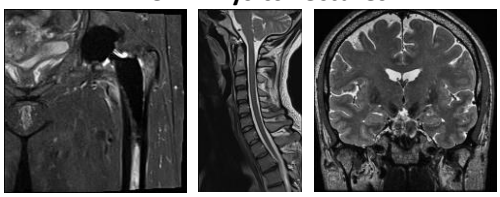
Magnetic Resonance Imaging

F.R.C.R. Physics Lectures



Lawrence Kenning PhD

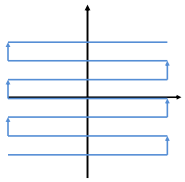
Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) [2]

- Diffusion Weighted Imaging (DWI)
- Dynamic Contrast Enhancement Imaging (DCE)
- Dynamic Contrast Susceptibility Imaging (DSC)
- Arterial Spin Labelling (ASL)
- Functional MRI (fMRI)

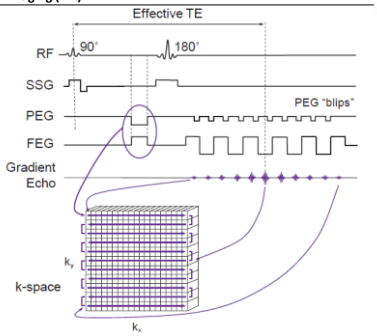
Echo Planar Imaging (EPI)

- EPI is the fastest acquisition method in MRI (100ms/ slice), but with limited spatial resolution
- Single-shot (can be run multi-shot)
  - Scan time = TR
- Inherently noisy
- Prone to distortions and ghosting
- Limited resolution (~128x128)
- Can be SE or GE based
- Widespread use in diffusion and fMRI



EPI: all lines of k-space per TR (typically 64 or 128)
Image time = TR

SE EPI



EPI: Preparation & Contrast

- For GE train a readout gradient is continuously applied, with positive & negative alternations
- With alternating gradient k-space scanned from left to right and back with each echo.
- At same time PE gradient may be permanent & constant (non-blipped) giving a zigzag trajectory or intermittent (blipped)

Echo Planar Imaging (EPI)

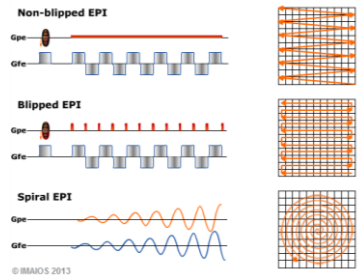
EPI: Preparation & Contrast

- Requires high performance gradients: need to allow rapid on-off switching of gradients.
  - Limits on how large this can be are determined by peripheral nerve stimulation
- Contrast determined by excitation pulse & possible magnetisation preparation
- Options:
  - GE-EPI: single RF pulse, with no preparation → T_2* weighting
  - SE-EPI: 90°-180° pulses → T_2 weighting
  - IR-EPI: 180° inversion pulse then RF excitation pulse → T_1 weighting
  - DW-EPI: preparatory pattern for diffusion weighting

Remarkable people. Extraordinary place.

Echo Planar Imaging (EPI)

Gradients and k-space filling



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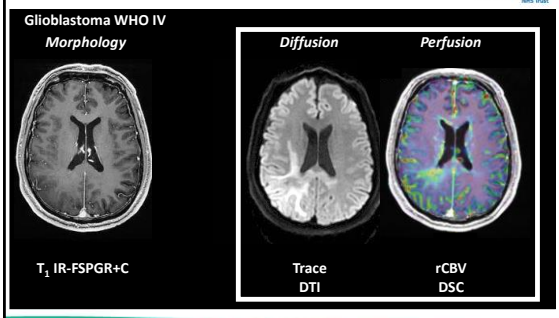

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Diffusion Weighted Imaging

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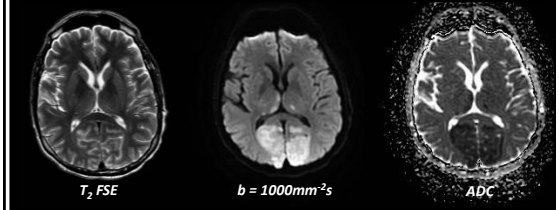
DWI

- DWI can provide real-time information about the extracellular environment



- Using DWI, alterations in water diffusion can be detected within a few minutes from onset of ischaemia
- Net increase of water detected as an increase of T_2 signal takes 1–4 hours

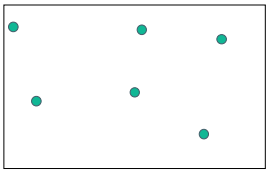
Remarkable people. Extraordinary place.

