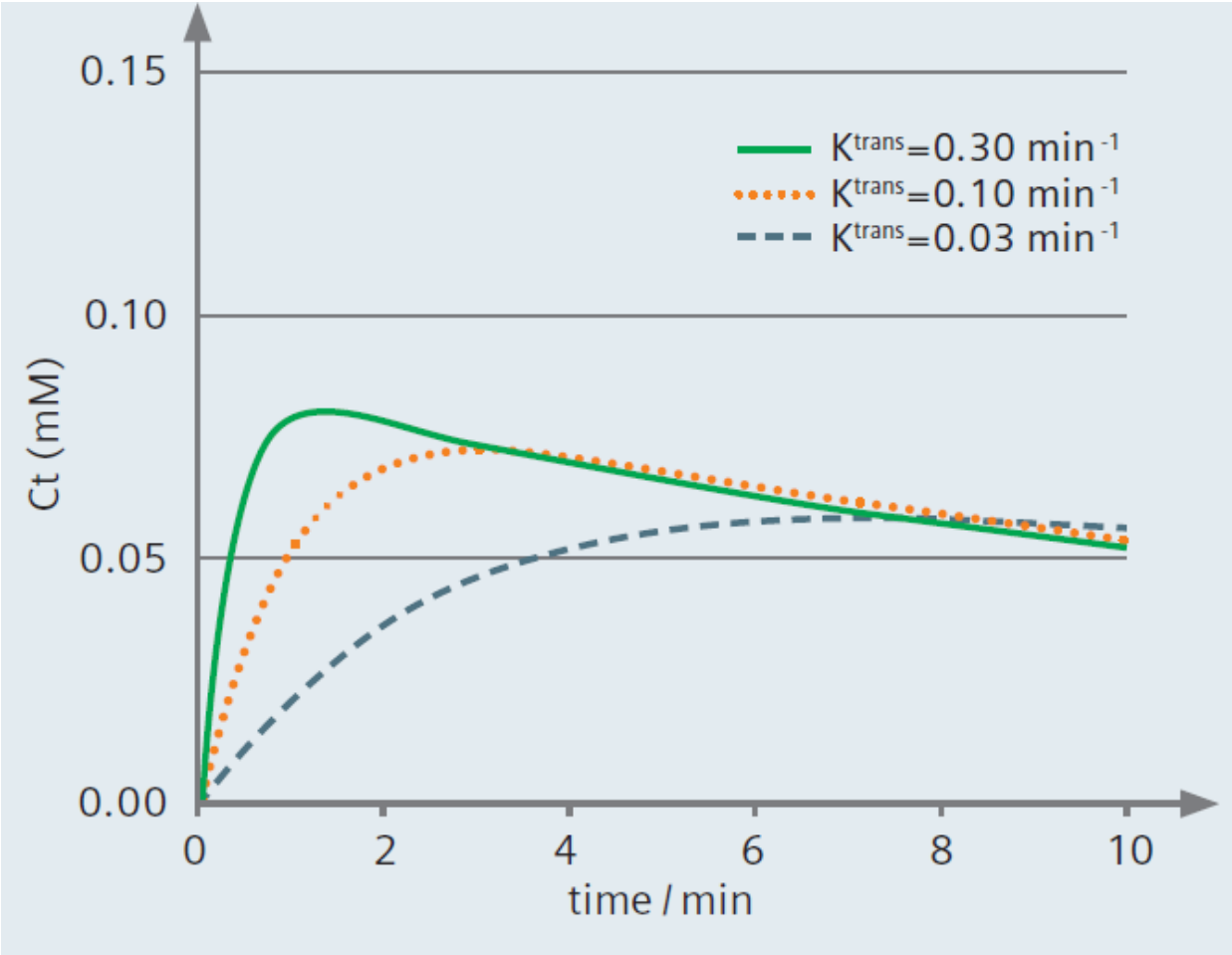
- Injection of Gd^{3+} gives a time-varying blood plasma concentration $C_p(t)$
  - measure in each subject (need $\Delta t < 3$ s)
  - use population average

K^{trans} – Transfer Constant

- Characterises the diffusive transport of low-molecular weight Gd^{3+} chelates across the capillary endothelium
- Used in assessing anti-angiogenic and anti-vascular therapies
- Leakage low enough then K^{trans} is permeability surface area product
  - multiple sclerosis lesions
  - ‘permeability’ imaging
- When permeability is high then then K^{trans} represents perfusion
  - tumour imaging
  - ‘perfusion’ imaging

Dynamic contrast-enhanced (DCE)

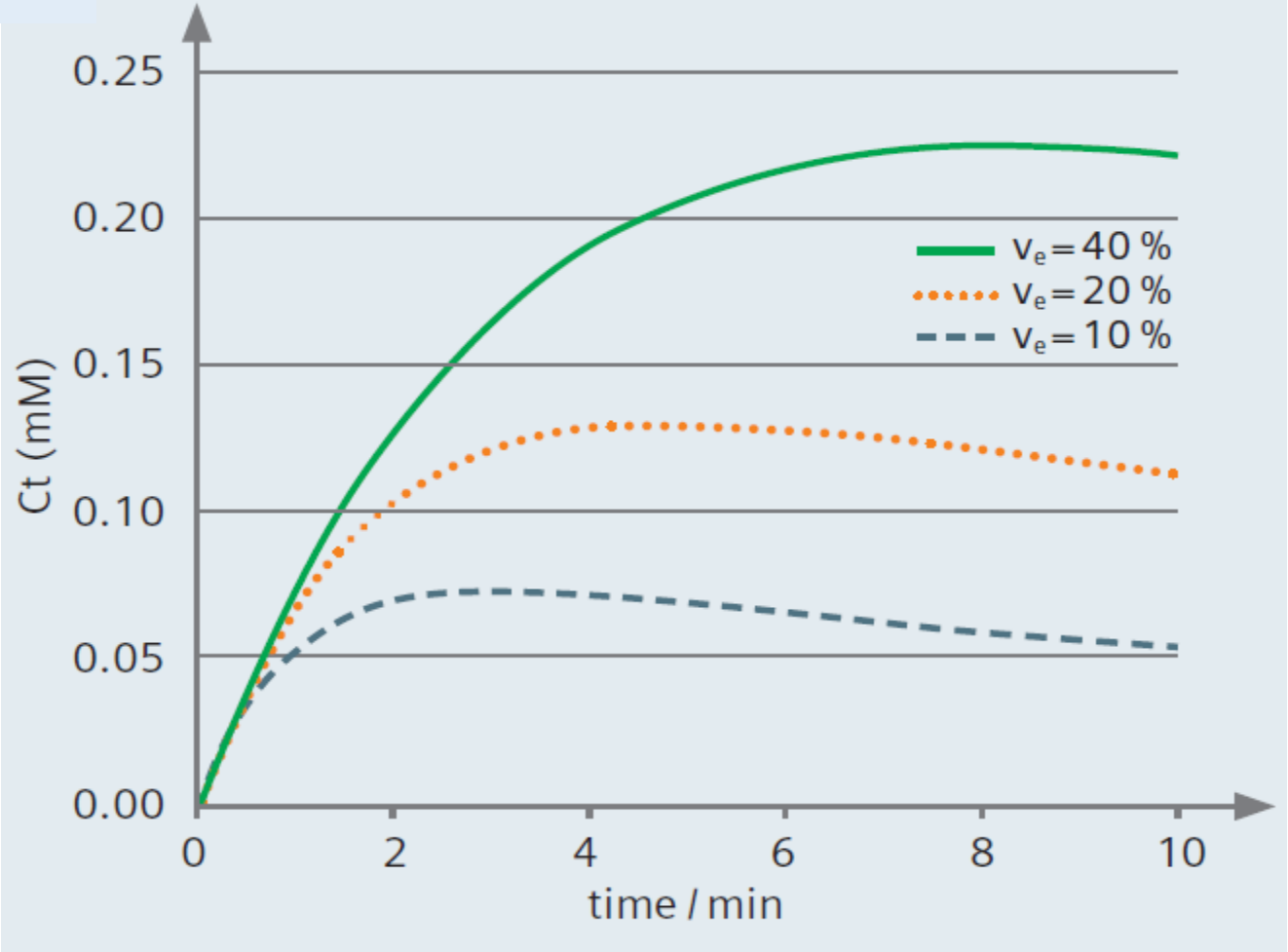
- Initial slope depends heavily on K^{trans}
  - higher K^{trans} corresponds to steeper slope



v_e – Fractional Volume of EES

- Gd^{3+} concentration sum of EES (v_e) and intravascular (v_p) contributions
- EES contribution dominates since v_e ~ 10-60 %
  - v_p is often small and ignored (~ 1-10%)
- Final peak value depends heavily on v_e
- Acquire data for long enough to sample the enhancement plateau
  - else v_e cannot be reliably measured

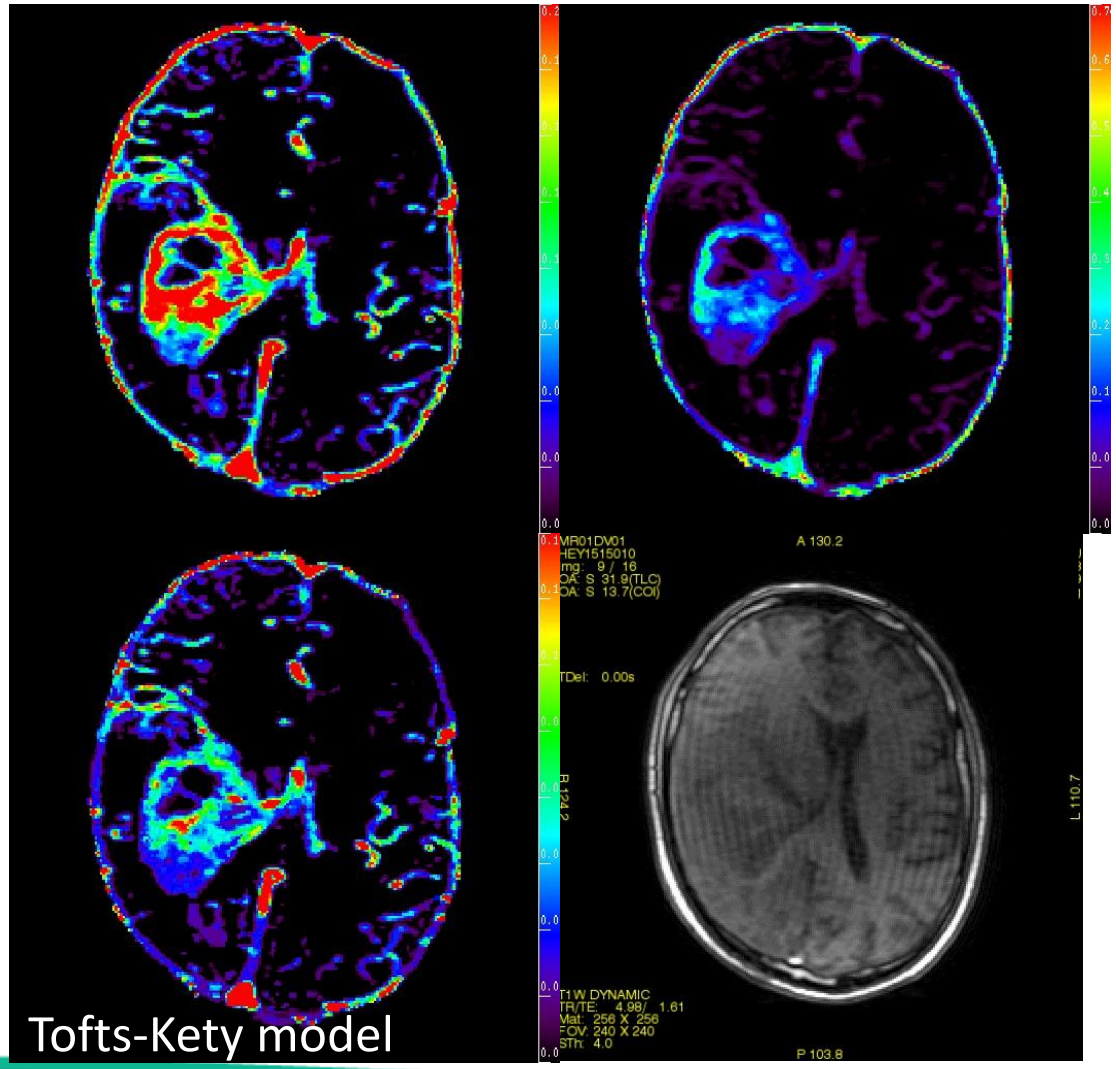
Dynamic contrast-enhanced (DCE)



Glioblastoma Multiforme

K^{trans} min^{-1}
(Permeability)

v_b
(blood volume fraction)

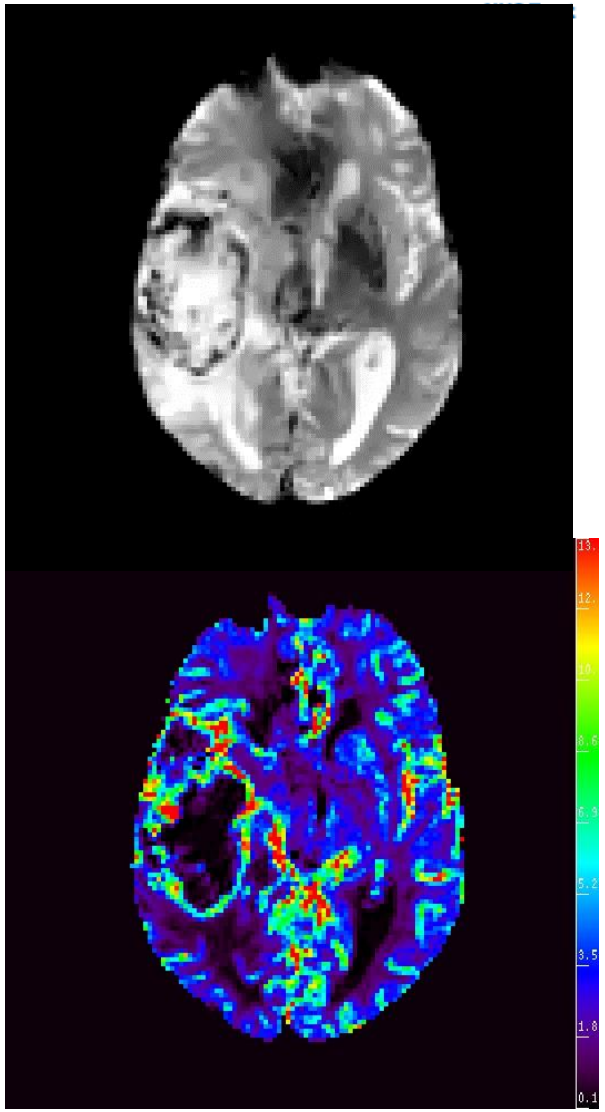


v_e
(extravascular extracellular space fraction)

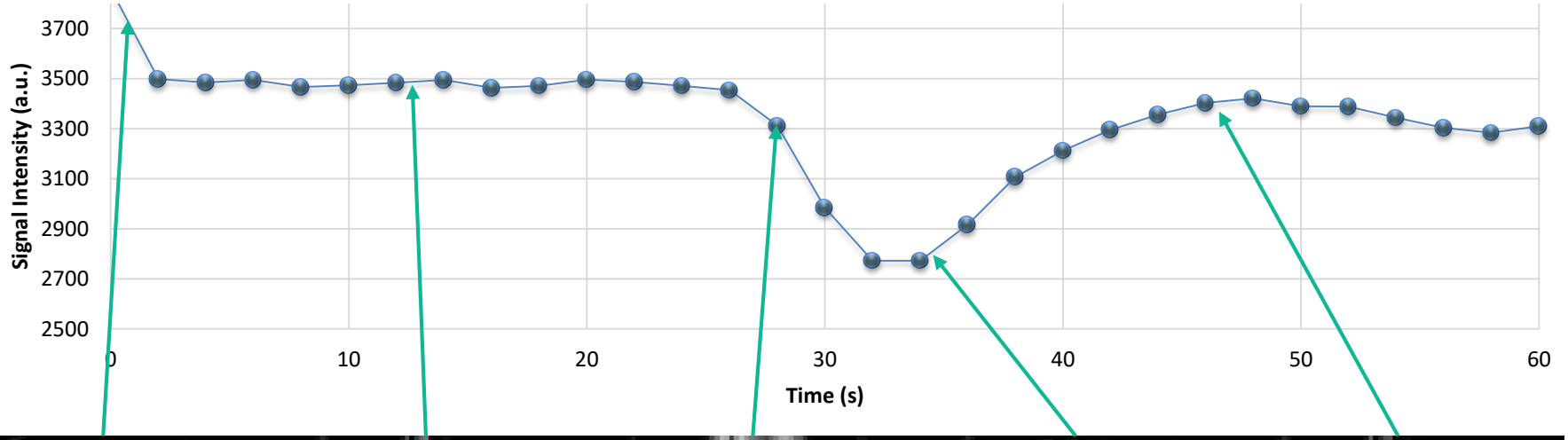
T_1 FSPGR

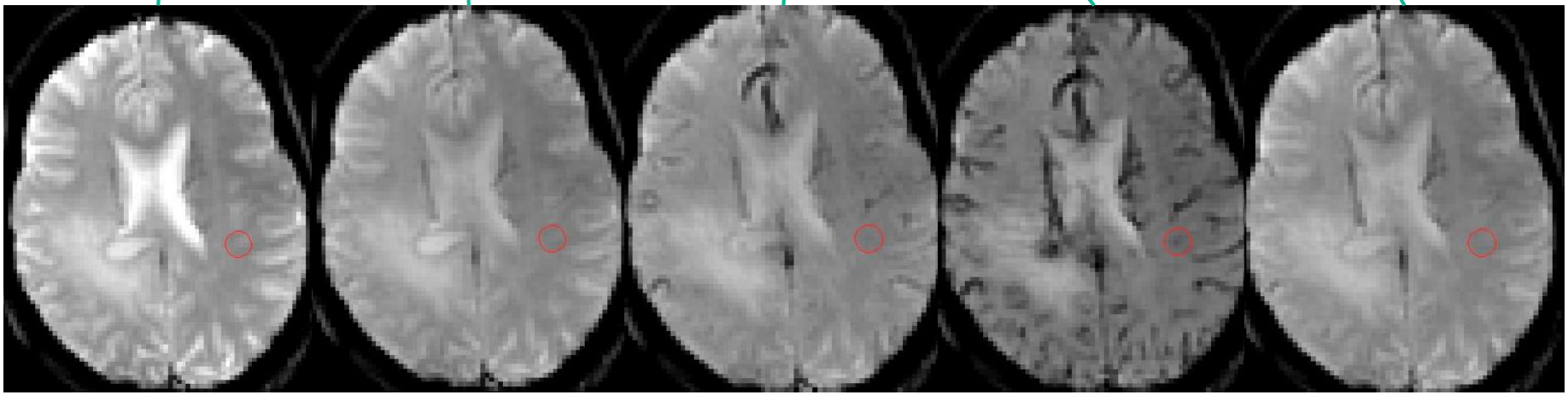
Overview of DSC MRI:

- Analyse dynamic signal changes following a bolus of Gd^{3+} contrast agent
- Observe first pass through tissue using a series of T_2- or T_2*-weighted MR images
- Susceptibility effect of the paramagnetic contrast agent leads to a signal decrease
- Signal can be converted to concentration
- Generate parametric maps for (relative) CBV, CBF and MTT

