NSI 1st Foundation Course
NIMHANS, Bengaluru 2015

Imaging for Brain Tumour Diagnosis

C.E.Deopujari, Sunila Jaggi
BHIMS, Mumbai

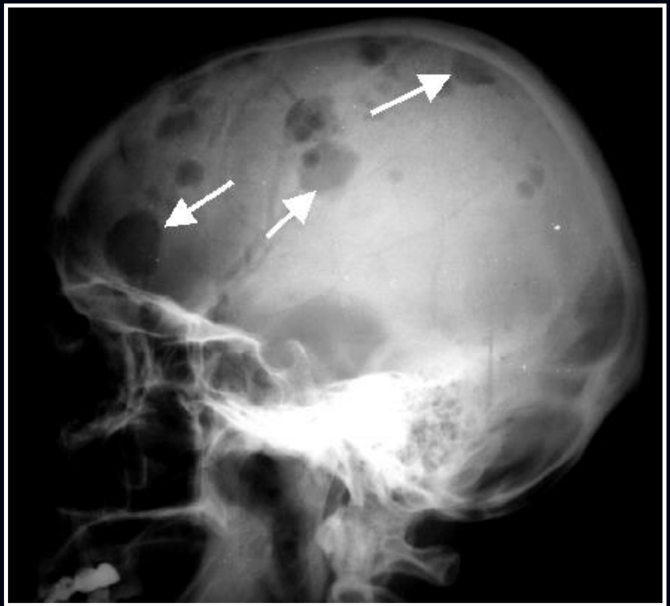
Discovery of X-Rays

On 8th November, 1895, a German physicist, **Wilhelm Conrad Röentgen**

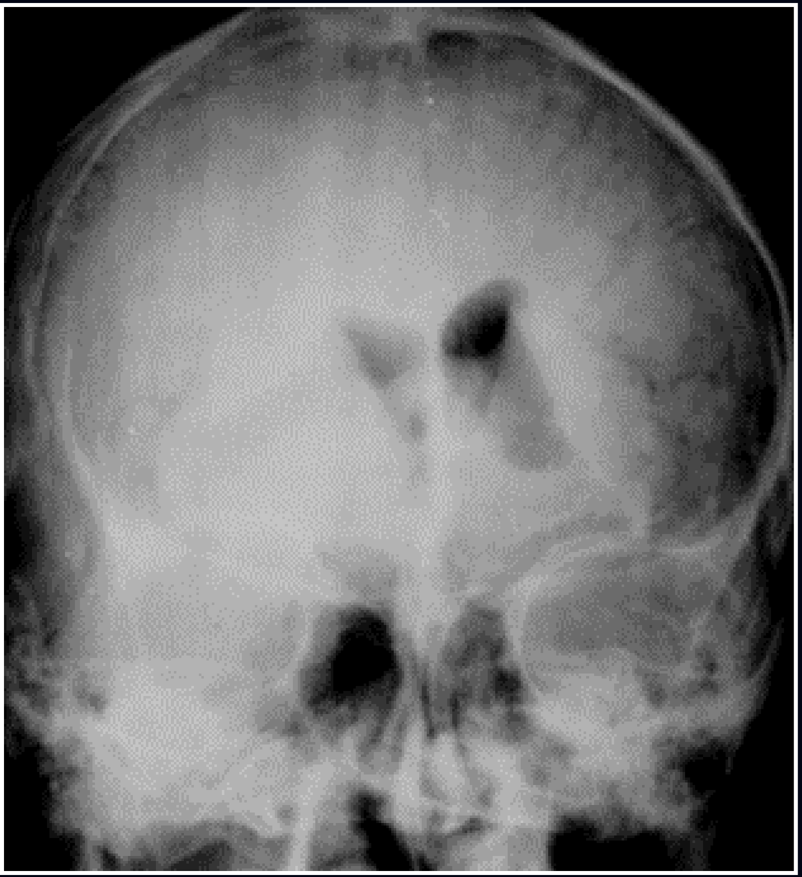
discovered X-rays while studying the phenomena of high voltage discharges in vacuum tubes.

- In 1901 was awarded the very first Nobel Prize in Physics

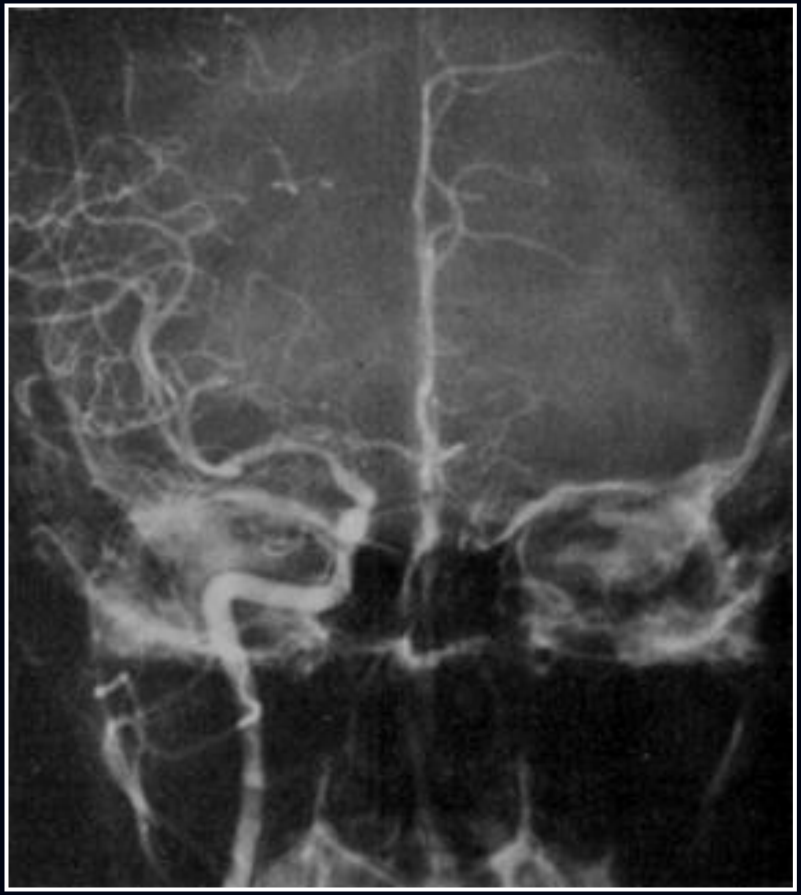
Neuroradiology



Pneumoencephalography



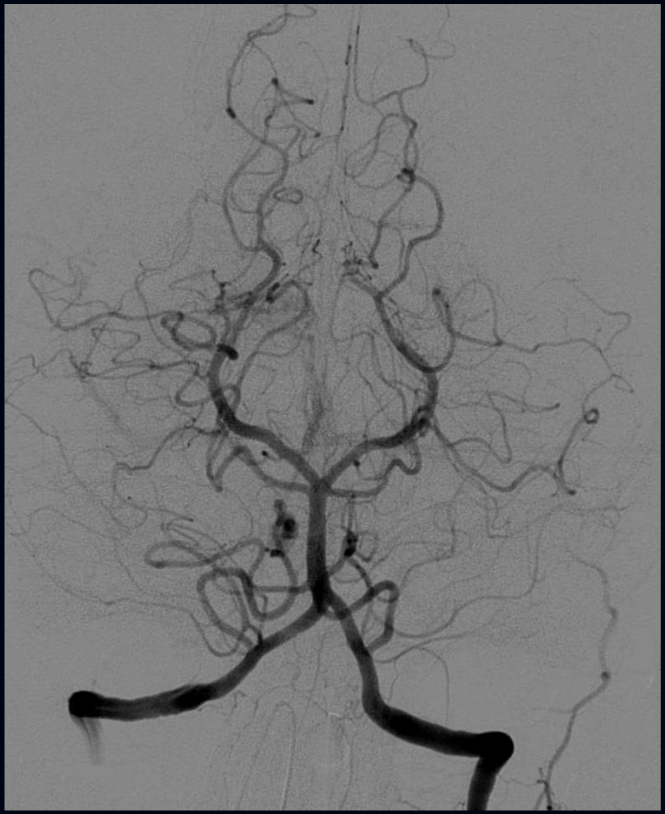
Cerebral angiography



1970's saw the discovery of advanced imaging techniques in the history of mankind

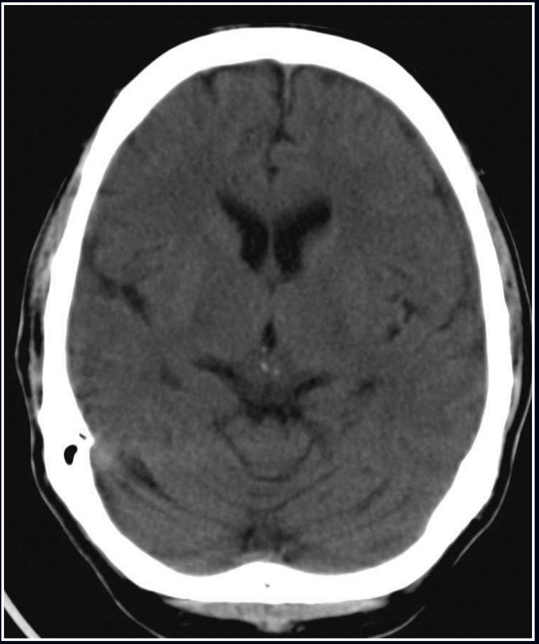
REVOLUTIONS IN NEUROIMAGING

Digital Subtraction Angiography (DSA)



Revolutions in Neuroimaging

Conventional → Cross-Sectional Imaging



Sir Godfrey Hounsfield
1919-2004

Invented CT Scan in 1972

A patient under examination by the computer-aided brain X-ray machine.

Brain X-rays assessed by computer

By John Roper
Medical Reporter

A British electronics company has developed an X-ray system which, it says, for the first time will make the investigation of tumours and other brain disorders far more precise and will help diagnosis greatly.

The machine, X-ray detectors combined with a digital computer, has been developed in the past three years by EMI. It enables vastly more information to be extracted than with conventional X-rays

The export cost of the equipment will be between £50,000 and £100,000, depending on whether the computer is built in or an external computer is linked up.

EMI, which is confident that the system will revolutionize clinical medicine and research, is mounting a big sales drive. Salesmen and technicians are going to America, Japan and elsewhere to sell what the company sees as an important British breakthrough in aids to investigation of brain disorders. Eastern European countries are expected to be particularly interested.

Research is going on into adapting the equipment for use in examination of other parts of the body, such as the lungs; but technical difficulties have to be overcome.

An advantage of the machine is that one operator with a modicum

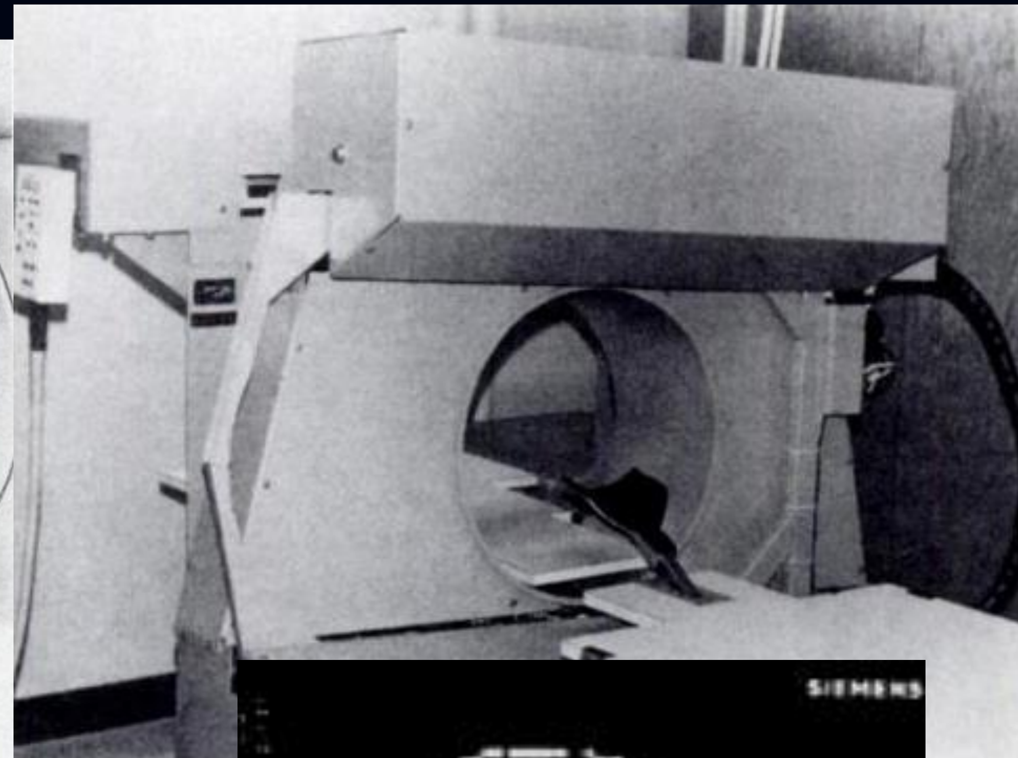
X-rays two adjacent slices of the brain, each one centimetre thick, by rotating round the patient's head and taking 56,000 readings.

These readings "learn" from each other and are fed to the computer which, solving 28,000 simultaneous equations, builds up a matrix of 25,000 points giving a highly accurate valuation of the material within the slices.

The system overcame the disadvantage of the low sensitivity of X-ray machines and the confusion of information on the plate caused by three-dimensional information being superimposed on a two-dimensional photograph.

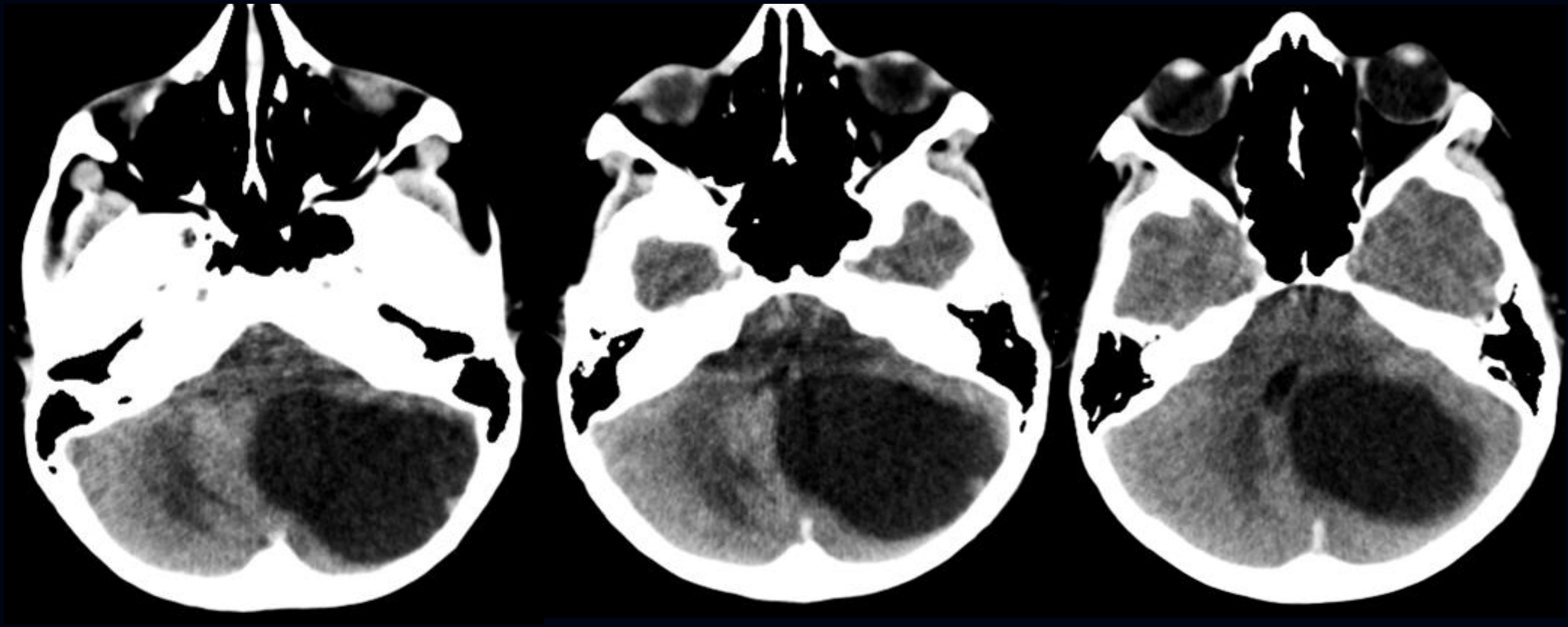
One examination does not cover the whole head, but in two and sometimes three examinations most of the brain is covered.