Thomalla *et al. The Lancet Neurology 2011, pg 978–86*

DWI

- Random movement 'walk' of particles in a fluid or gas is known as: Brownian Motion (Robert Brown, 1827)
- Caused by thermal motion (agitation)





- Free diffusion

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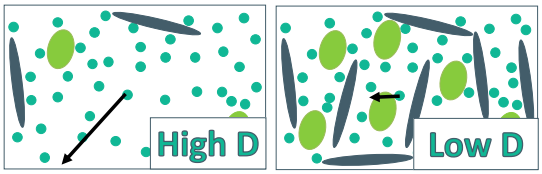
DWI



- *in vivo* molecular diffusion in tissue is not free, due to interactions with macromolecules, fibres and membranes
- Reveal microscopic details about tissue architecture
- Einstein's equation for diffusion due to Brownian motion $\langle r^2 \rangle = 6D\tau$
- $\langle r^2 \rangle / 6\tau$ = distance/time = D = self diffusion coefficient

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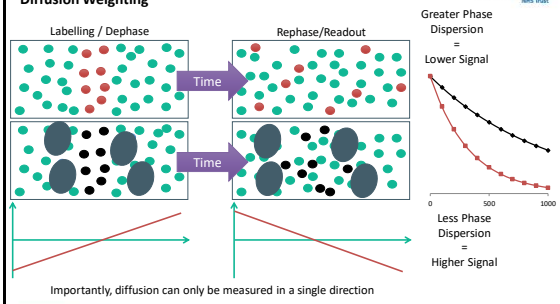
DWI

Diffusion Weighting



Importantly, diffusion can only be measured in a single direction

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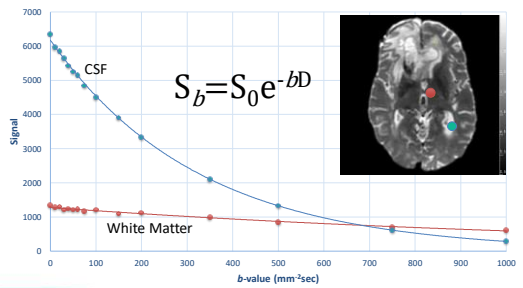
DWI

Signal Decay



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Stejskal and Tanner. *Spin Diffusion Measurements: Spin Echoes in the Presence of a Time Dependent Field Gradient J. Chem. Phys. 42, 288 (1965)*

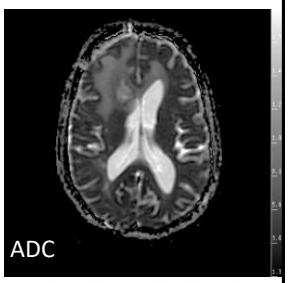
DWI

Apparent Diffusion Coefficient (ADC)

$$S_b = S_0 e^{-bD}$$

$$\text{ADC} = D = \frac{-1}{b} \ln \frac{S_b}{S_0}$$

$$\text{ADC} = \text{mm}^2/\text{sec}$$



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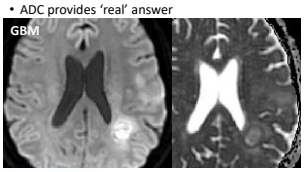
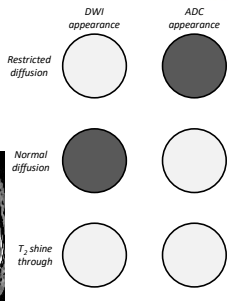
DWI

Artefacts - T_2 Shine-Through

- High signal on DW images
  - not due to restricted diffusion
- Caused by long T_2 values in lesions
  - mimicking restricted diffusion
- Seen in many pathologies
  - sub-acute infarctions
  - epidermoid cysts
- ADC provides 'real' answer





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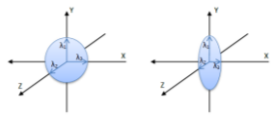
DTI

Iso- / Aniso- trophic diffusion

Isotropic Diffusion	Anisotropic Diffusion
1x 10^{-3} mm^2/sec	1x 10^{-3} mm^2/sec



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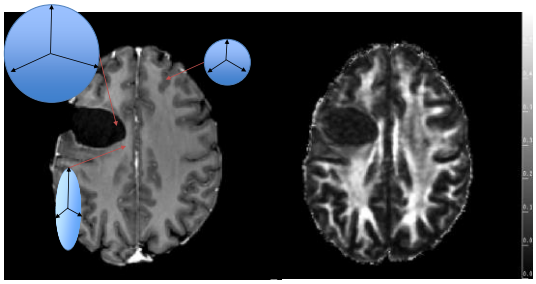
DTI

Anisotropy Mapping



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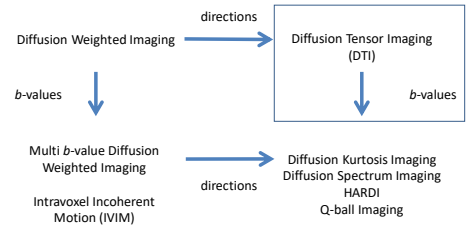
DTI