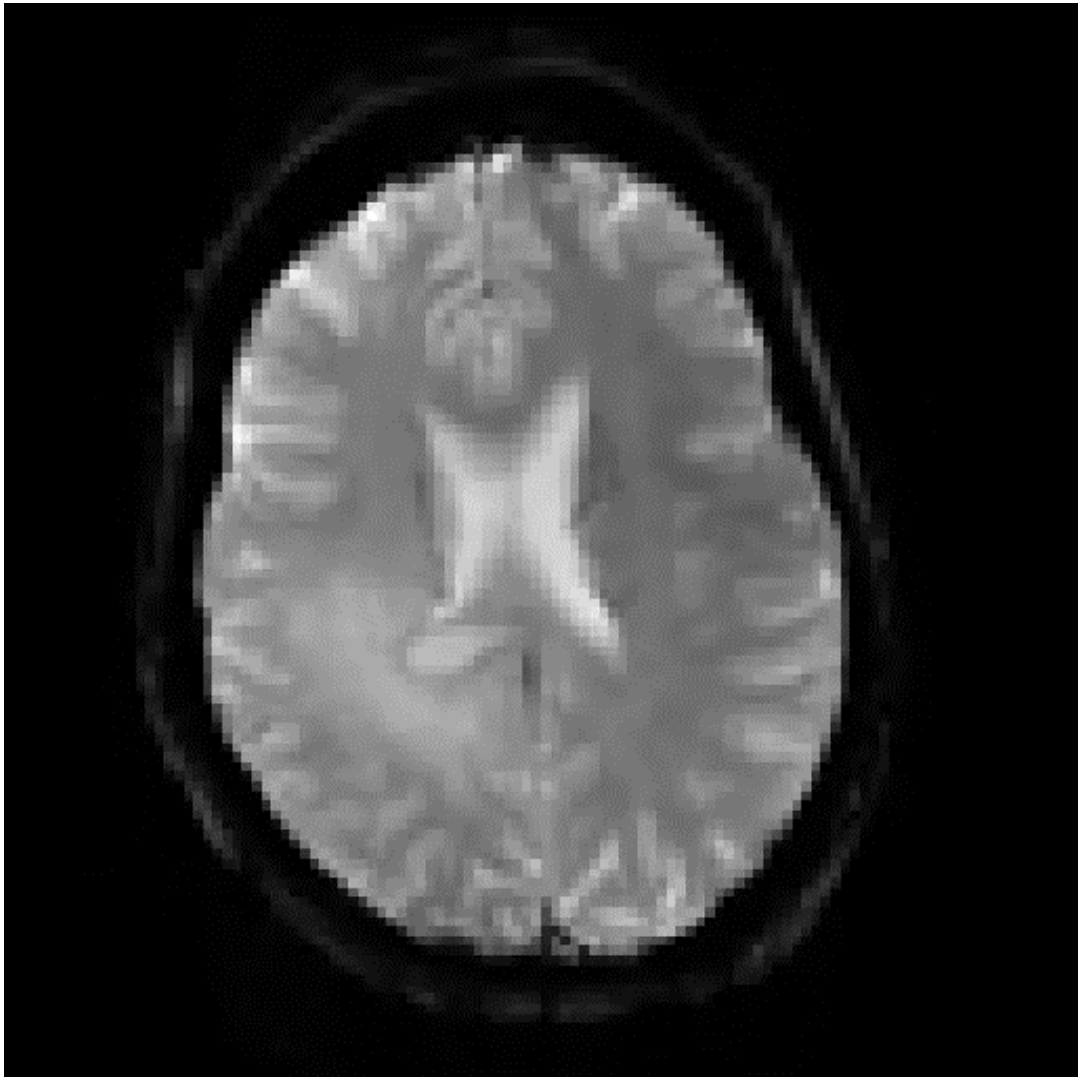


The Signal Time Course

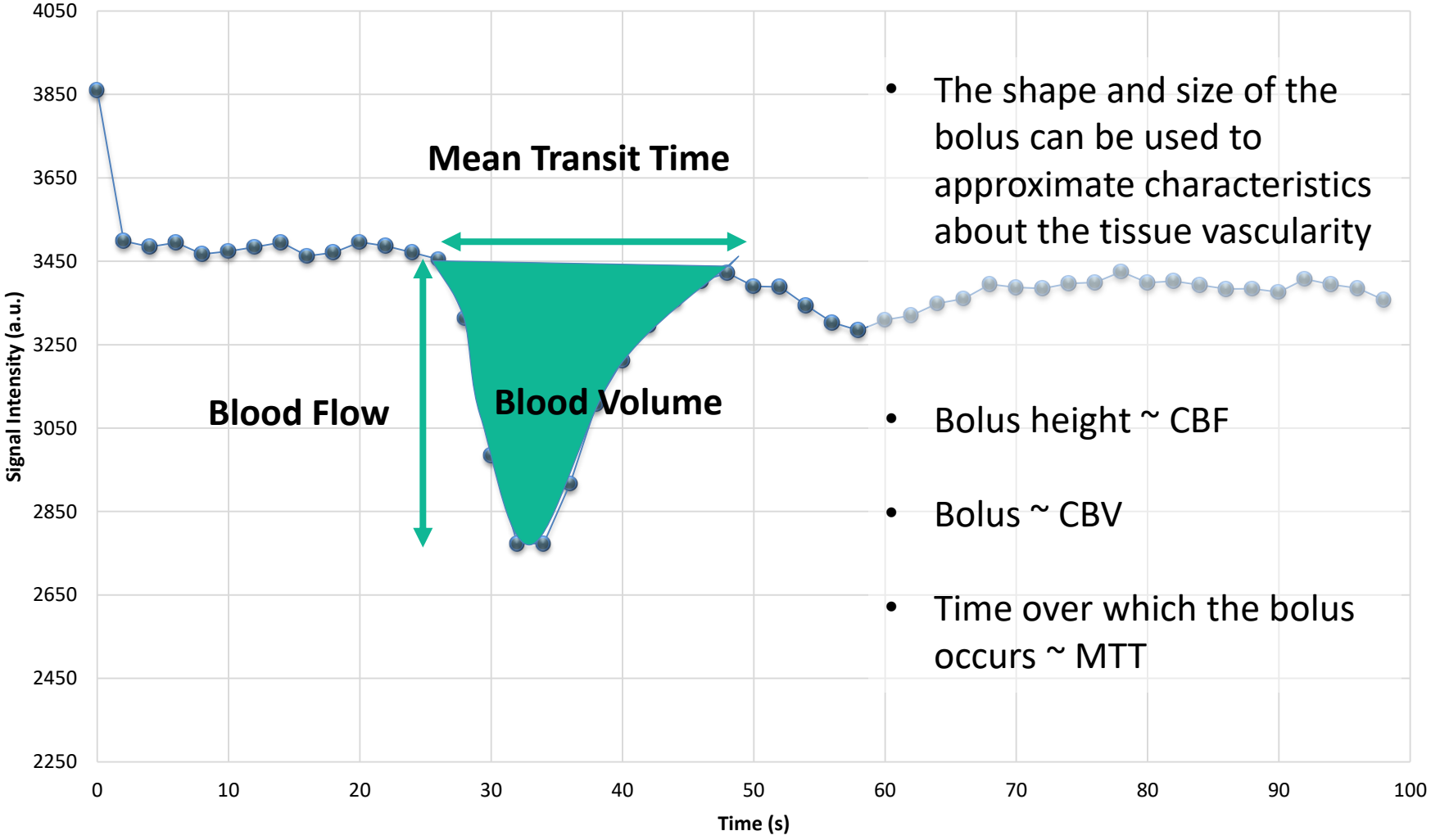




Dynamic susceptibility contrast (DSC)

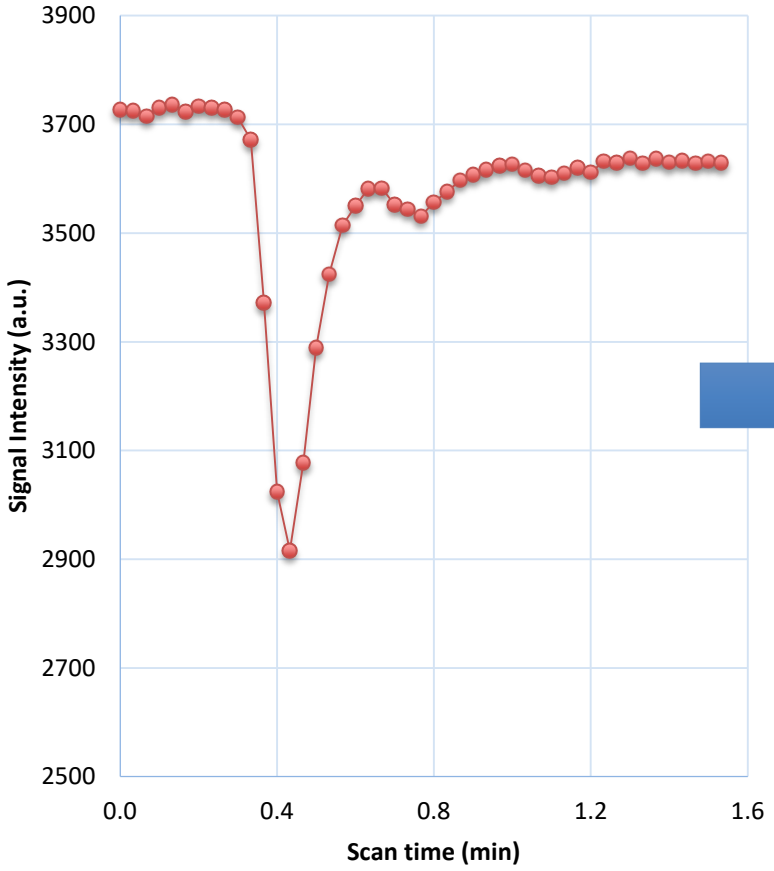


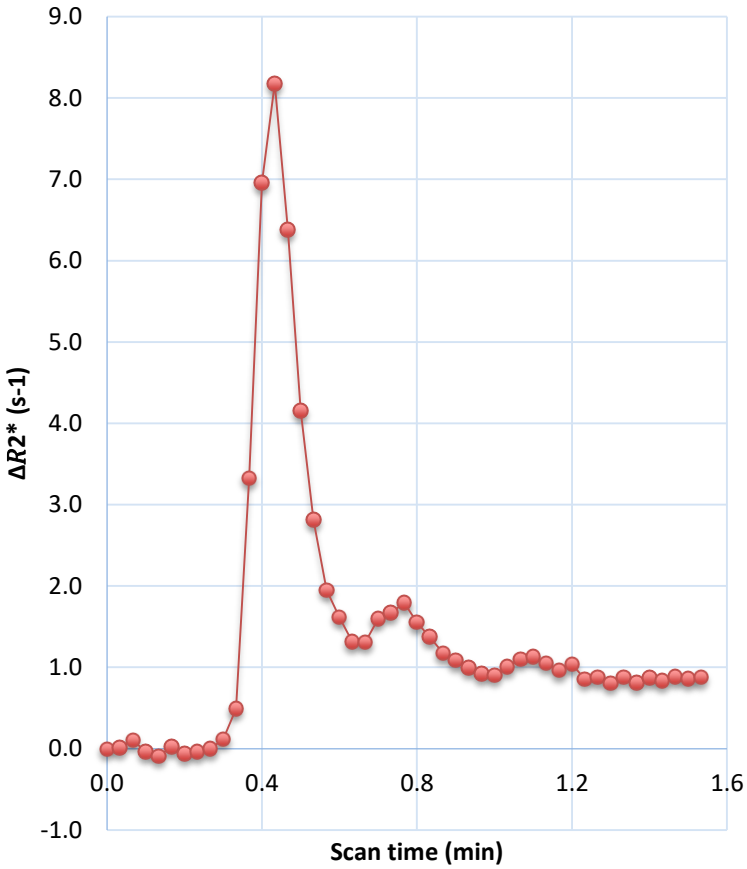
The Signal Time Course



- The shape and size of the bolus can be used to approximate characteristics about the tissue vascularity
- Bolus height ~ CBF
- Bolus ~ CBV
- Time over which the bolus occurs ~ MTT

Signal to Concentration:

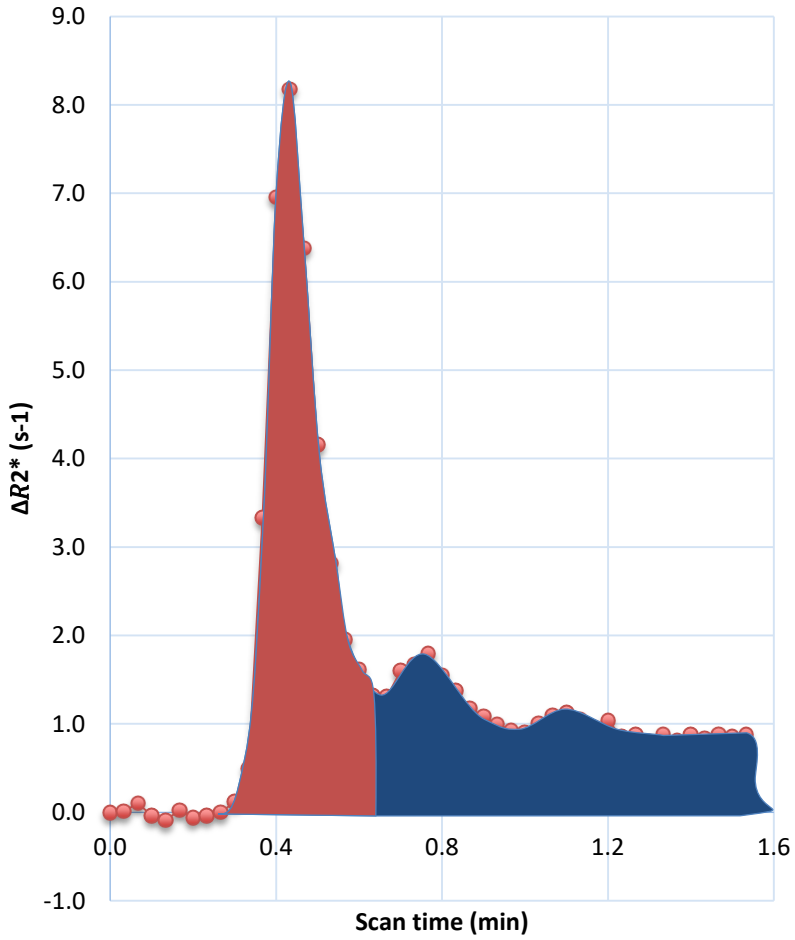


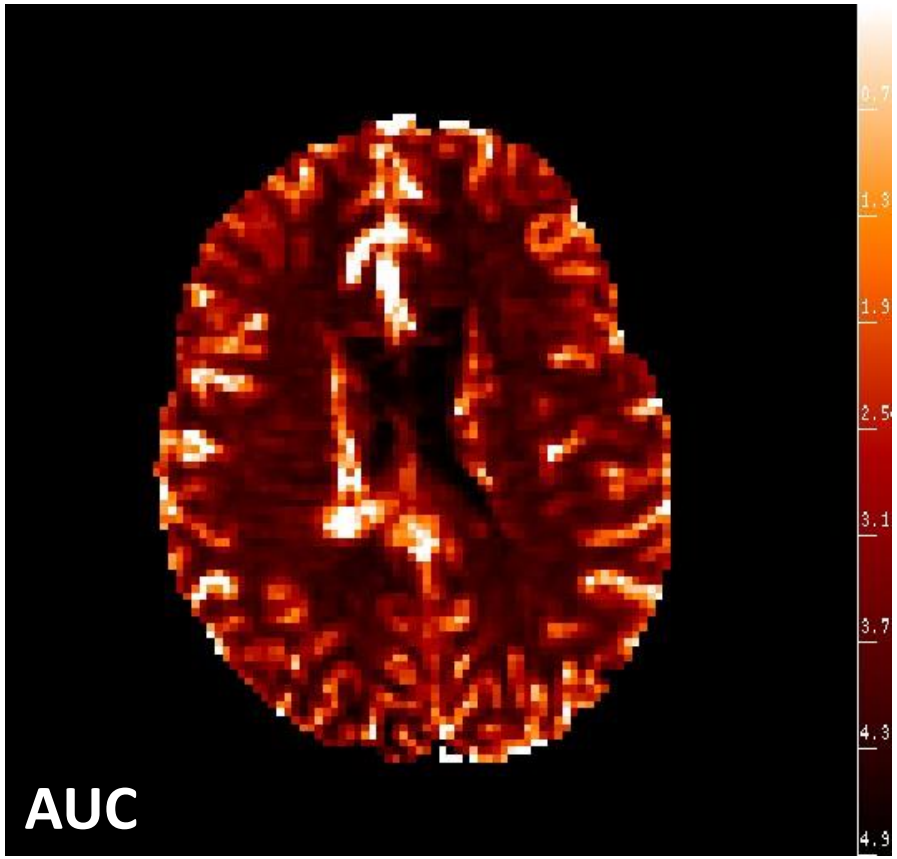


$$\Delta R_2^*(t) = -1/TE \; ln(S(t)/S_0)$$

Dynamic susceptibility contrast (DSC)

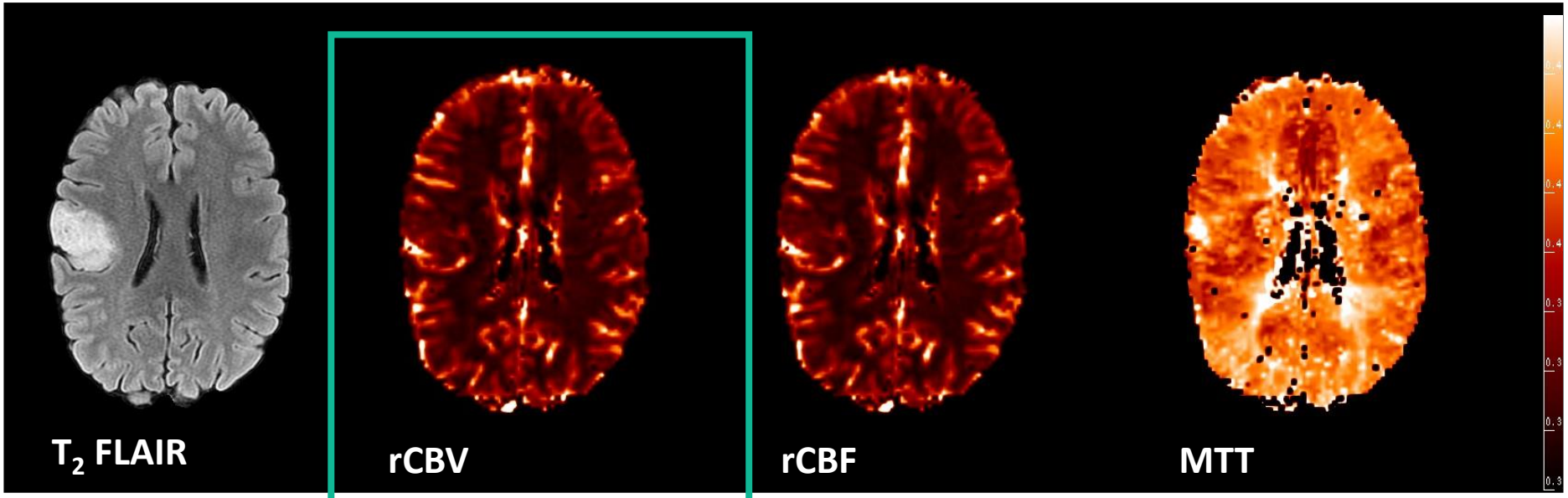
Area Under Curve / Negative Enhancement Integral:





Dynamic susceptibility contrast (DSC)

DSC Derived Parameters



- ml of blood per 100g of brain (%)
- rCBV (%) = ΔR_2* brain / ΔR_2* artery
- Typically 3-5% in brain
- Most common DSC parameter for oncology imaging

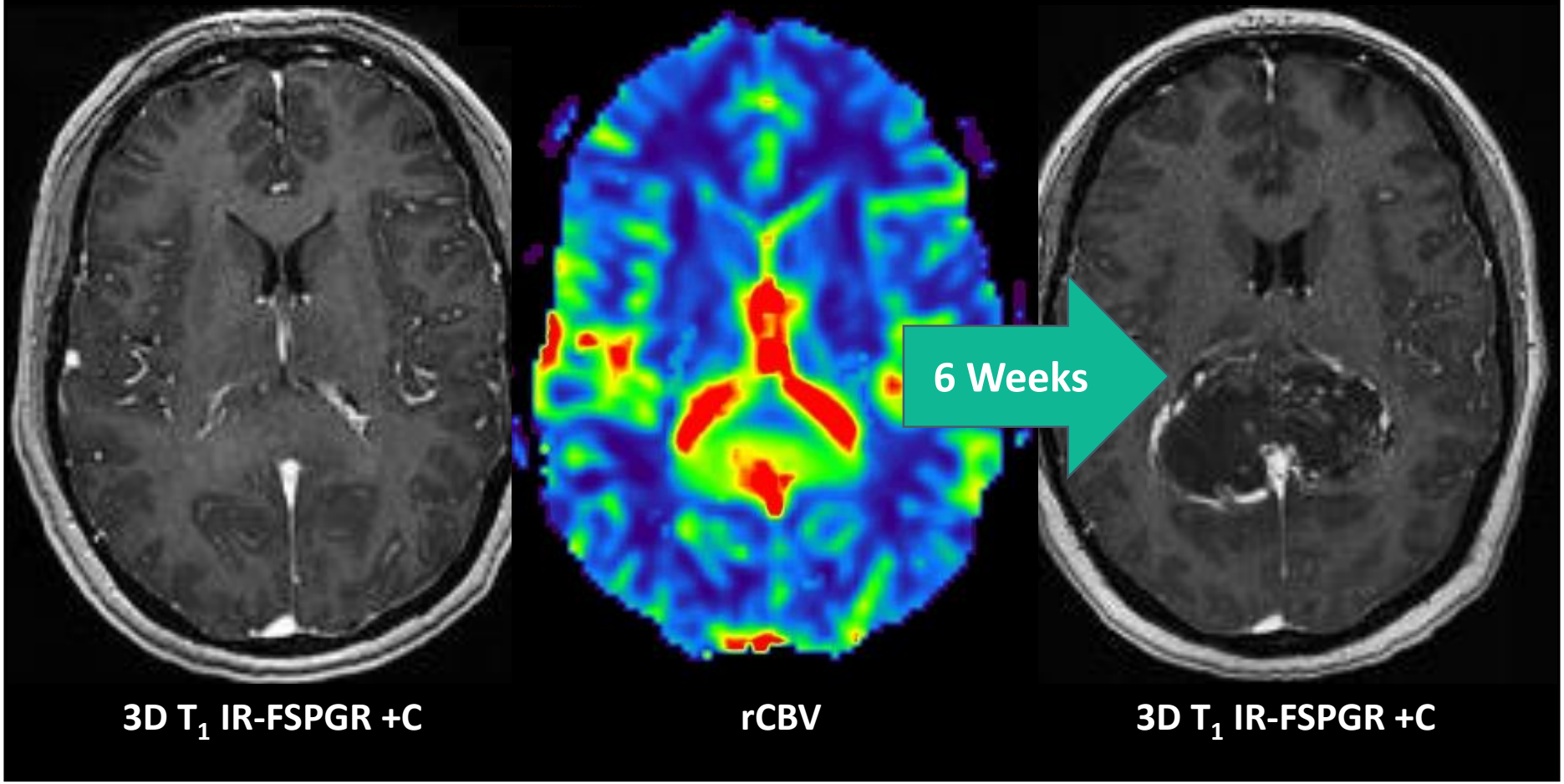
- GM blood flow ~60ml/100g/min
- WM blood flow ~20ml/100g/min
- <10ml/100g/min in cell death
- Similar characteristics to CBV in oncology but different for stroke

- Average time blood spends in the capillary bed MTT [seconds]
- Typical time is 3-5 seconds
- More prevelent in stroke imaging

$$MTT = \frac{CBV}{CBF}$$

Dynamic susceptibility contrast (DSC)

Glioblastoma WHO IV – Increased rCBV prior to BBB disruption



DSC-MRI Acquisition Wish List:

- Rapid bolus injection of Gadolinium based contrast agent using a power injector
- High Concentration Agent (1M)
- T_2 (SE) or T_2* (GRE) weighted single shot EPI Sequence
- High Temporal Resolution
- Compliant Patient!