Mr Hounsfield added that the

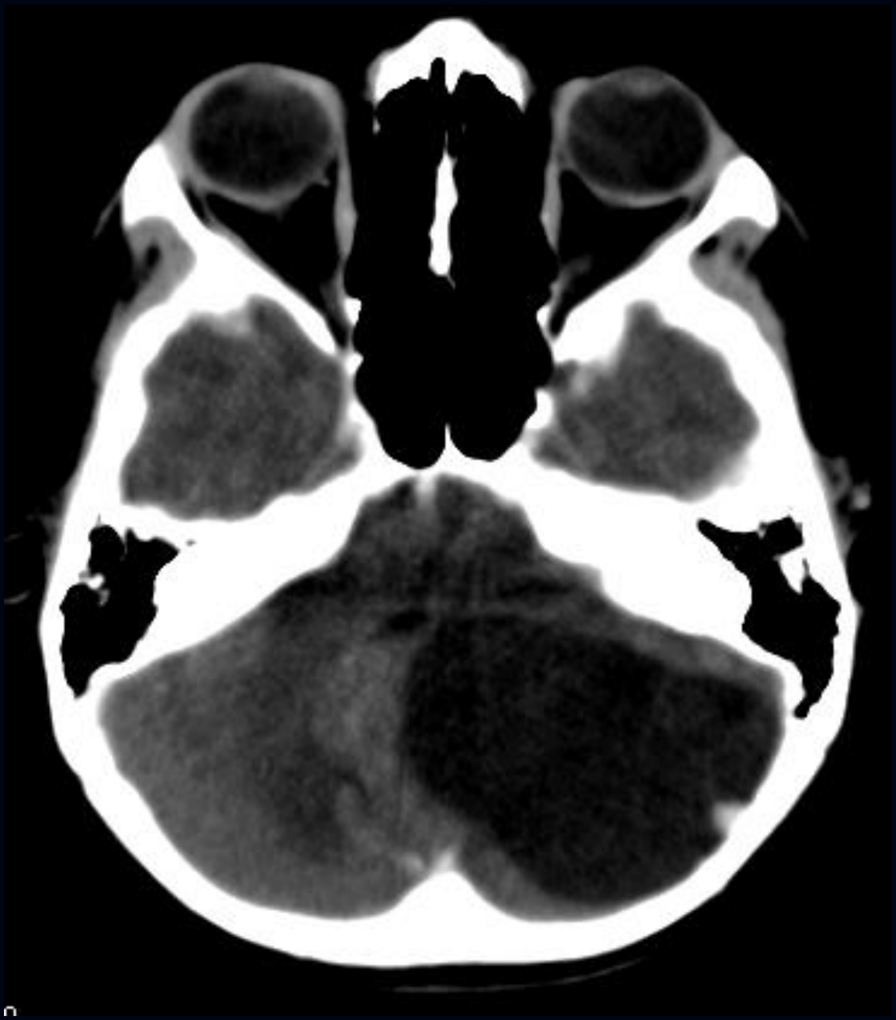


First CT Scan machines - 1974

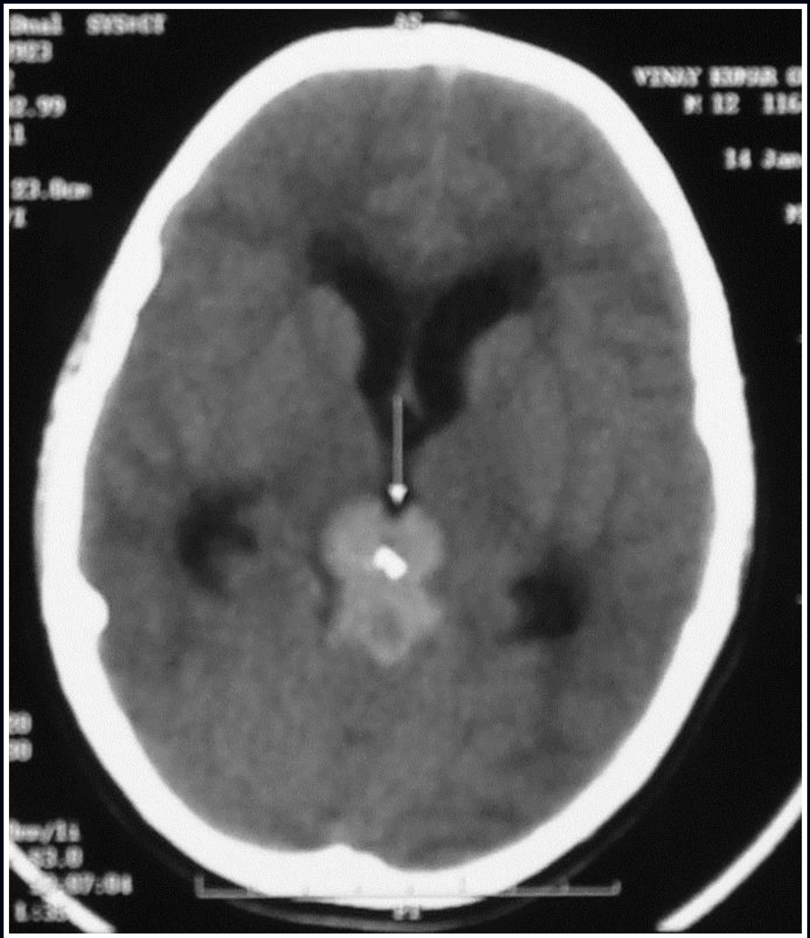
Plain CT Scan

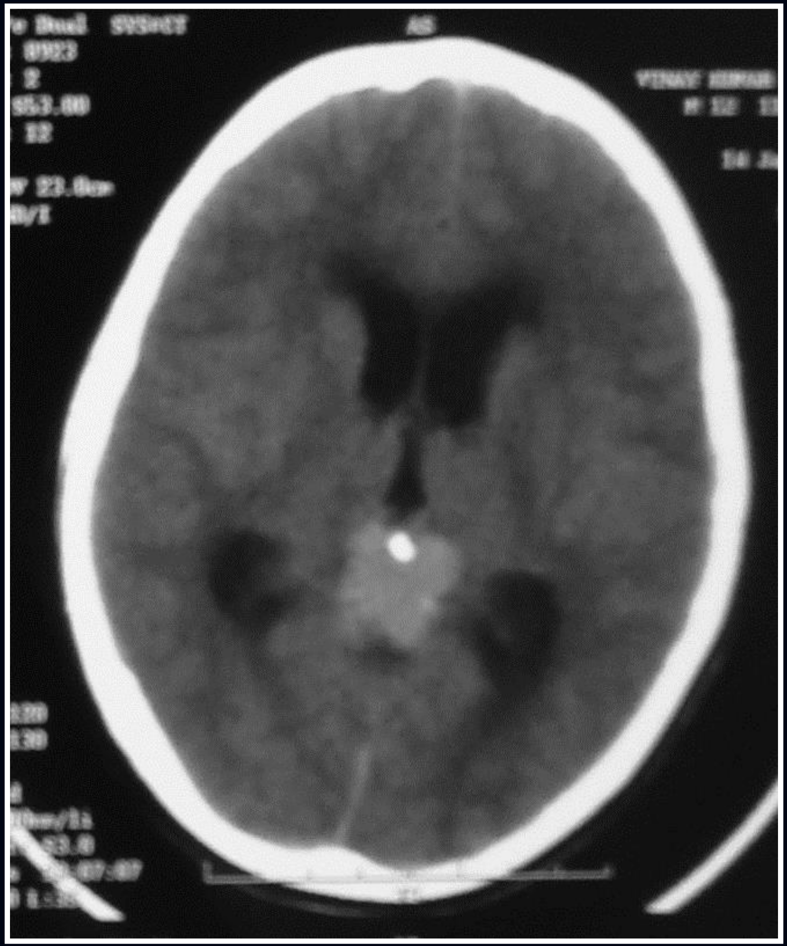


Post-Contrast CT Scan

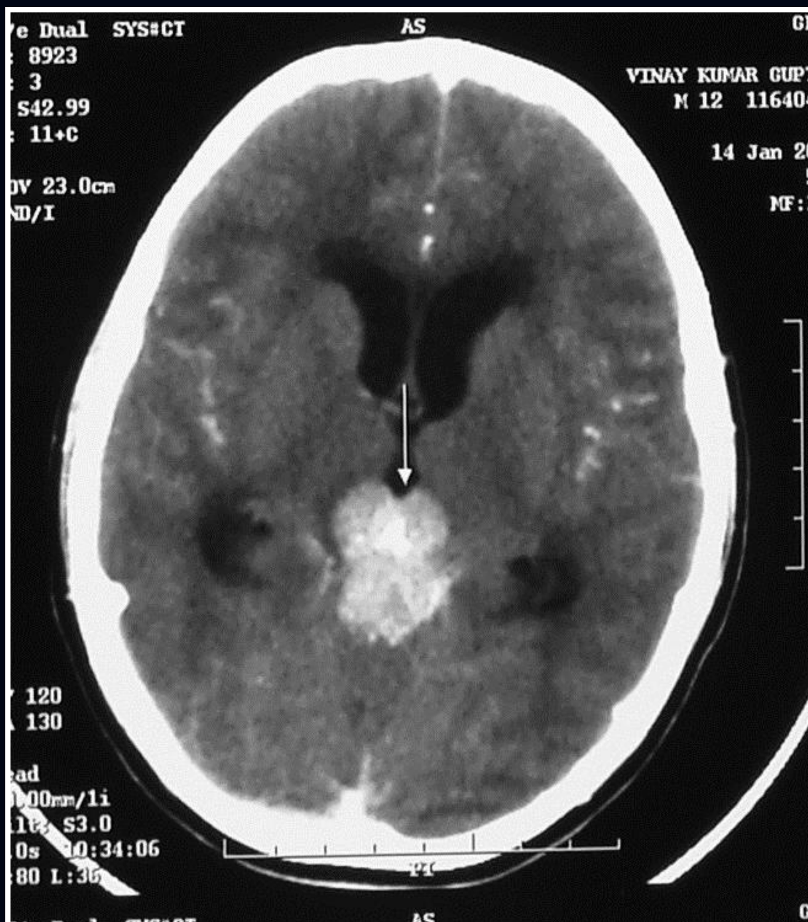


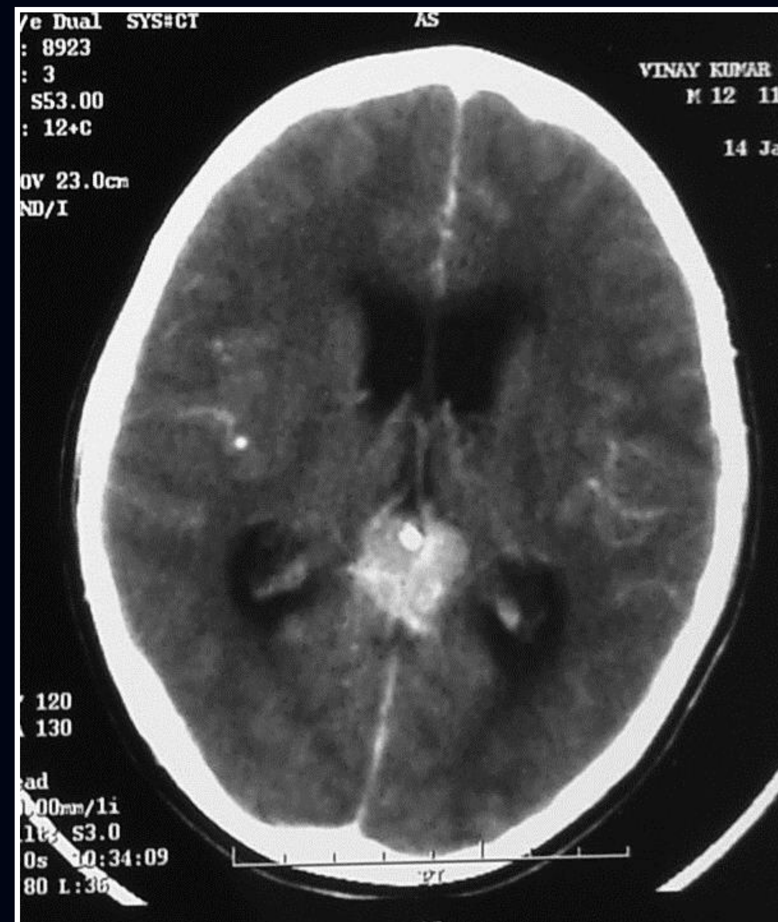
Plain CT Scan

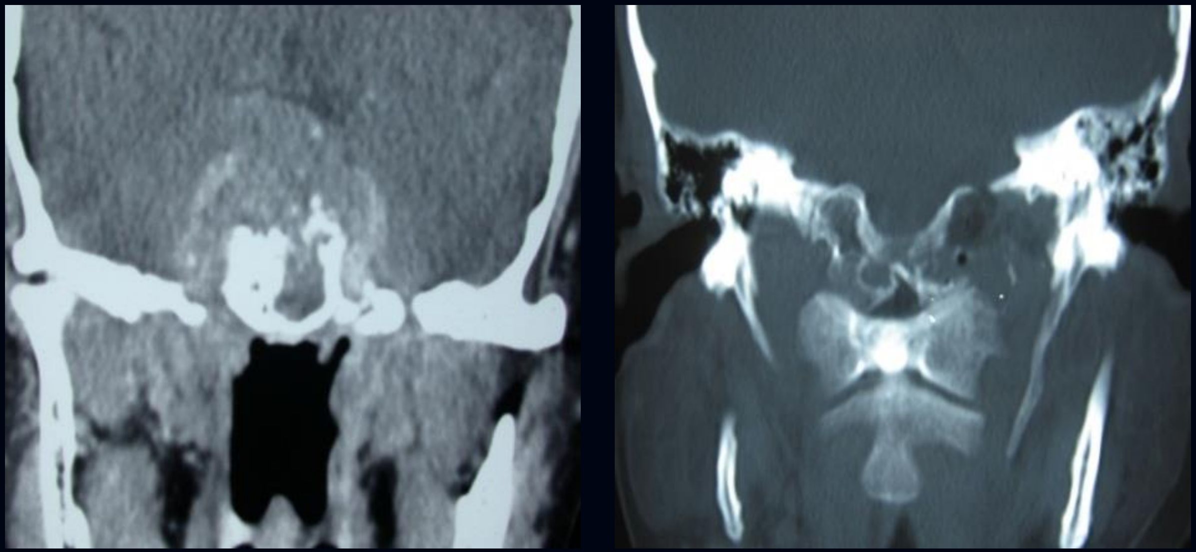




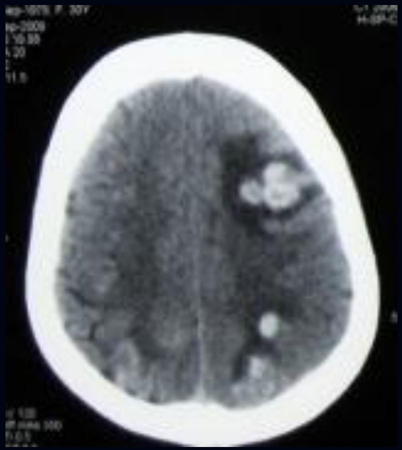
Post-Contrast CT Scan







CT showing bony destruction of clivus in a case of chordoma and (b) widening of jugular foramina in a case lower cranial nerve schwannoma.



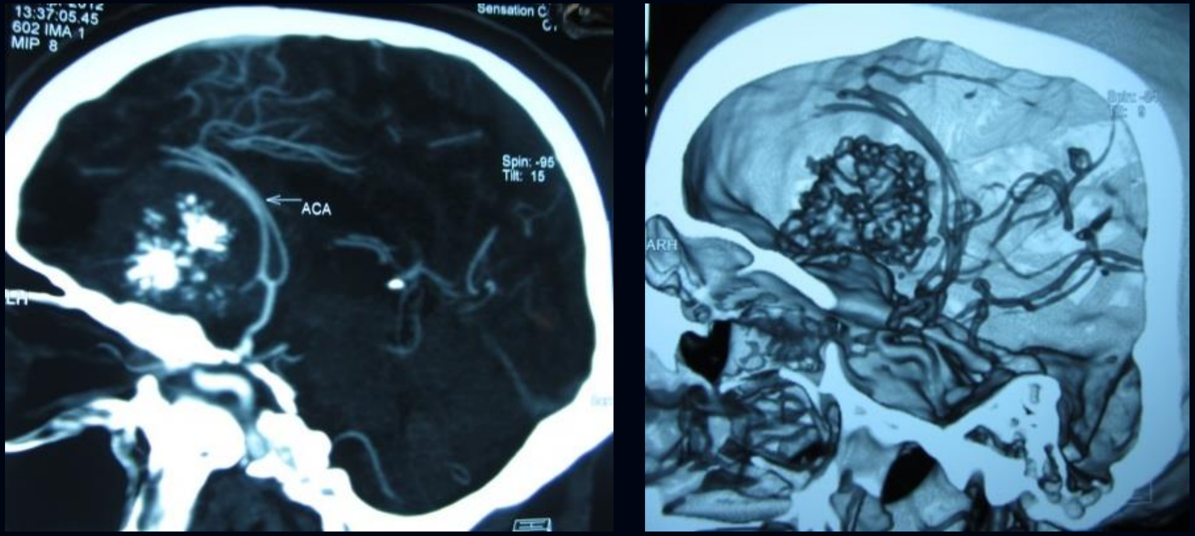
CT scan showing haemorrhage in a metastatic tumour

CT Scan

CT Scan showing Calcification in a suprasellar craniopharyngioma

CT scans showing intra tumoral calcification in a sub frontal meningioma. She also had skull base hyperostosis.

3 D CT Angiography



3D CT angiography images showing the relationship and displacement of the blood vessels due to a Skullbase meningioma.

Magnetic Resonance Imaging (MRI)

First MRI machine in 1977

Dr Raymond Damadian & Colleagues

Further advances in Technology

Anatomical → Functional

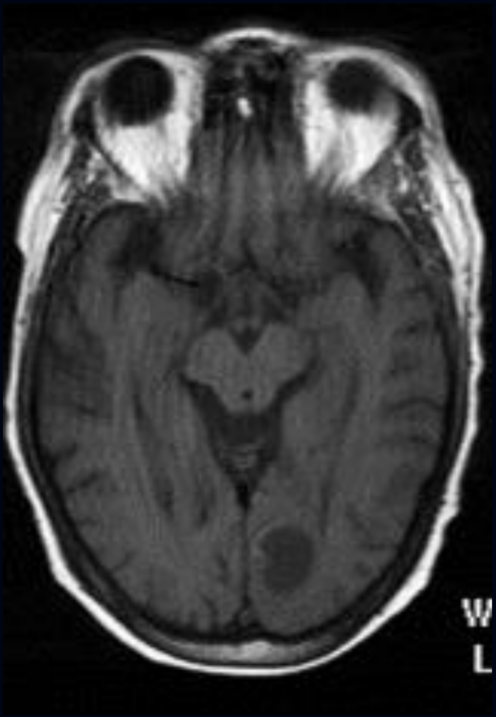
MOTSA

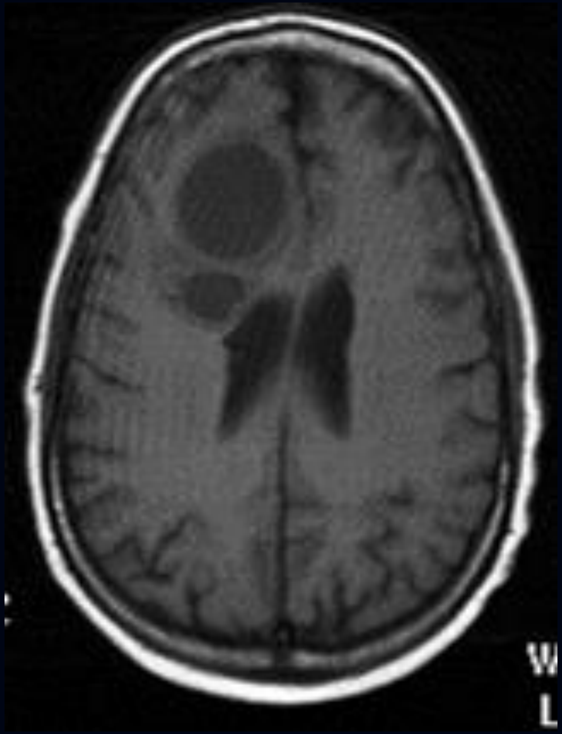
- Multiple Overlapping Thin Slab Acquisition
- Imaging volume is divided into multiple overlapping slabs. These slabs are then combined into single volume of data
- Combines advantages of 2D(larger area of coverage) and 3D(high resolution)