Variations of diffusion imaging



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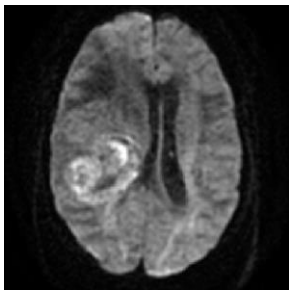
DTI

The Tensor

$$\begin{matrix} Dxx & Dxy & Dxz \\ Dxy & Dyy & Dyz \\ Dxz & Dyz & Dzz \end{matrix}$$

- D_{xx}, D_{yy}, D_{zz} are the diffusion in the main axis
- Assume that: $D_{xy} = D_{yx}$ $D_{xz} = D_{zx}$ $D_{yz} = D_{zy}$
- Therefore: only 6 elements are needed to create the tensor.
- 6 non-collinear gradient directions



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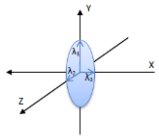
DTI

The Tensor

For each voxel:

eigenvalues eigenvectors

$$\begin{matrix} Dxx & Dxy & Dxz \\ Dxy & Dyy & Dyz \\ Dxz & Dyz & Dzz \end{matrix} \xrightarrow{\text{SVD}} \begin{matrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{matrix} [e_1\ e_2\ e_3]$$



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

$$FA = \sqrt{\frac{3}{2}} \sqrt{\frac{(\lambda_1 - ADC)^2 + (\lambda_2 - ADC)^2 + (\lambda_3 - ADC)^2}{\lambda_1^{\,2} + \lambda_2^{\,2} + \lambda_3^{\,2}}}$$

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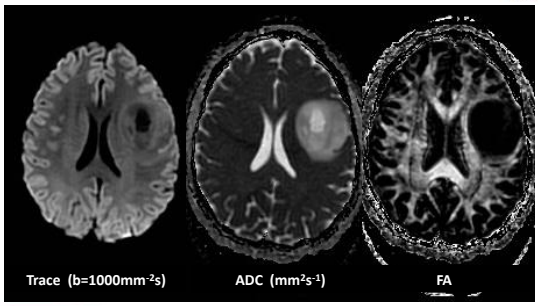
DTI

Low Grade Glioma



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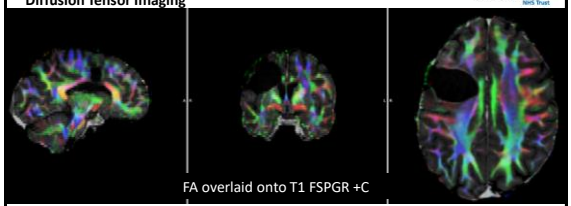
DTI

Diffusion Tensor Imaging



Red	=	magnitude of eigenvector(1)	Right-Left
Green	=	magnitude of eigenvector(2)	Anterior-Posterior
Blue	=	magnitude of eigenvector(3)	Superior-Inferior

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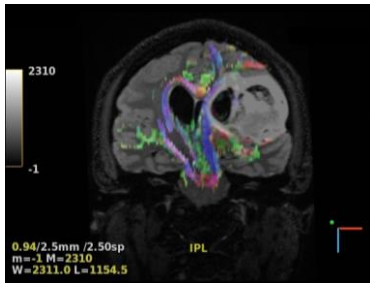
DTI

DTI Tractography for Surgical Planning

- Best possible resection
- Preserve eloquent areas and major white matter tracts
- Minimise postoperative morbidity



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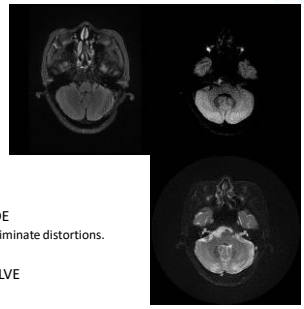
DWI

Susceptibility Issues

- Susceptibility Sources
  - Bone
  - Air
  - Hemosiderin
  - Dental work / clips
  - Tissue boundaries
- Solution?
  - Brain DWI PROPELLER / BLADE
    - FSE read-out, to minimize or eliminate distortions.
  - Multishot DWI – MUSE/RESOLVE



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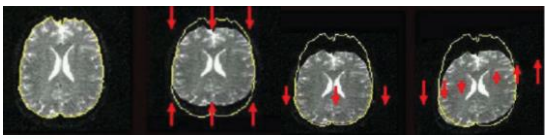
DWI