DSC-MRI Protocol:

Acquisition Timings

- Total acquisition time around 2 minutes (90-120s)

- Recommended to inject after at least 10 baseline phases

Other Scanner Parameters

• FOV	20x20cm	(20x20 - 24x24cm)
• Matrix	128x128	(64x64 - 256x56)
• Slice thickness	5mm	(3 - 5mm)
• Number of slices	11	(5-20)
• Slice gap	1 mm	(0 - 1mm)
• Volume duration	1 TR	

- Temporal coverage (number of volumes) 40-120 total time points

Artefacts:

Hemosiderin

- Causes a local susceptibility effect
- Bolus cannot be visualised when the signal is already low (in the noise floor)
- Can cause a gross underestimation of the tumour cerebral blood volume

Metallic Objects

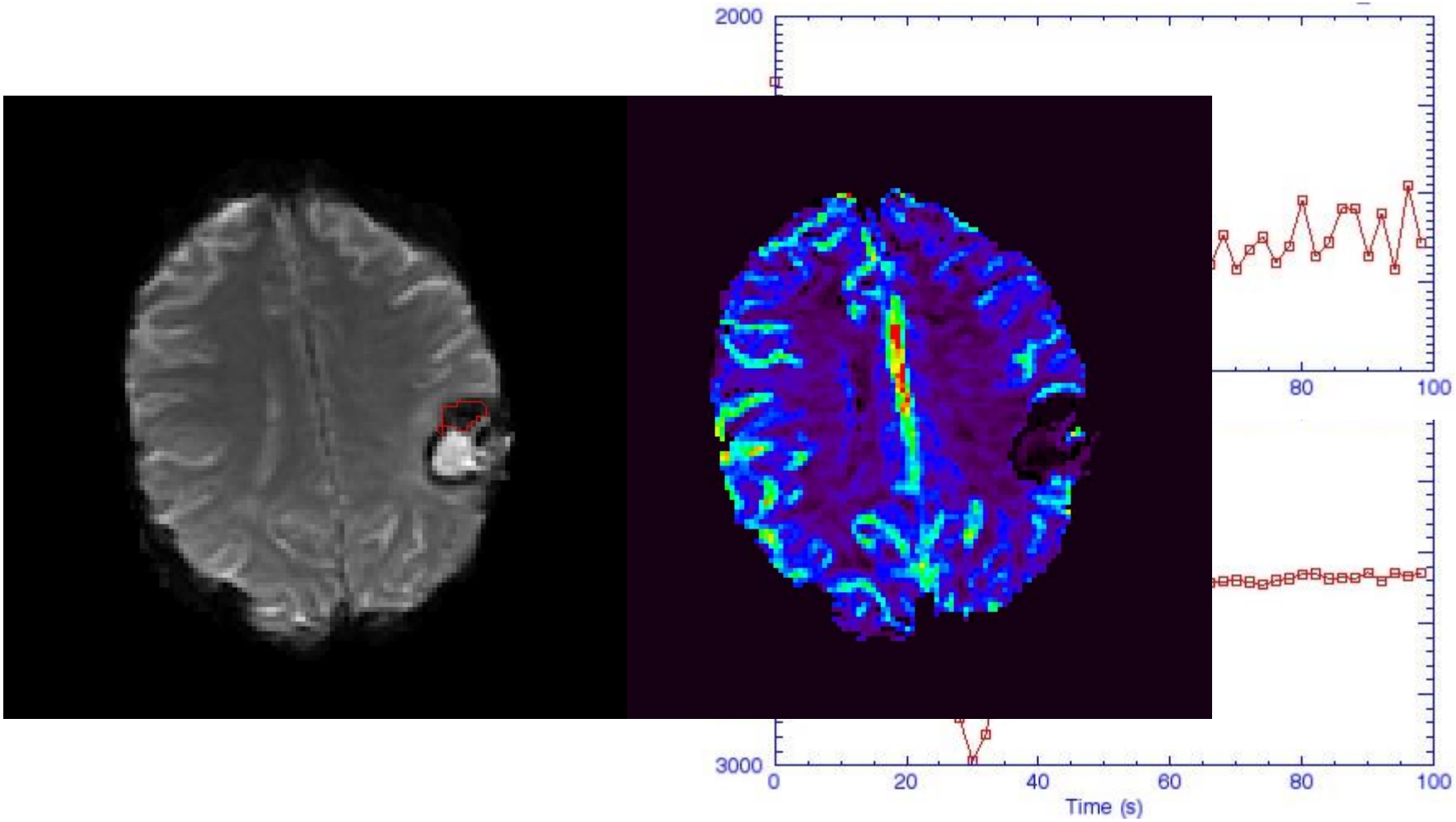
- Objects such as surgical clips also cause local susceptibility artefacts which obscure the bolus effect from the contrast agent
- Limits the use of DSC for detecting residual tumour within the first week of surgery due to blood products and surgical clips

Air-Tissue Interface

- Given the sequence is susceptibility-weighted, regions adjacent to a tissue-air interface are often lost
- The underlying echo-planar sequence is also subject to the same eddy current problems as experienced with DWI (distortion)

Dynamic susceptibility contrast (DSC)

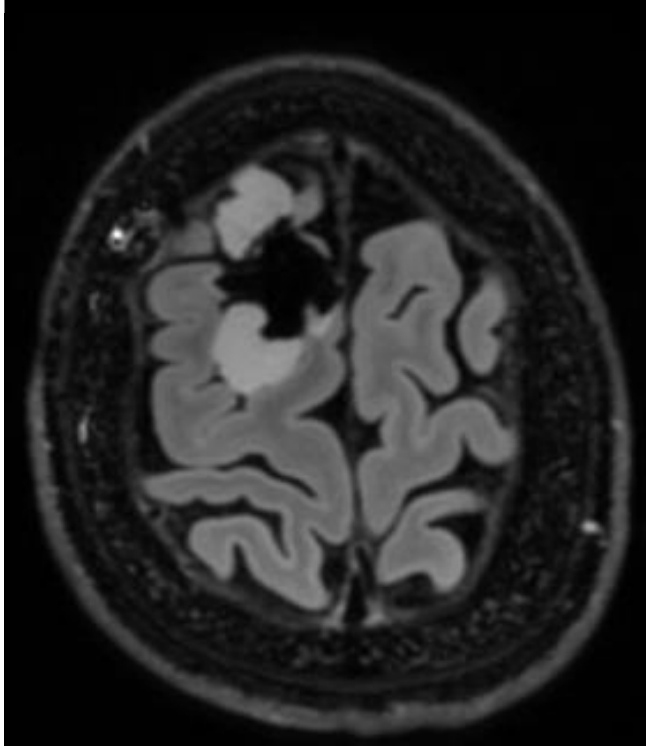
Artefacts:



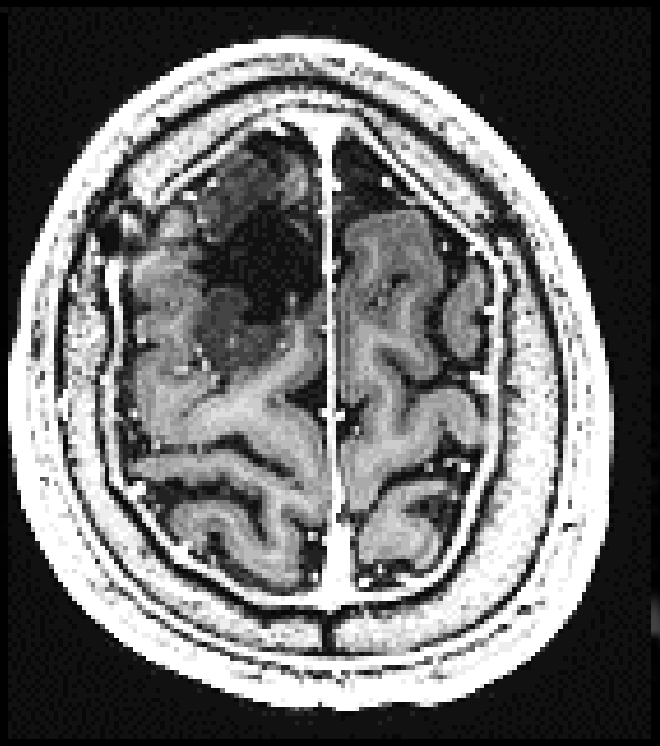
Tumours:

- CBV measurements from DSC-MRI can be used as an adjunct to conventional imaging to help assess:
    - degree of neovascularisation in brain tumours
    - evaluate tumour grading and malignancy
    - identify tumour-mimicking lesions (such as radiation necrosis cerebral abscess, and tumefactive demyelinating lesion (TDL))

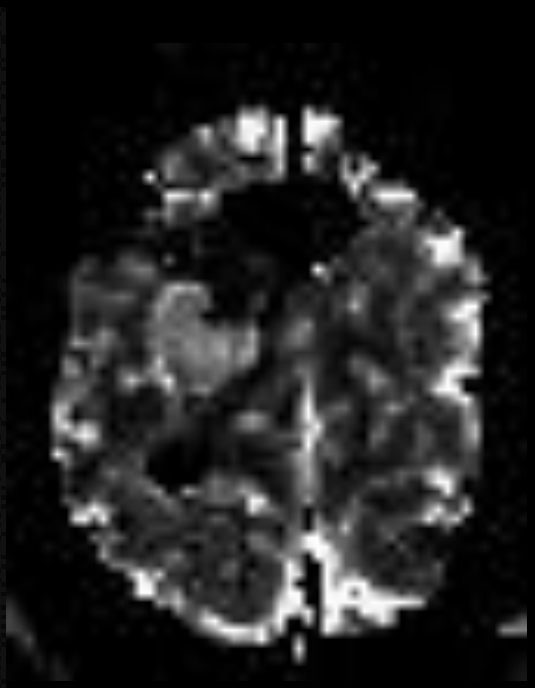
LGG (Oligoastrocytoma WHO II in 2005) – Increased rCBV prior to BBB disruption



3D T2 FLAIR CUBE FS MPR



3D T_1 IR-FSPGR +C



rCBV

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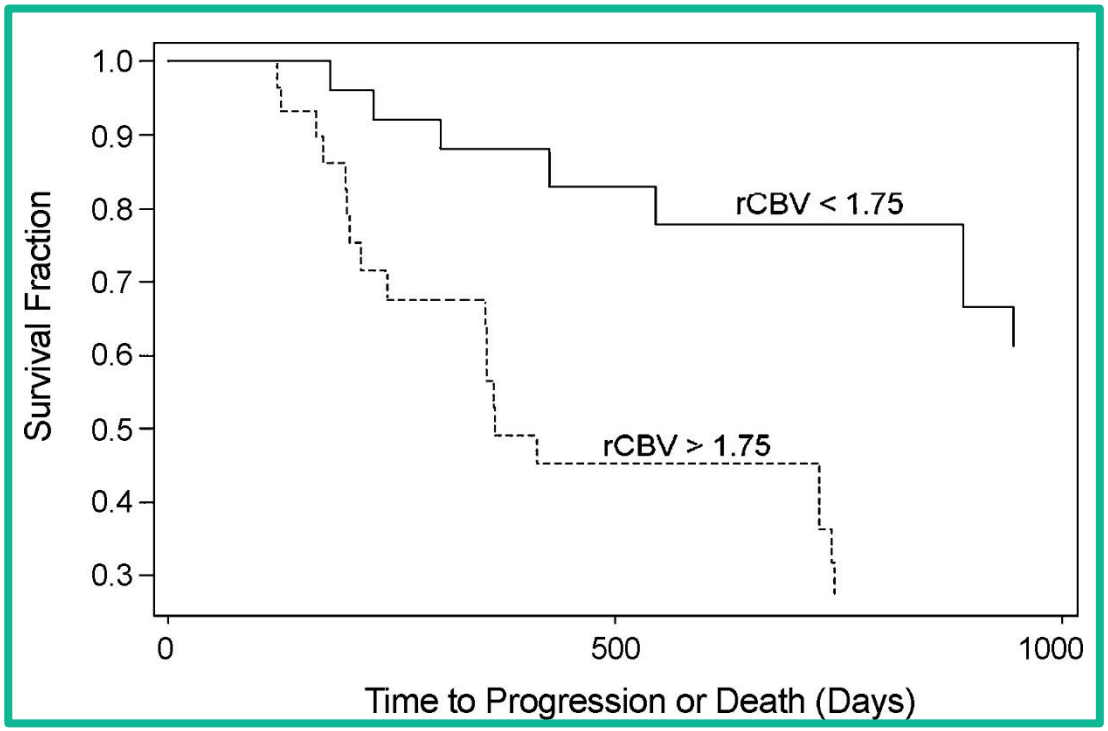
Low-grade gliomas: dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging - prediction of patient clinical response. Law *et al.* 2006.



- "Kaplan–Meier survival curves for time to progression within groups with low (rCBV < 1.75) and high (rCBV > 1.75) at both institutions.
- Patients with low-grade glioma with low rCBV at baseline have a probable median time to progression of 889 days, whereas the median time to progression among subjects with high rCBV is 365 days."

Quantification: Hot Spot Approach

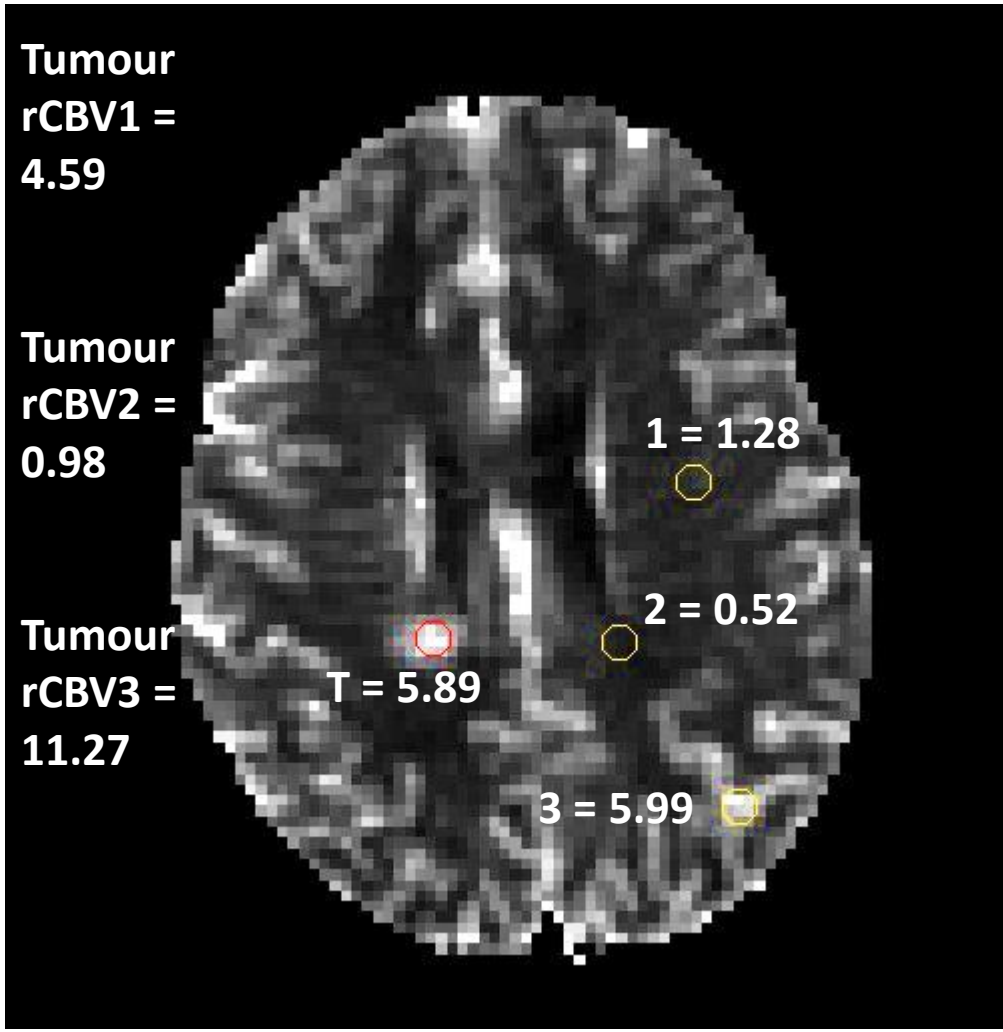
- Regional calculation of perfusion parameters in tumours is commonly performed by manual placement of region of interests (ROIs) around a portion or the entire lesion

- $rCBV = CBV_{TUM} / CBV_{REF}$

- The main limitation of the hot-spot approach is the reference tissue

- Difficult in cases with large amounts of mass effect

- Consistent reference tissue is vital



Dynamic susceptibility contrast (DSC)

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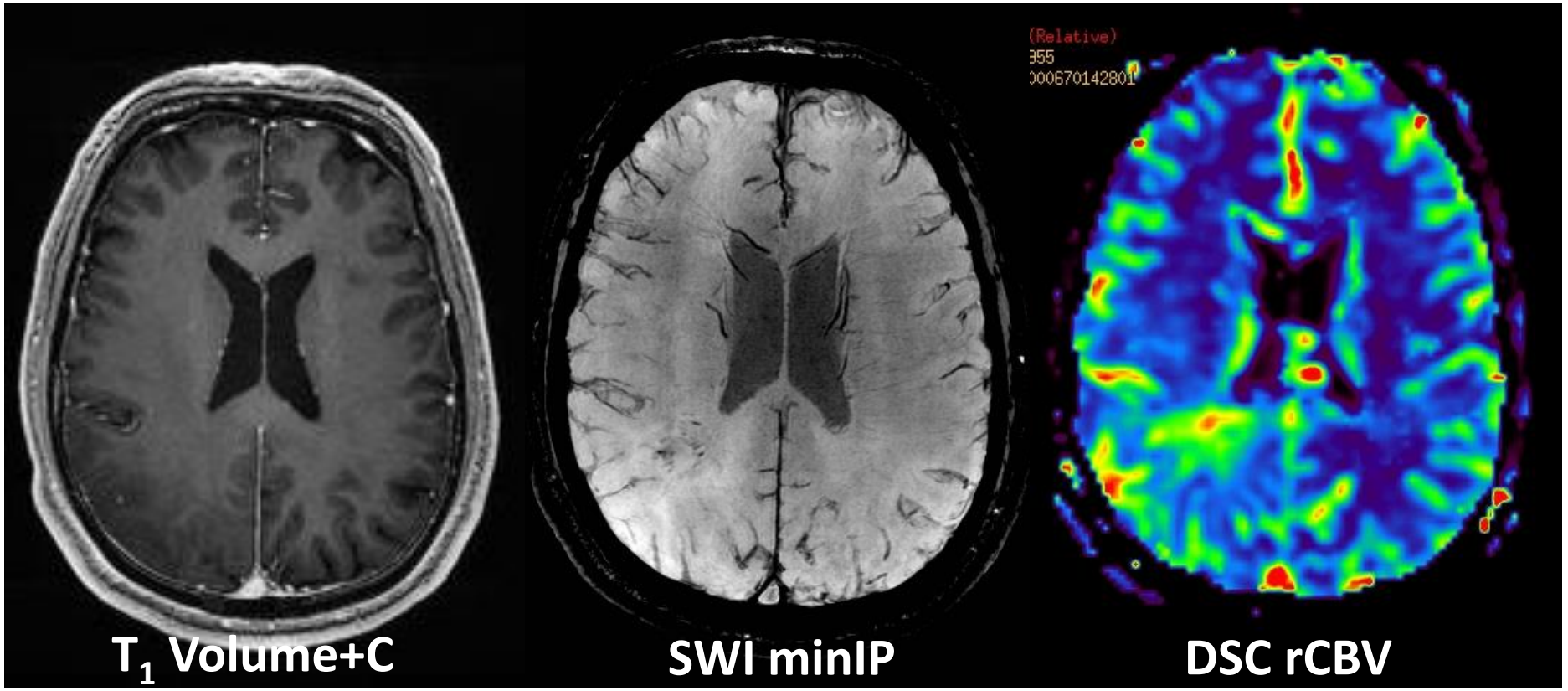
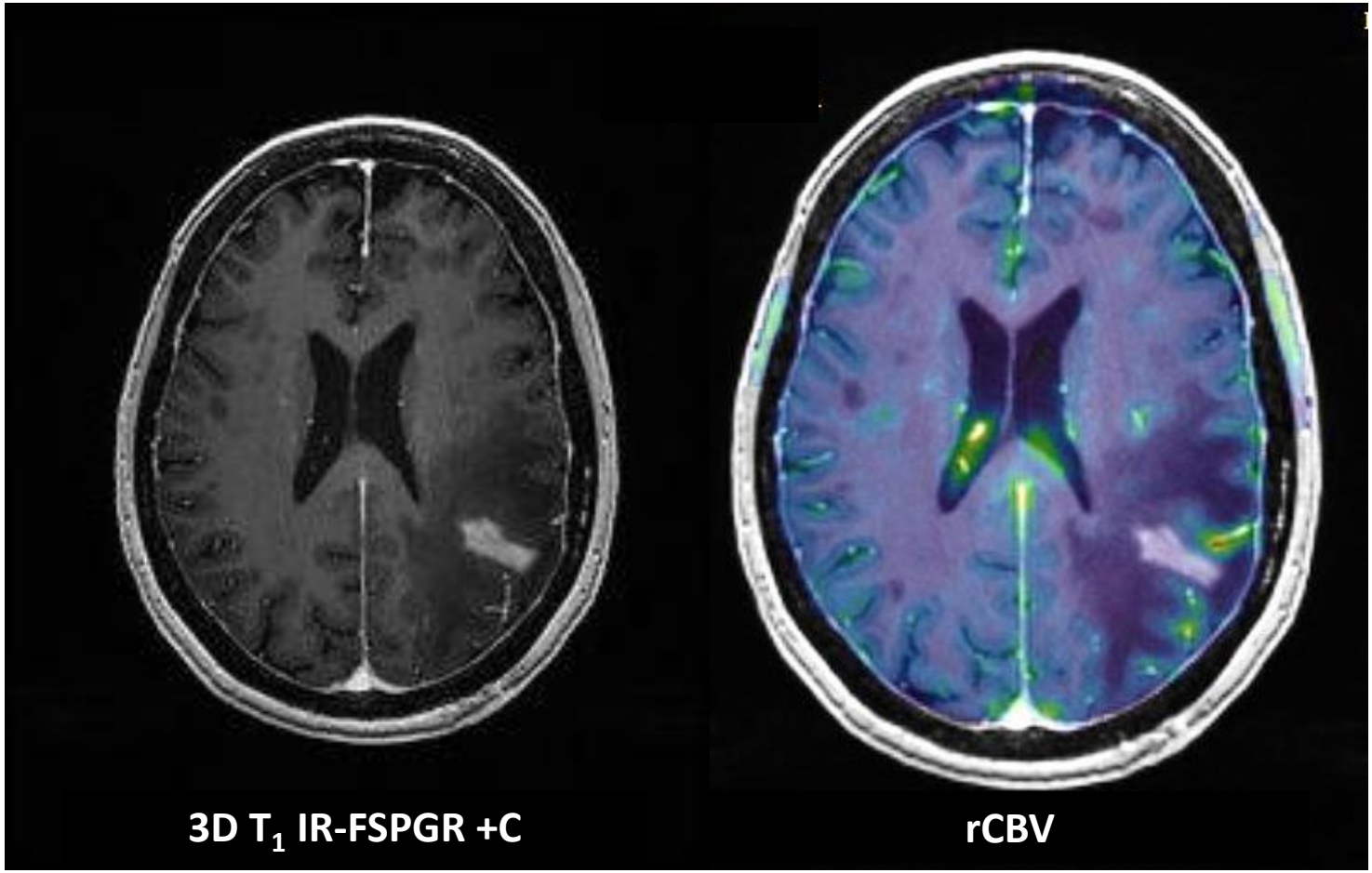
Glioblastoma WHO IV