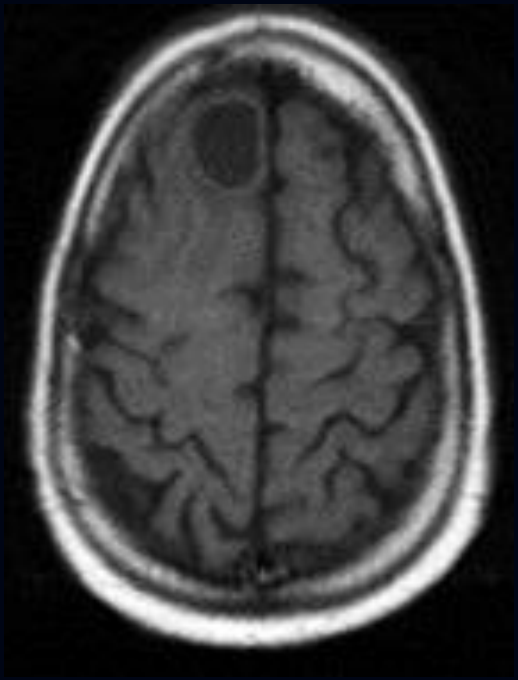
Basic MRI sequences

- T1W
- T2W
- FLAIR
- CET1W

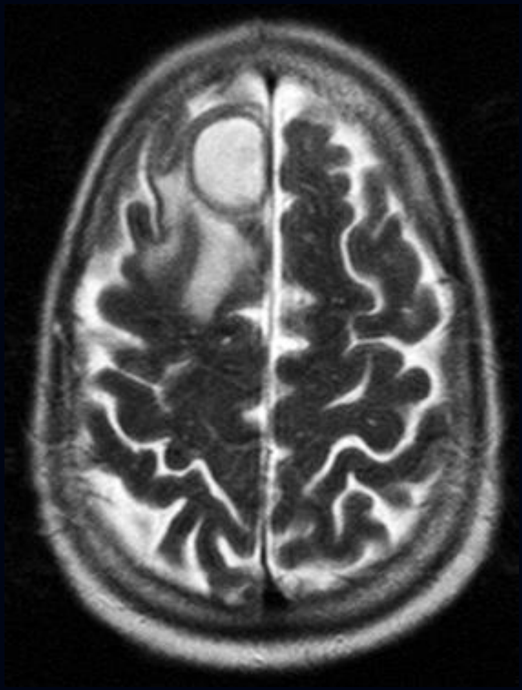
T1W



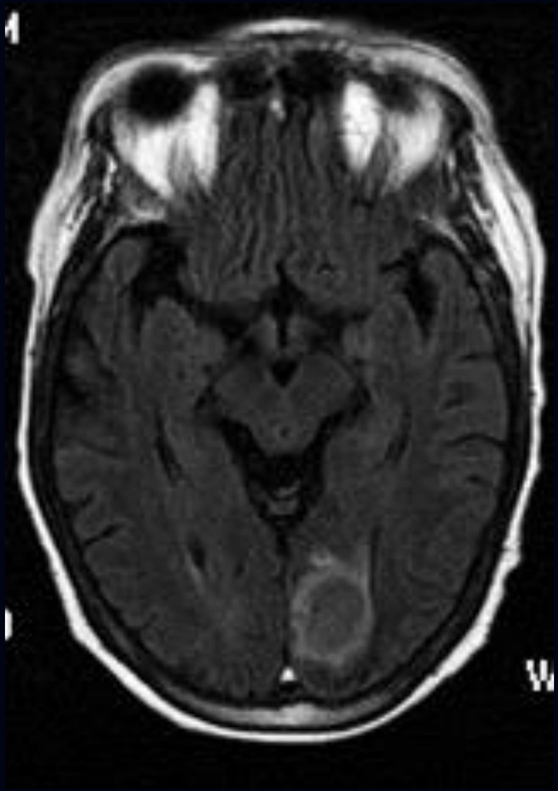


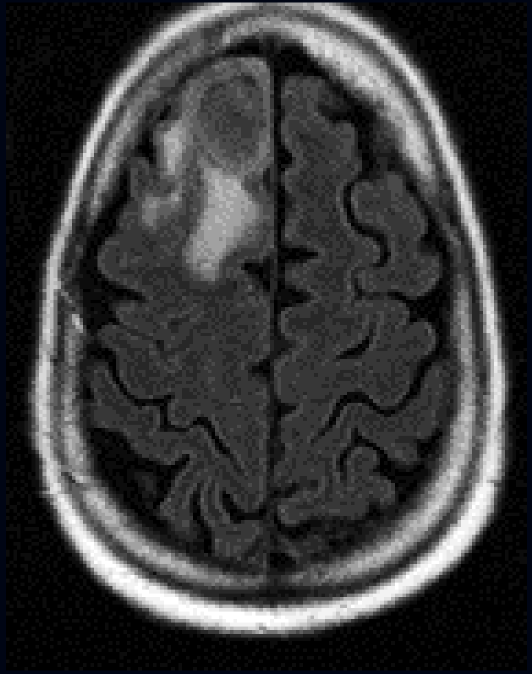


T2W

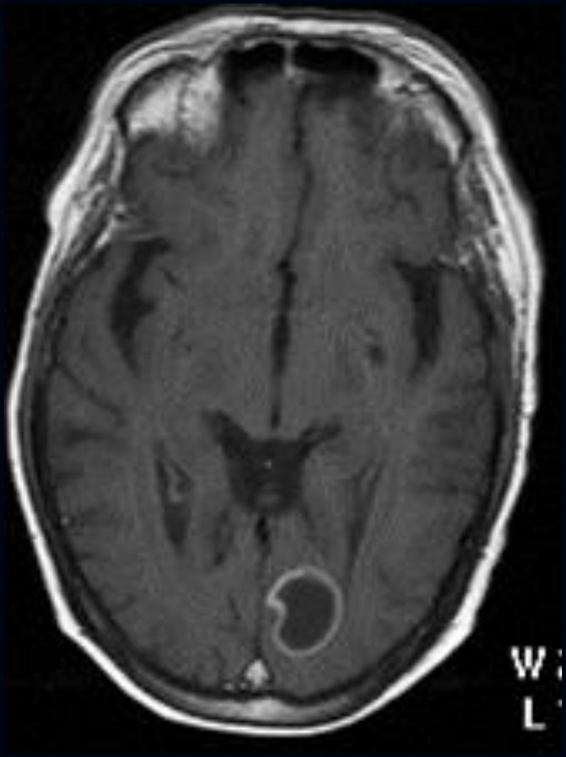


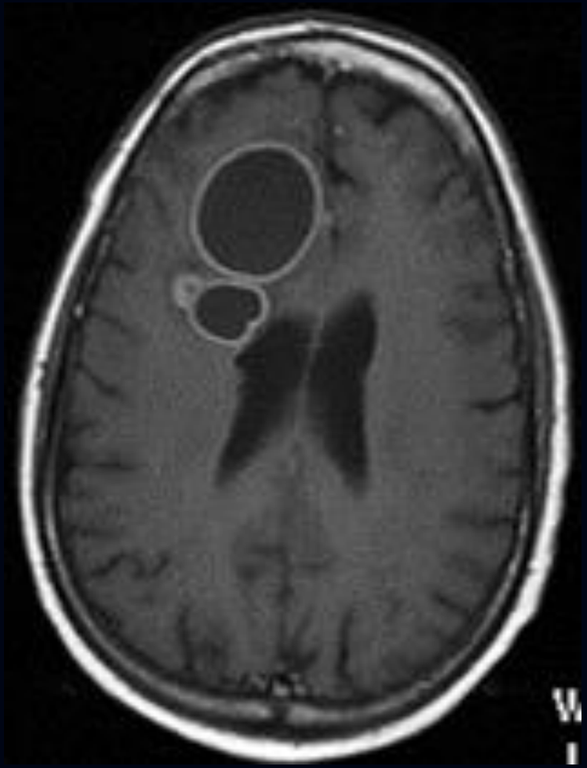
FLAIR

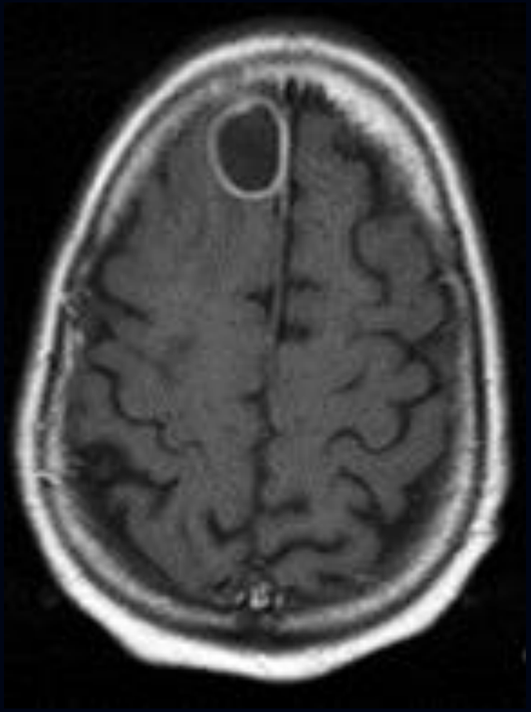


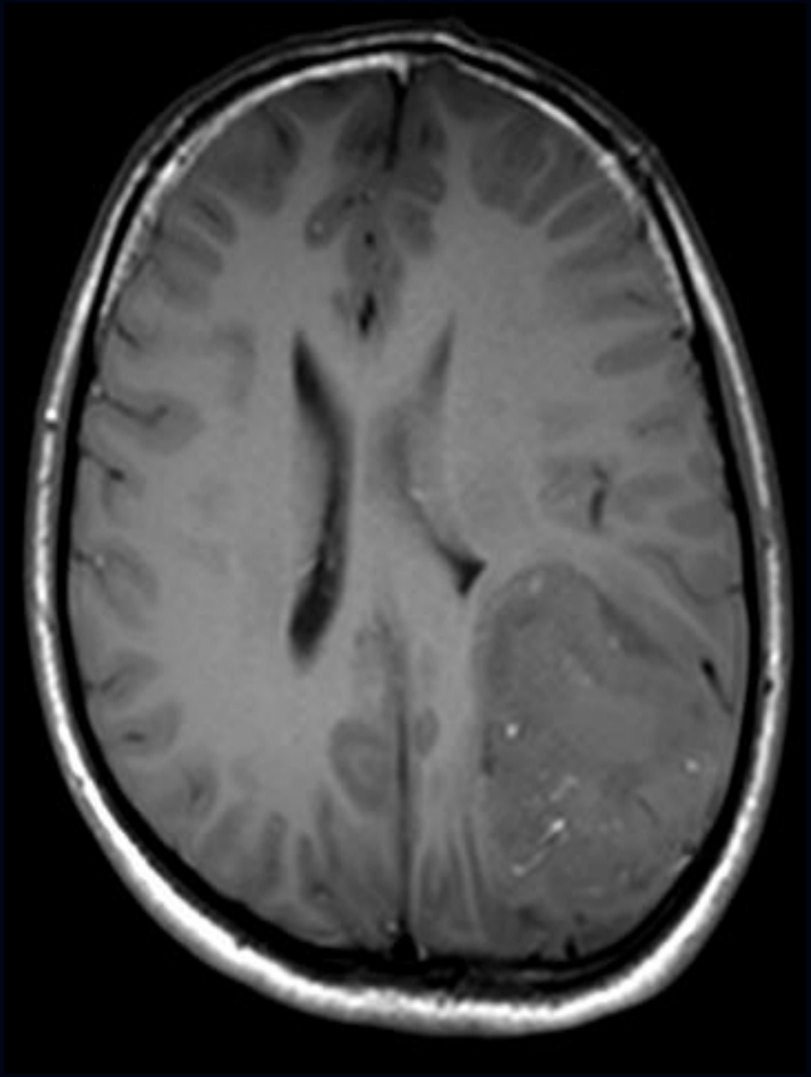


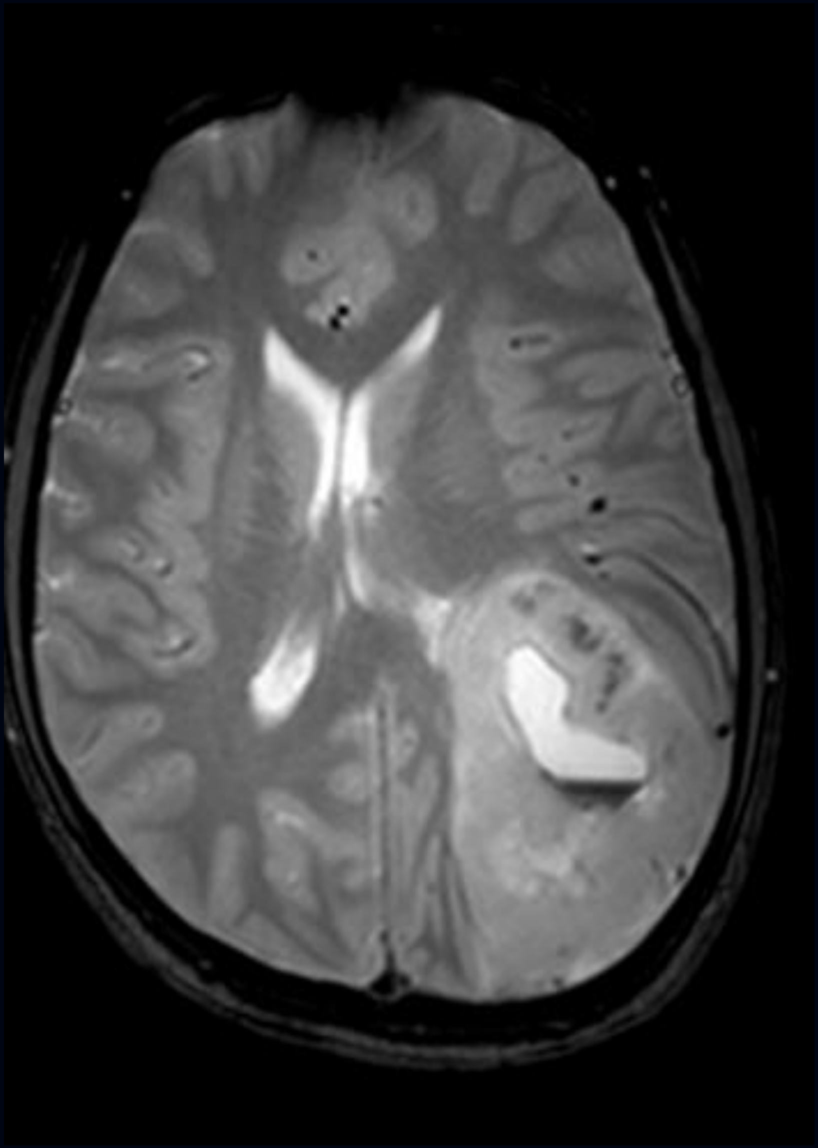
Post-Contrast

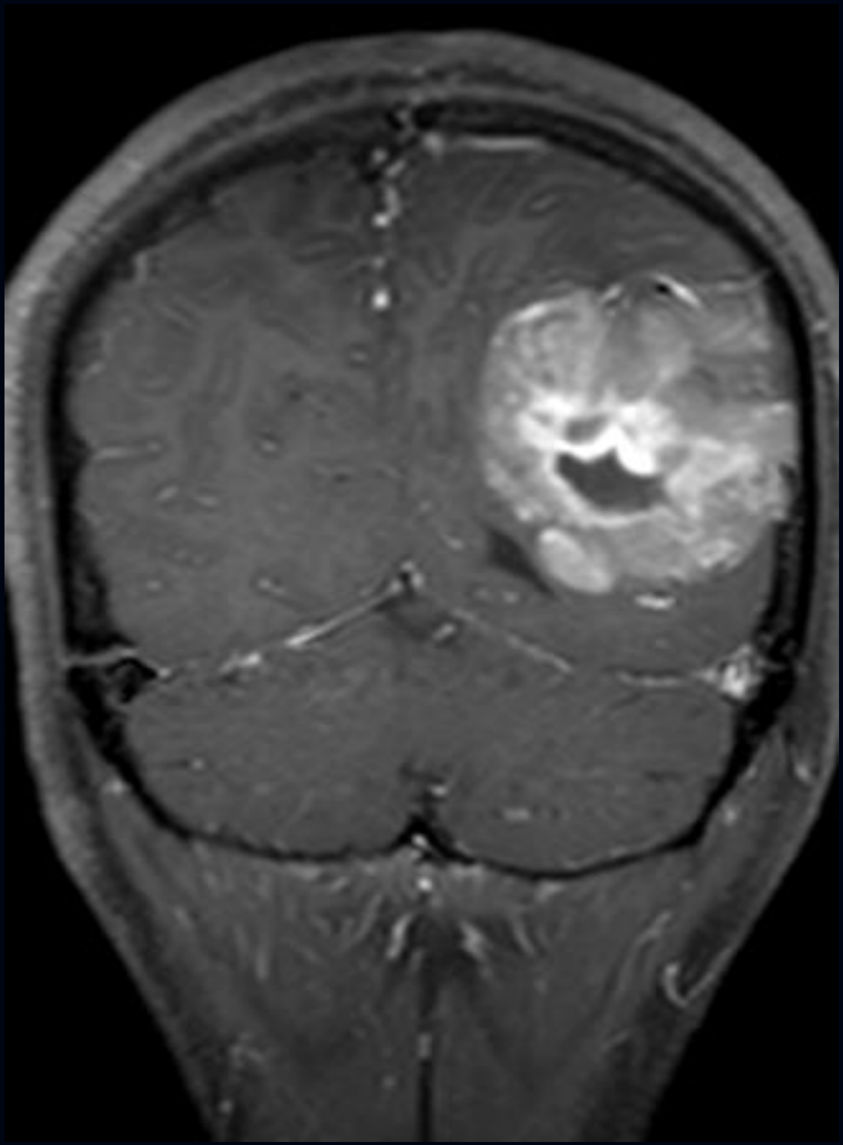


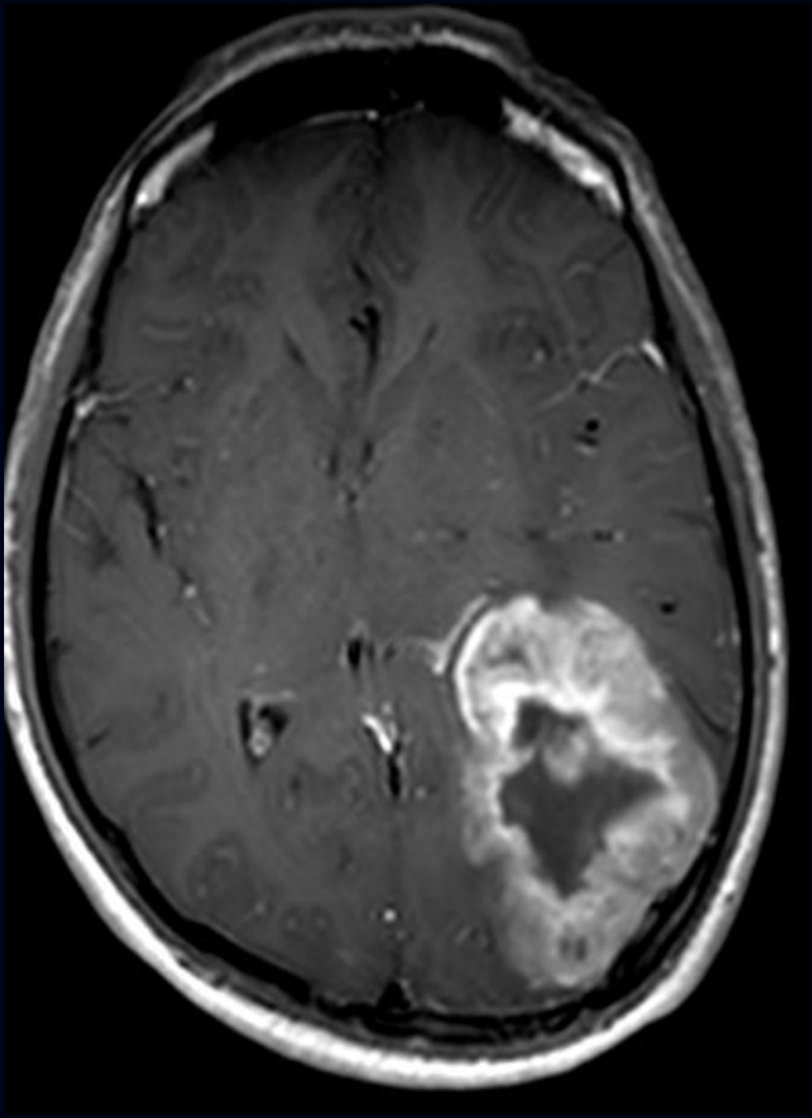


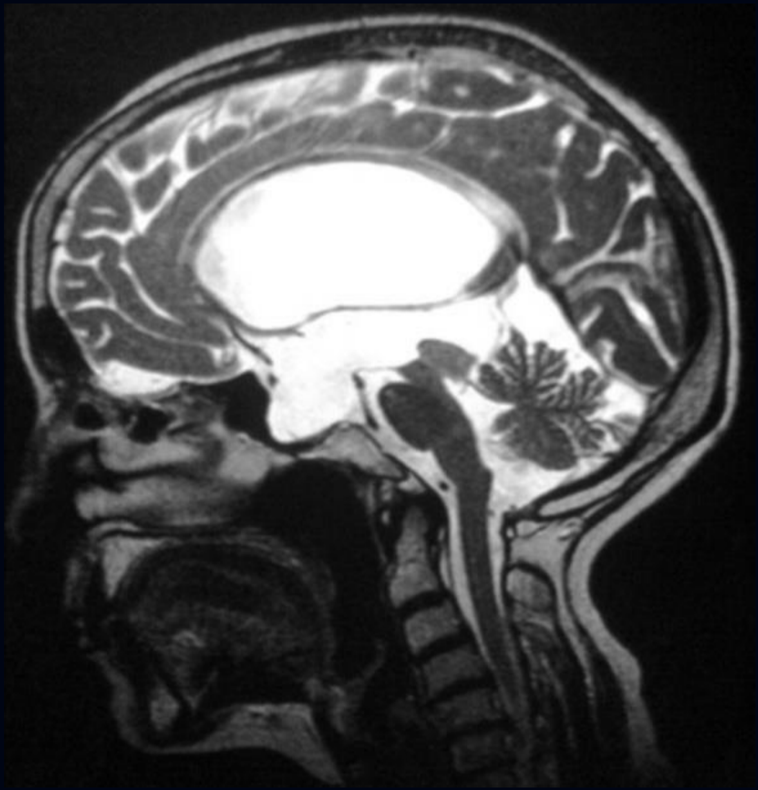


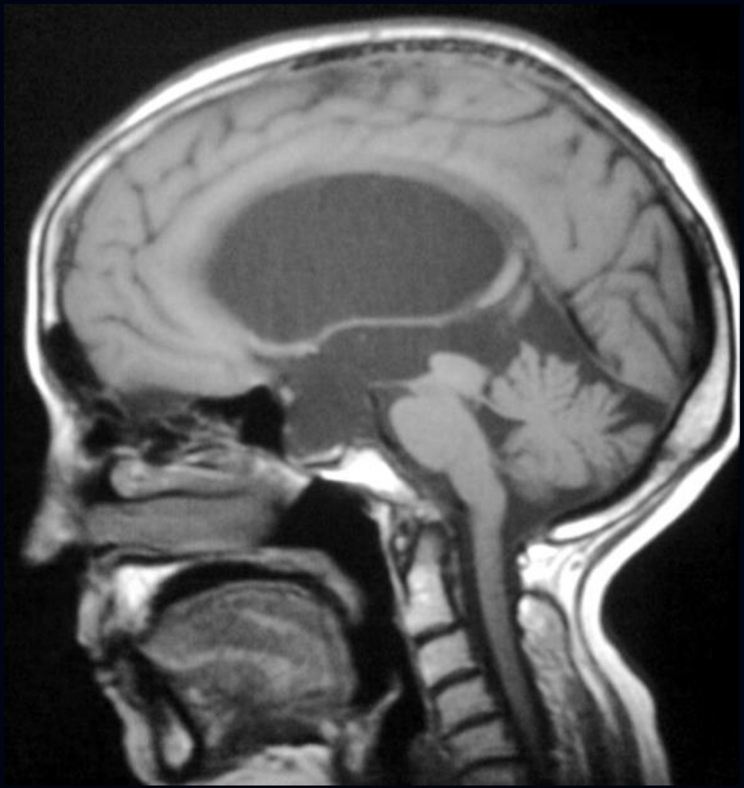






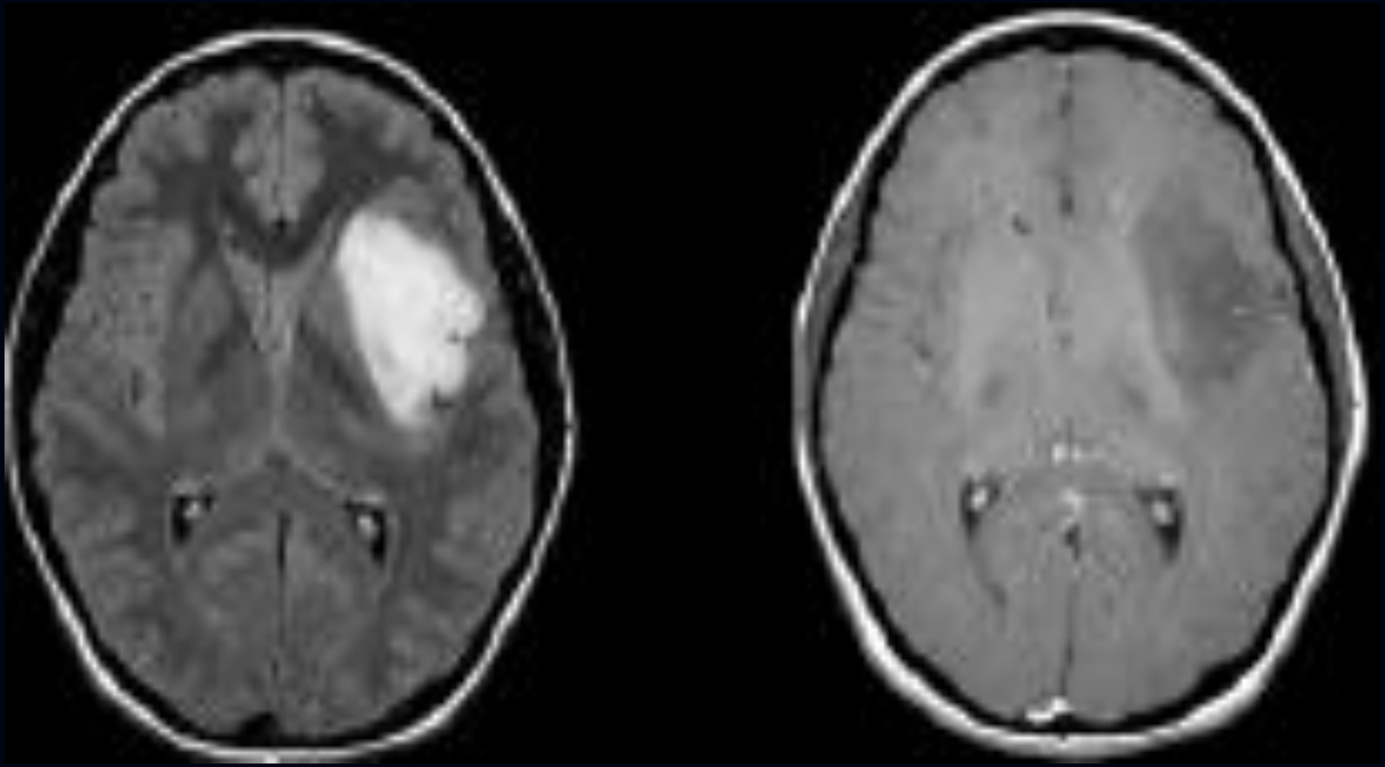






Tectal plate glioma presenting with hydrocephalus.

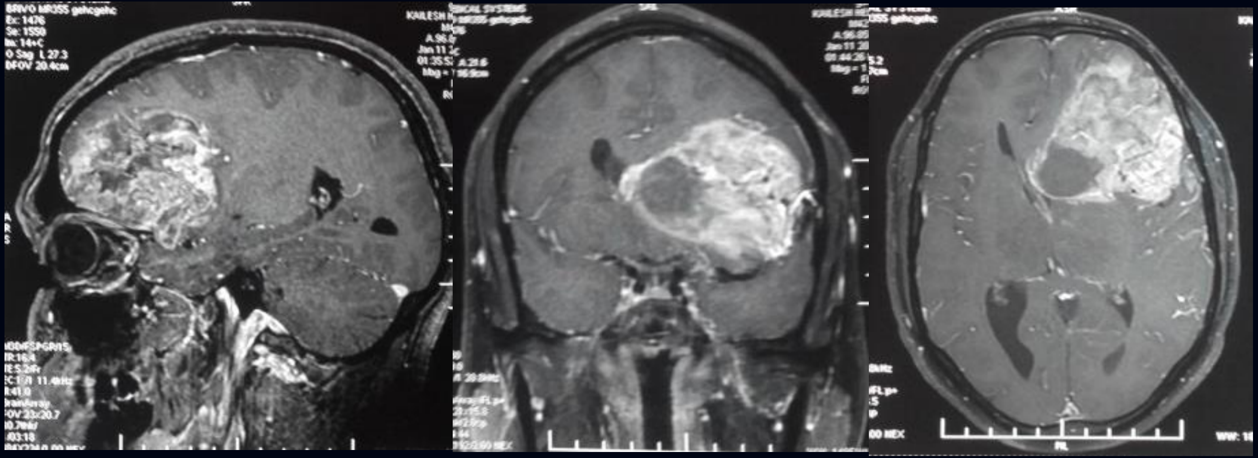
ASTROCYTOMA



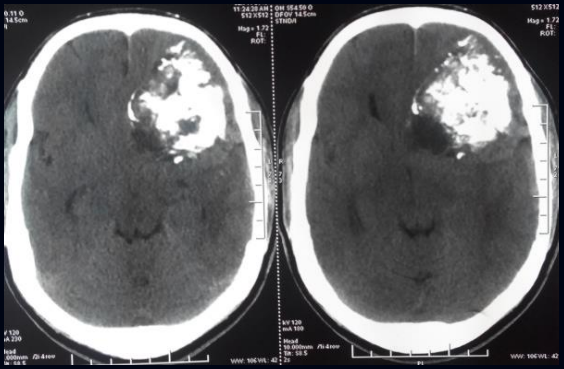
MRI T1WI image showing hyperintense lesion and post contrast scan showing no contrast enhancement, suggestive of a low grade astrocytoma.

Pontine glioma : diffuse lesion with focal enhancement

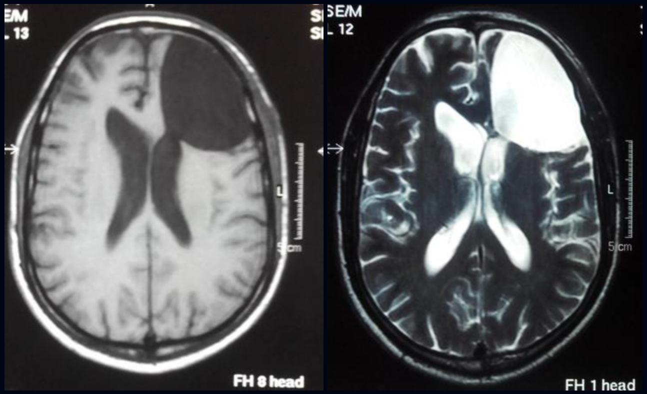
OLIGODENDROGLIOMA



(a) MRI showing a large left frontal heterogeneously enhancing oligodendroglioma



(b) CT of the same patient showing calcification and



(c) postoperative images with complete tumour resection.

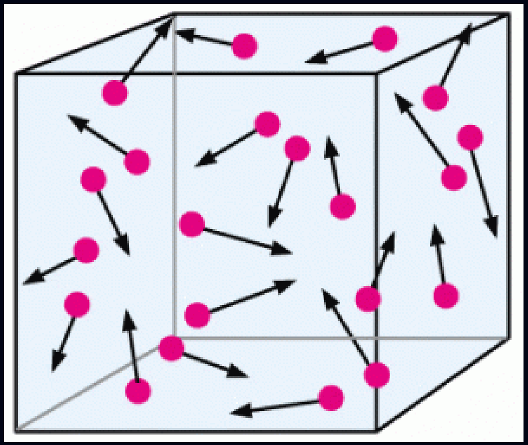
MR Advanced Imaging

- Diffusion
- DTI
- Spectroscopy
- Perfusion
- Angiography
- BOLD imaging (fMRI)

DIFFUSION IMAGING

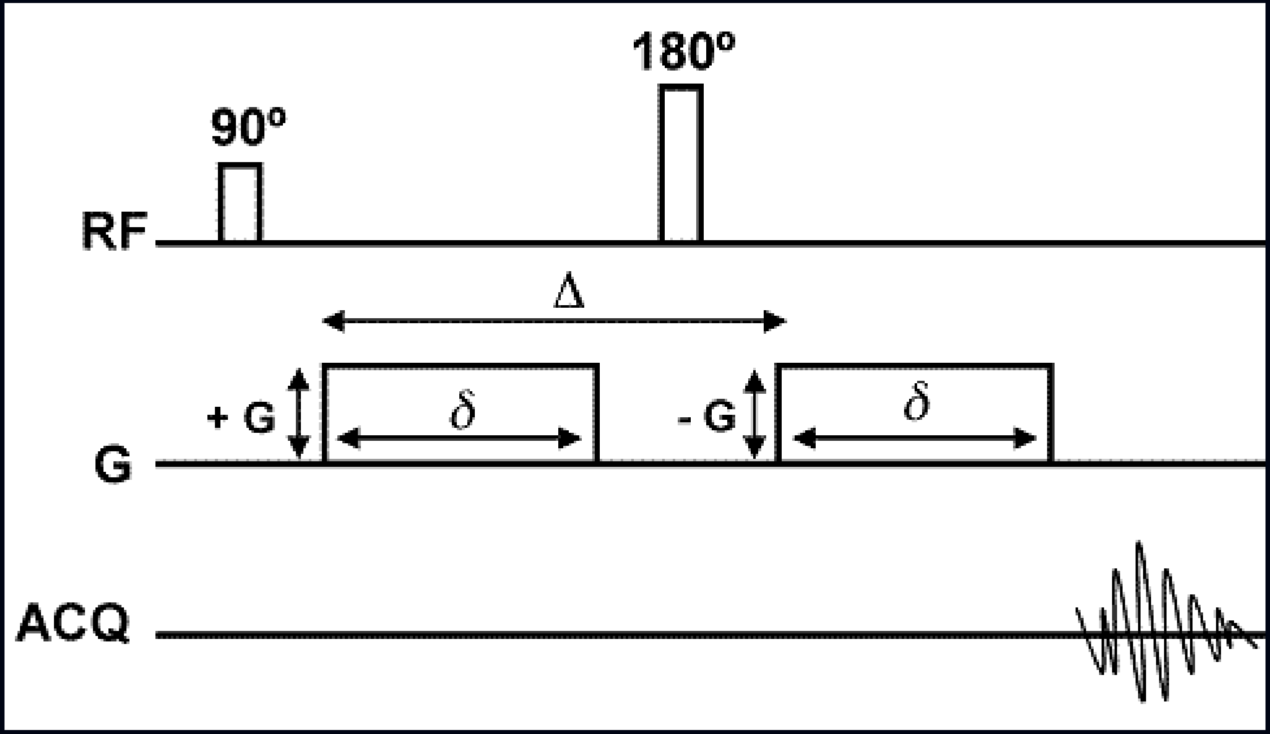
Diffusion

- Random thermally driven motion of water molecules ("Brownian Motion")
- It is higher in gases/liquids (ventricles) & lower in solids (brain)
- It should not be mistaken for bulk flow of particles as in blood vessels
- 2 Types:
  - **Isotropic** – Equal in all directions
  - **Anisotropic** – Not uniform in all directions and instead moves preferentially in some directions (White matter)



Diffusion – Basic Concept

Stejskal and Tanner described in 1965



90 deg pulse and 1st Diffusion gradient

Molecules acquire phase shifts of transverse magn

180 deg pulse and 2nd Diffusion gradient

Rephasing of stationary spins (“Bright Signal”)

Phase shifts in mobile molecules -- incomplete rephasing -- Signal loss (“Dark Signal”)

Diffusion Imaging

- Signal intensity of a voxel of tissue is calculated as:

$$S = S_0 \times \exp[-b \times D]$$

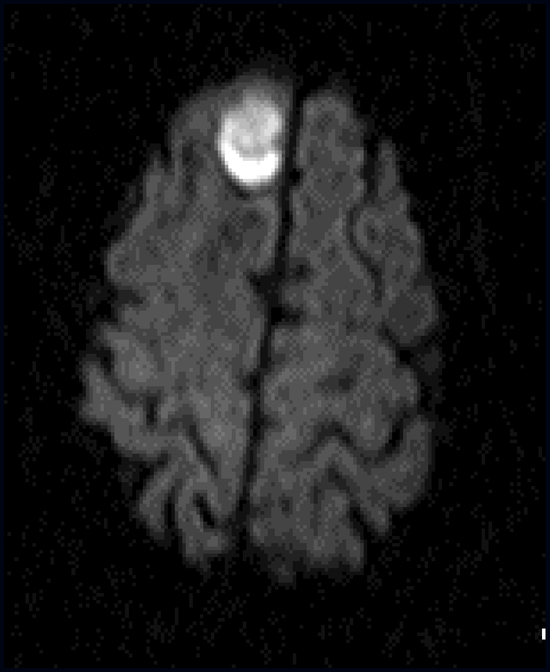
b = Gradient factor
S_0 = Signal intensity on T2W image (i.e. b = 0)
D = Diffusion co-efficient