Eddy Currents

- large, rapidly switched magnetic field gradients induce eddy currents in the conductive structures of the scanner
- produce additional unwanted magnetic fields
- field gradient at the sample differs from the prescribed field gradient, resulting in a difference between the actual and prescribed b-matrix
- slowly decaying field during readout of the image causes geometrical distortion



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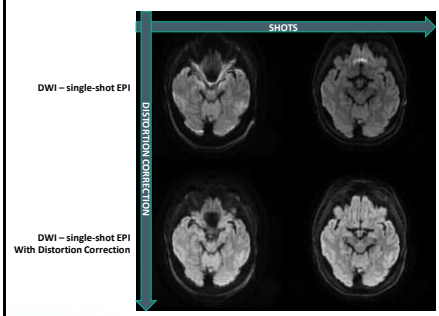
Artifacts and Pitfalls in Diffusion MRI - Le Bihan et al, JMRI 2006

DWI



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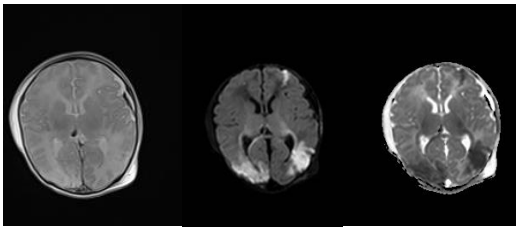
DWI

Hypoxic Injury



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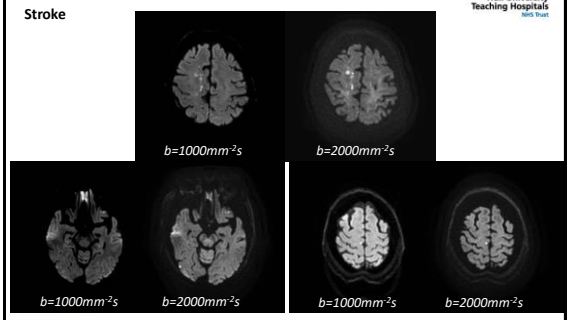
DWI

Stroke



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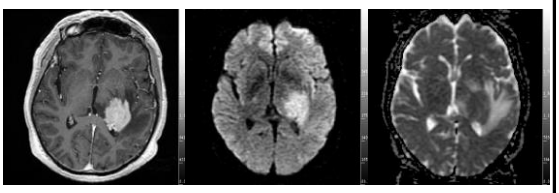
DWI

Lymphoma



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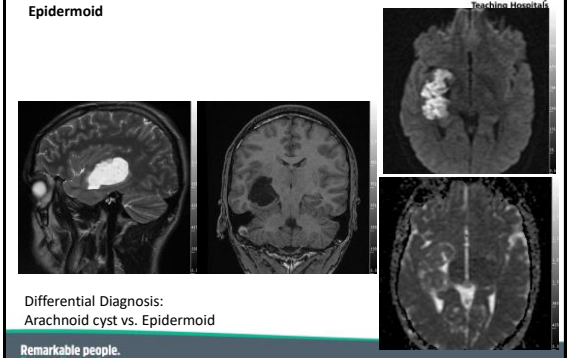
DWI

Epidermoid



Differential Diagnosis:
Arachnoid cyst vs. Epidermoid

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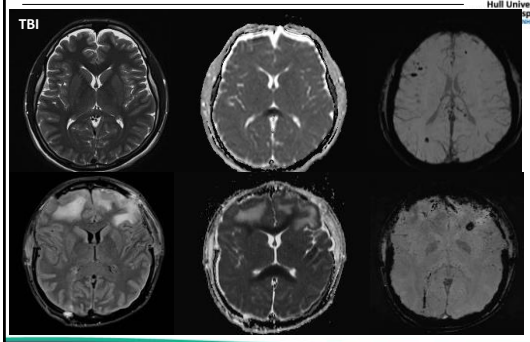
DWI

TBI



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DWI

Prostate DWI



Lesion in the peripheral zone of the gland apex

Remarkable people. Extraordinary place.

DWI

Whole Body DWI



Whole Body DWI

Remarkable people. Extraordinary place.

DWI

Summary

- Diffusion weighted imaging is highly sensitive to tissue environment
- Traditionally used to examine extracellular conditions of tissue (DWI)
- Can be used to interrogate tissue structure (DTI)
- Select *b*-value according to ADC of the tissue being scanned
- Beware of T_2 shine through
- Diffusion is not just for stroke!

Remarkable people. Extraordinary place.