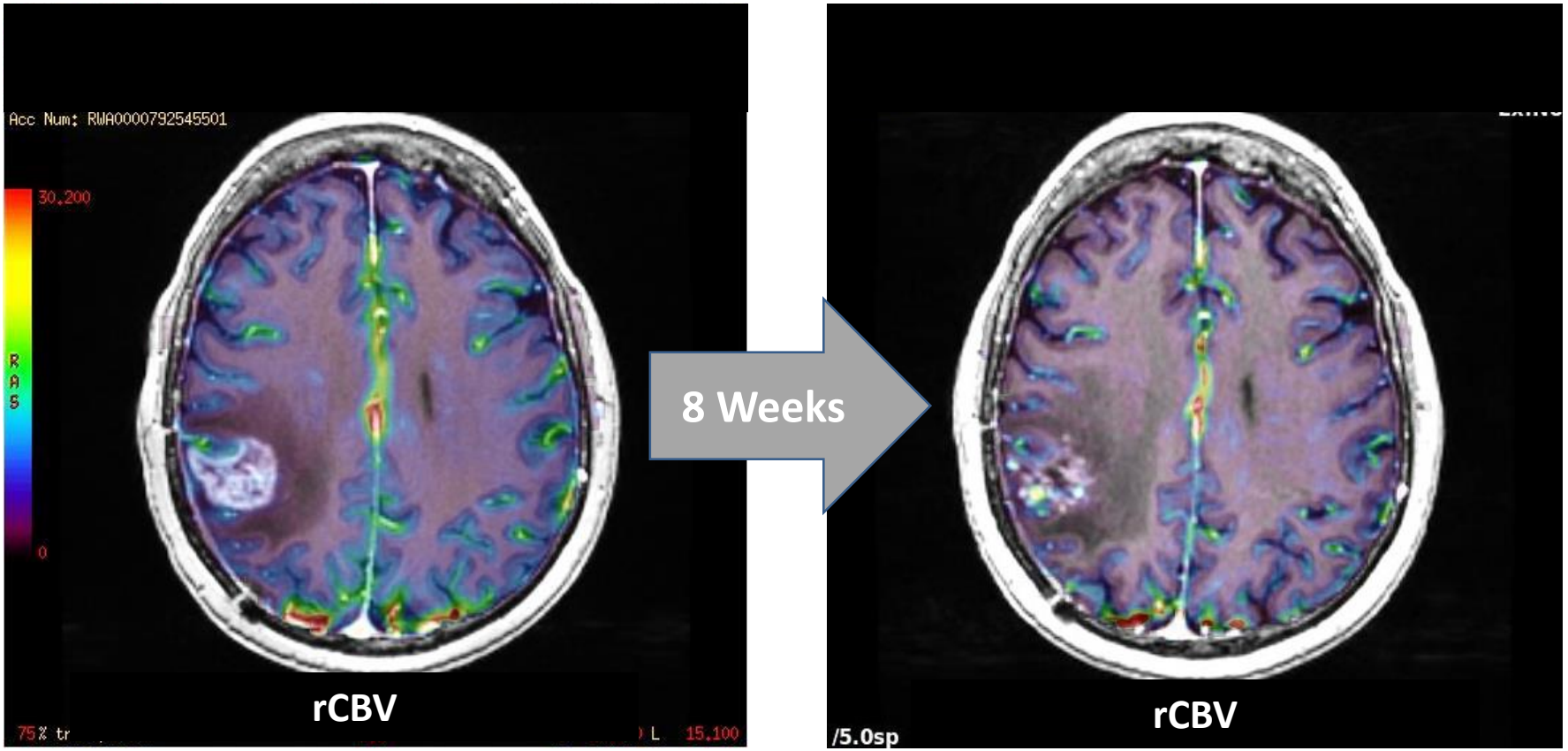


CNS Lymphoma



Dynamic susceptibility contrast (DSC)

Pseudo-progression



Dynamic susceptibility contrast (DSC)

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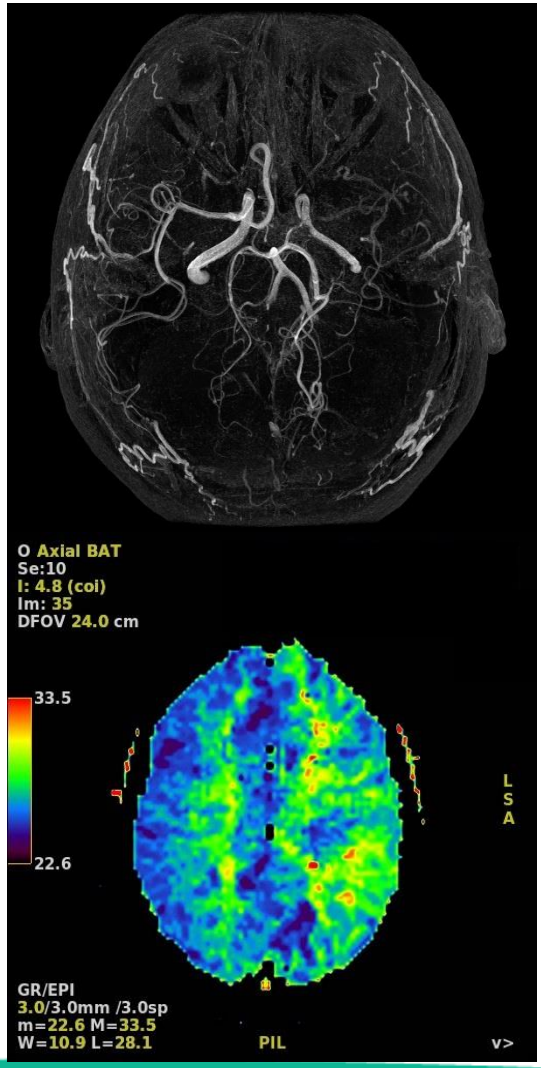
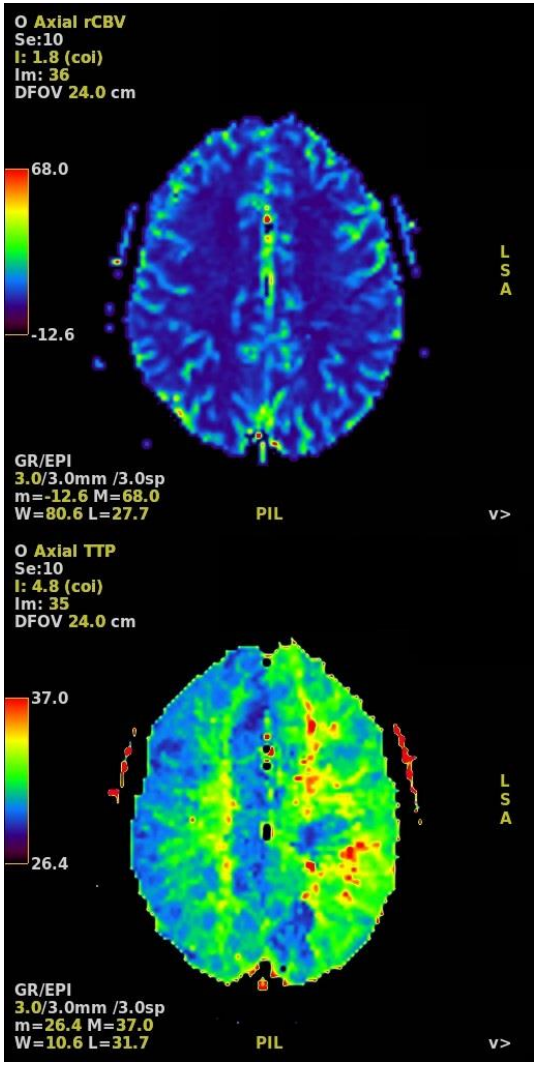
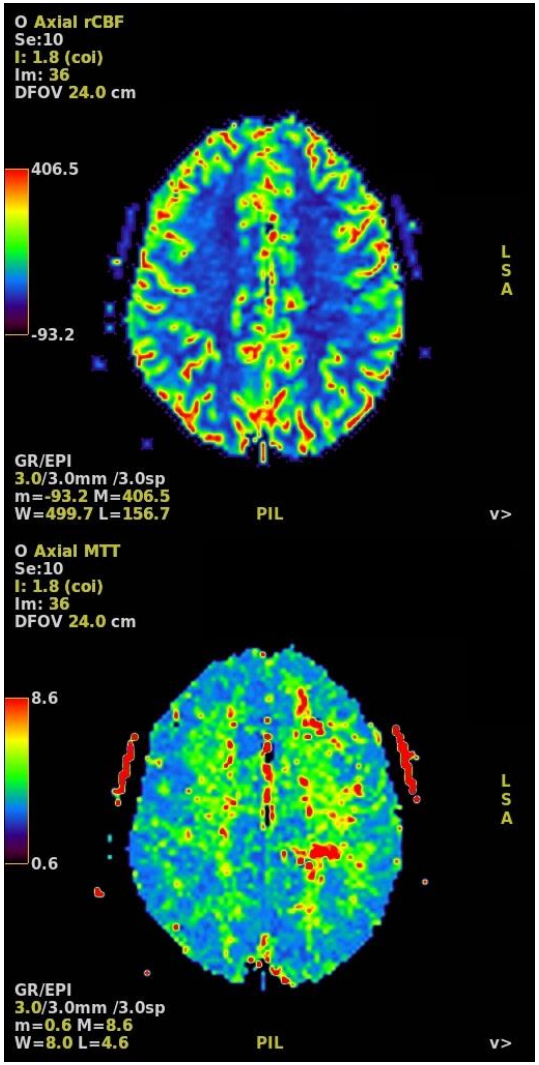
Moya-moya

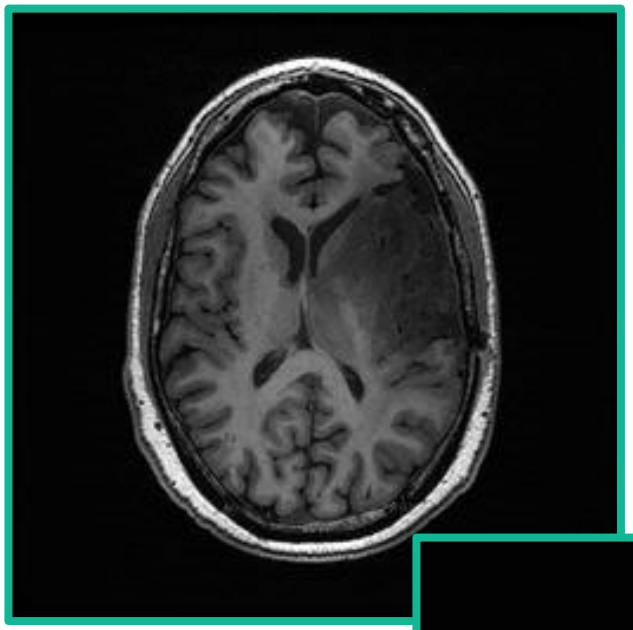


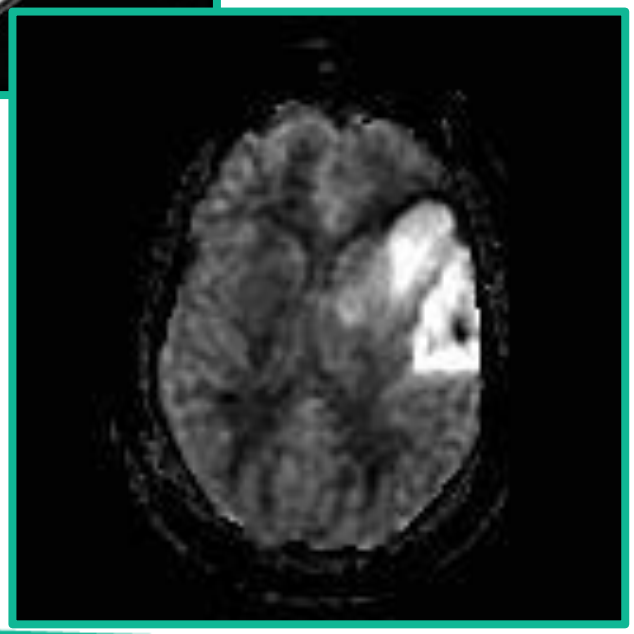




Awareness of arterial spin labelling (ASL)

- Contrast-free, non-invasive perfusion technique
- Enables whole brain cerebral blood flow (CBF) measurements
- Ideal for patients in whom contrast in contraindicated (low GFR, pregnant etc.)
- More robust in regions of high susceptibility compared to DSC





Awareness of arterial spin labelling (ASL)

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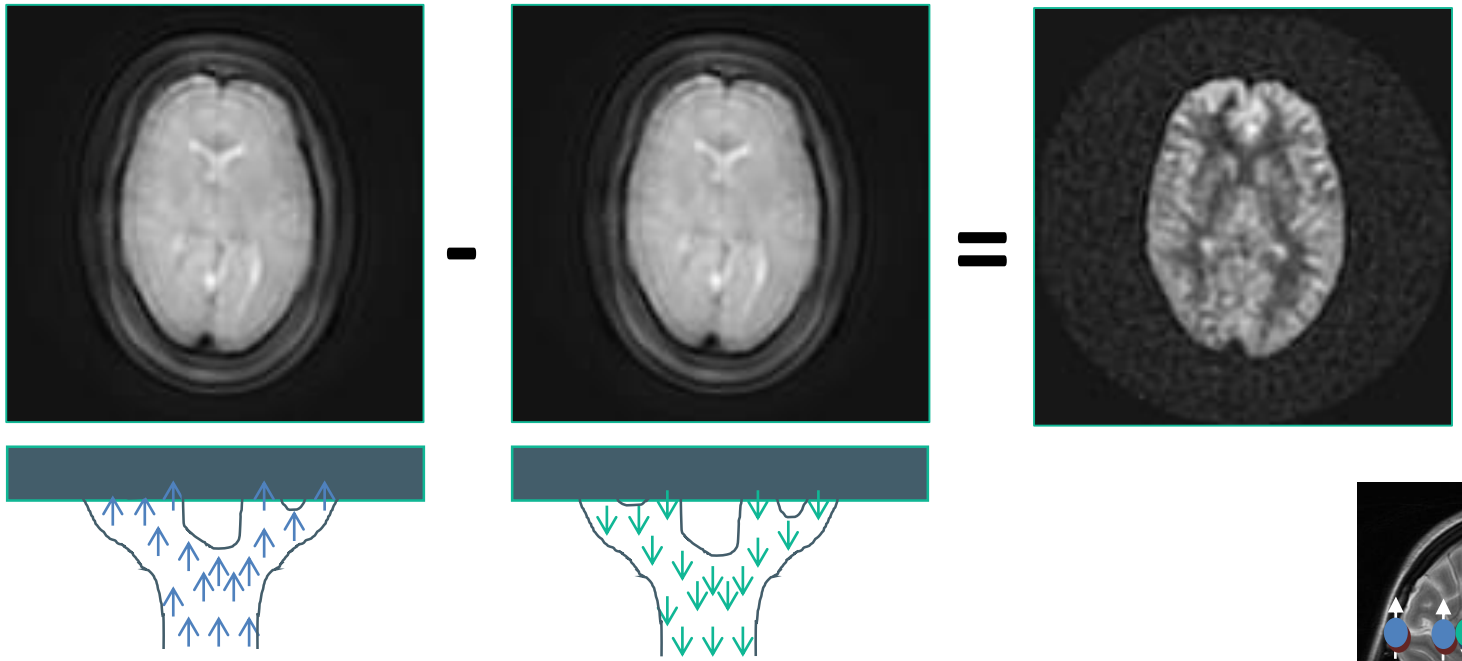
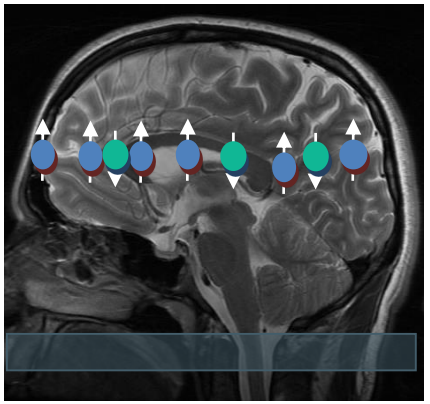
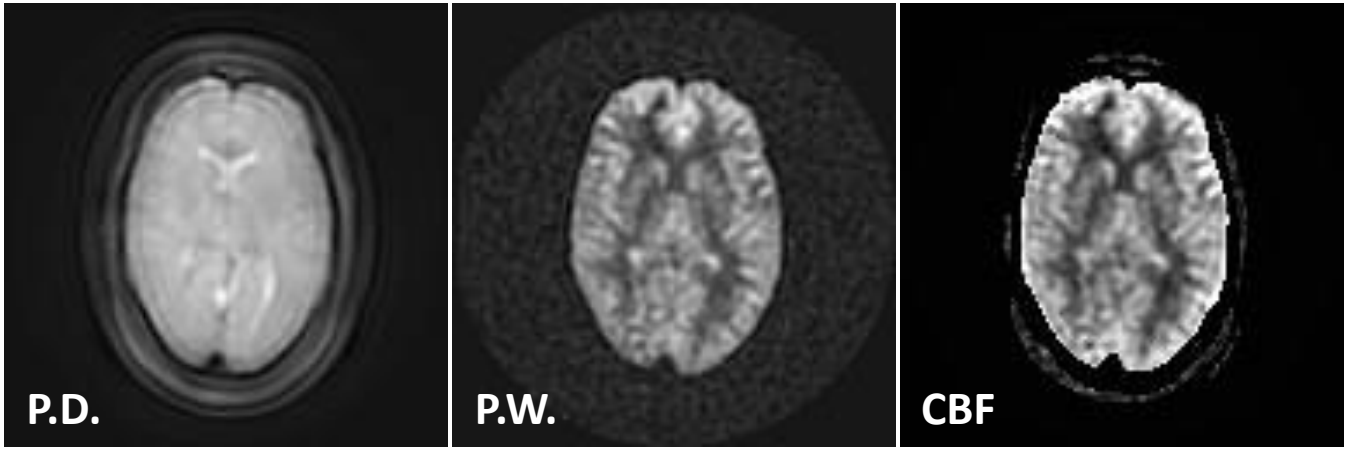
Control (Non-inverted) **Inverted Blood Image** **Perfusion Weighted Image**





- spatially selective inversion continuous pulse is applied that, in effect, labels protons as they move into tissue
- inverted blood results in a decreased signal on a proton density image

Awareness of arterial spin labelling (ASL)



$$CBF = 6000 * \lambda \frac{\left(1 - \exp\left(-\frac{ST(s)}{T_{1t}(s)}\right)\right)\exp\left(\frac{PLD(s)}{T_{1b}(s)}\right)}{2T_{1b}(s)\left(1 - \exp\left(-\frac{LT(s)}{T_{1b}(s)}\right)\right)\varepsilon * NEX_{PW}\left(\frac{PW}{SF_{PW}PD}\right)}$$

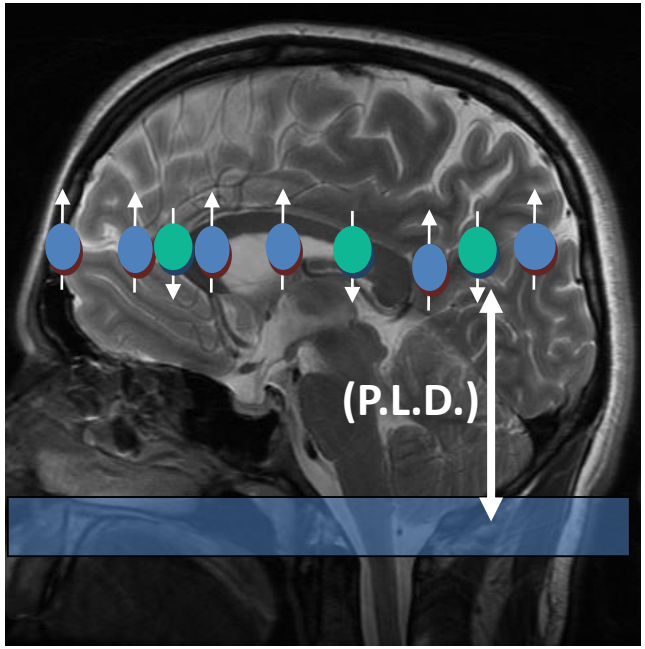
Assumption

Measured

where T1b is T1 of blood and is assumed to be 1.6s at 3T and 1.4s at 1.5T. The partial saturation of the reference image (PD) is corrected for by using a T1t of 1.2s (typical of gray matter) ST is saturation time and is set to 2s. The partition coefficient λ, is set to the whole brain average, 0.9. The efficiency, ε, is a combination of both inversion efficiency (0.8) and background suppression efficiency (0.75) resulting in an overall efficiency of 0.6. PLD is the post labeling delay used for the ASL experiment. LT is the labeling duration if is set to 1.5s for the current version. PW is the perfusion weighted or the raw difference image. SF_{PW} is the scaling factor of PW sequence NEX_{PW} is the number of excitation for PW images. The CBF is reported in ml/100gm/min units.