Diffusion Coefficient

- Diffusion of a particle depends upon several factors like the type of particle, temperature & the environment in which diffusion takes place

- Hence, during routine MR imaging, as the rate of molecular motion is influenced by many factors, only apparent (and not true) diffusion co-efficient can be calculated

Diffusion weighted images

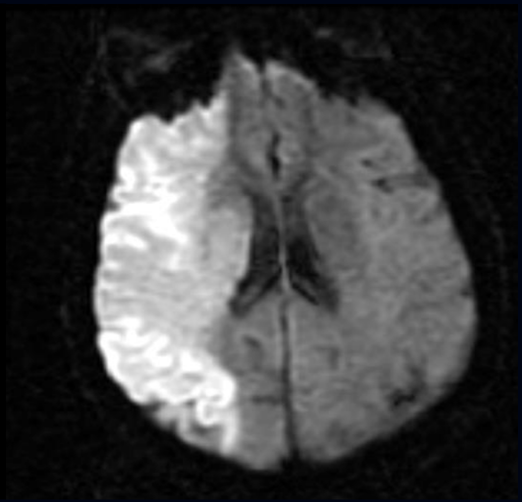


Apparent Diffusion Coefficient (ADC)

ADC images can be obtained either graphically or mathematically

T2 - image

Isotropic Diffusion-Weighted Image

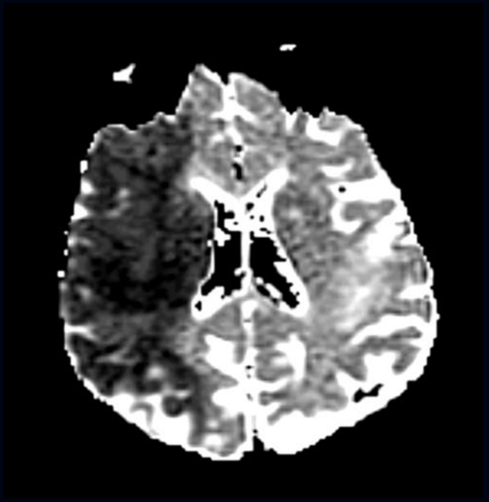


Stroke is Bright

Mathematical Combination

- + x /

ADC image

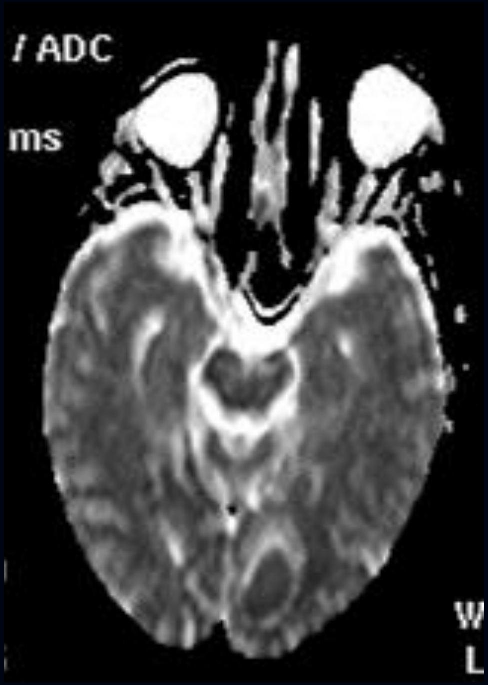


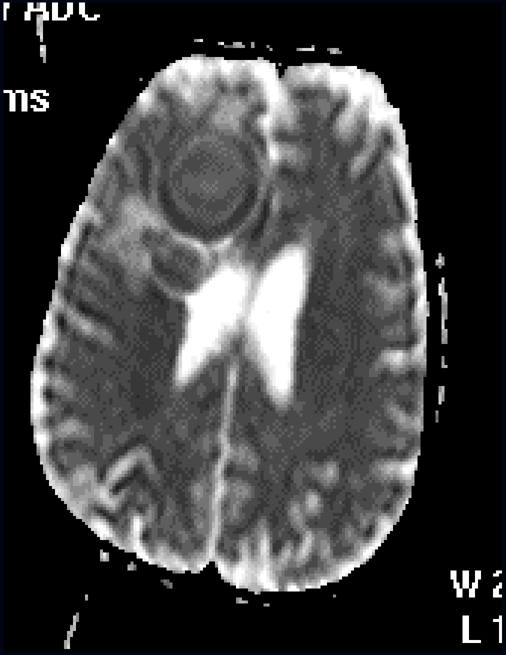
Stroke is Dark

ADC

- Images of ADC are called “ADC Maps”
- Area with reduced ADC (restricted diffusion) will be Bright on DW images & will turn Dark on ADC maps
- ADC is not equal in all directions in brain (WM) i.e. anisotropic
- Therefore diffusion gradients are applied in 3 different directions(x, y, z)
- Average image – TRACE Diffusion image

ADC Maps



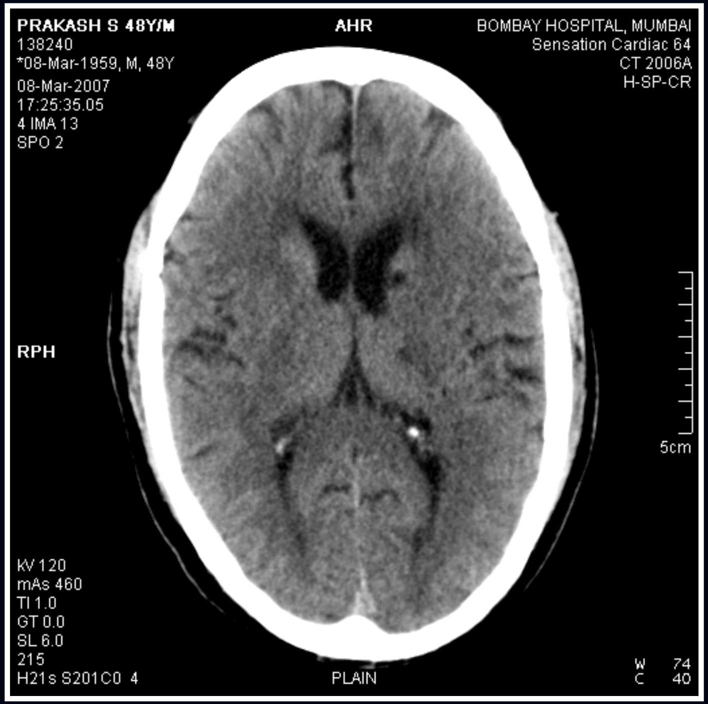


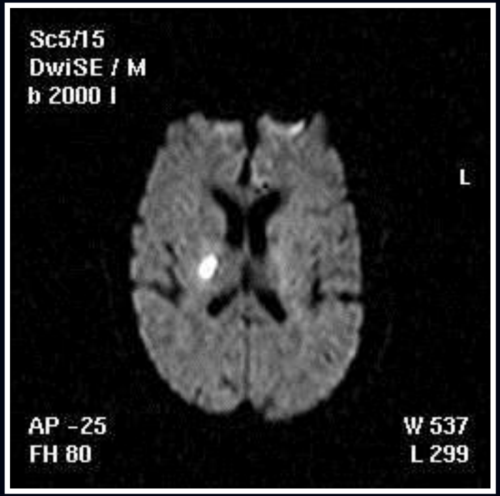
DIFFUSION - Applications

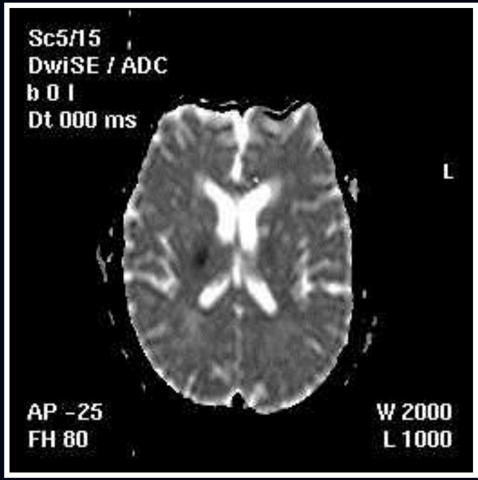
- Acute ischemic stroke
- Hemorrhage (Hyperacute & late subacute)
- Intra-axial masses (glioma, lymphoma, metastases)
- Epidermoid v/s Arachnoid Cyst
- Cerebral abscess, Herpes encephalitis, CJD
- Trauma
- Demyelination

Diffusion Imaging

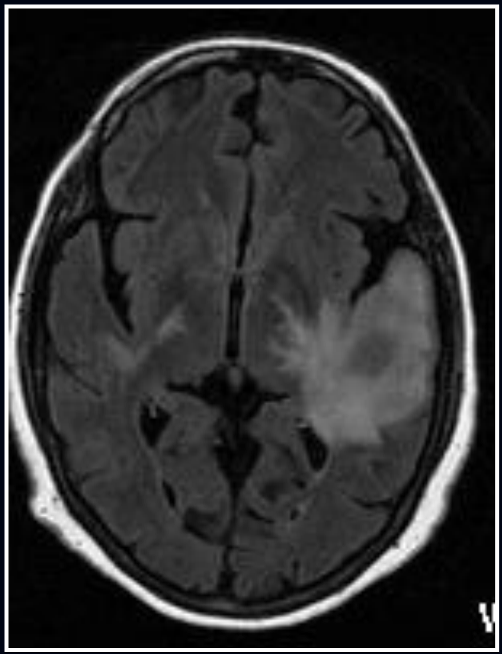
- Normal CT

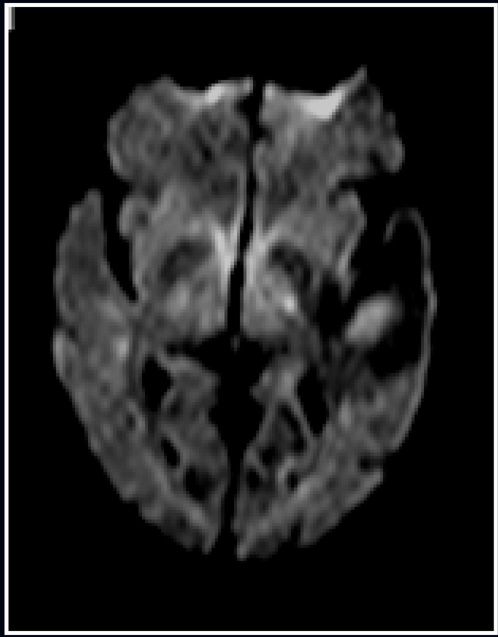


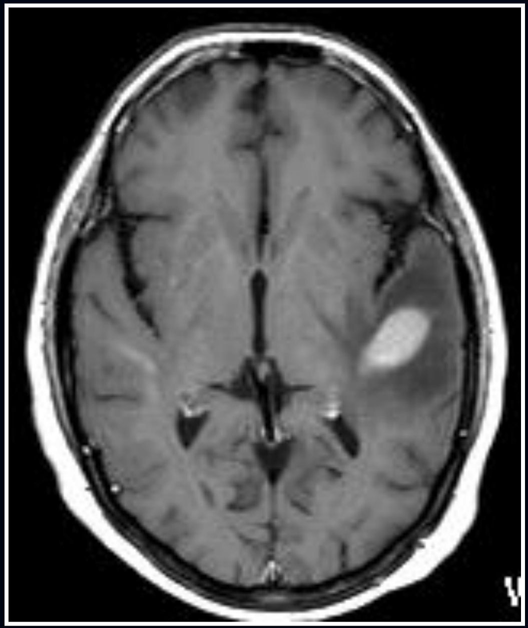


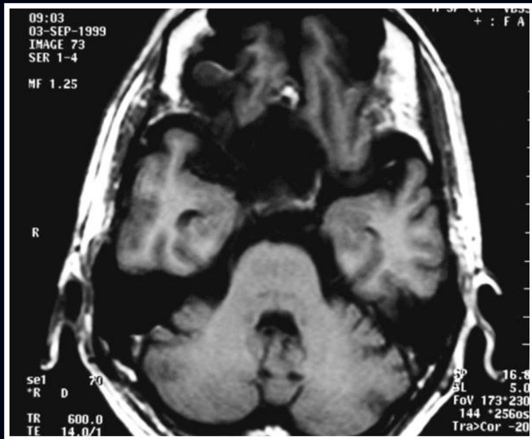


Primary CNS Lymphoma





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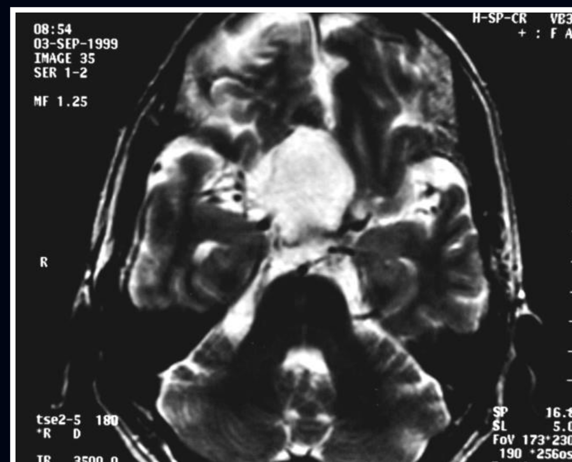
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SL 5.0
FoV 173*230
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IMAGE 92
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MF 1.25
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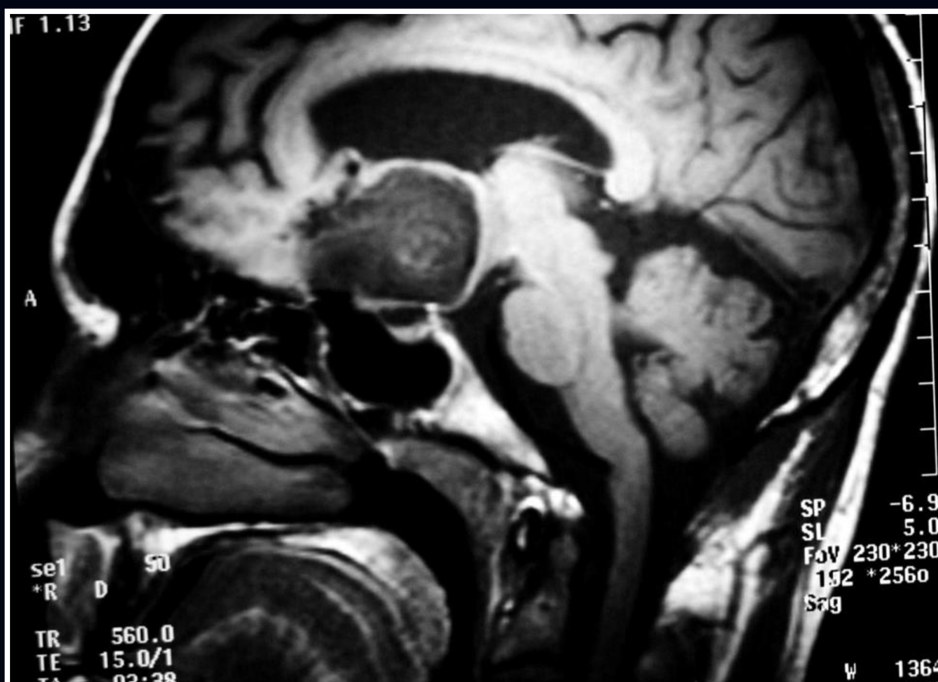
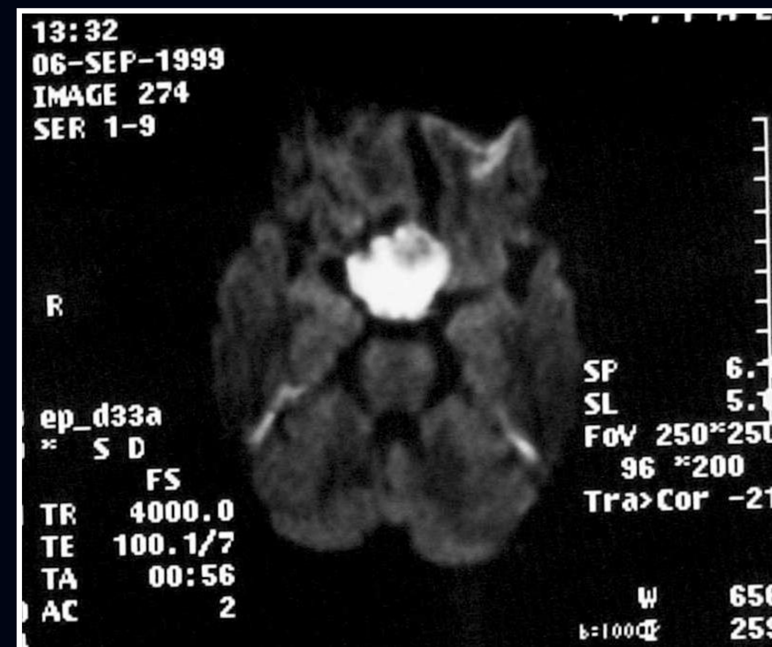
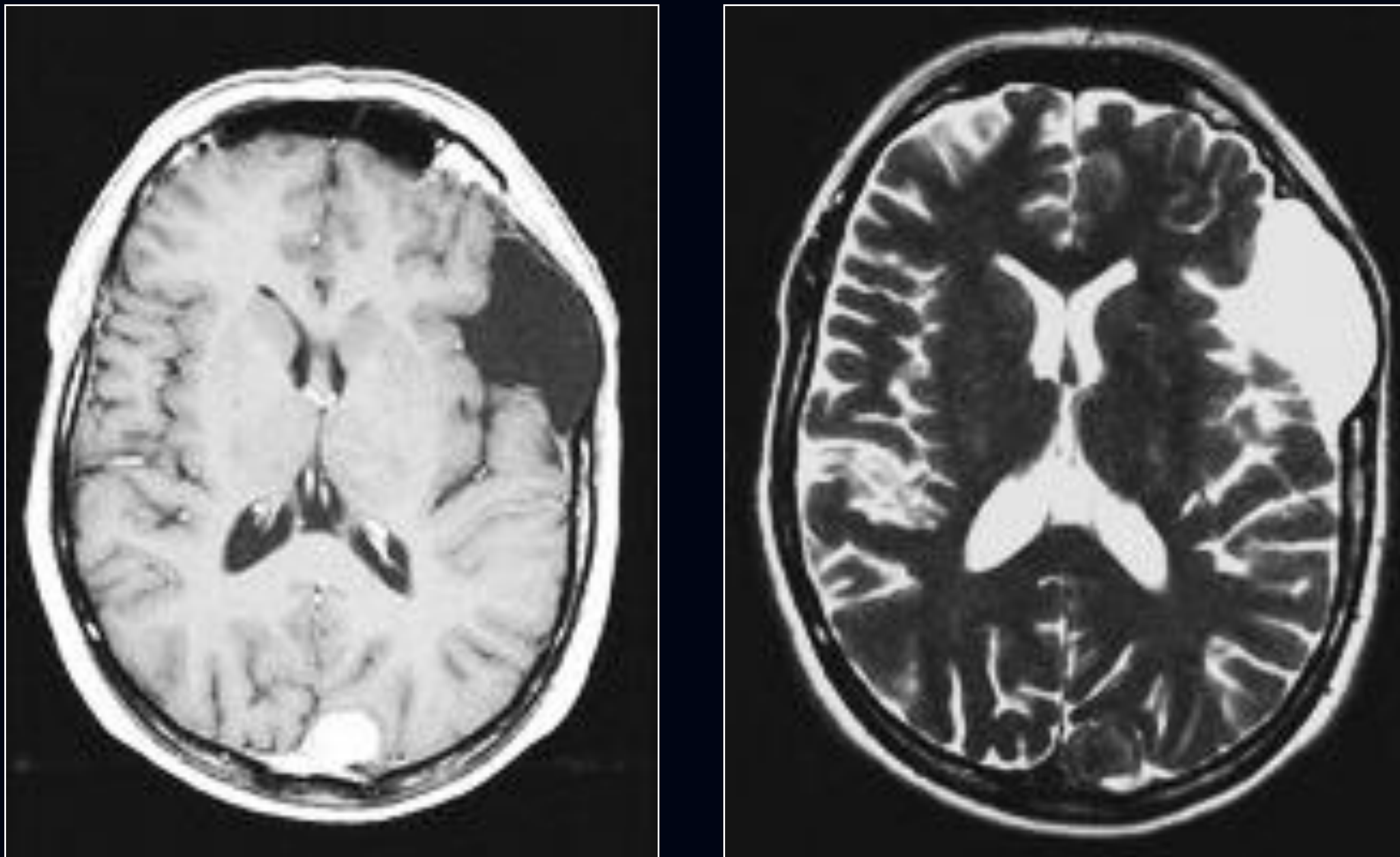
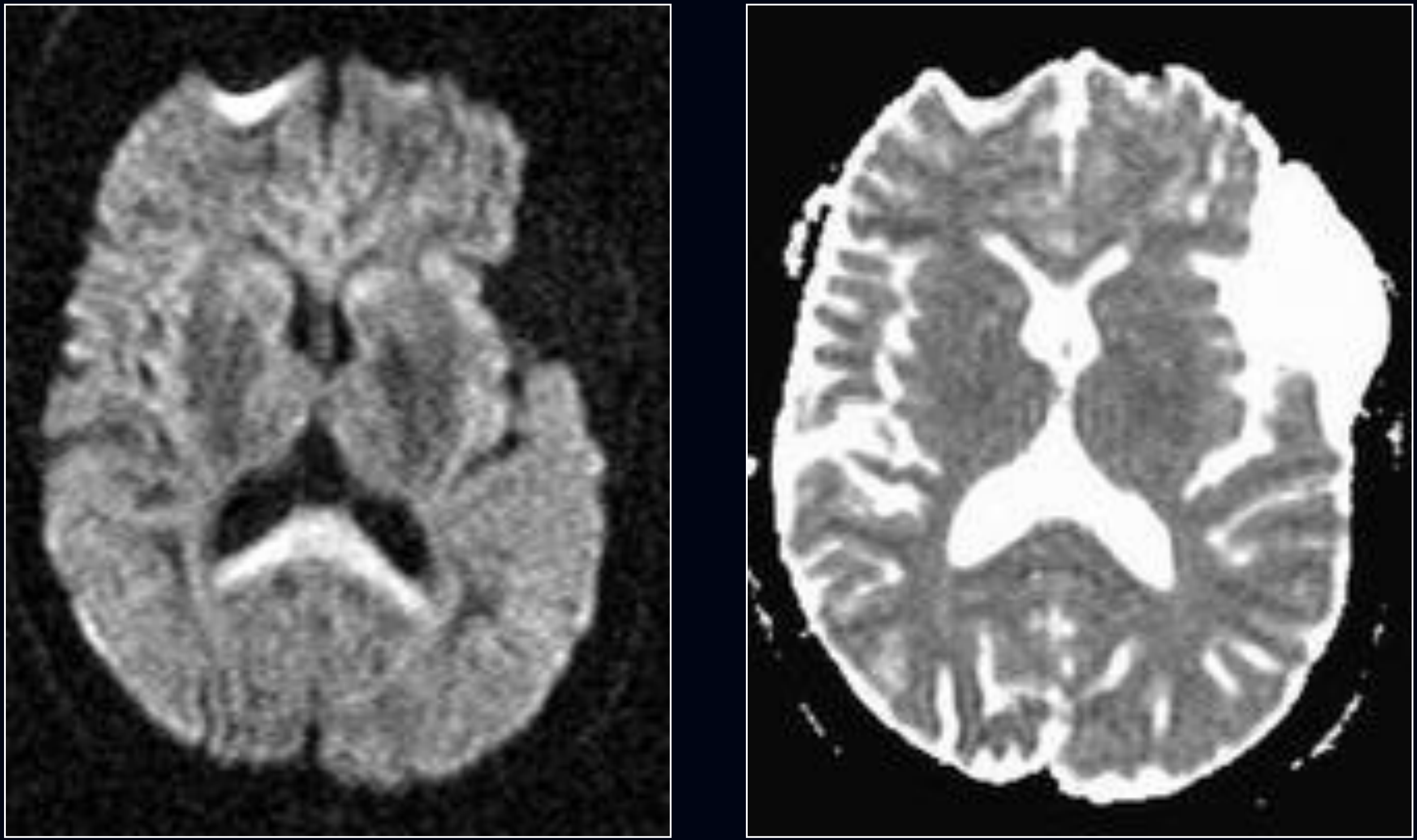
Suprasellar Epidermoid