Dynamic Contrast Enhanced (DCE) MRI

Hull University Teaching Hospitals NHS Trust

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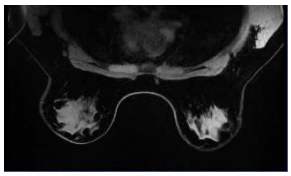
DCE

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



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DCE

Image Acquisition

- Initial T_1 measurement so signal can be converted to concentration
  - 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

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DCE

Ideal Dynamic Sequence

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

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DCE

DCE Image Analysis

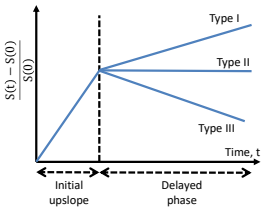
- Can analyse DCE data with varying levels of complexity
- Can depend on data available
- Visual inspection
- Empirical analysis
- Pharmacokinetic modelling

Remarkable people. Extraordinary place.

DCE

Visual Inspection

- Type I – progressive enhancement pattern
  - continuous increase in signal
  - considered benign (~9% malignant)
- 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



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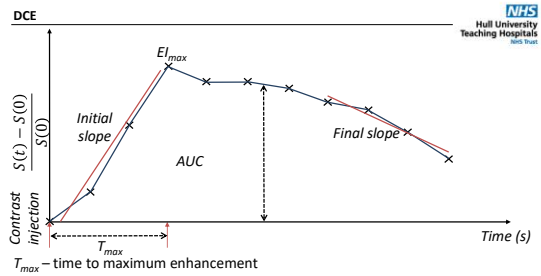
DCE

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

Remarkable people. Extraordinary place.

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

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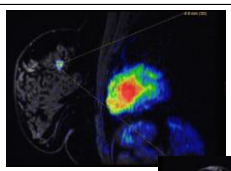
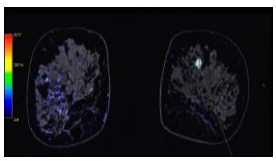
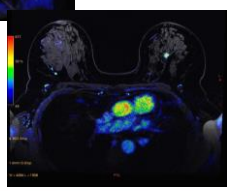
DCE

Breast Malignancy

Percentage enhancement curves







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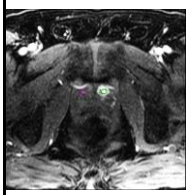
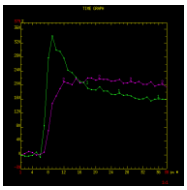
DCE

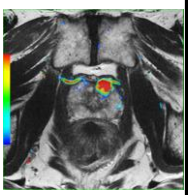
Prostate Malignancy



LAVA-FLEX source data



Percentage enhancement curves



Positive integral enhancement map overlaid onto T2 FSE

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DCE

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

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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*

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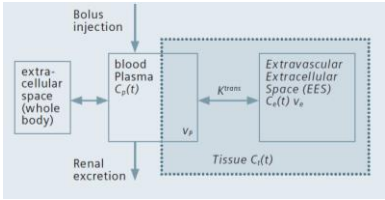
DCE

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

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DCE

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

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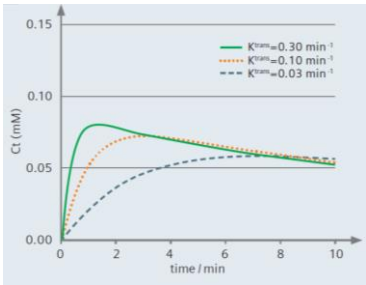
DCE

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



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DCE

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

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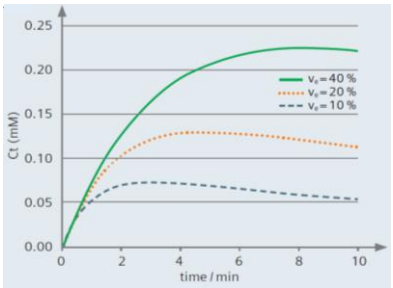
DCE



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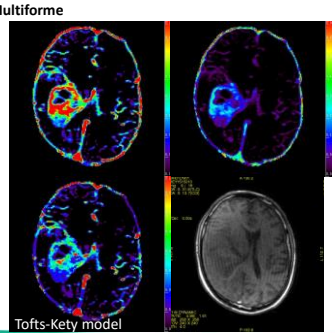
DCE

Glioblastoma Multiforme

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

v_b (blood volume fraction)



v_e (extravascular extracellular space fraction)

T_1 FSPGR

Tofts-Key model

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Dynamic Susceptibility Contrast (DSC) MRI

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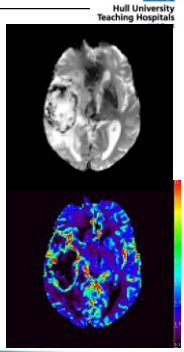
DSC

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



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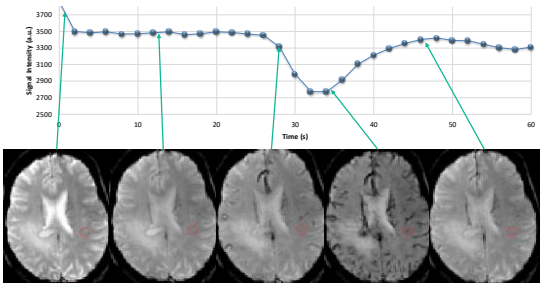
DSC