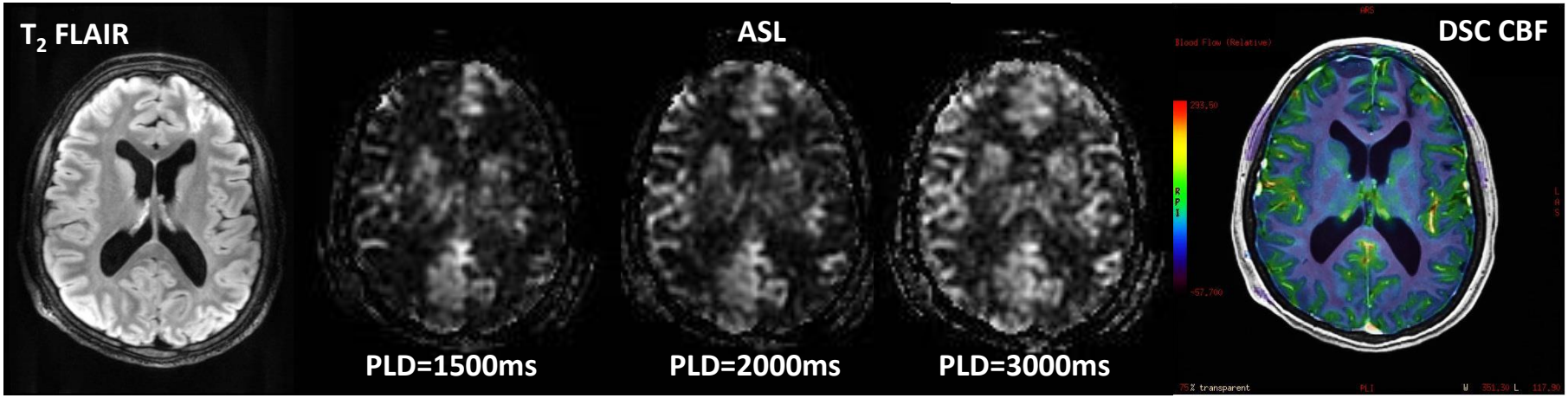
MR systems 25.0 Operator Manual/Training Tool, English
5500865-1EN (04/2015) Rev.4 © 2015 General Electric Company

Awareness of arterial spin labelling (ASL)

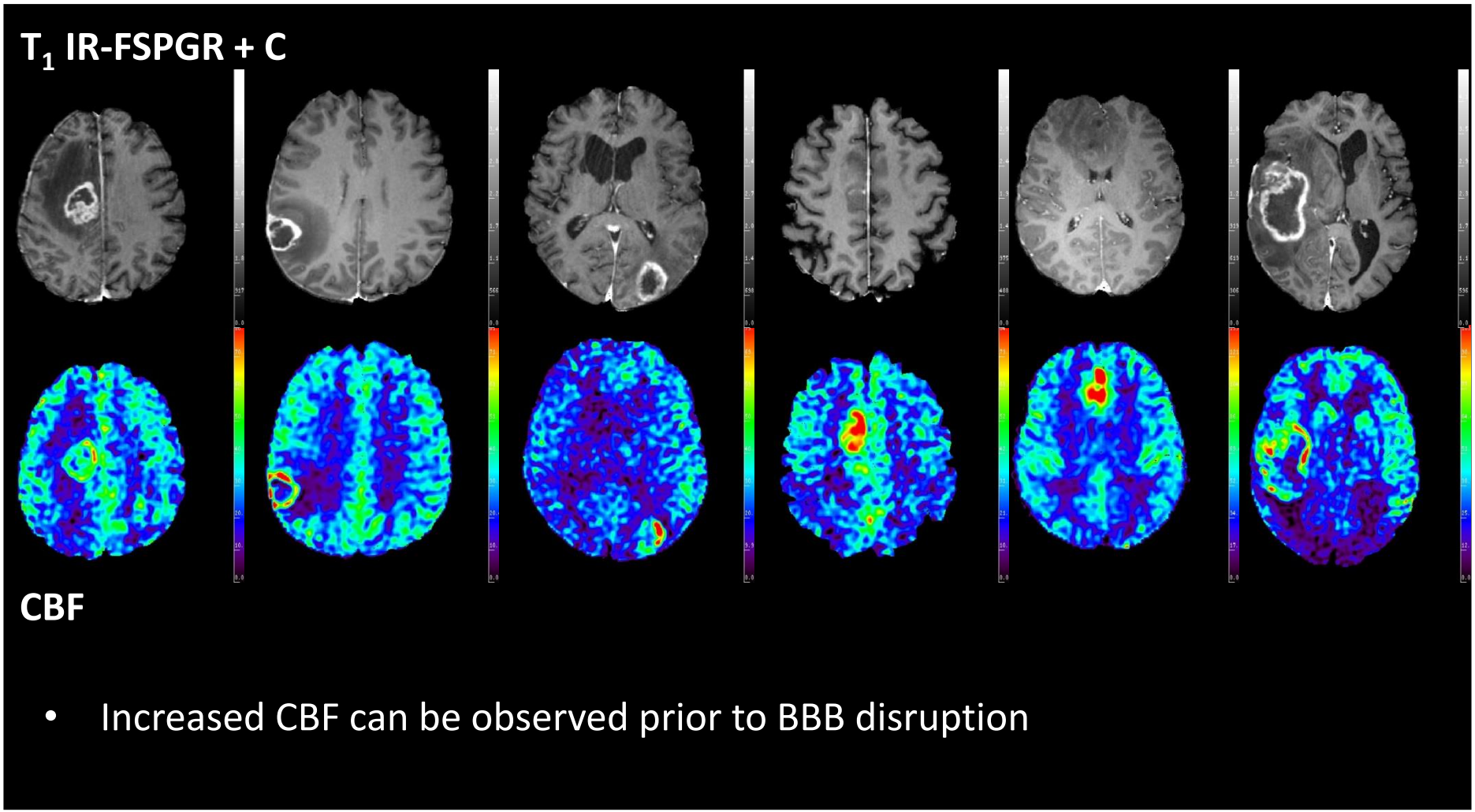


- Time from labelling to the capillary bed is known as the pulse labelling delay (P.L.D.)

- Paediatrics = 1500ms
- Normal adults = 2000ms
- Elderly patients = 2500ms
- Moya Moya = 3000ms

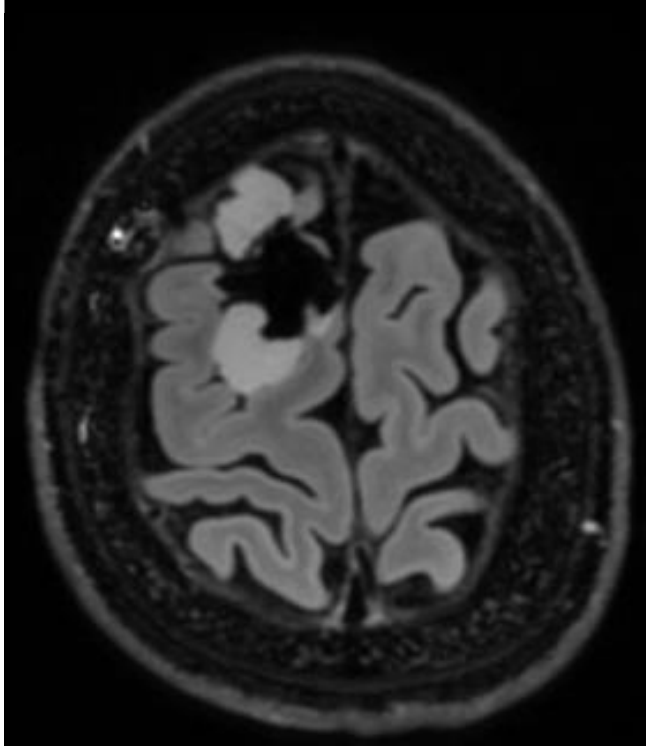


Awareness of arterial spin labelling (ASL)

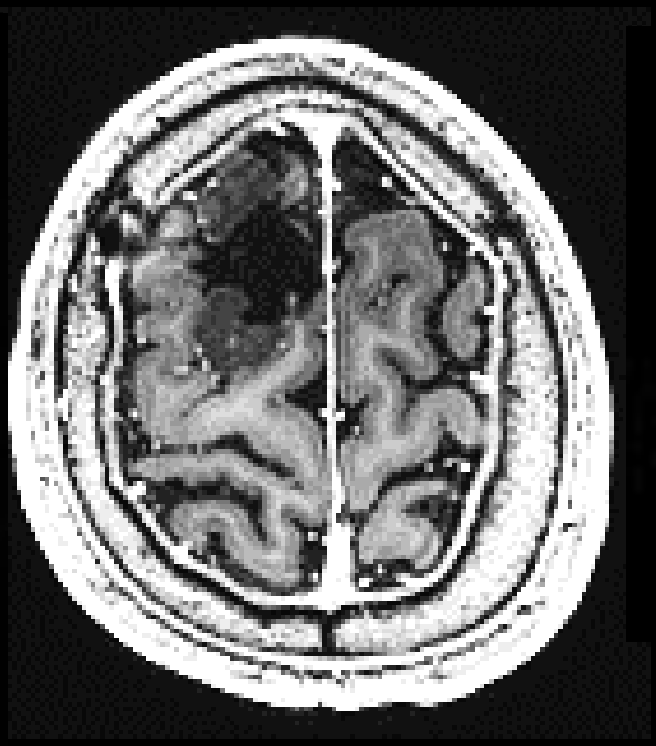


- Increased CBF can be observed prior to BBB disruption

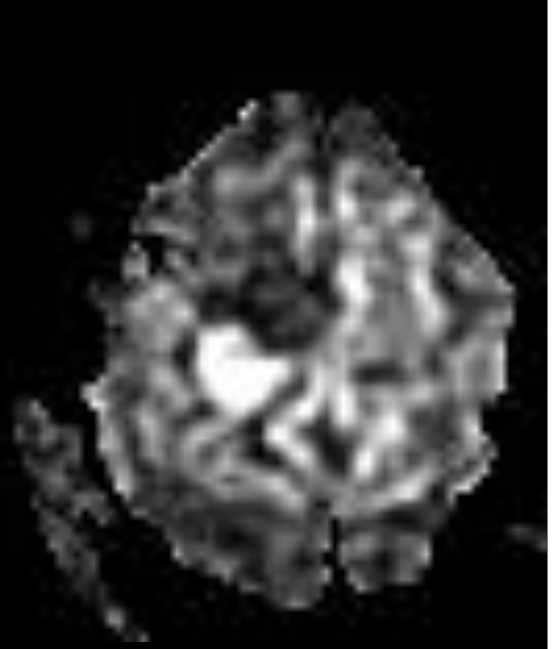
LGG (Oligoastrocytoma WHO II in 2005) – Increased CBF prior to BBB disruption



3D T2 FLAIR CUBE FS MPR



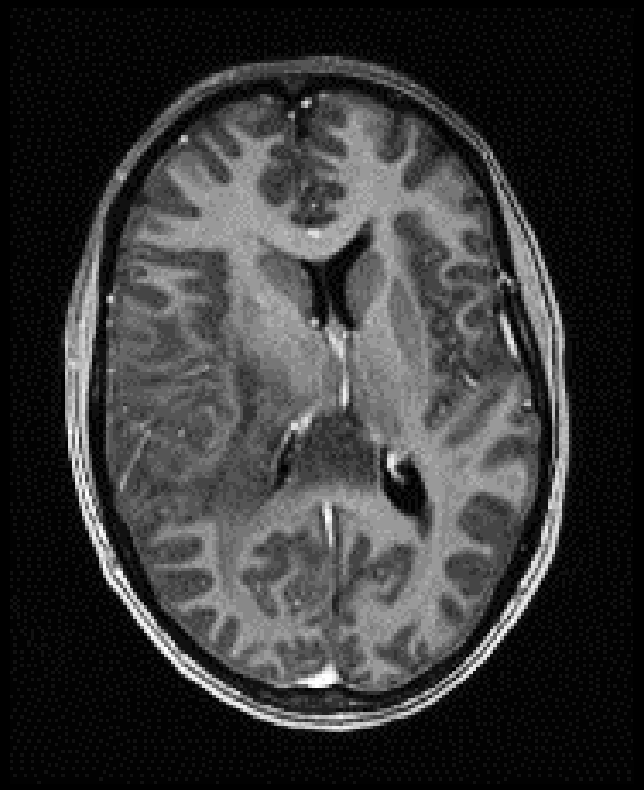
3D T_1 IR-FSPGR +C



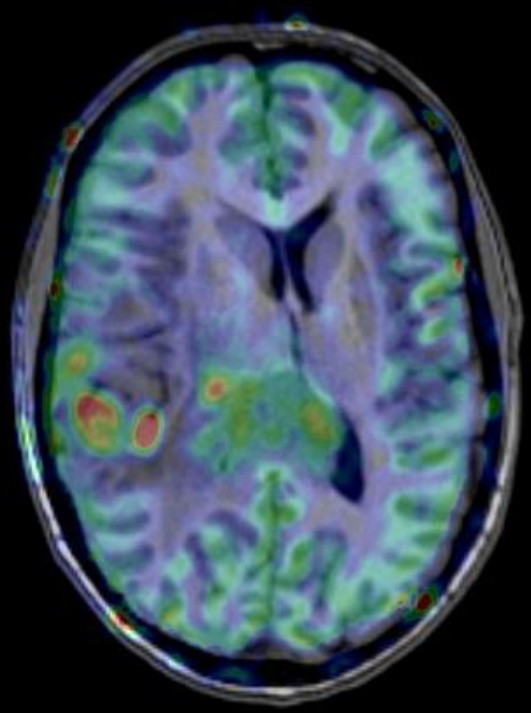
CBF

Awareness of arterial spin labelling (ASL)

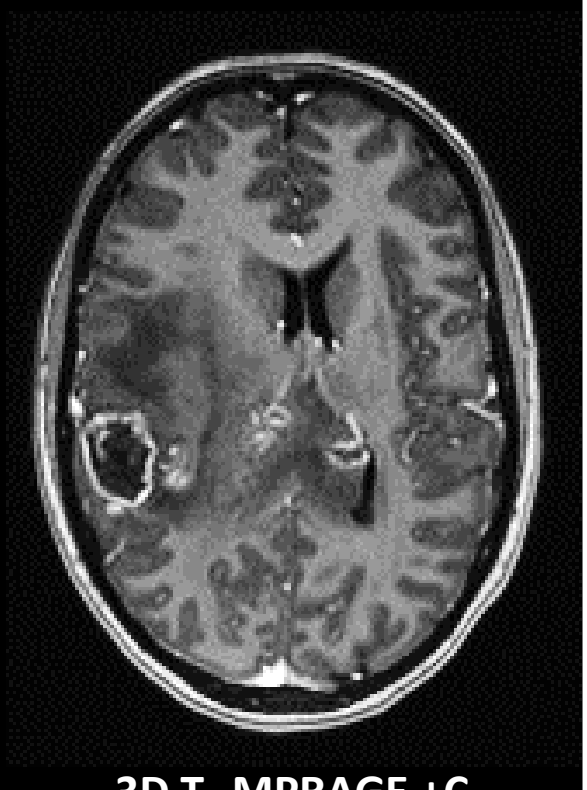
GBM WHO IV IDH-ve – Increased CBF prior to BBB disruption



3D T_1 MPRAGE +C



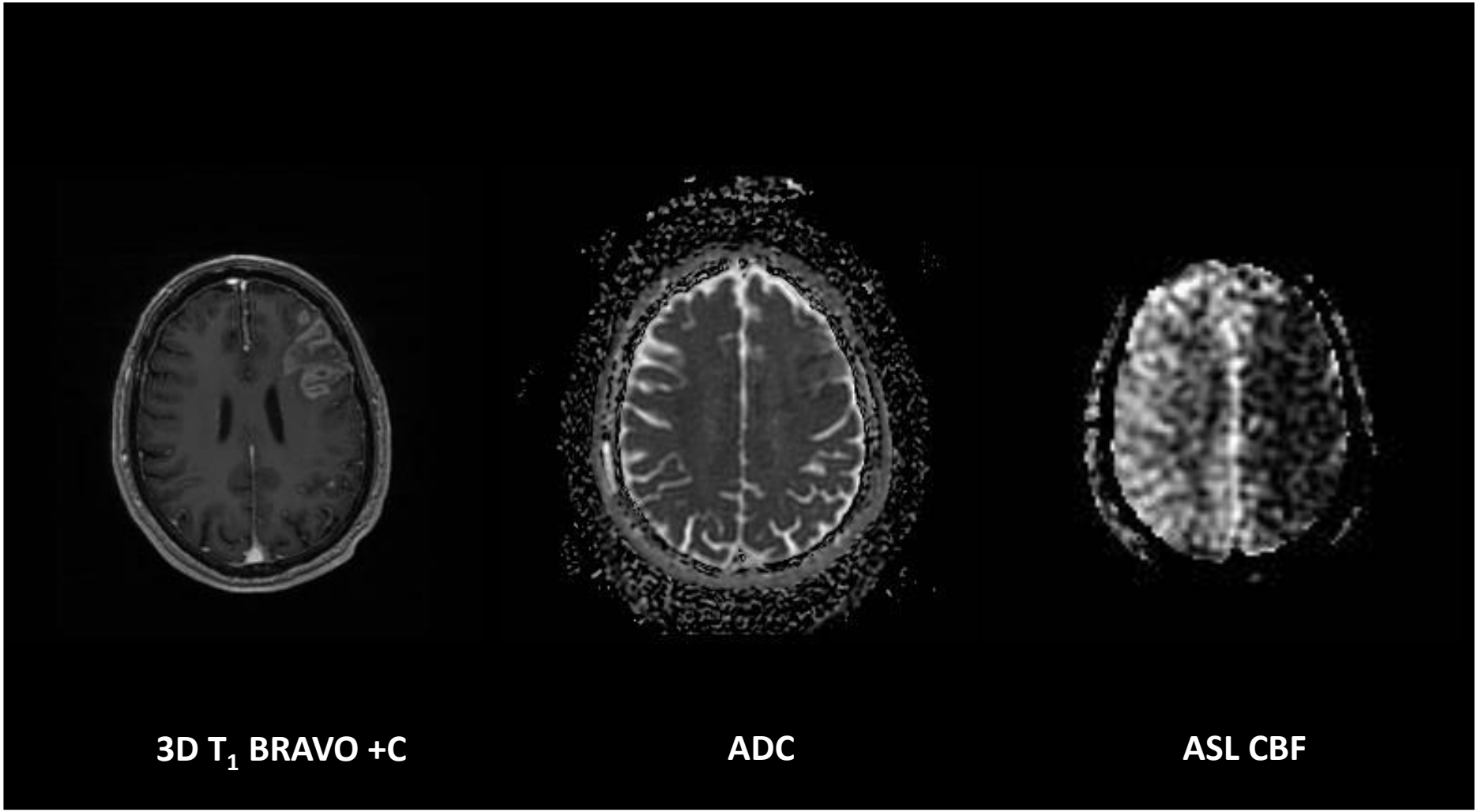
CBF fused
3D T_1 MPRAGE +C



3D T_1 MPRAGE +C
+ 6 Weeks

Awareness of arterial spin labelling (ASL)

Stroke



Awareness of arterial spin labelling (ASL)

LGG on conventional imaging – 3T Premier

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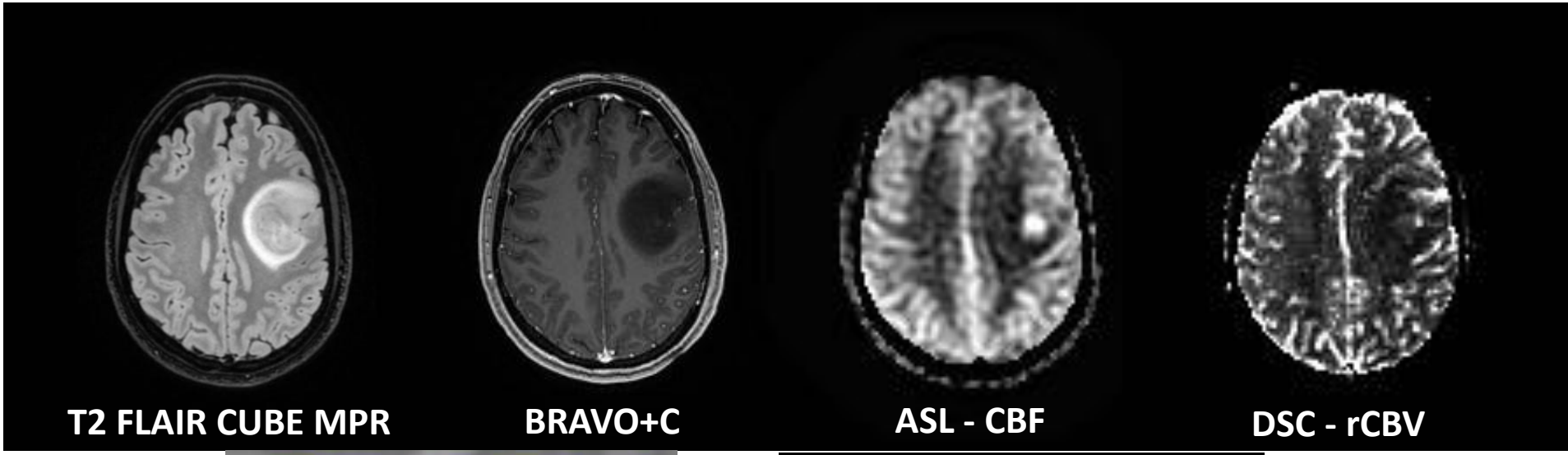
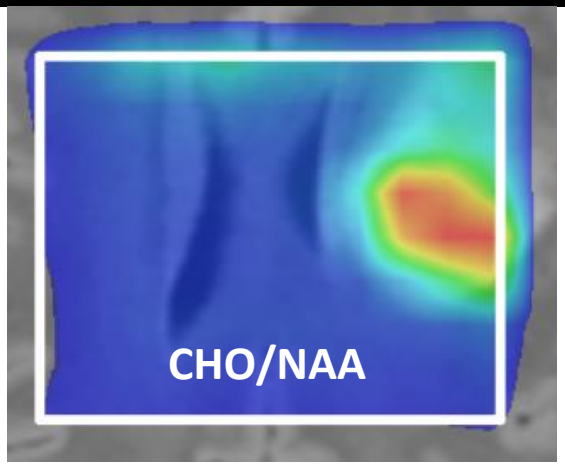
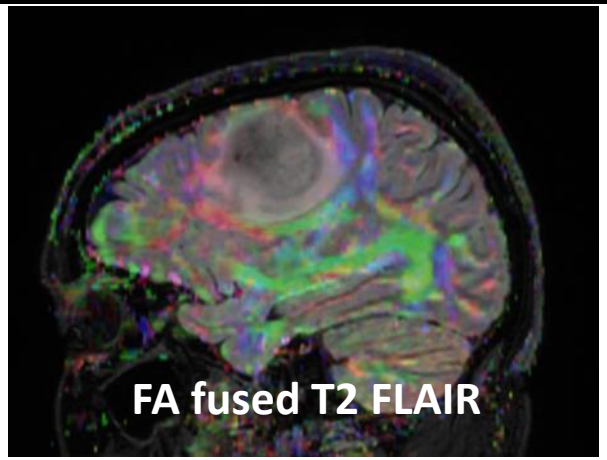
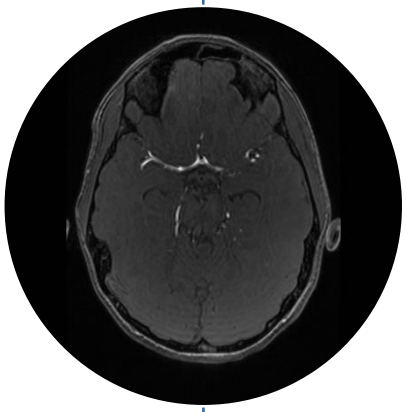