Arachnoid Cyst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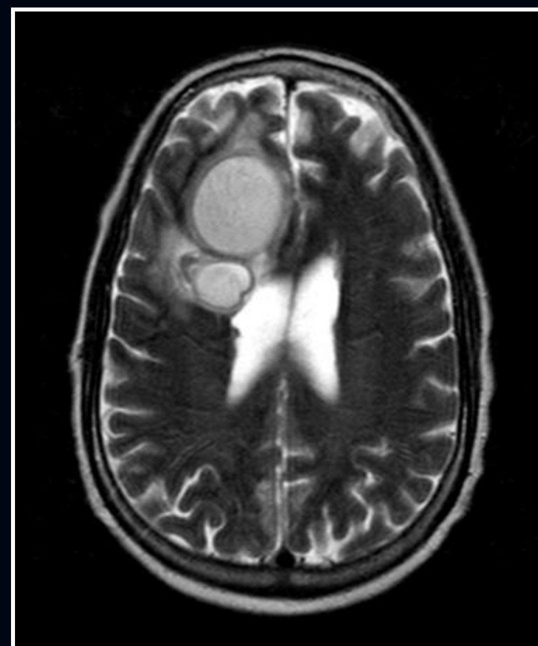
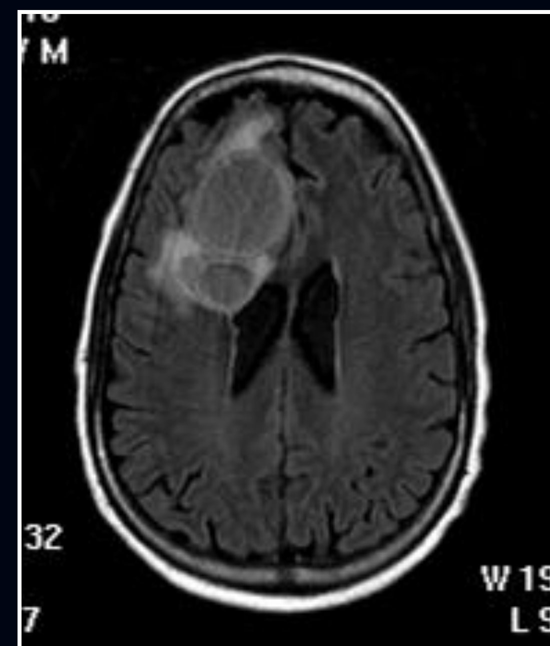
7


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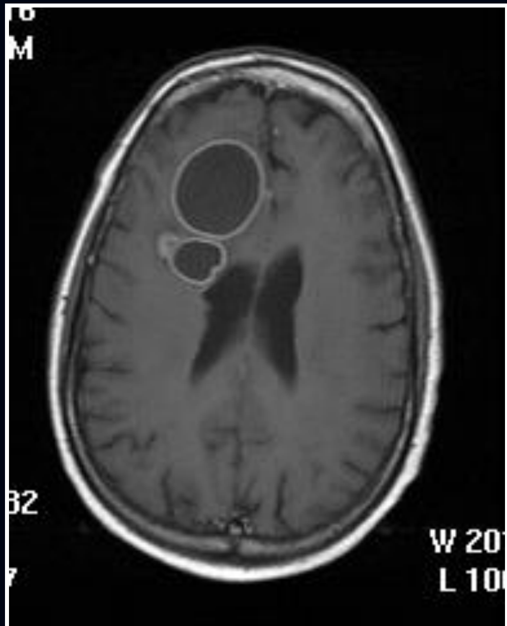
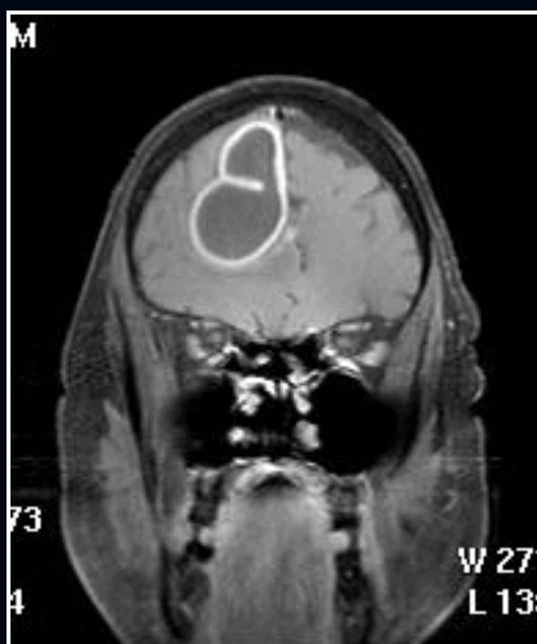
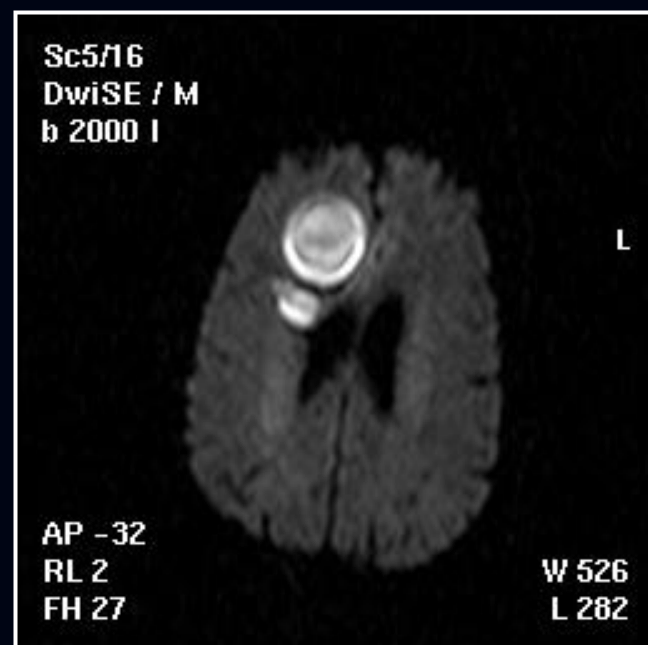


BRAIN ABSCESS





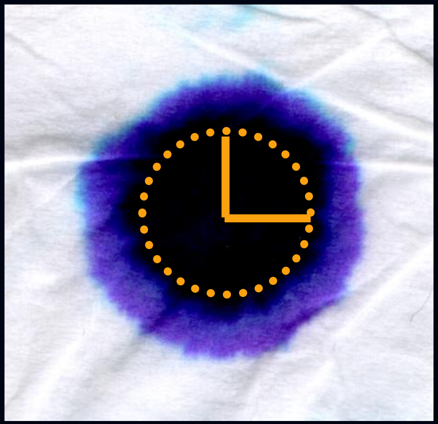
DIFFUSION TENSOR IMAGING

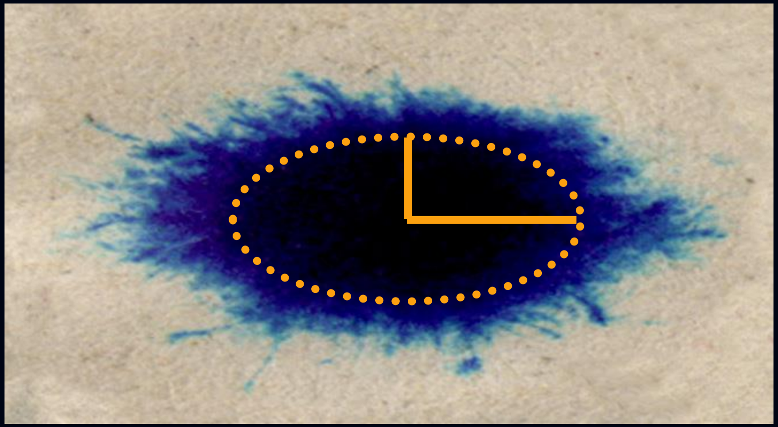
- Diffusion
  - Brownian motion
- Diffusion Weighted Imaging (DWI)
  - Single Direction
- Diffusion Tensor Imaging (DTI)
  - Multidimensional

Diffusion

- Isotropic – Equal in all directions

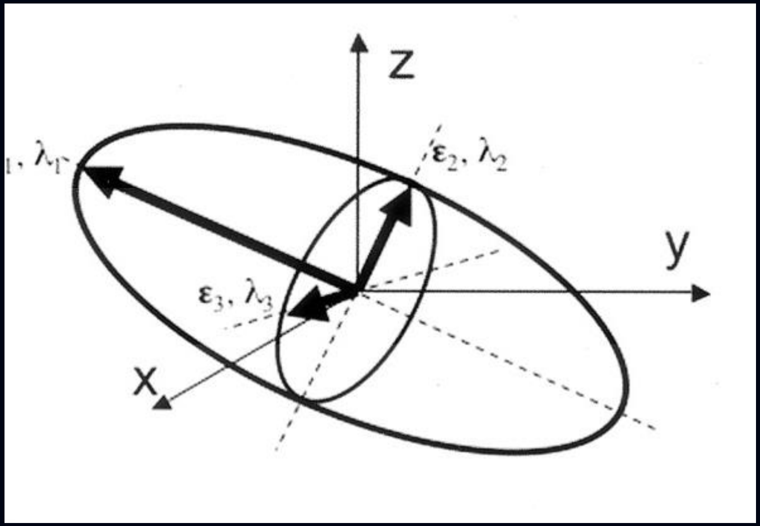
- Anisotropic – Not the same in all directions (White matter)
  - Due to axonal membranes,myelination,extracellular bulk flow,capillary blood flow and intracellular streaming





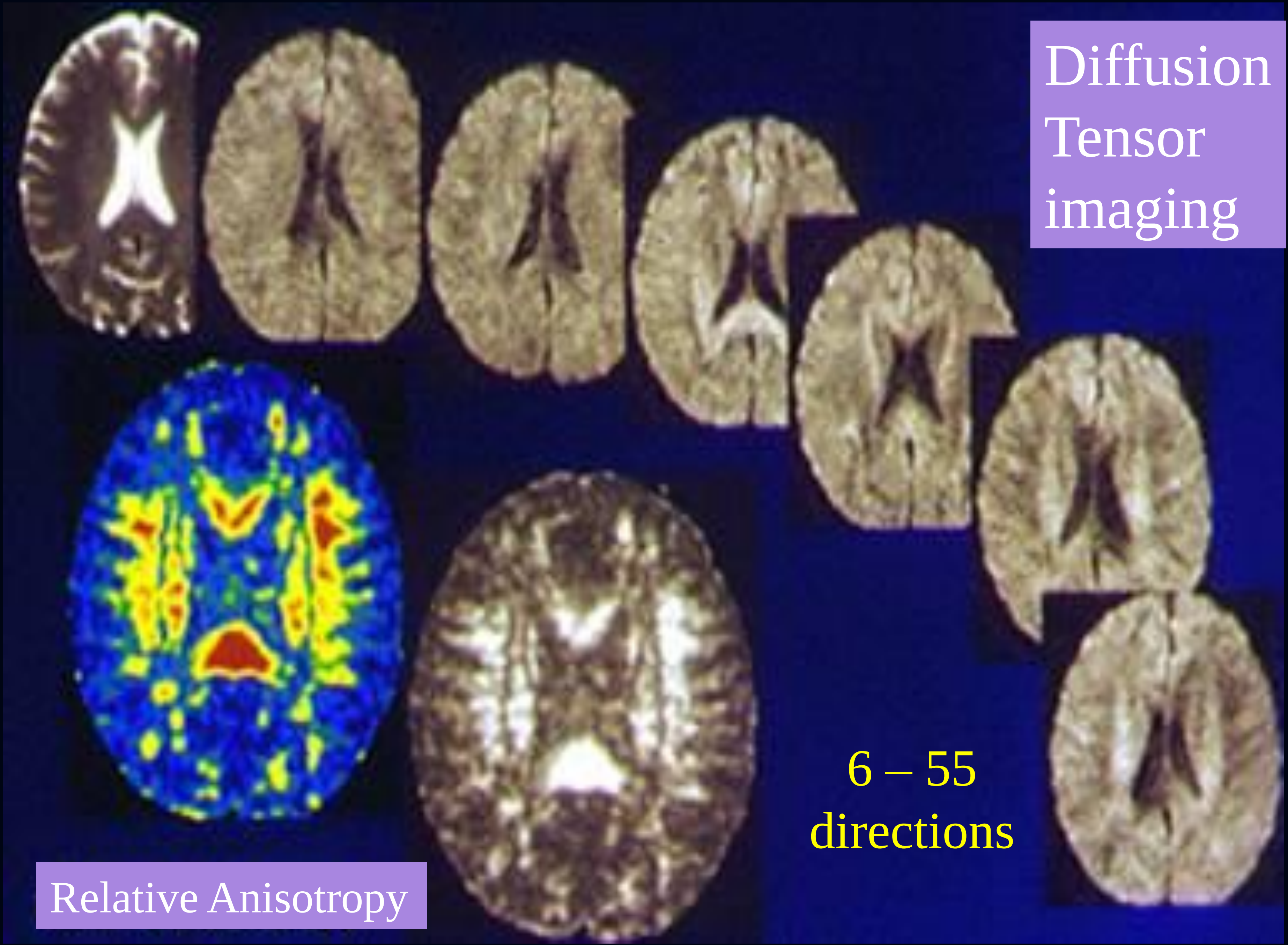
Diffusion Tensor

- Mathematical description of diffusion in direction and magnitude in three-dimensional space
- Abstract mathematic entity
- **Quantifiable measure** of directionally restricted (anisotropic) diffusion in highly organized tissues (e.g. white matter) (Basser and Pierpaoli, *J Magn Reson B* 1996;111:209-219)

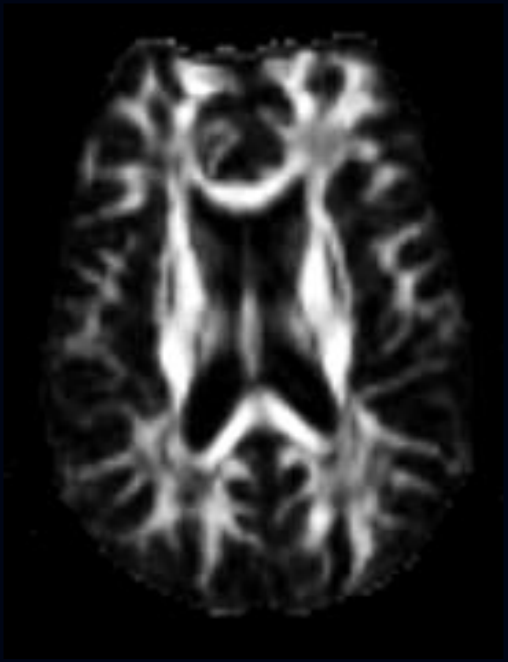


Diffusion Tensor Imaging

- Images are acquired in multiple directions (minimum 6 to 55)
- Linear algebraic procedure – Diagonalization
- 3 eigenvectors and 3 eigenvalues
- Calculate Anisotropy metrics – “Fractional Anisotropy” (FA) value (ranges from 0 to 1)
- FA Maps
- Colour coded FA maps


Diffusion Tensor imaging
6 – 55 directions
Relative Anisotropy

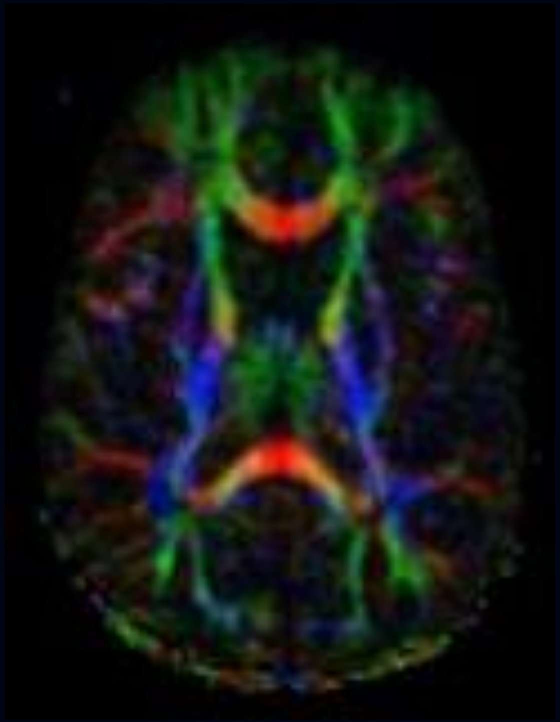
Fractional anisotropy image

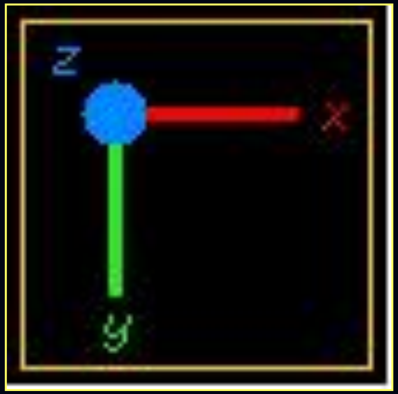


- White pixels = high FA values
- Dark pixels = low FA values

- White matter = more restriction, high anisotropy – **white**
- Cortex = less restriction, lower anisotropy – **dark**

Color coded "fractional anisotropy map"

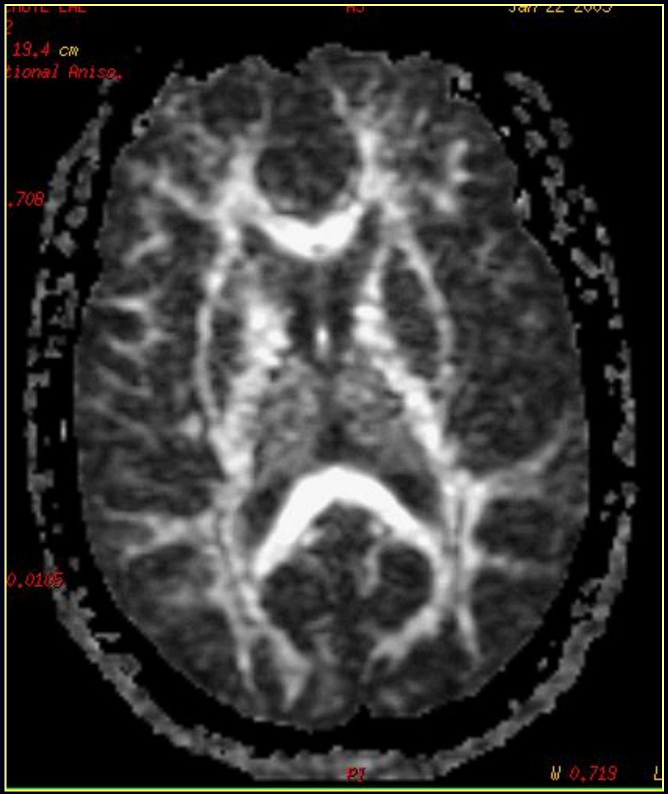


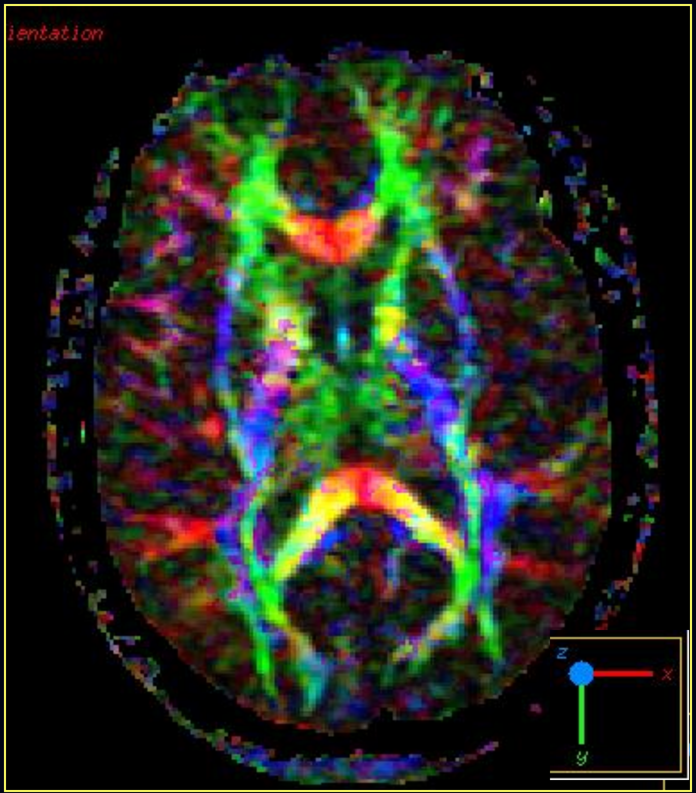


Pixels displayed in colors to reveal predominant direction of tensor

- Green = Ant to Post or Post to Ant
- Red = Rt to Lt or Lt to Rt (corpus callosum)
- Blue = Sup to Inf or Inf to Sup (pyramidal tracts)