The Signal Time Course



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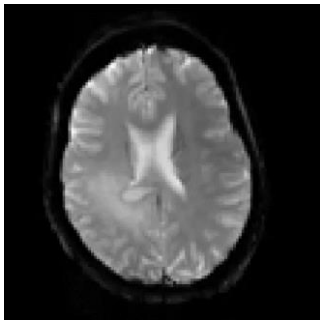
DSC



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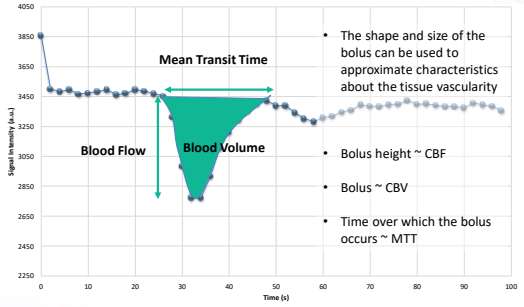
DSC

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

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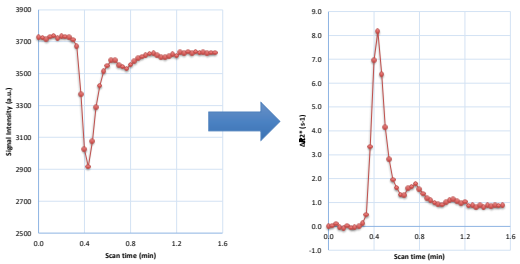
DSC

Signal to Concentration:



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

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DSC

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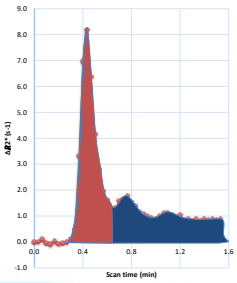
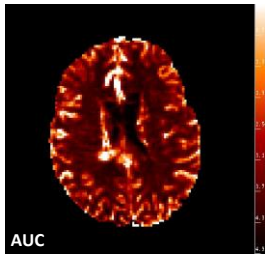
Area Under Curve / Negative Enhancement Integral:





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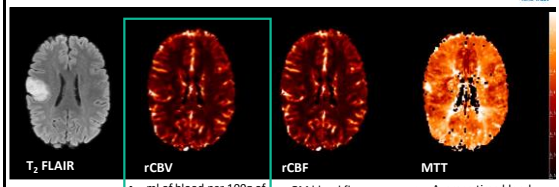
DSC Derived Parameters



T_2 FLAIR	rCBV	rCBF	MTT
	• 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 $MTT = \frac{CBV}{CBF}$

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DSC

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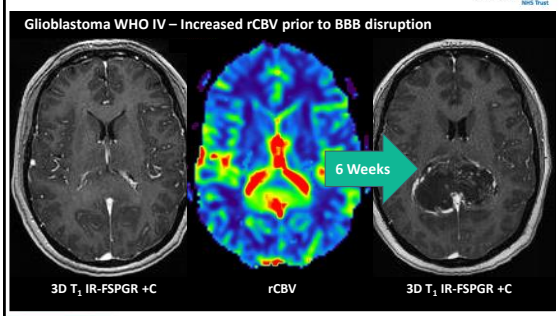
Glioblastoma WHO IV – Increased rCBV prior to BBB disruption



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DSC

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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!



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DSC

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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

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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)

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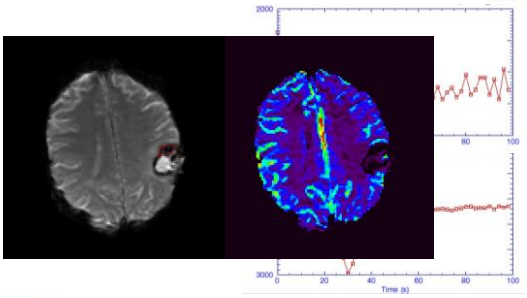
DSC

Artefacts:



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DSC

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))

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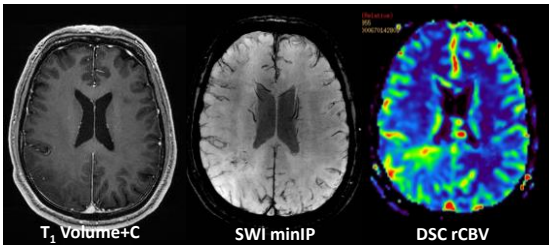
DSC