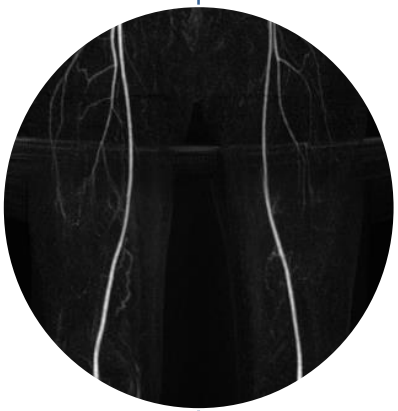


MR angiography (MRA) techniques

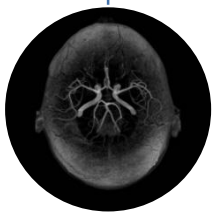
Magnetic Resonance Angiography (MRA)



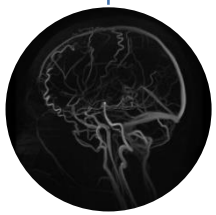
Non-Contrast



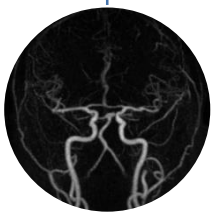
Contrast Enhanced



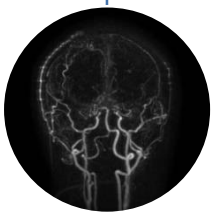
Time of Flight



Phase Contrast



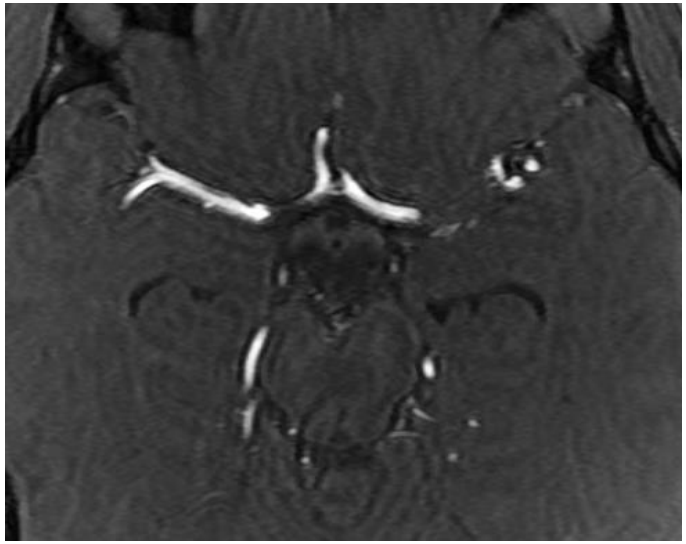
Fluoroscopic-Triggering

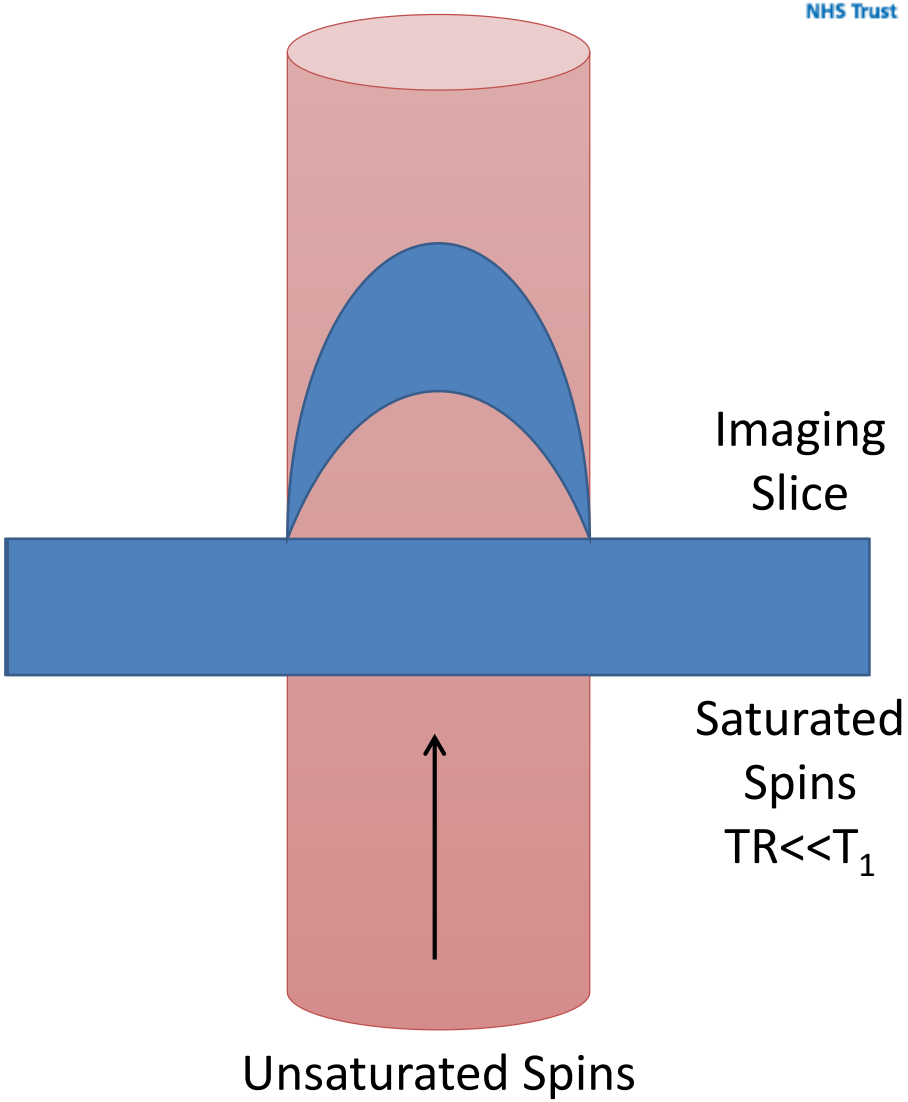


Time-resolved MRA

Time of Flight (TOF)

- TOF MRA utilises gradient echo sequences with short TE/TR to saturate the signal from stationary spins
- Spins flowing into the imaging slice with full magnetisation have high signal





Time of Flight (TOF)

- Based on the phenomenon of **flow-related enhancement** of spins entering into an imaging slice.
  - As a result of being unsaturated, these spins give more signal that surrounding stationary spins.

- The strength of the vascular signal depends on:
  - Flow velocity and type
  - The length and orientation of the vessel

- Limitations
  - Signal loss from spin dephasing when flows are complex or turbulent (stenosis), when flow is too slow
  - Poor signal suppression of the stationary tissues with short T_1 relaxation time (fat, atheroma, haematoma, thrombus)

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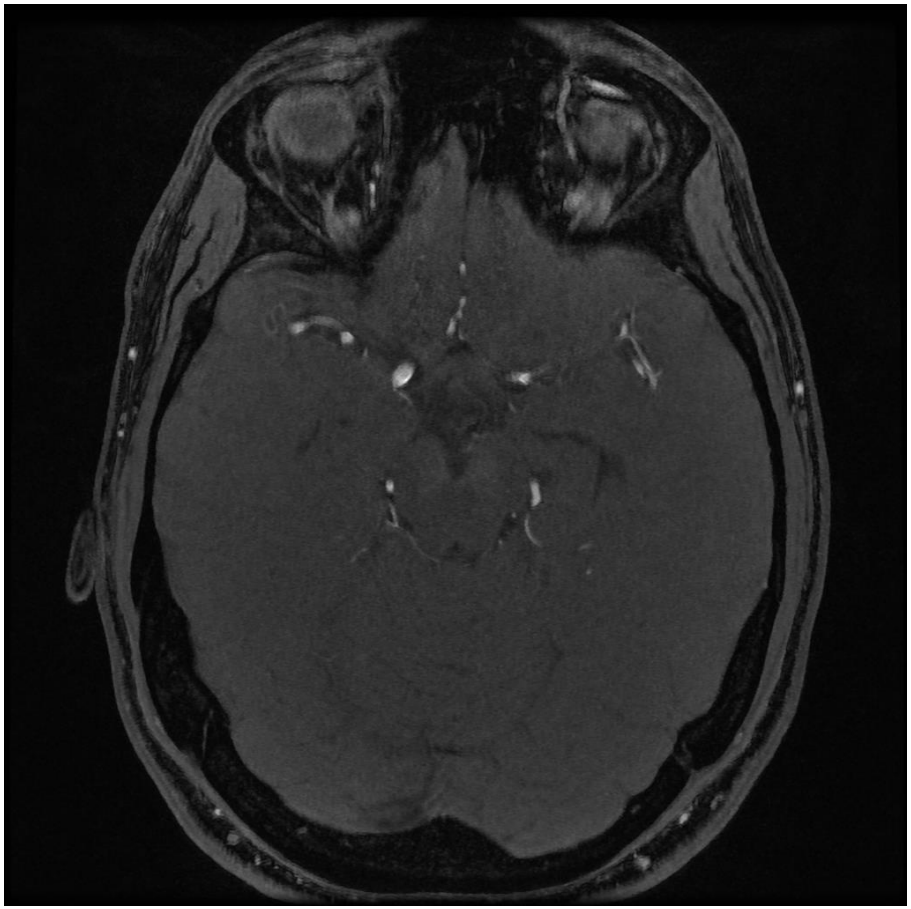
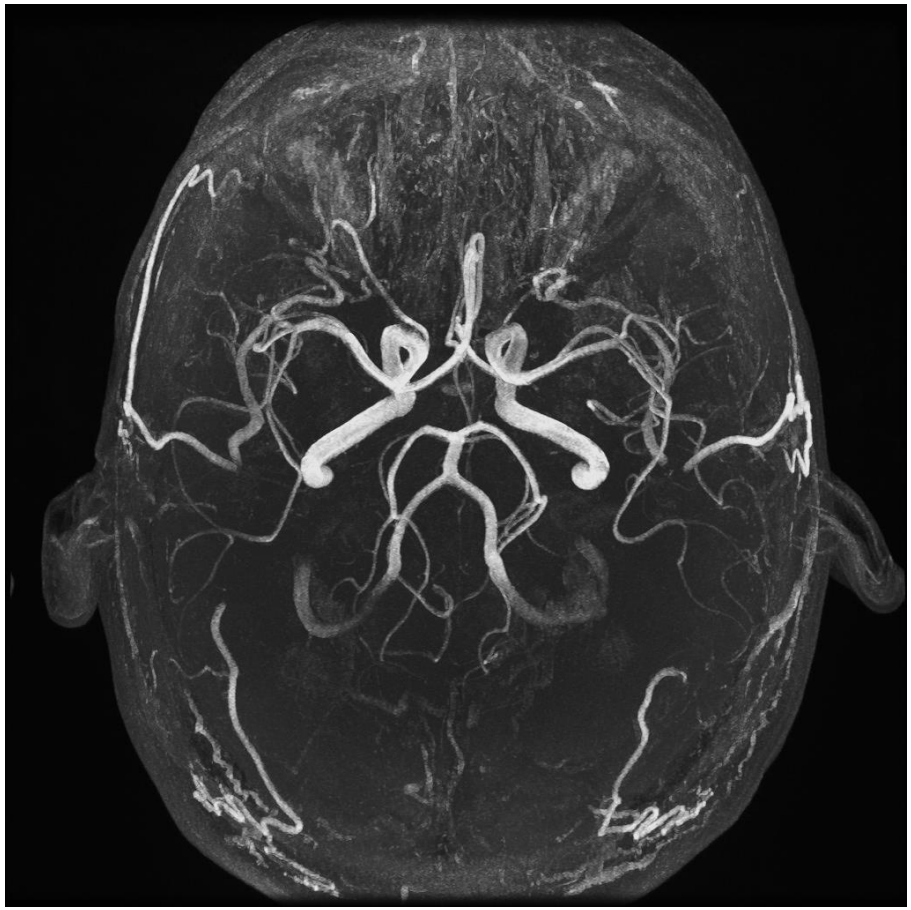
MR Angiography: Time of Flight (TOF)

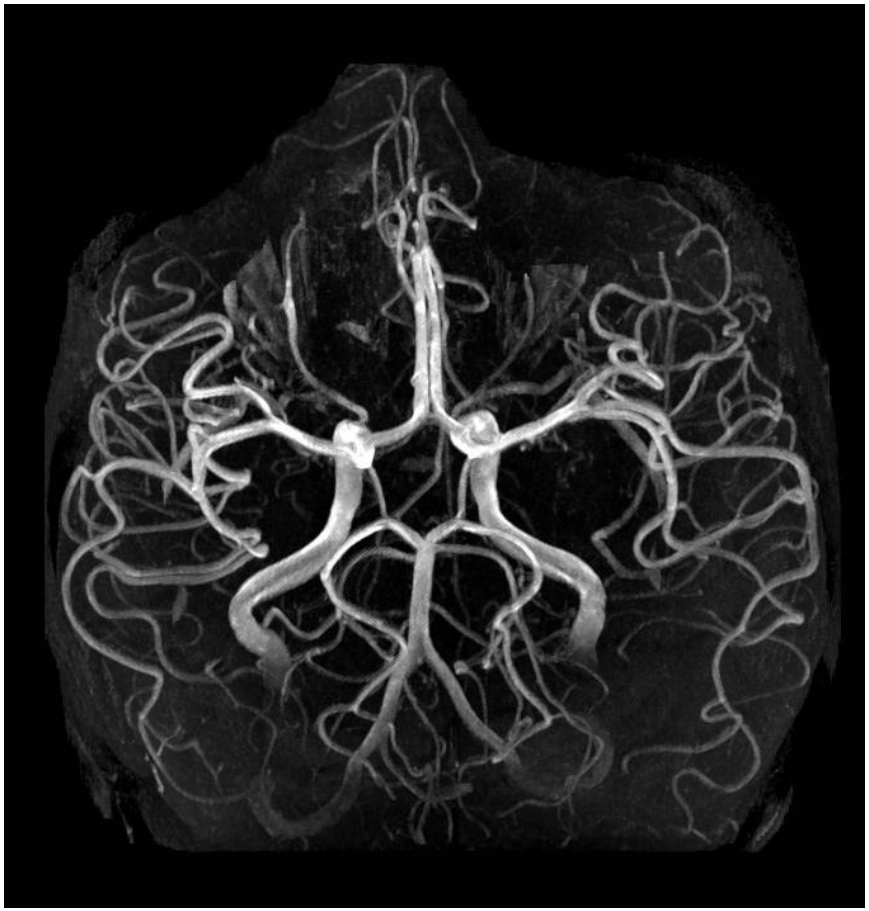


TOF Source Data

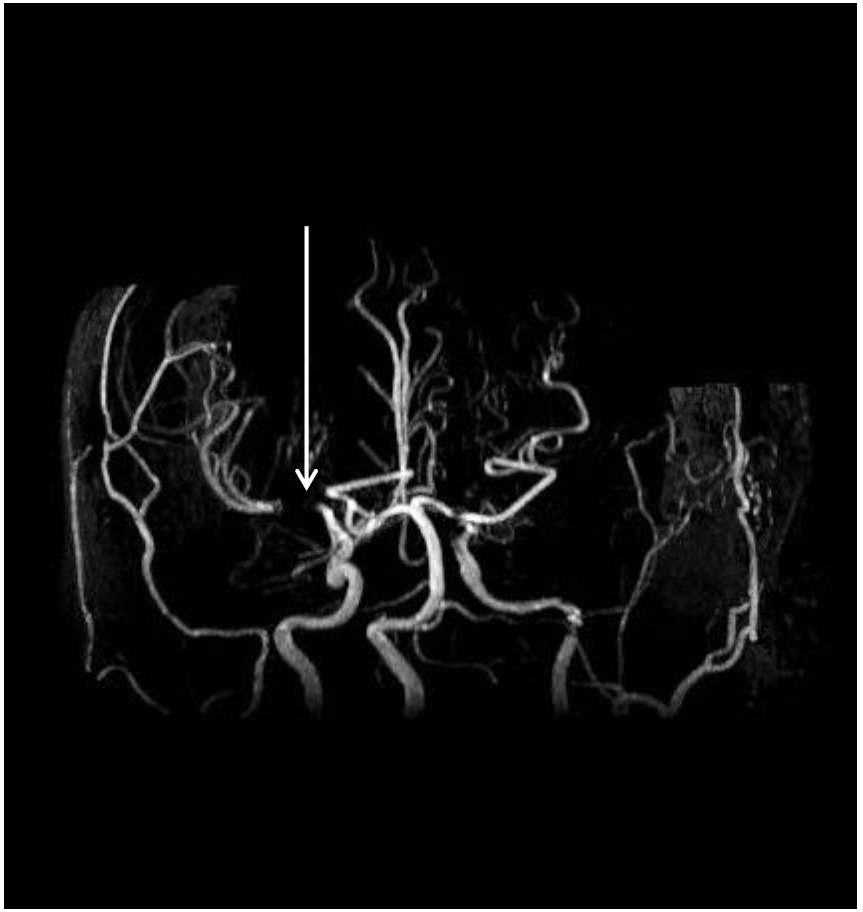


TOF MIP

MR Angiography: Time of Flight (TOF)