FA MAPS

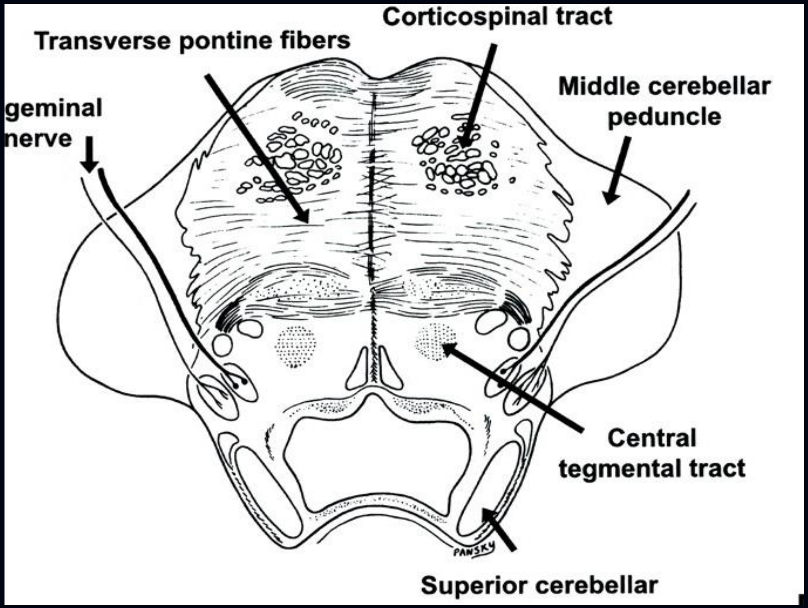


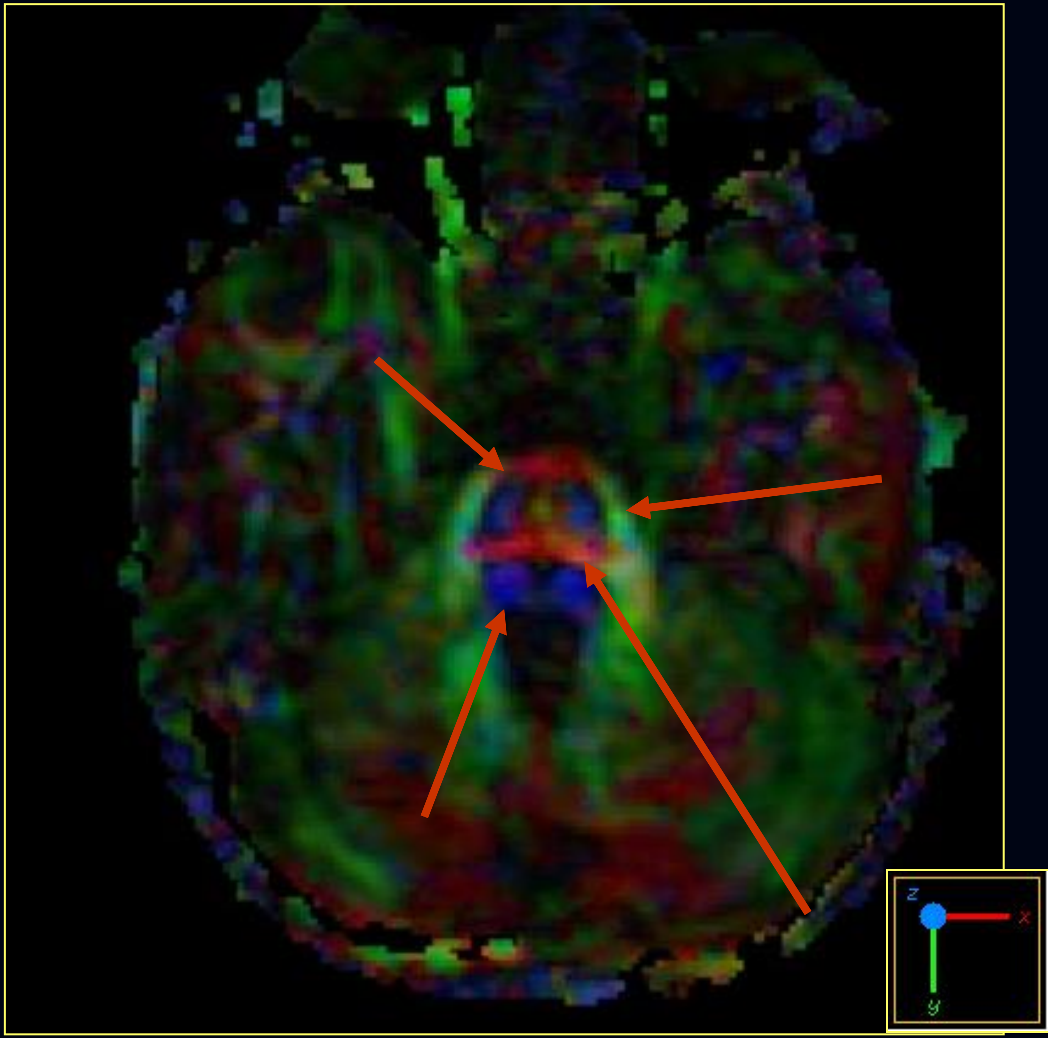


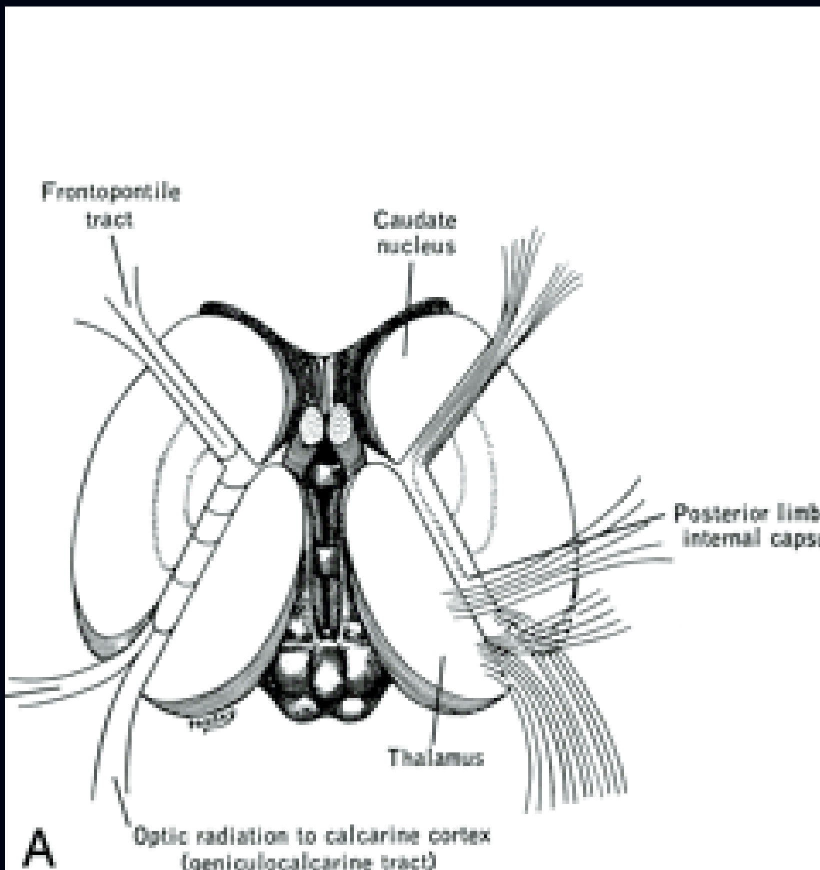
without directional information

with directional information

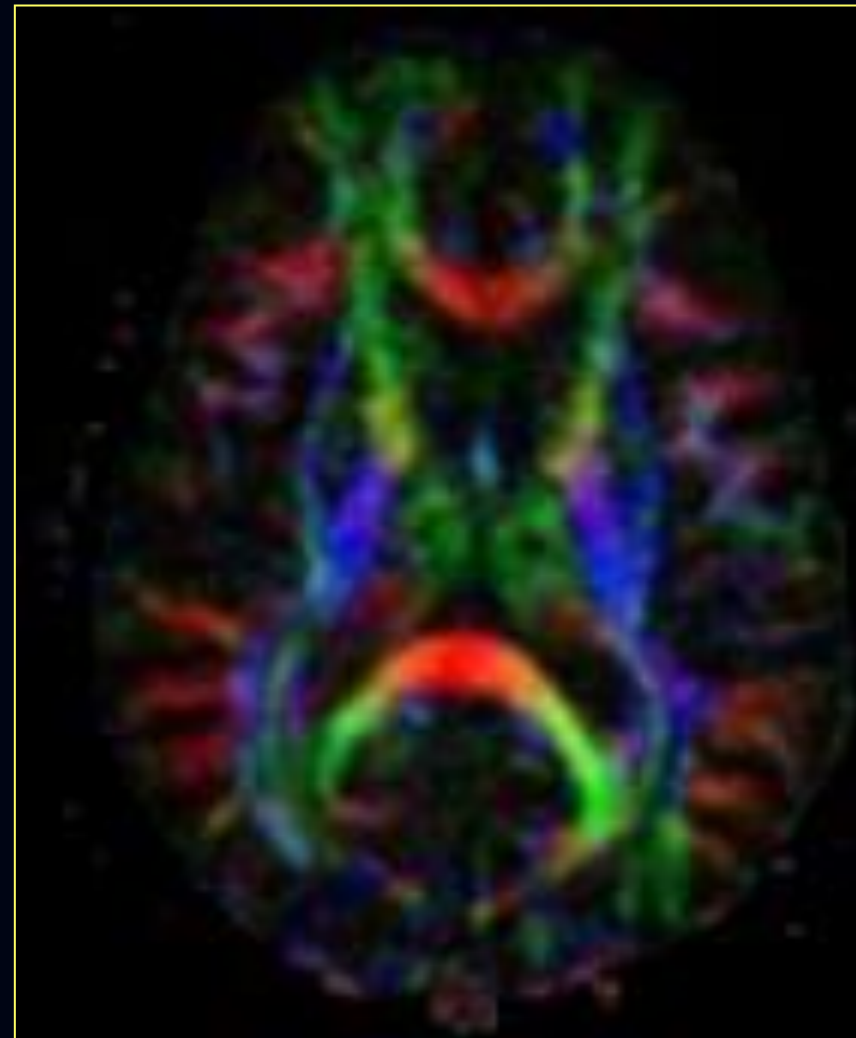
Brain stem


Corticospinal tract
Transverse pontine fibers
Middle cerebellar peduncle
geminal nerve
Central tegmental tract
Superior cerebellar
PANSKY


z
x
y

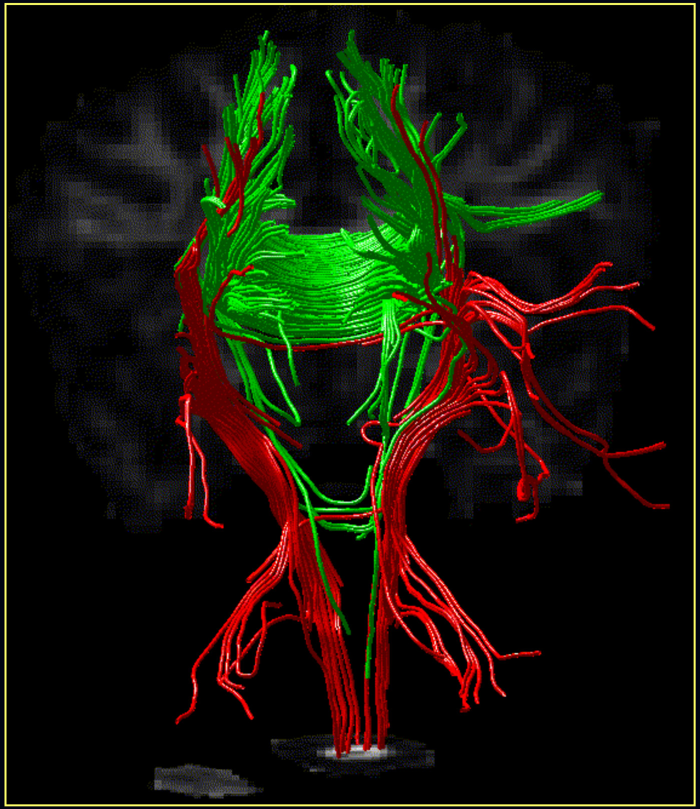


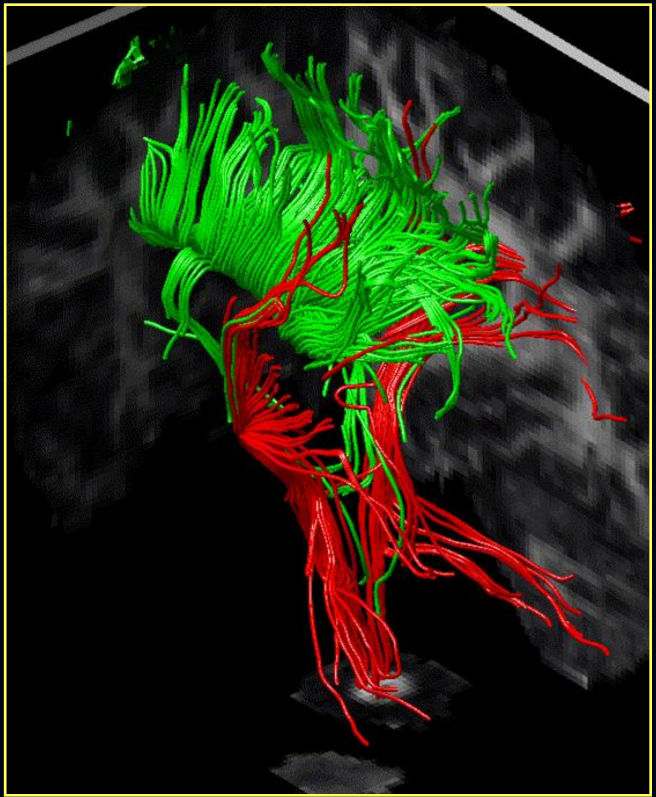
Frontopontile tract
Caudate nucleus
Posterior limb internal capsu
Thalamus
A
Optic radiation to calcarine cortex (geniculocalcarine tract)



- Diffusion Tensor Imaging can be used to reconstruct white matter tracts **(FIBER TRACTOGRAPHY)**

- “Eloquent” major white matter tracts can be depicted and any alteration in their anatomy can be evaluated





WM FIBER Classification

- Association Fibers
- Projection Fibers
- Commissural Fibers

Association Fibers

- Interconnect cortical areas in each hemisphere
  - Cingulum
  - Superior and inferior occipitofrontal fasciculi
  - Uncinate fasciculus
  - Superior longitudinal (arcuate) fasciculus
  - Inferior longitudinal (occipitotemporal) fasciculus

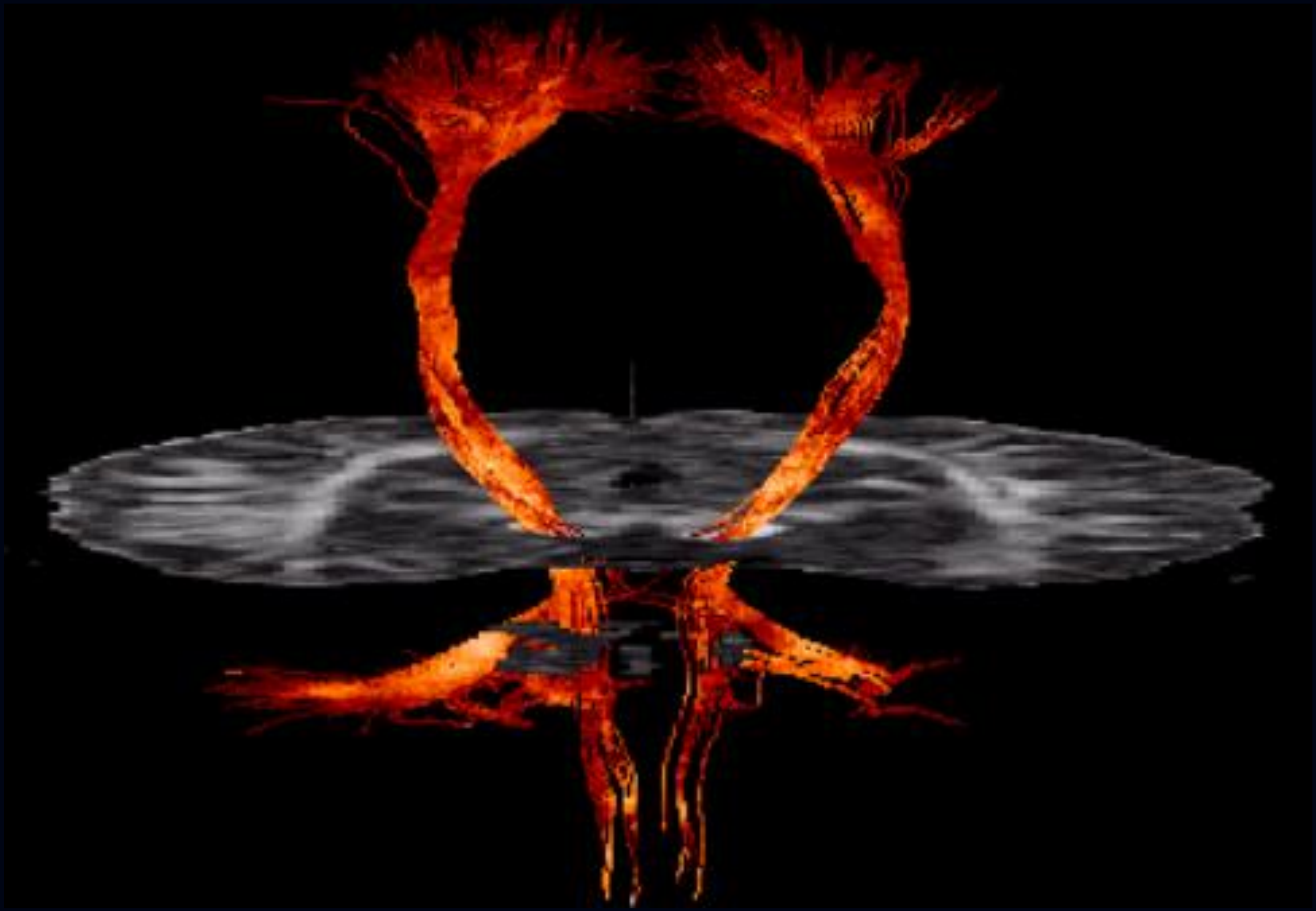
Projection Fibers

- Interconnect cortical areas with deep nuclei, brainstem, cerebellum and spinal cord (Efferent and Afferent)
  - Corticospinal tracts
  - Corticobulbar tracts
  - Corticopontine tracts
  - Geniculocalcarine tracts (optic radiations)

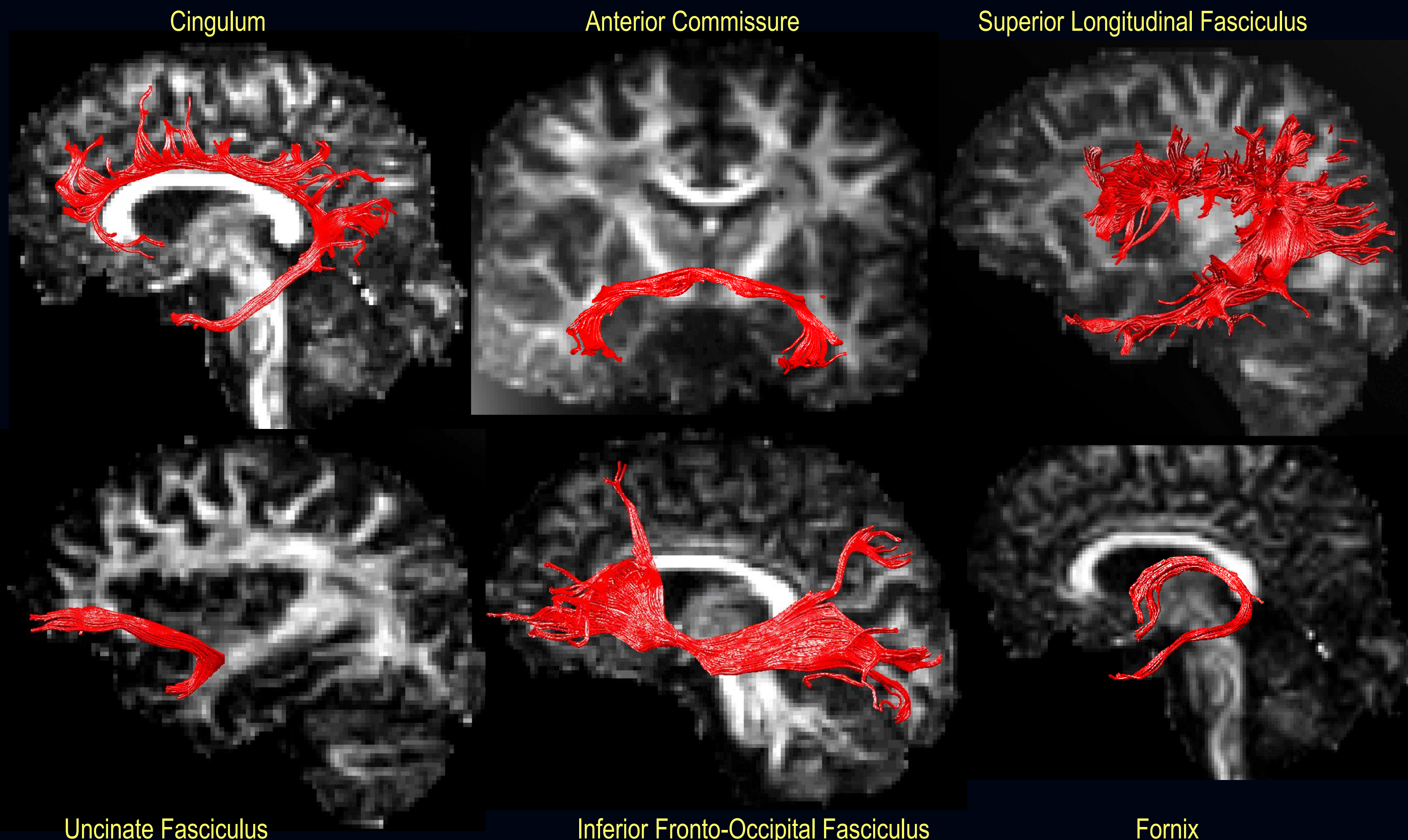
Commissural Fibers

- Interconnect similar cortical areas between opposite hemispheres
  - Corpus callosum
  - Anterior commissure

Cortico-Spinal Tract Mapping



$$T = \sqrt[3]{3b/2\gamma^2G^2}$$



Evaluation of Fibers

1. Fiber tract volume
2. Anatomical distribution of tract
3. Presence or absence of tract in the expected position
4. Compare fibers with opposite side in FA Map image

Note: Except corpus callosal rest of the fibers are analyzed and compared with opposite side(RT-LT)

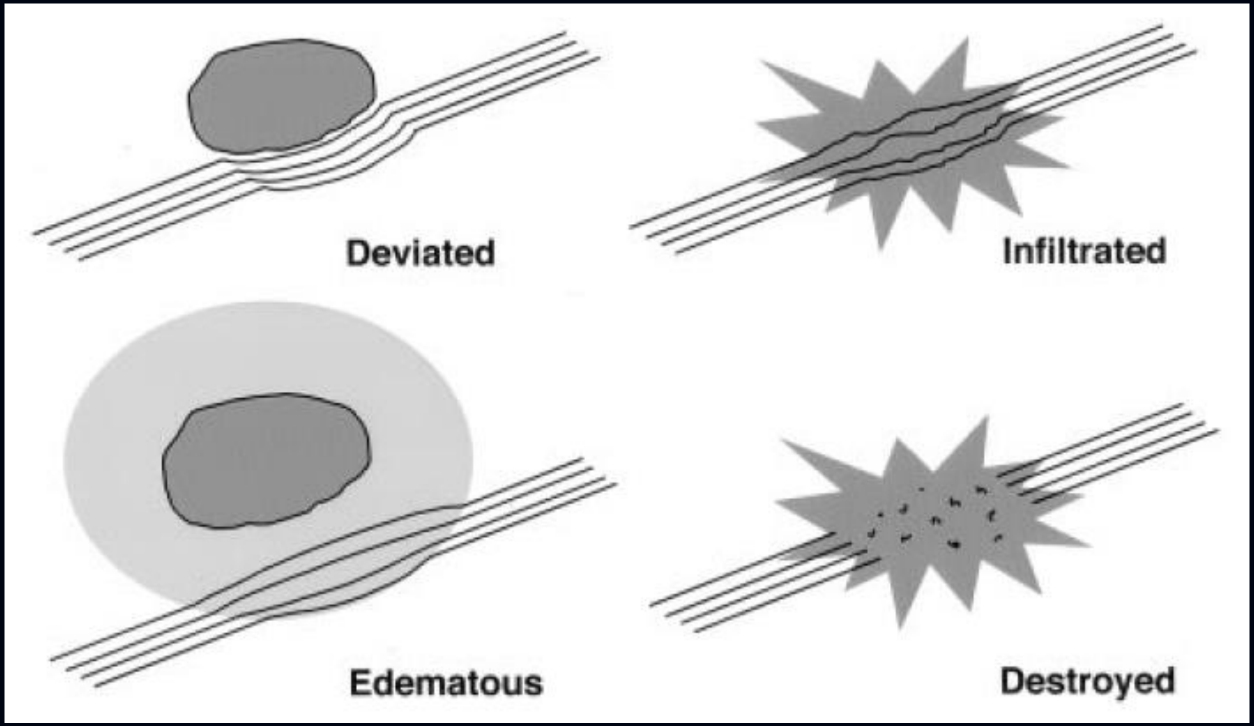
Brain Tumours – Goal of Surgery

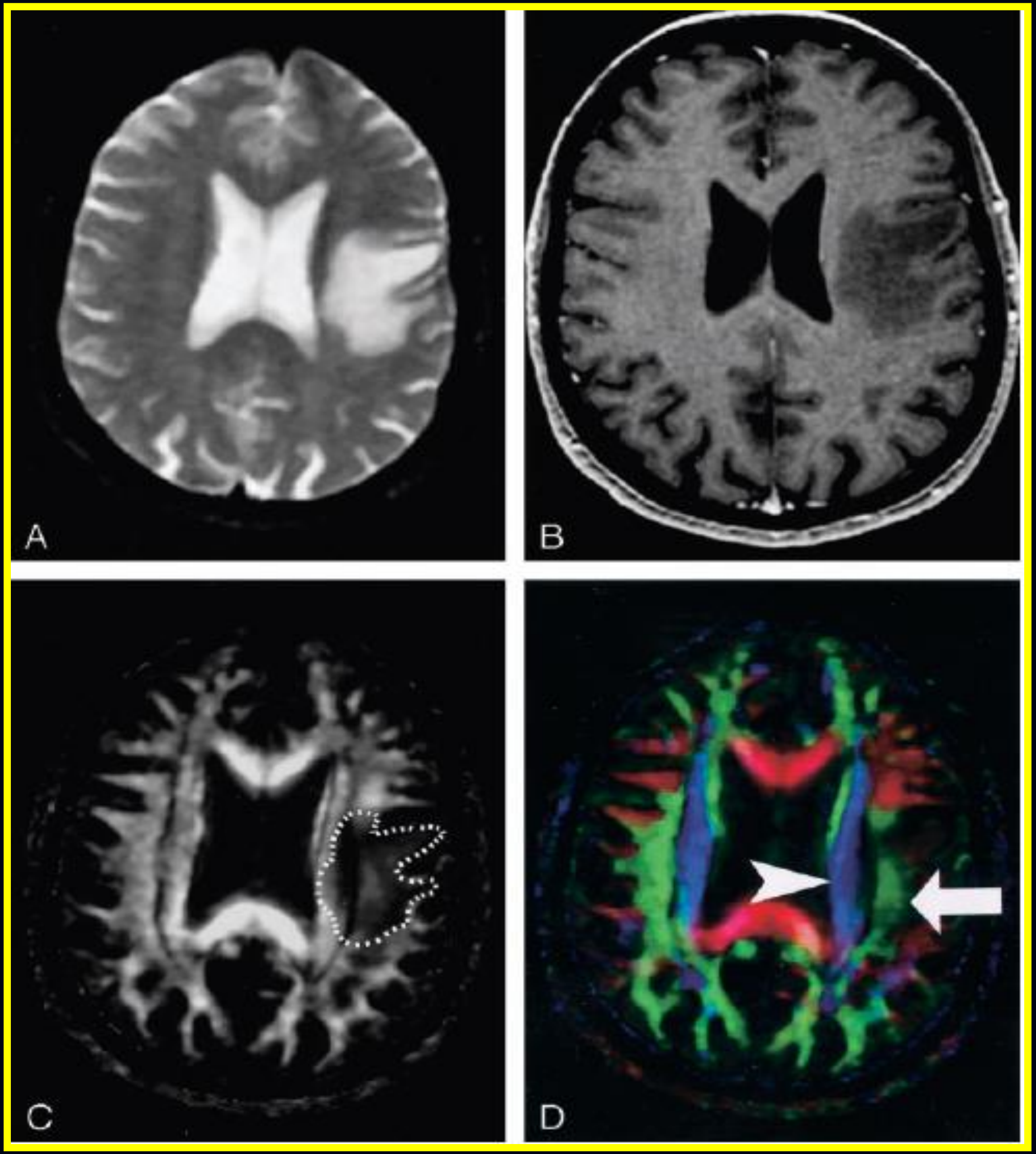
- Maximise tumour resection
- Minimise postoperative neurological deficits