Glioblastoma WHO IV



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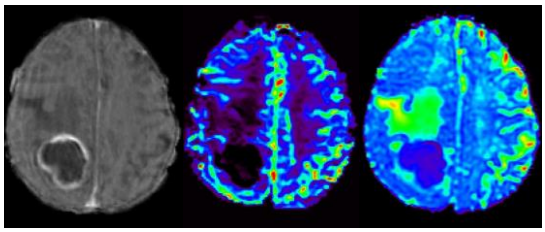
DSC

Abscess



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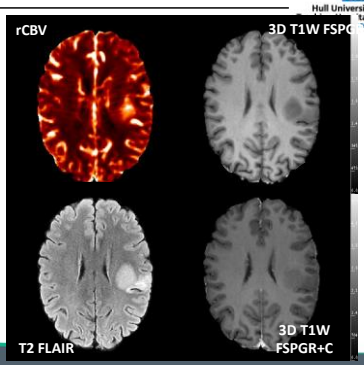
DSC

Glioblastoma WHO IV

Relative Cerebral Blood Volume fitted with Boxerman Model 'leakage corrected'



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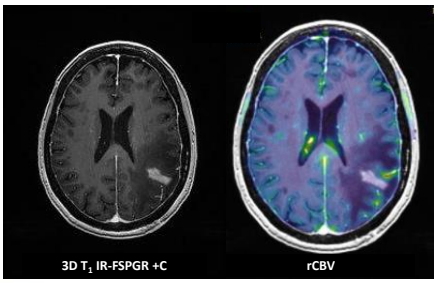
DSC

CNS Lymphoma



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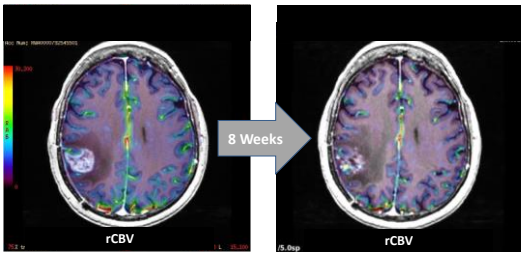
DSC

Pseudo-progression



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DSC

Summary

- DSC Perfusion MR imaging is a relatively new and promising imaging tool
- Can be used for:
  - tumour grading
  - staging
  - monitoring of treatment
- Potentially help determine efficacy of novel therapeutic agents, especially antiangiogenic therapy
- Short imaging and processing times makes perfusion MR imaging a useful tool that can easily be incorporated as part of the routine clinical evaluation of intraaxial lesions
- Main limitation is the standardised quantification of CBF and CBV

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Arterial Spin Labelling (ASL)

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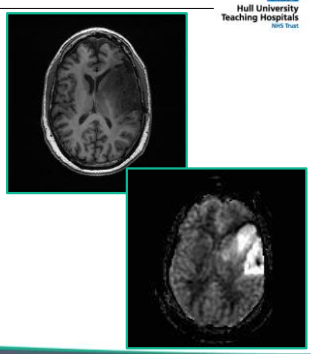
ASL

- 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



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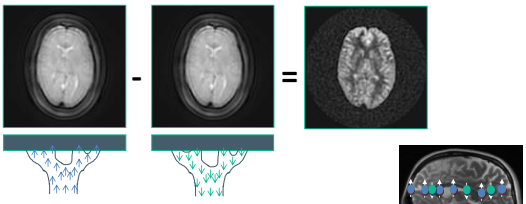
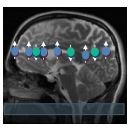
ASL

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

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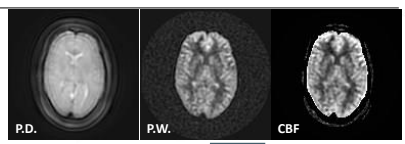
ASL



$$CBF = 6000 * \lambda \frac{\left(1-\exp\left(-\frac{ST(s)}{T_{1t}(s)}\right)\right)\exp\left(\frac{PLD(s)}{T_{1b}(s)}\right)}{2T_{1b}(s)\left(1-\exp\left(-\frac{LT(s)}{T_{1b}(s)}\right)\right)\varepsilon^4 NEX_{PW}} \left(\frac{PW}{SF_{PW}PD}\right)$$

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 T1 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 (0.7), 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.