TOF MIP



TOF MIP

MR angiography (MRA) techniques - Time of flight

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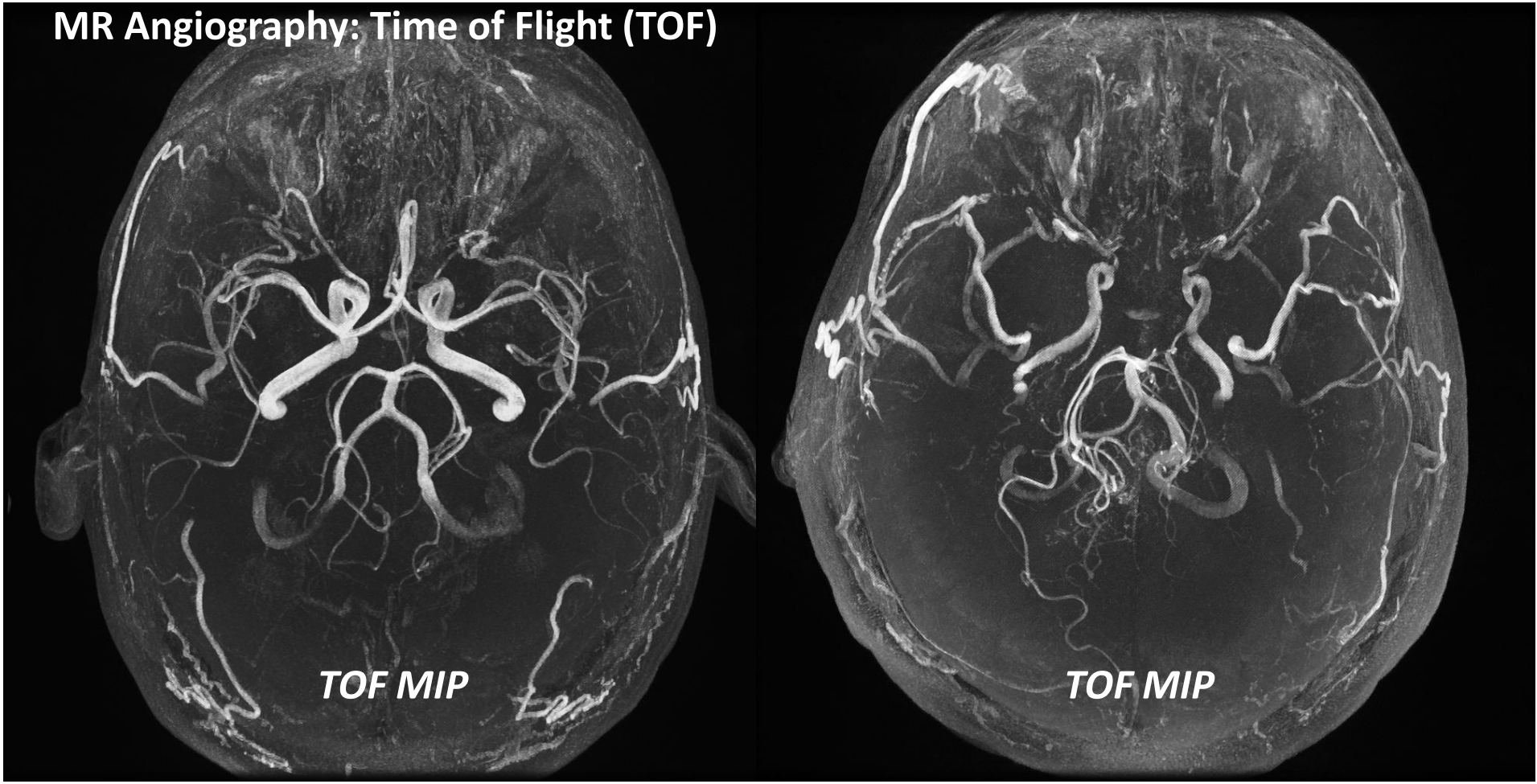
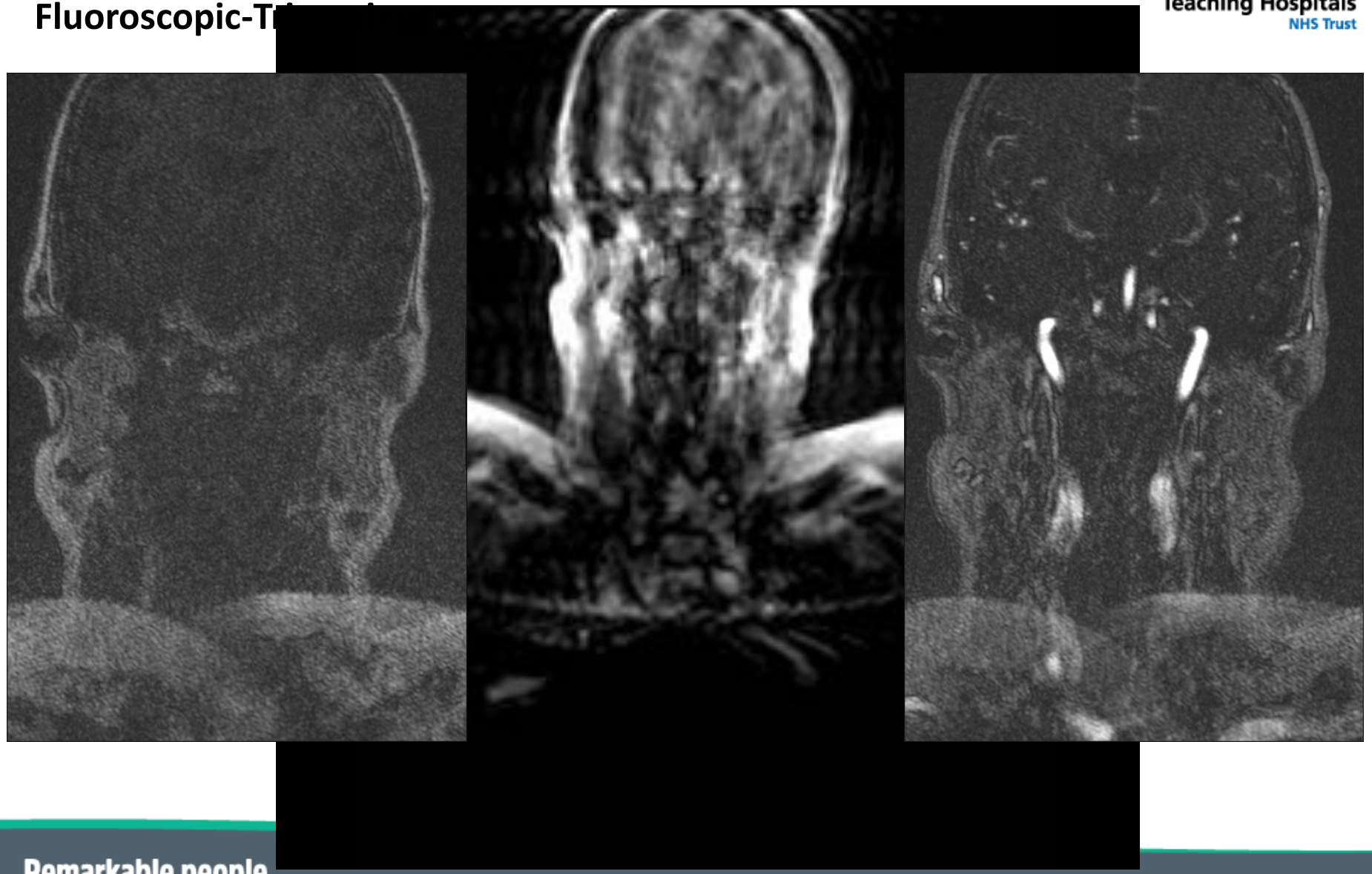


Contrast Enhanced (CE) MRA

- Contrast agent shortens relaxation time of blood
- Not reliant on saturation effects, relatively independent of flow dynamics
- Short TR reduces background signal and scan time
- Timing of arterial bolus and acquisition important

MR angiography (MRA) techniques – Contrast-Enhanced

Fluoroscopic-T



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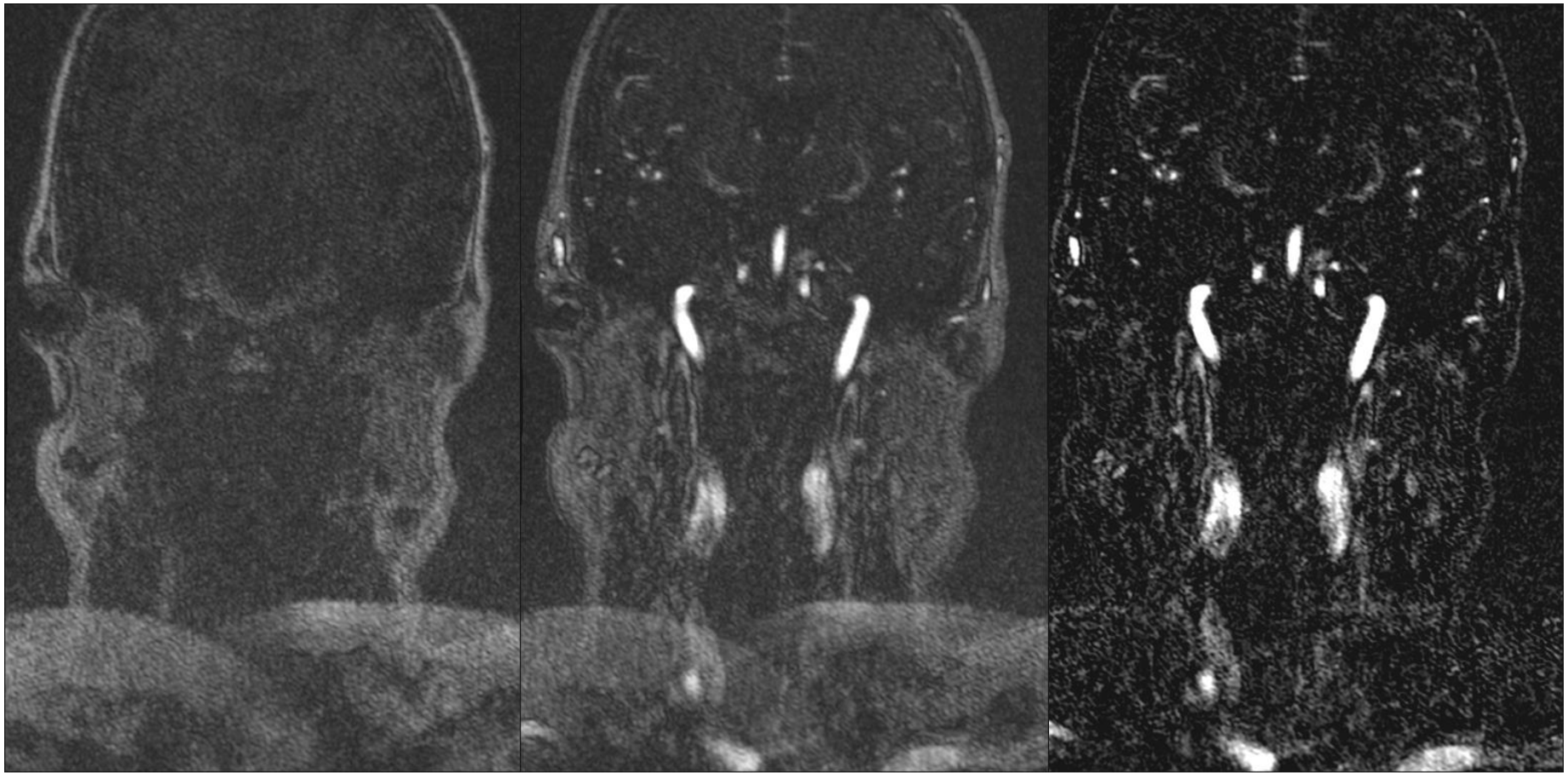
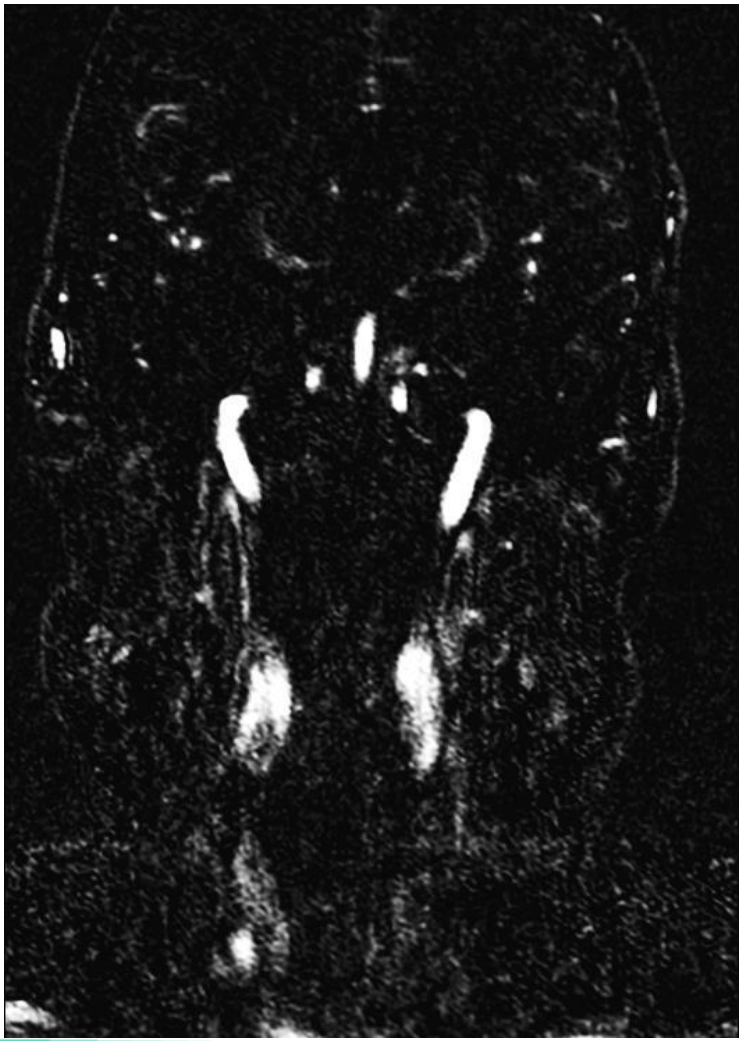
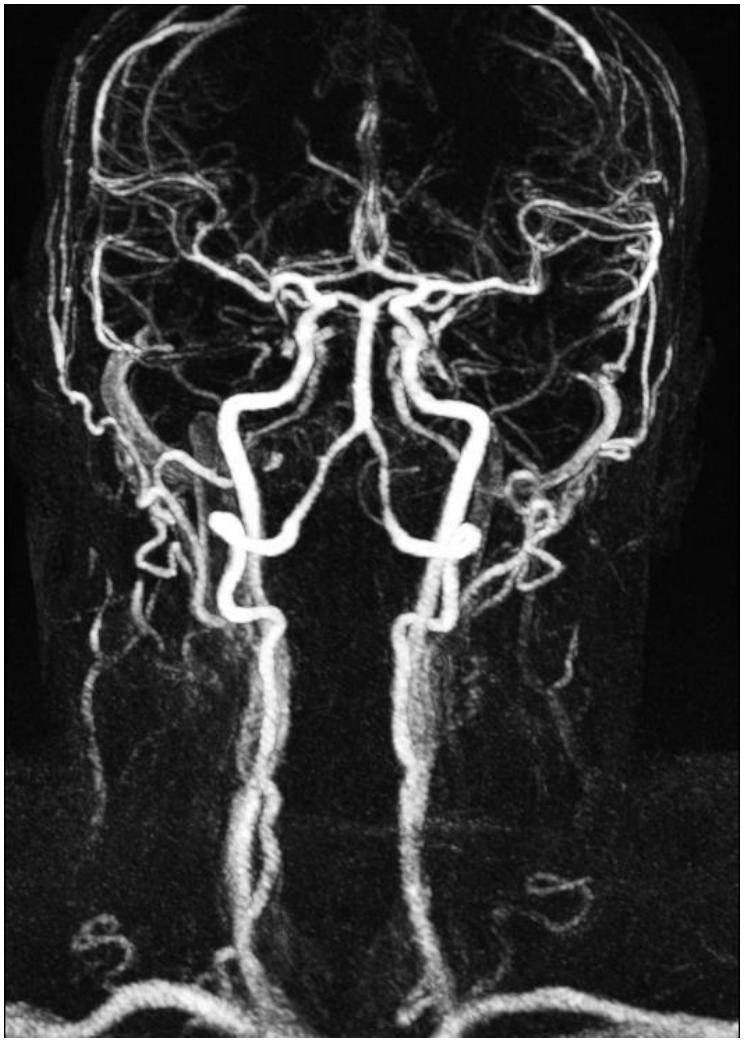
Fluoroscopic-Triggering



Fluoroscopic-Triggering





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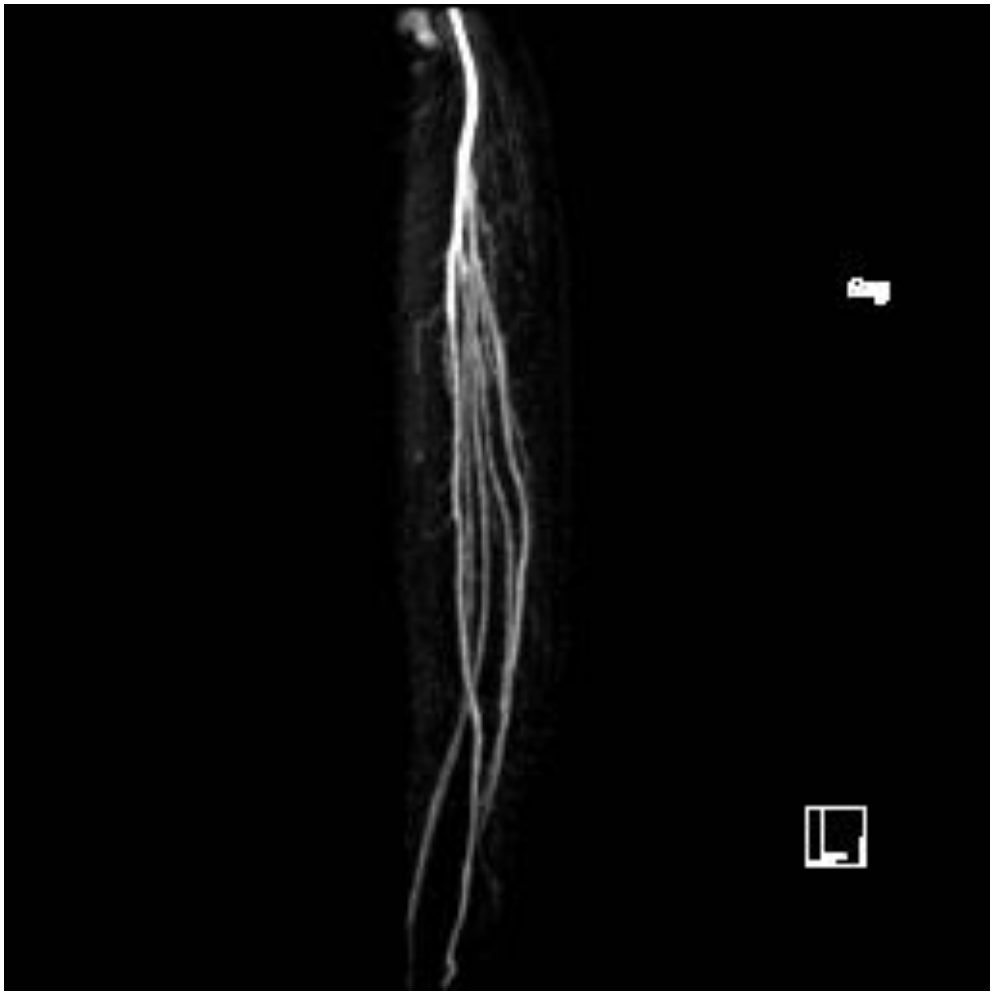
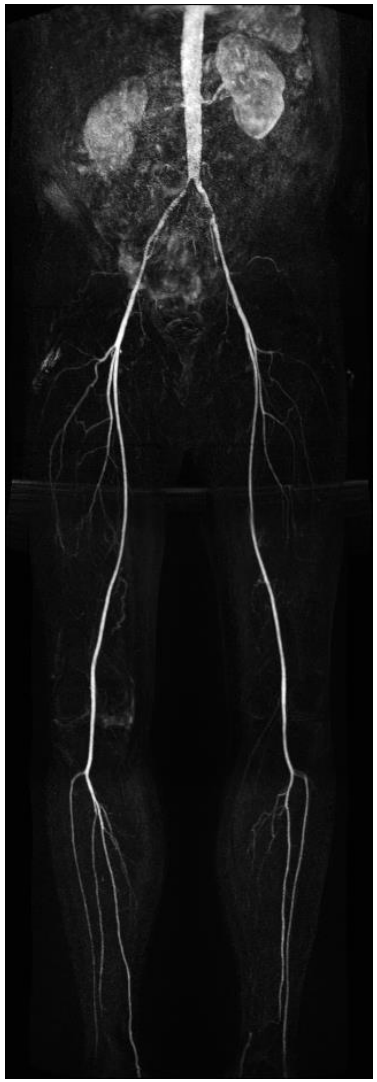
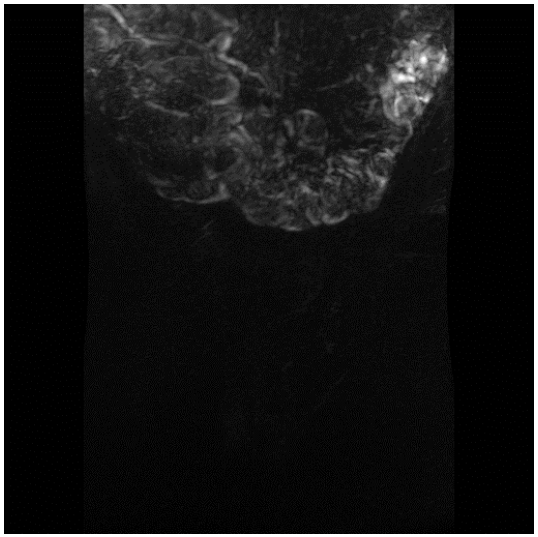
Fluoroscopic-Triggering





Contrast Enhanced (CE) MRA: Time-resolved MRA

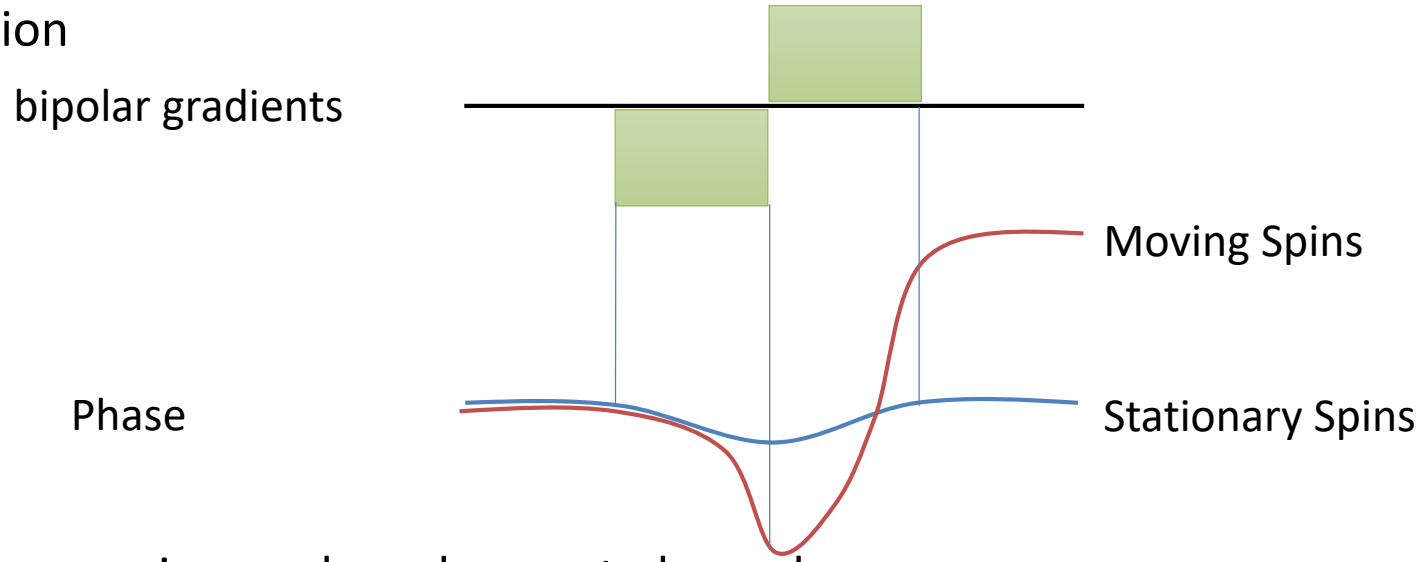
- Time-resolved MRA techniques use view-sharing
- Although the details of these methods vary, all begin by acquiring a non-contrast, full-resolution image (all of k-space) of the area of interest
- During passage of the contrast bolus, the centre of k-space is sampled more frequently than the periphery, which is updated only periodically
- The data from the different partial k-space samplings are combined to create a series of time-resolved images with satisfactory spatial resolution.
- The original non-contrast image can be used as a mask for subtraction to improve vascular conspicuity.