Pre-operative and intra-operative mapping of tumour and its relationship to surrounding structures

WM Tracts - Patterns

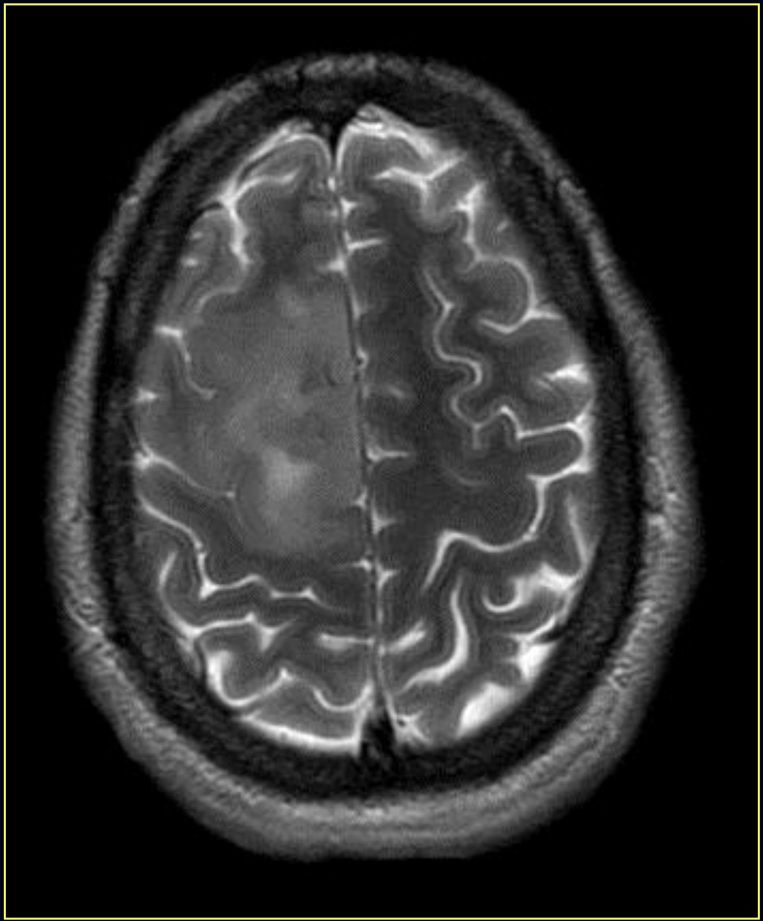
- Intact but displaced
- Edematous / Infiltrated
- Destroyed

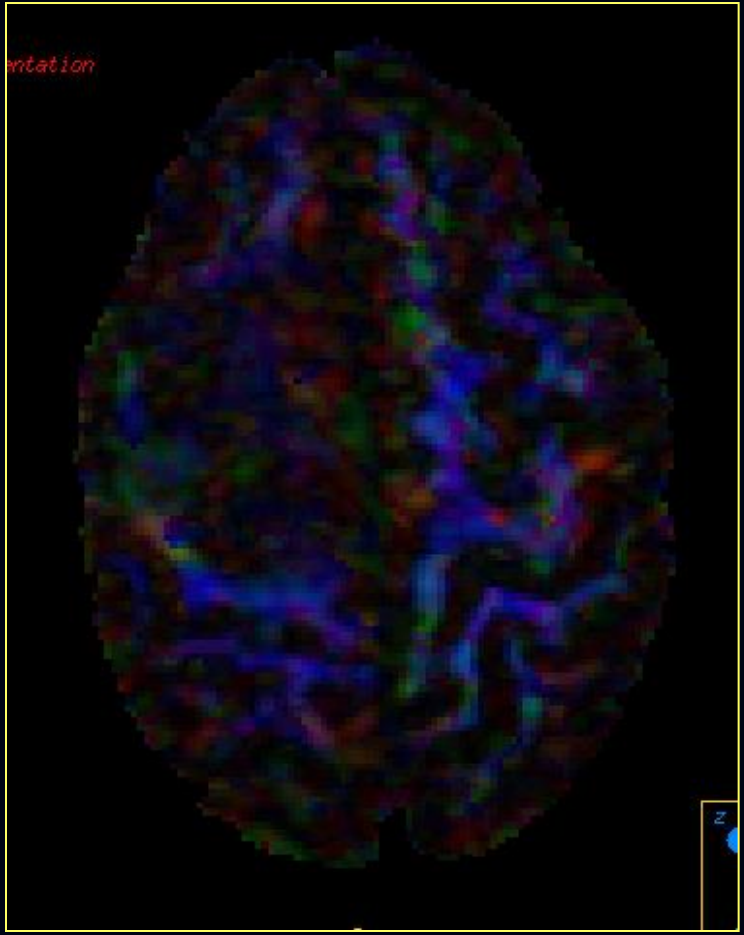




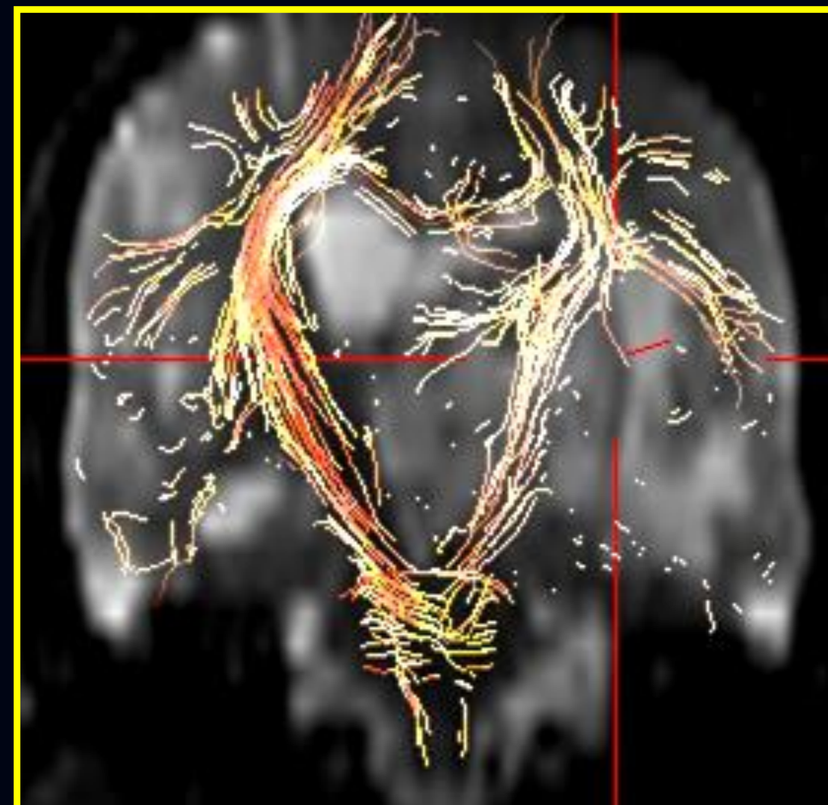
Edema

Tumour destroying WM tracts

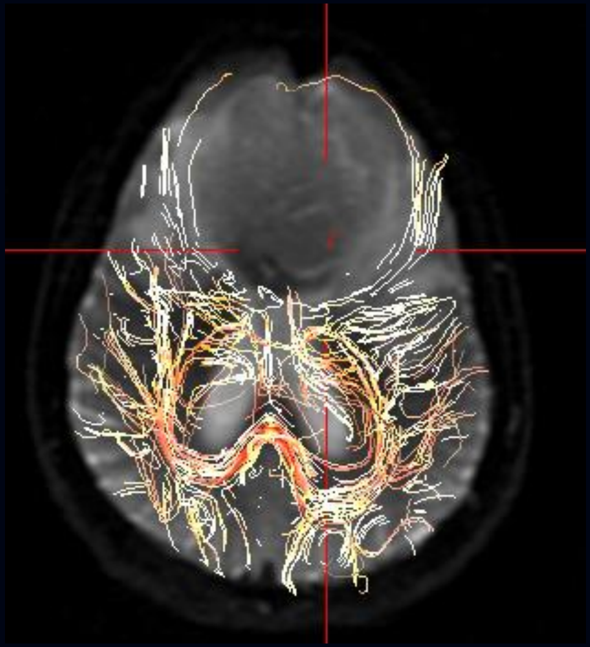
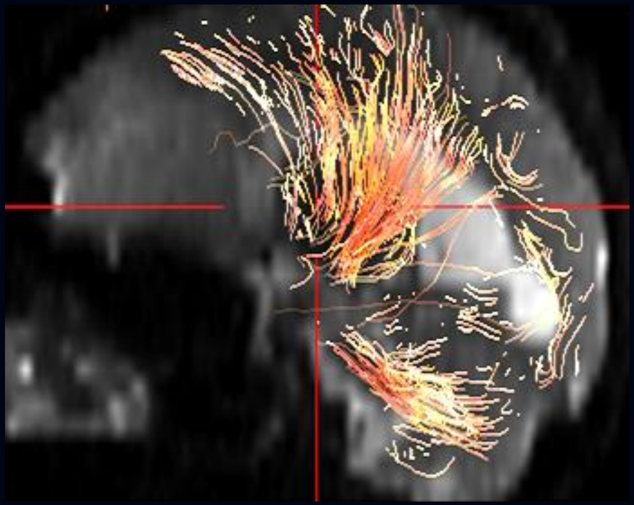
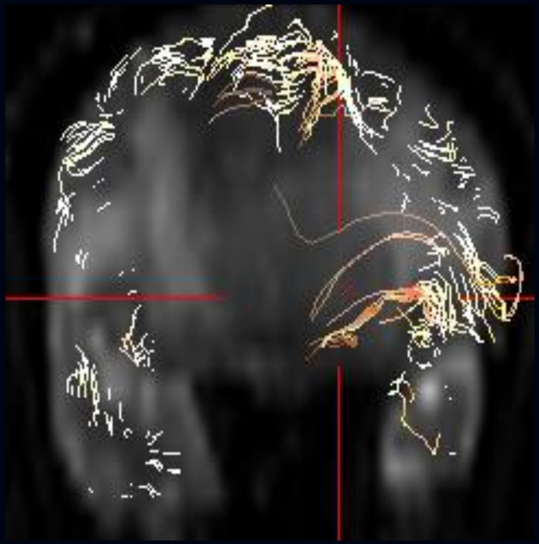




GBM



Meningioma

Other Applications

- DTI is able to detect WM damage and recovery after brain injury
- DTI can characterise Wallerian degeneration of WM tracts remote from infarction zone secondary to subacute or chronic ischemia
- Imaging occult disease
  - neuropsychiatric applications
    - schizophrenia
    - dementia (MID vs DAT)
  - epilepsy
  - brain maturation
- Imaging spinal cord disease – prognosis
- In the future, DTI may provide useful prognostic information for recovery of motor function after stroke

DTI - Limitations

- Heavily operator dependent
- Cannot differentiate between afferent and efferent tracts
- Problem of fiber crossing, kissing and branching
- Lack of standardisation
- Motion artifacts – voluntary/involuntary
- Age variation
- Long learning curve, more studies required

MR SPECTROSCOPY

MR Spectroscopy

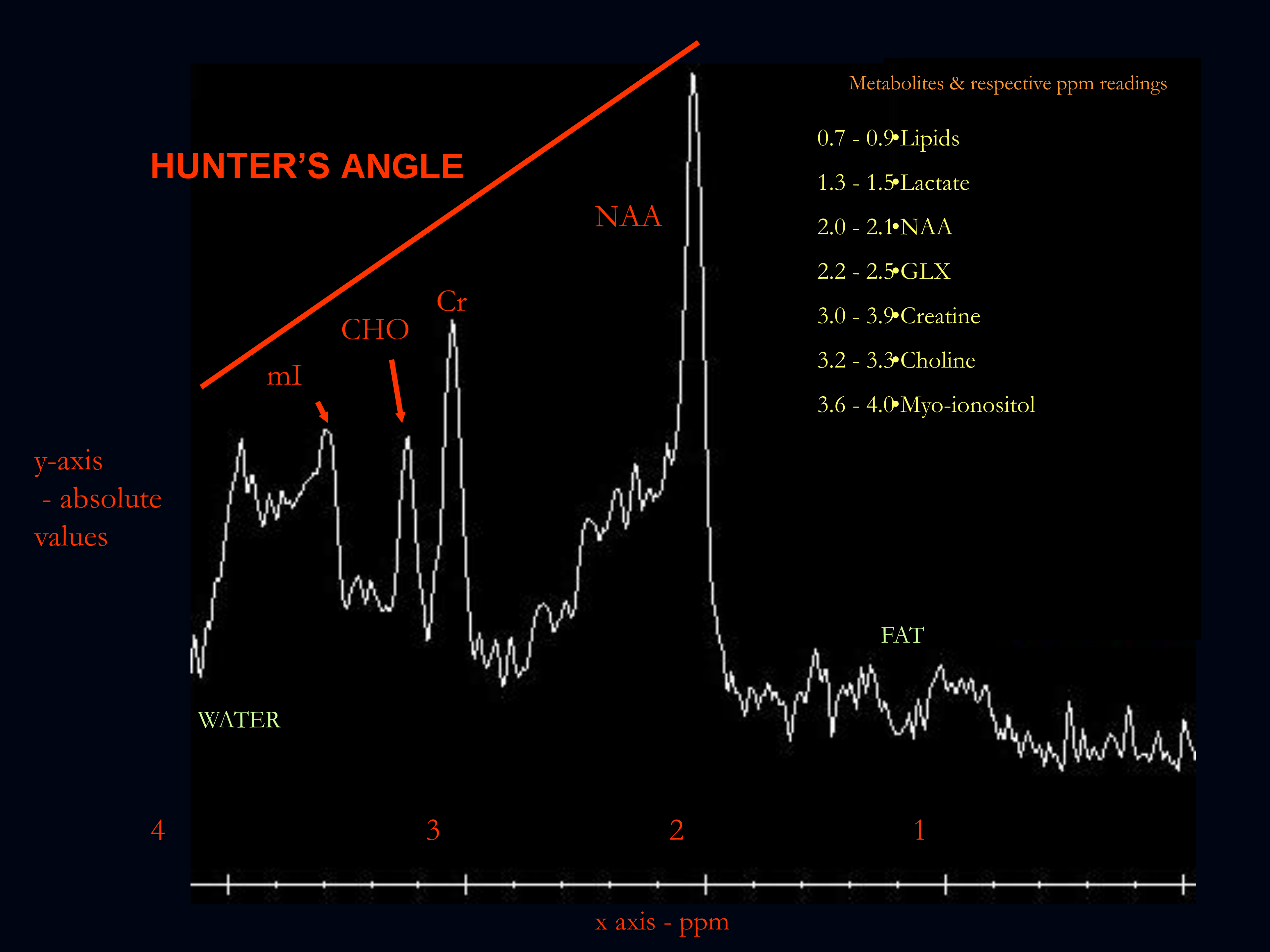
- It is a non-invasive method of providing metabolic information about the brain
- MRS enables tissue characterization on a biochemical level surpassing that of conventional magnetic resonance imaging
- MRS is most useful when augmented with a comprehensive patient evaluation that includes the clinical history and imaging studies
- MRS does not replace conventional MRI but complements the information provided by it

What is the difference between MRI and MRS?

- Basically, MRI and MRS are the same technique, differing only in the manner in which data are presented.
- In MRI, the signal obtained in the time domain is used to generate an image.
- In MRS, the Fourier transform of the magnetic resonance signal in the time domain is used to generate a frequency domain spectrum of components that make up the image.

MR Spectroscopy

- At least one localization sequence is necessary
- Volume of interest (VOI)
- Suppression of water signal
- Detection of signal from protons other than water
- Frequency maps
- Types - Single / multivoxel



HUNTER'S ANGLE
NAA
Cr
CHO
mI
Metabolites & respective ppm readings
0.7 - 0.9•Lipids
1.3 - 1.5•Lactate
2.0 - 2.1•NAA
2.2 - 2.5•GLX
3.0 - 3.9•Creatine
3.2 - 3.3•Choline
3.6 - 4.0•Myo-ionositol
y-axis
- absolute
values
FAT
WATER
4
3
2
1
x axis - ppm

Metabolite	Location (ppm)	Clinical significance
NAA	2.0	Marker for adult healthy neurons
Creatine	3.0	Internal reference
Choline	3.25	Cell membrane turnover
Lactate	1.33	Hypoxia (anaerobic metabolism)
Lipid	1.3	Necrosis
Myoinositol	3.56	Osmotic regulator
Glx(gln/glu)	2.2-2.4	Indicator of destructive process
Water	4.7	

DIFFERENT TYPES OF SEQUENCES

- **PRESS - point resolved spectroscopy**
- **STEAM – stimulated echo acquisition mode**

  - **Short TE – 31 ms**
  - **Long TE – 136 ms – Invert lactate**

    - 270 ms - Lipid suppressed

APPLICATIONS

- BRAIN TUMORS
- INFECTIONS
- EPILEPSY
- METABOLIC DISEASES & WM DISORDERS
- DEMENTIA

BRAIN TUMORS

1. Differentiating Neoplastic from non-neoplastic brain lesions.

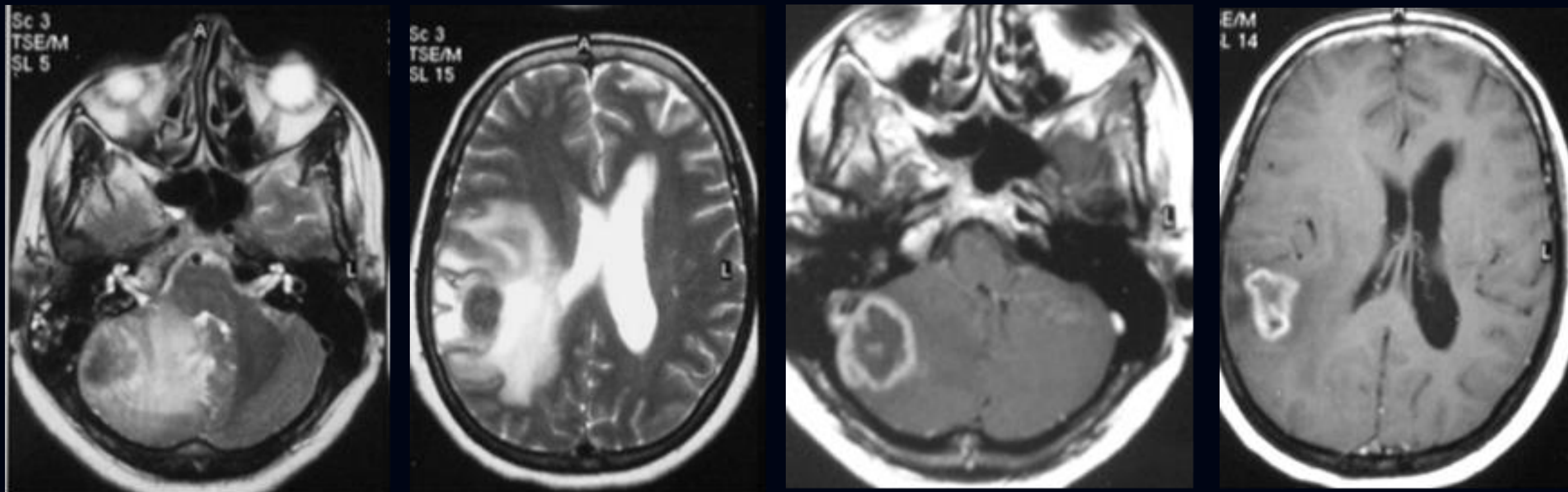
2. Suggesting Tumor histology, grade

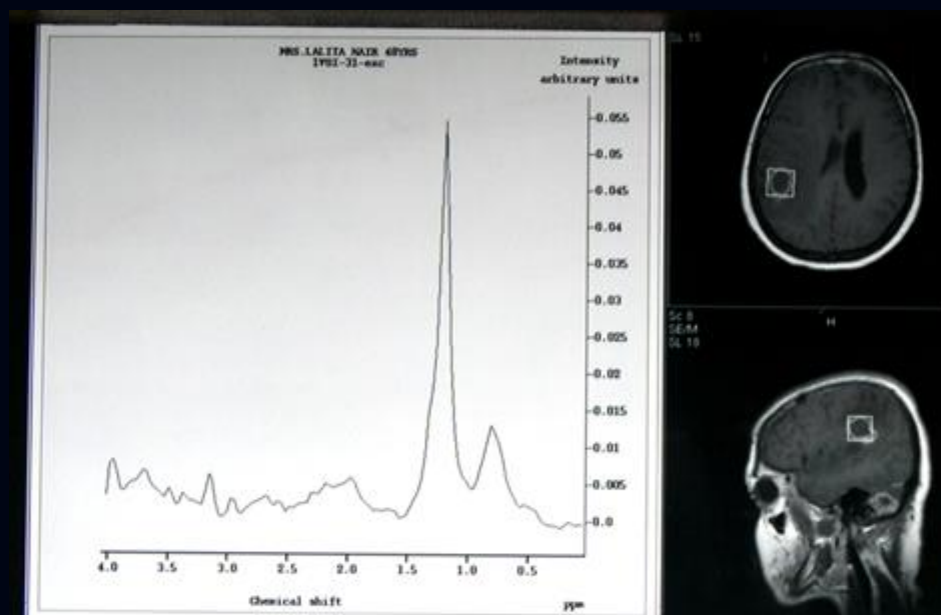
3. Indicating the ideal site of biopsy.

4. Assessing therapeutic response - recurrence v/s radiation necrosis

BASIC PATTERN IN BRAIN TUMORS

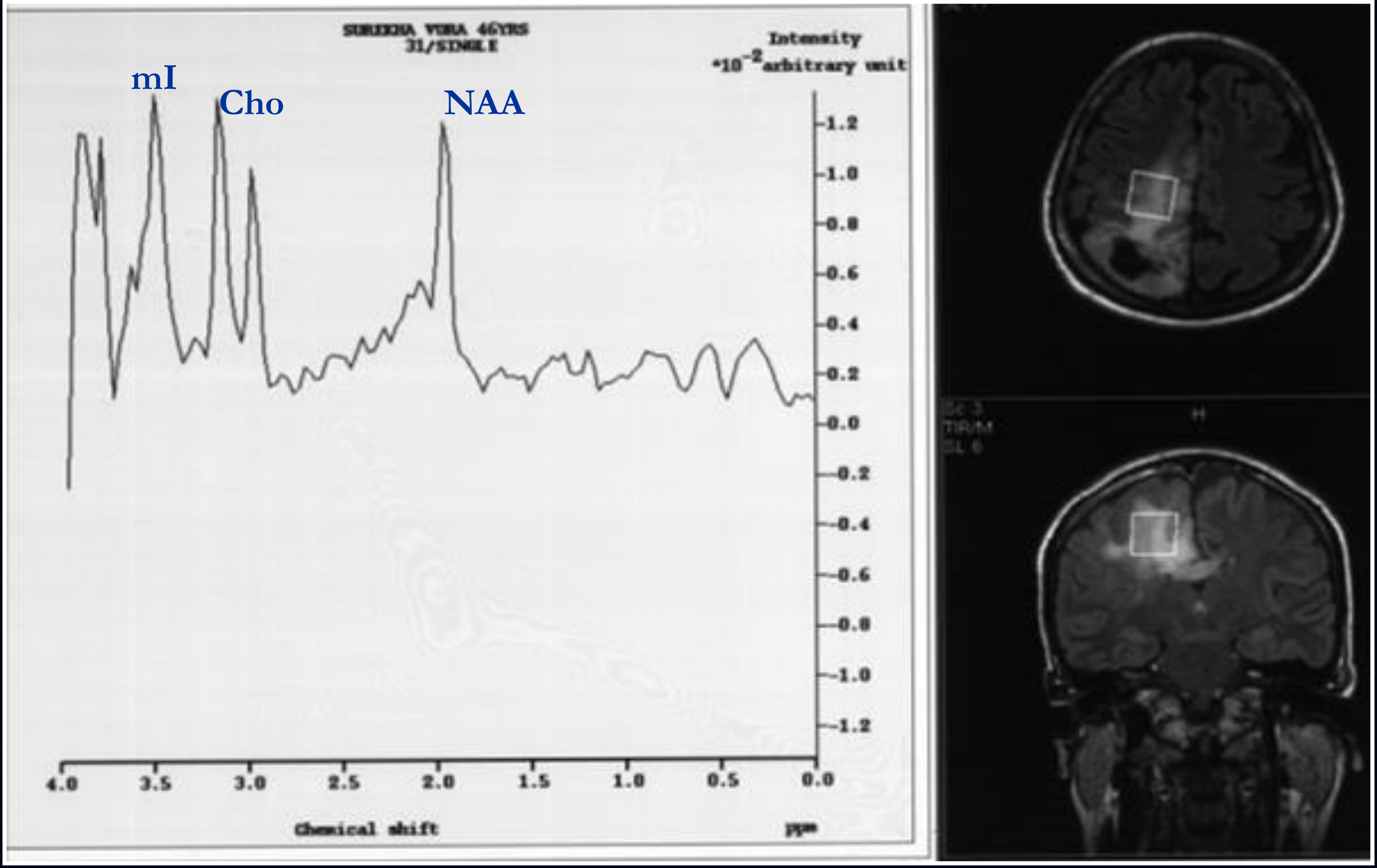
- Decreased NAA and NAA / Creatine ratio
- Increased Choline and Choline / Creatine ratio
- Elevated Lipid, Lactate in some tumors.