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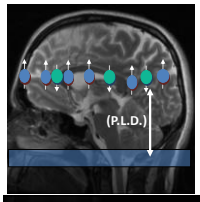
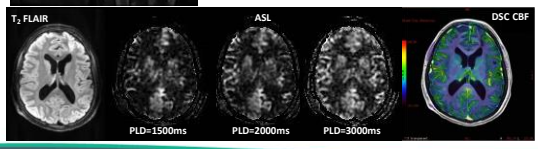
MR systems 25.0 Operator Manual/Training Tool, English
5500865-1EN (04/2015) Rev.4 © 2015 General Electric Company

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



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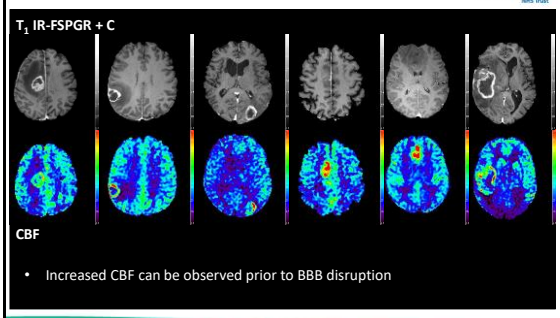

- Increased CBF can be observed prior to BBB disruption

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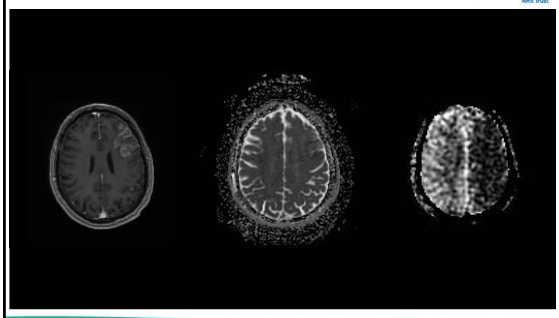
ASL



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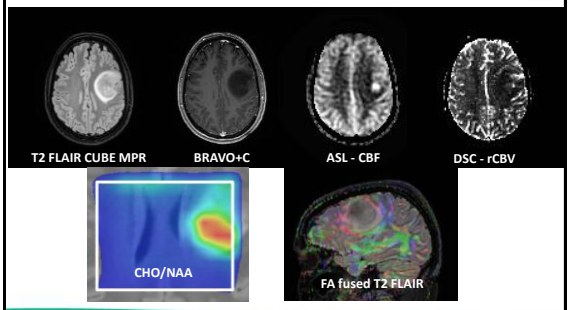
Cases

LGG on conventional imaging – 3T Premier



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Functional MRI (fMRI)

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fMRI

- Permits brain activation to be non-invasively studied (unlike PET)
- Example of endogenous contrast
- Utilises the change in MR signal which stems from changes in blood oxygen when the brain is active
- Uses blood-oxygen-level dependent (BOLD) technique
- Neuronal activity provokes an increase in oxygen consumption and higher increase in local blood flow
- Expressed as relative increase in oxyhaemoglobin compared to deoxyhaemoglobin

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fMRI

- Deoxyhaemoglobin is paramagnetic and causes a gradient which attenuates signal (shortens T_2*)
- Neuronal activity causes increase in blood flow
- Oxyhaemoglobin fraction increases signal increase on T_2* or T_2-W images



Gradient echo EPI sequence

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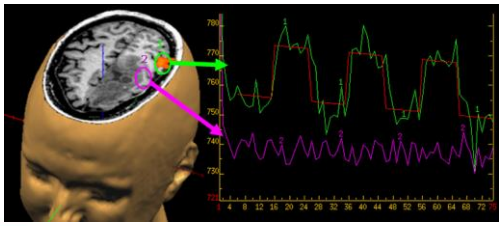
fMRI

REST TASK REST TASK REST TASK REST



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fMRI



- fMRI used in Neurosurgical Planning

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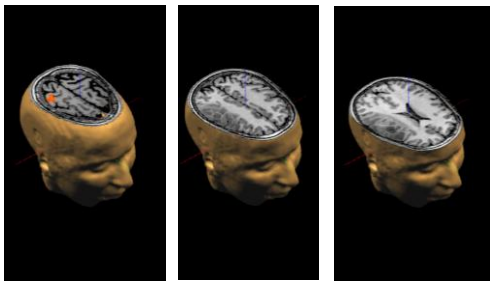
fMRI



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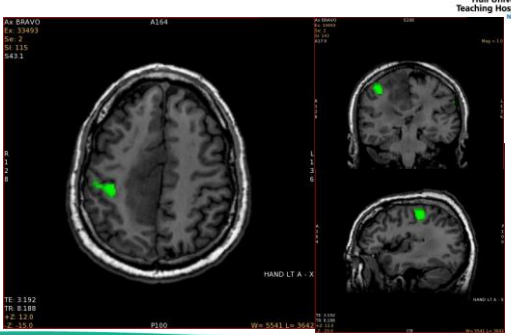
fMRI



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Question

Pulse sequences in MR

A. Echo-planar imaging (EPI) provides highly detailed images

B. Restricted diffusion shows a high signal and is abnormal in diffusion weighted images of stroke.

C. Deoxygenated haemoglobin is paramagnetic; this is the basis for functional MRI

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