Phase-Contrast (PC) MRA

- Bipolar gradient pair used to sensitise flow (flow encoding in 1 direction)

- bipolar gradients are two gradients with same magnitude but opposite gradient direction

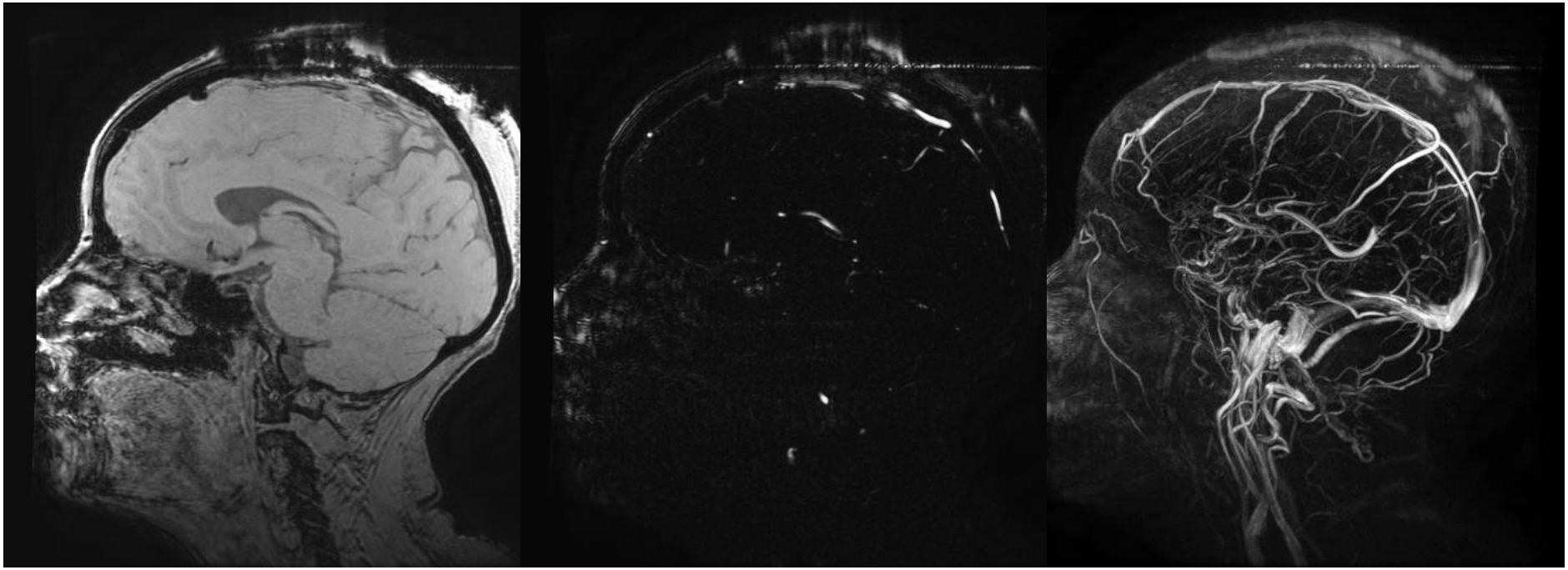


- Stationary spins re-phased: no net phase change

- Moving spins experience net phase shift proportional to blood velocity leading to loss of signal flow appears dark

Phase-Contrast (PC) MRA

- This information can be used directly to determine the velocity of the spins. Alternatively, the image can be subtracted from one acquired without the velocity encoding gradients to obtain an angiogram



PC Source Data **PC Subtraction Data** **PC MIP**

Phase-Contrast (PC) MRA

- Velocity Encoding (VENC) is a parameter that must be specified before performing a phase-contrast study

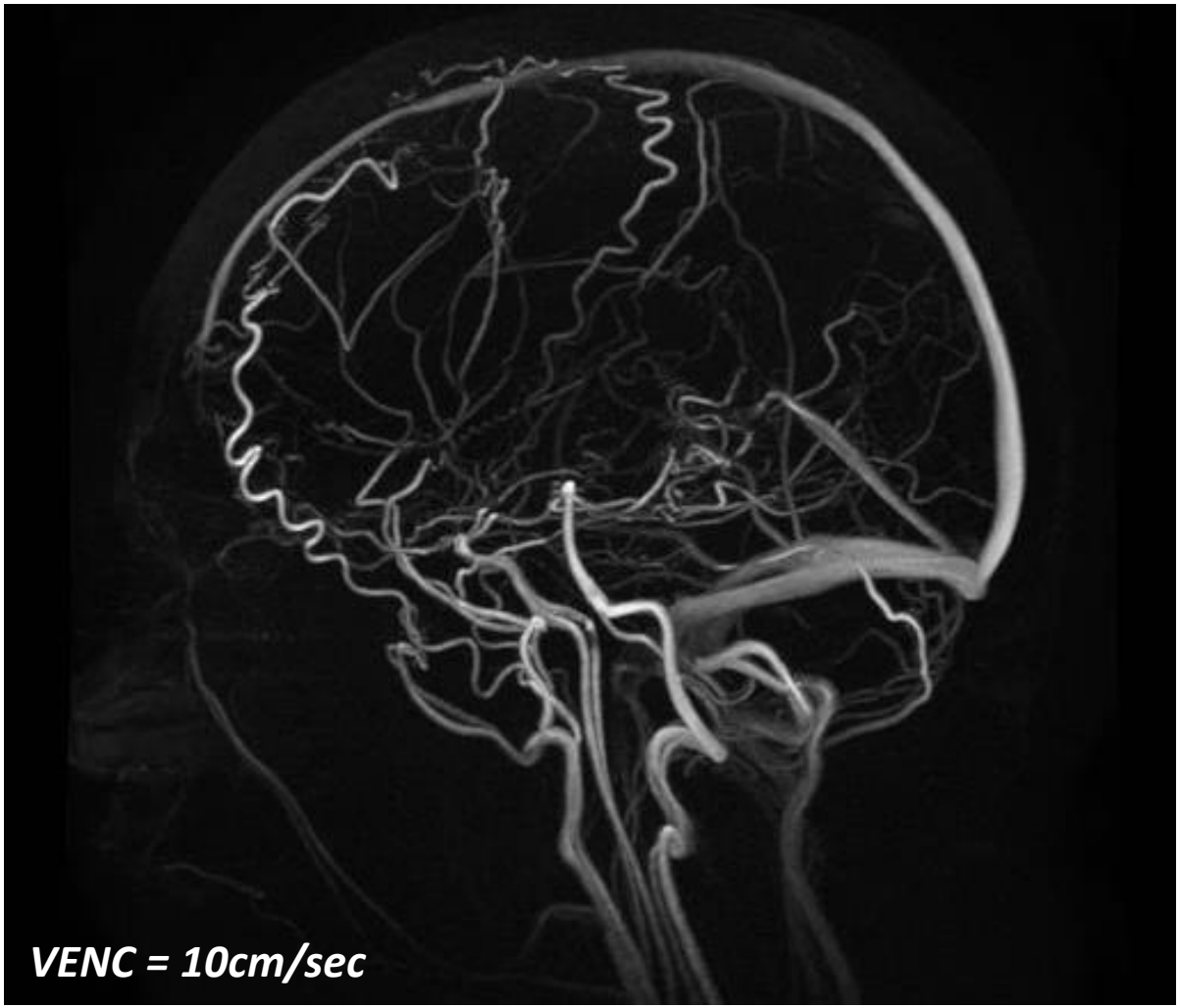
- Units of cm/sec, should be chosen to encompass the highest velocities likely to be encountered within the vessels of interest

- If VENC is set to 50 cm/sec, for example, flows in the range of ±50 cm/sec can be accurately represented by a set of phase shifts spanning from −180° to +180°

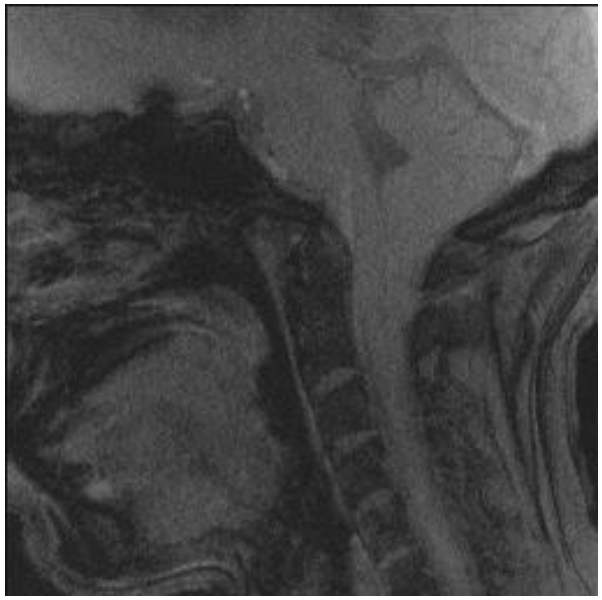
- If the selected VENC is set too high, the range of flows imaged will span only a limited phase shift range

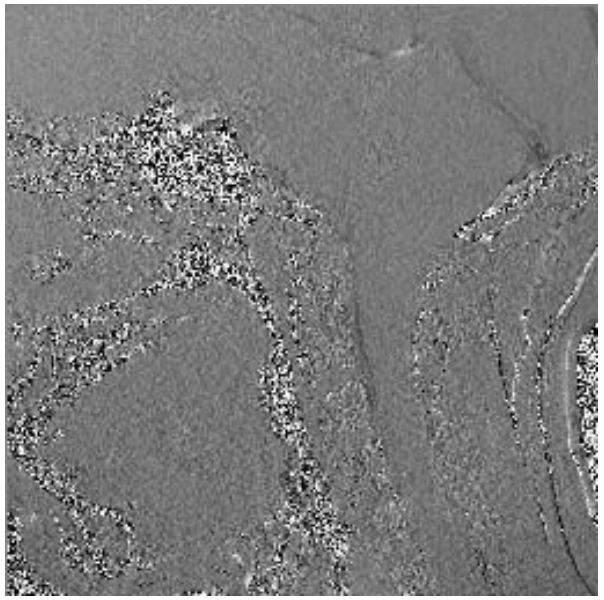
- Generally:
  Arterial imaging => VENC=40-50cm/sec
  Venous imaging => VENC=5-10cm/sec

MIP Phase contrast imaging (Inhance 3D Velocity)

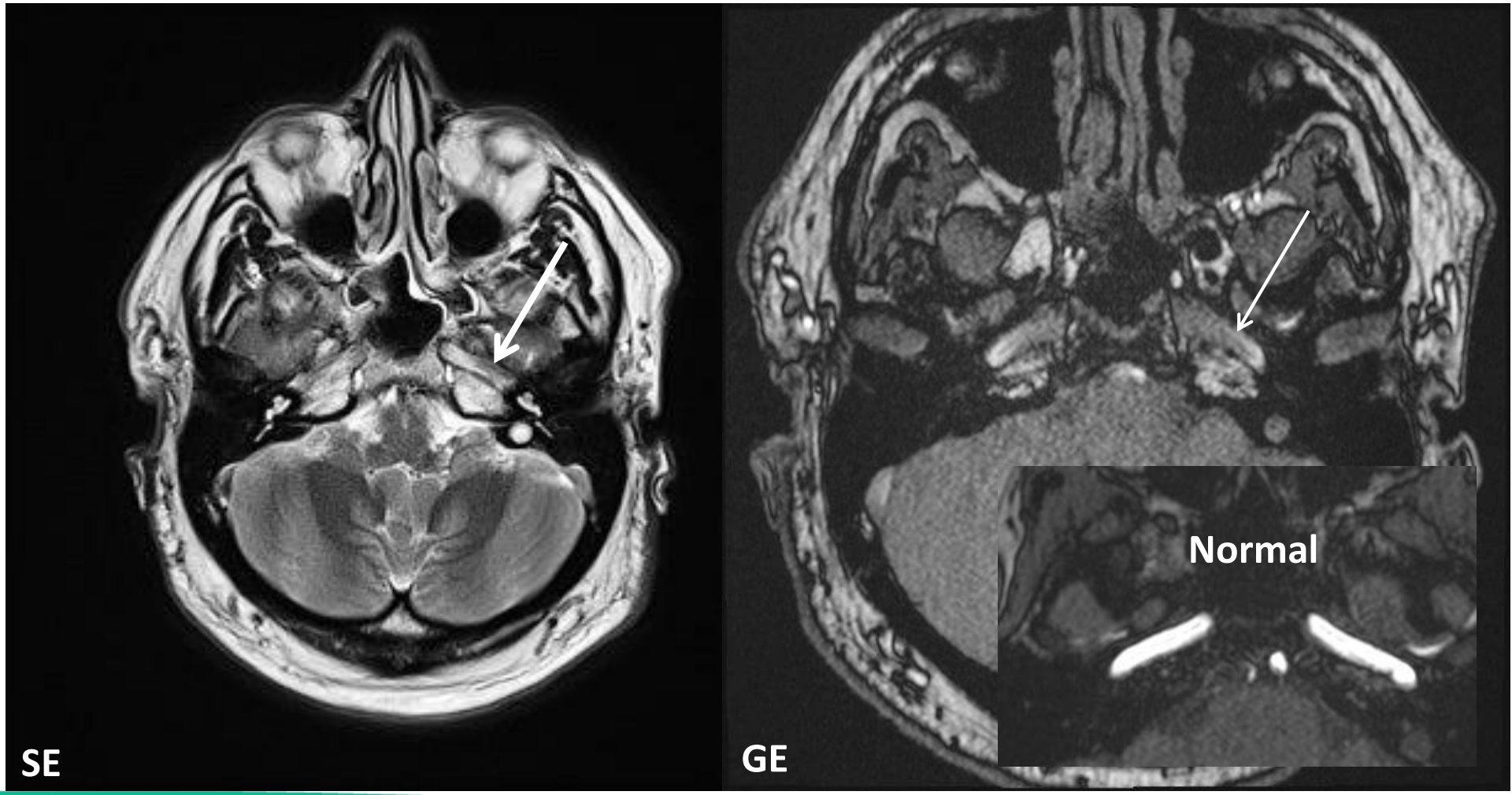


Phase Contrast CSF Flow Studies

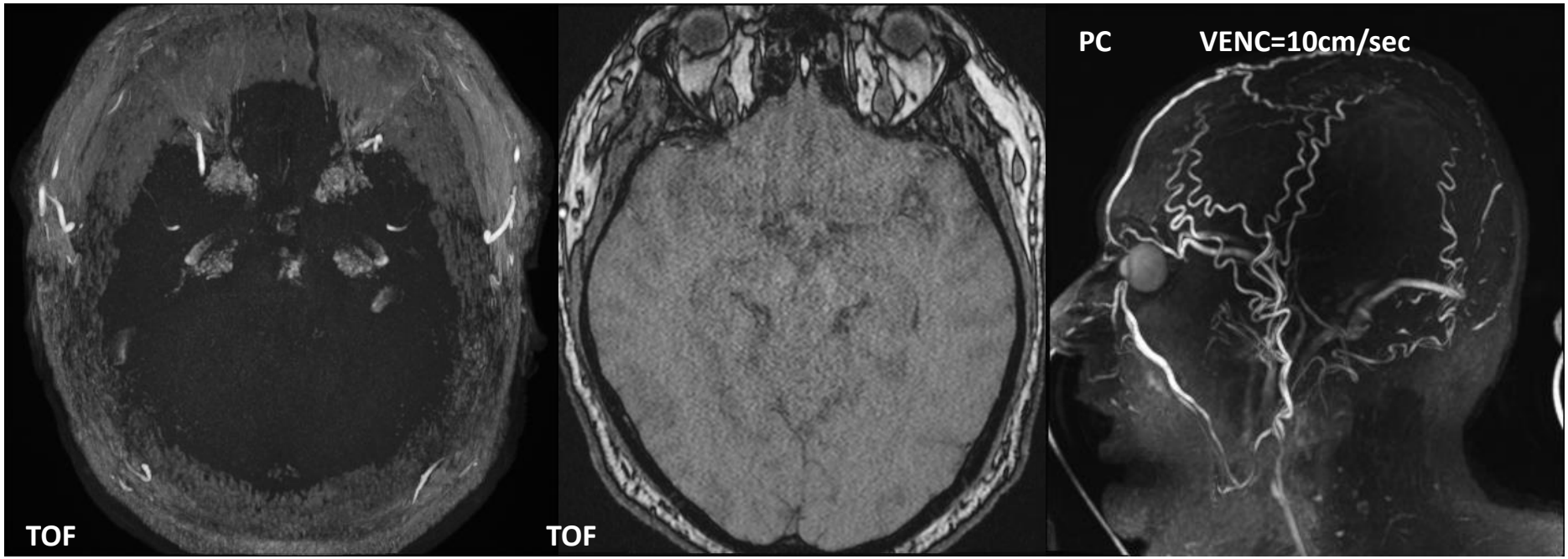




Abnormal flow

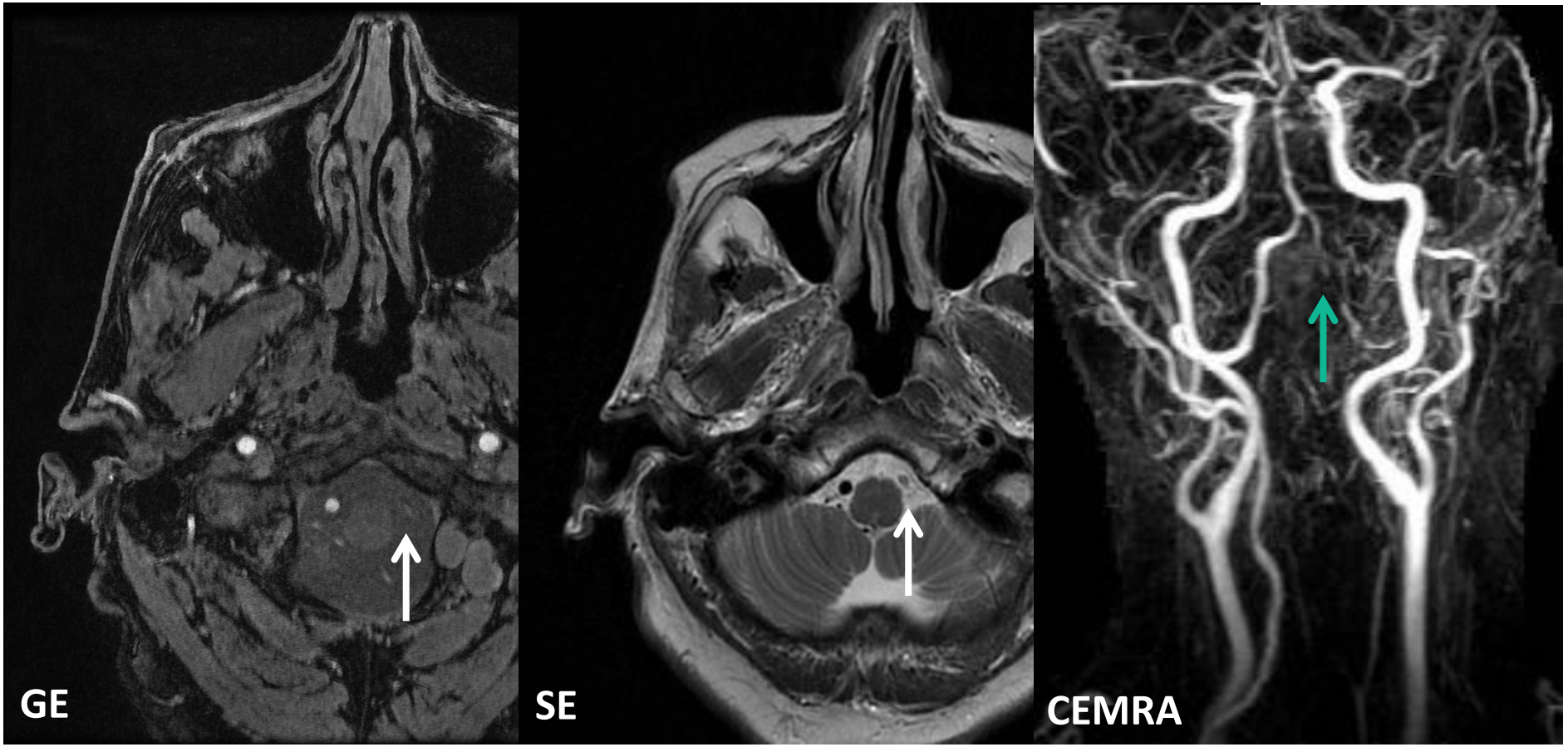


MR Angiography: Multimodal Imaging



MR Angiography: Multimodal Imaging

NHS
Hull University Teaching Hospitals
NHS Trust



7.8 Flow-related MR techniques

- Dynamic contrast-enhanced (DCE)
  - *Multiphase contrast enhanced T_1 weighted imaging. Usually gradient echo based for rapid image acquisition. Image repeatedly at the same locations to observe enhancement and subsequent washout*

- Perfusion MRI
  - Dynamic susceptibility contrast (DSC)
    - *Signal change following a bolus of Gd^{3+} contrast agent. Observe first pass through tissue using a series of T_2- or T_2*-weighted MR images. Susceptibility effect of the paramagnetic contrast agent leads to a signal decrease. Signal can be converted to concentration. Generate parametric maps for (relative) CBV, CBF and MTT*

  - Awareness of arterial spin labelling (ASL)
    - *Non-contrast perfusion imaging. Only CBF. Pre-contrast only*

7.8 Flow-related MR techniques

- DCE for myocardial perfusion, oncology
  - *Curve shape. Empirical Analysis. PK modelling. Breast, prostate, head and neck. Temporal vs spatial resolution*

- MR angiography (MRA) techniques,
  - Time of flight
    - *Based on the phenomenon of flow-related enhancement of spins entering into an imaging slice. As a result of being unsaturated, these spins give more signal that surrounding stationary spins.*

  - Contrast-enhanced
    - *Contrast agent shortens relaxation time of blood. Not reliant on saturation effects, relatively independent of flow dynamics. Short TR reduces background signal and scan time. Timing of arterial bolus and acquisition important. Time resolved MRA.*

7.8 Flow-related MR techniques

- Phase contrast
  - *Bipolar gradient pair used to sensitise flow. Stationary spins re-phased: no net phase change. Moving spins experience net phase shift proportional to blood velocity leading to loss of signal flow appears dark. Also used for CSF flow studies.*