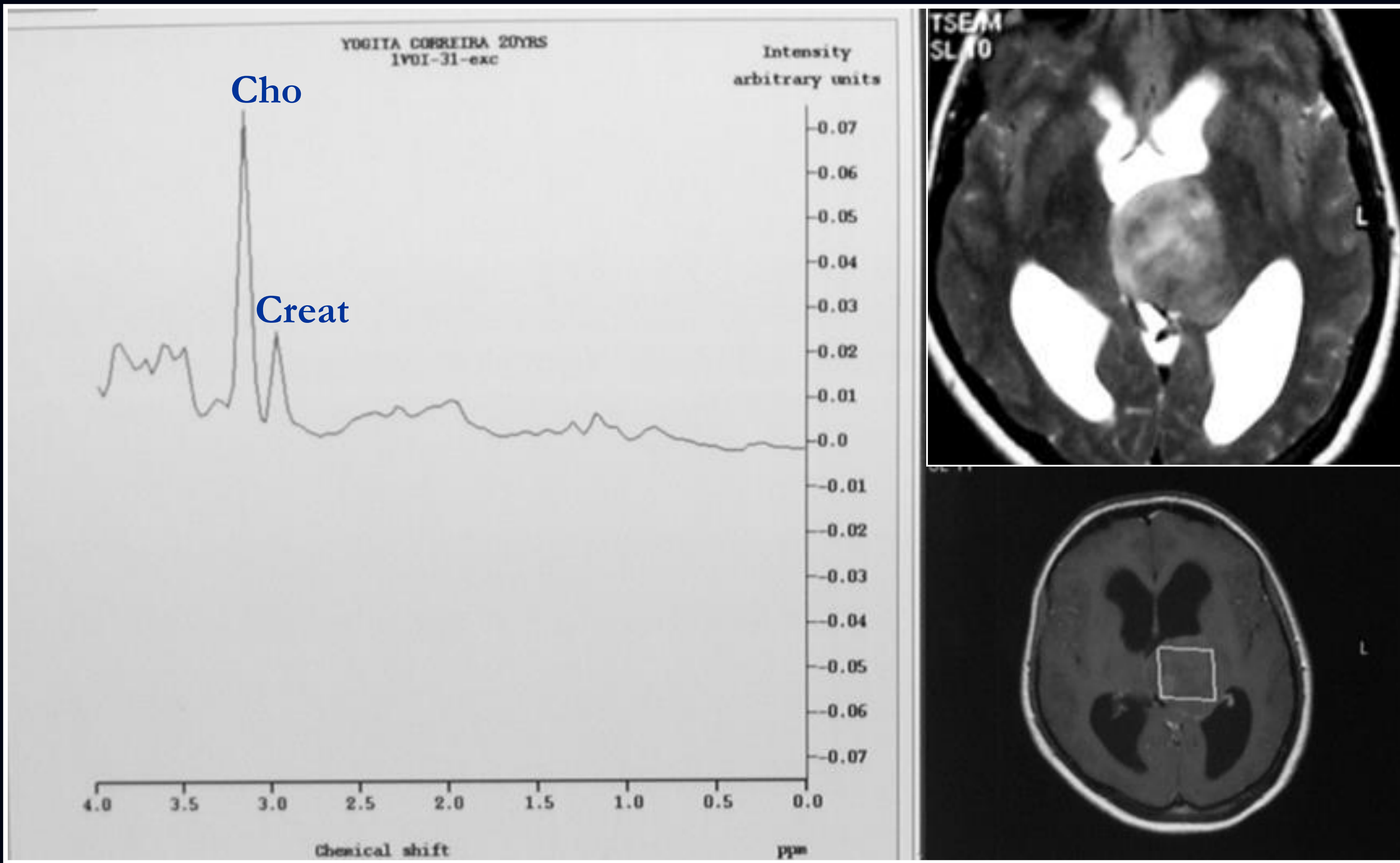


Tuberculomas

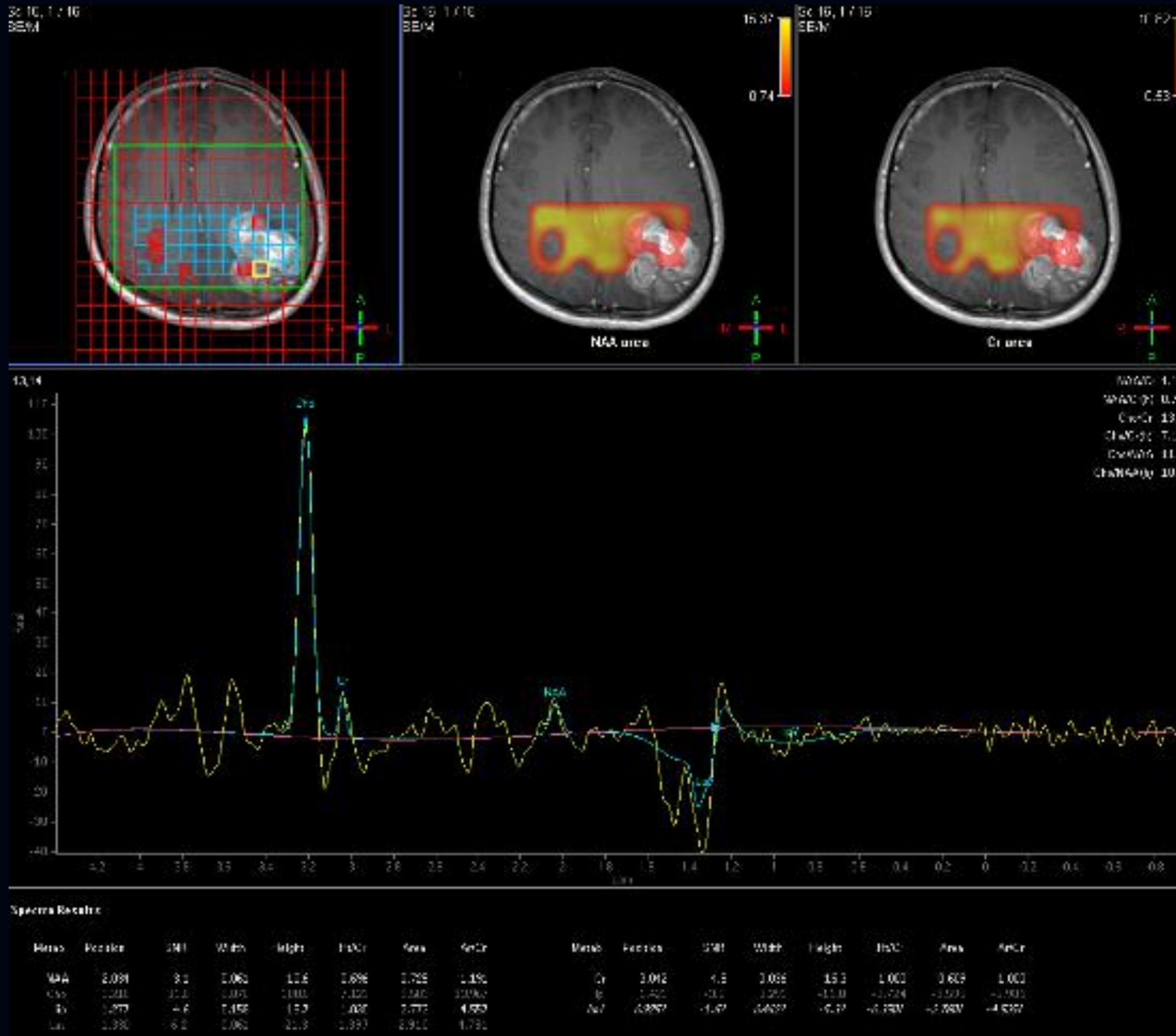
LOW GRADE GLIOMA



HIGH GRADE GLIOMA

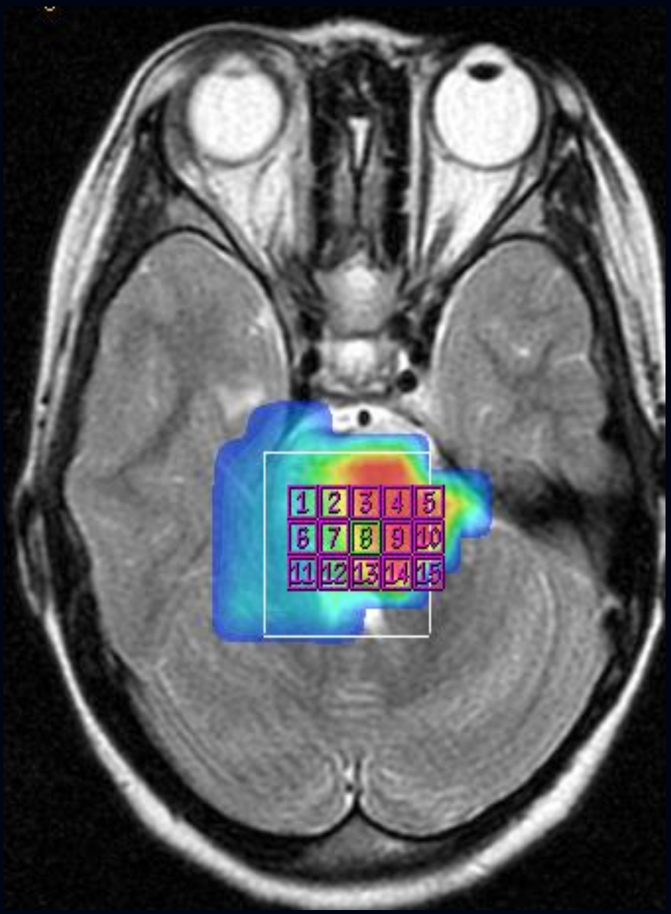


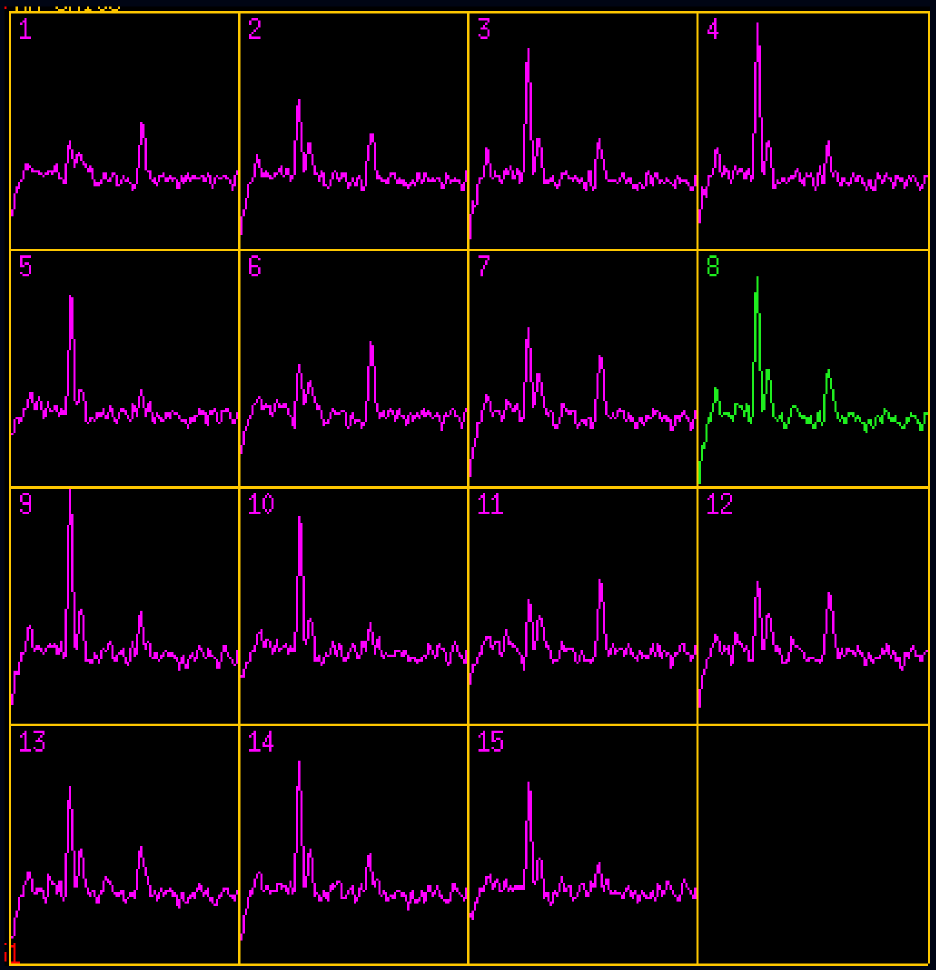
MR
Spectroscopy



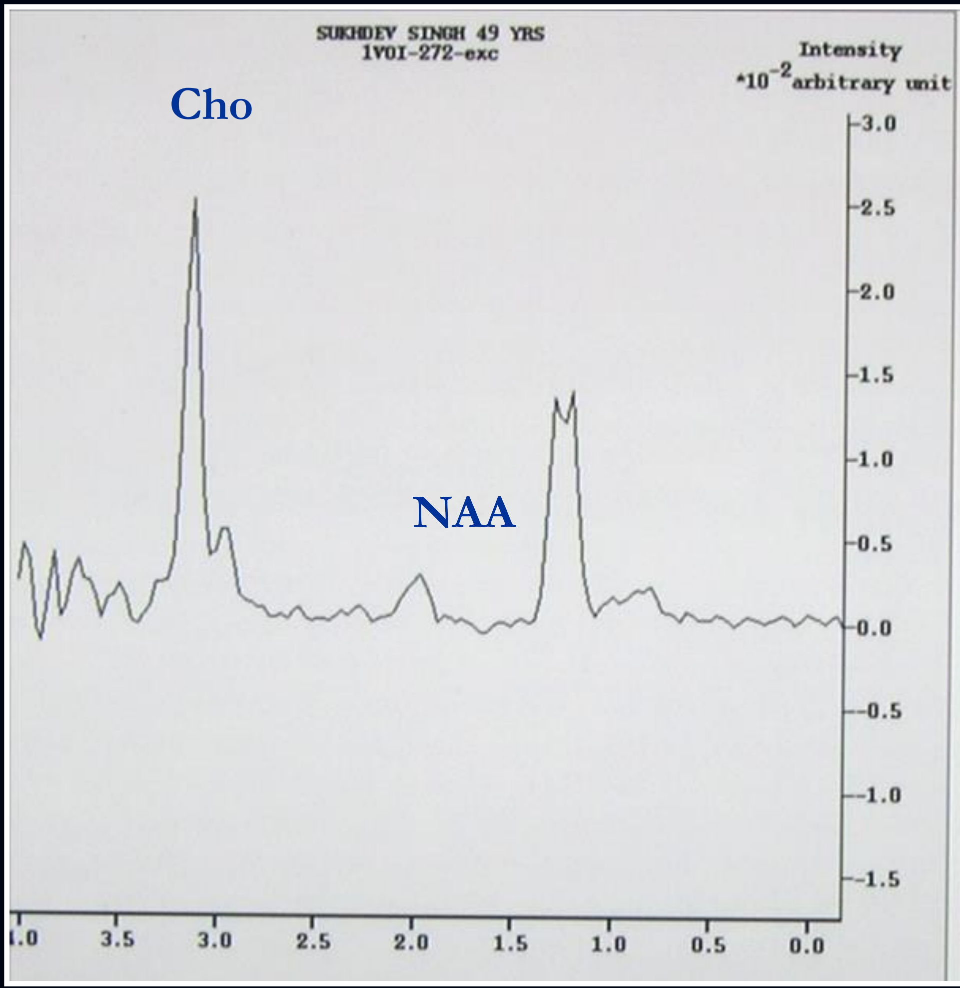
MRS in Glioblastoma showing high choline peak

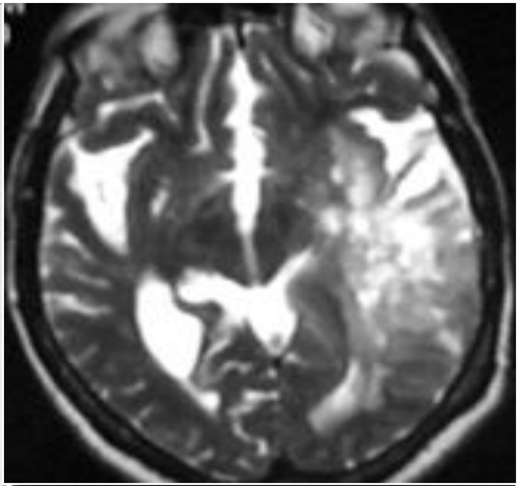
MULTIVOXEL SPECTROSCOPY
To indicate the ideal site of biopsy

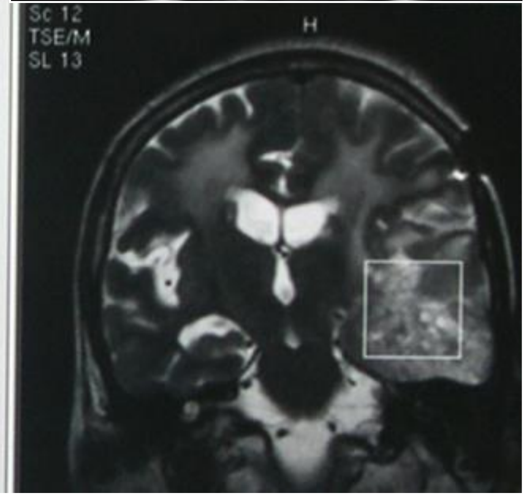




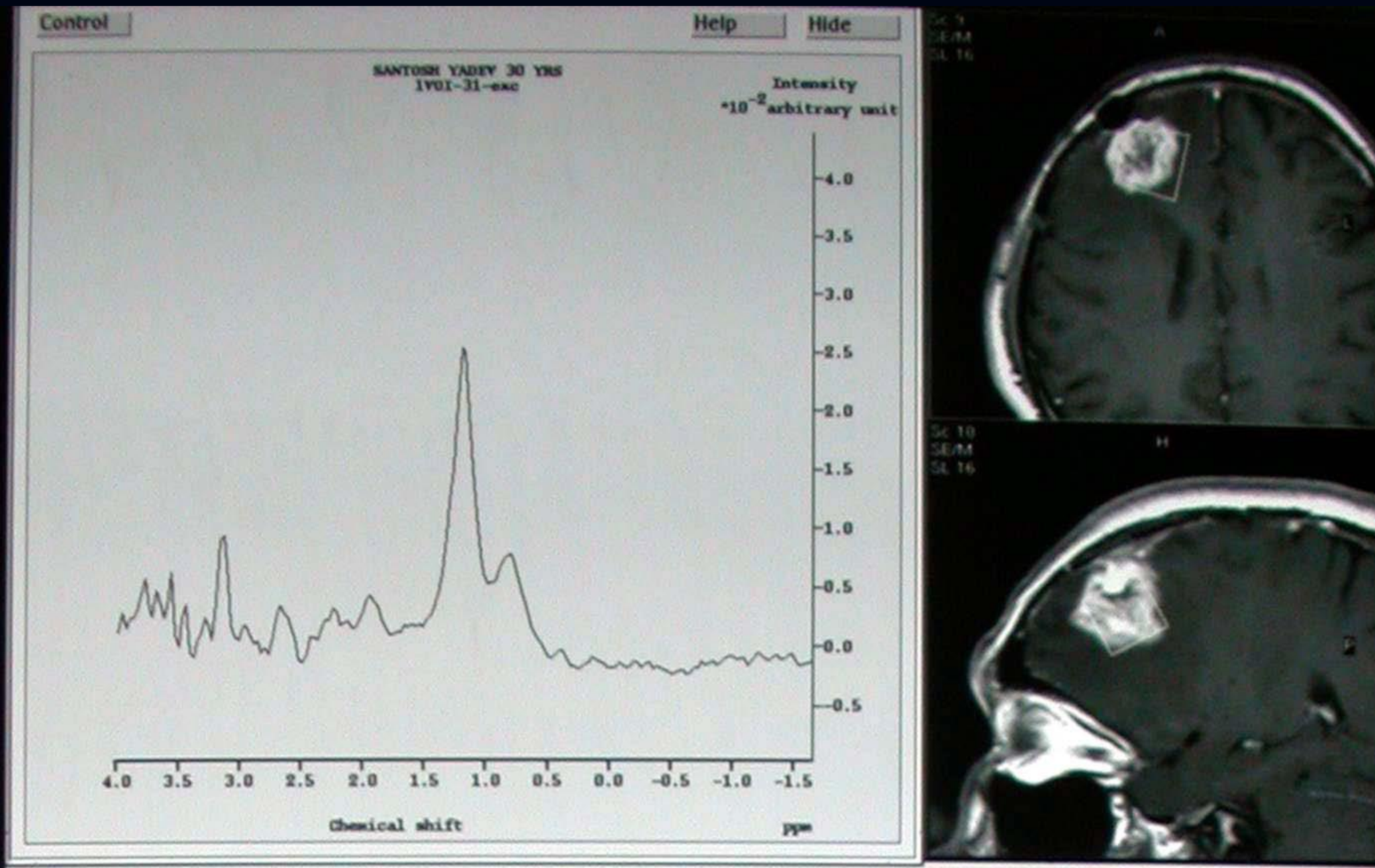
POST OP/RT RECURRENCE

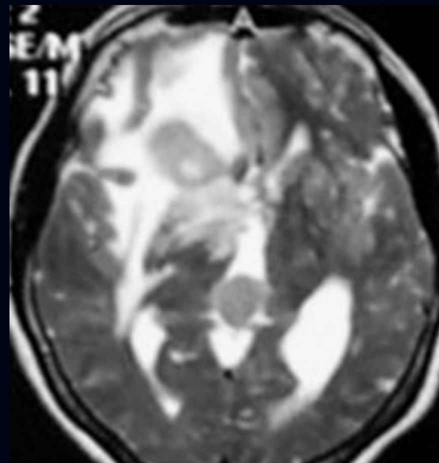


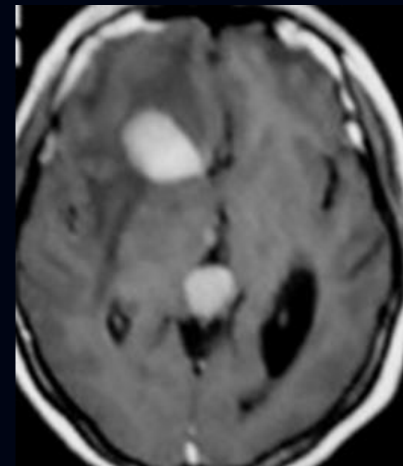


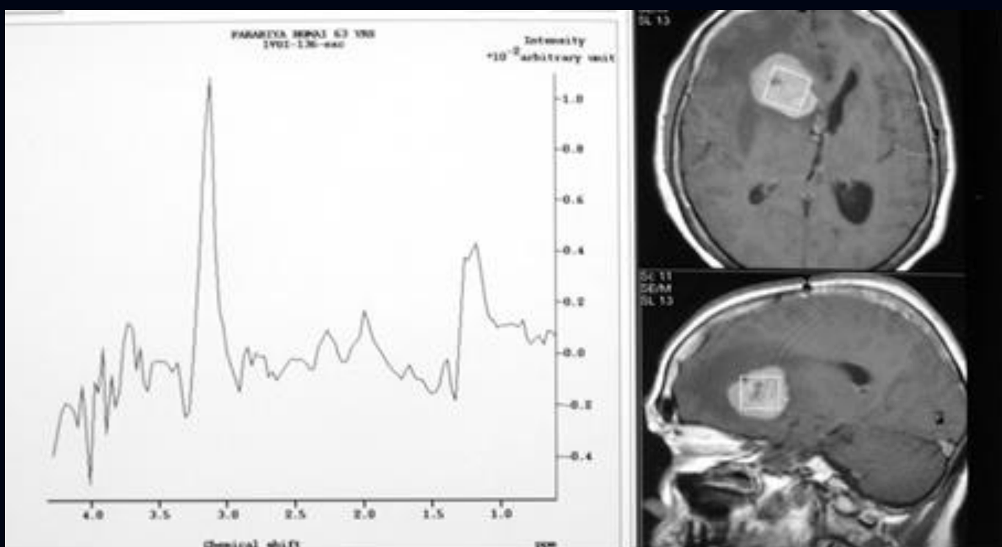


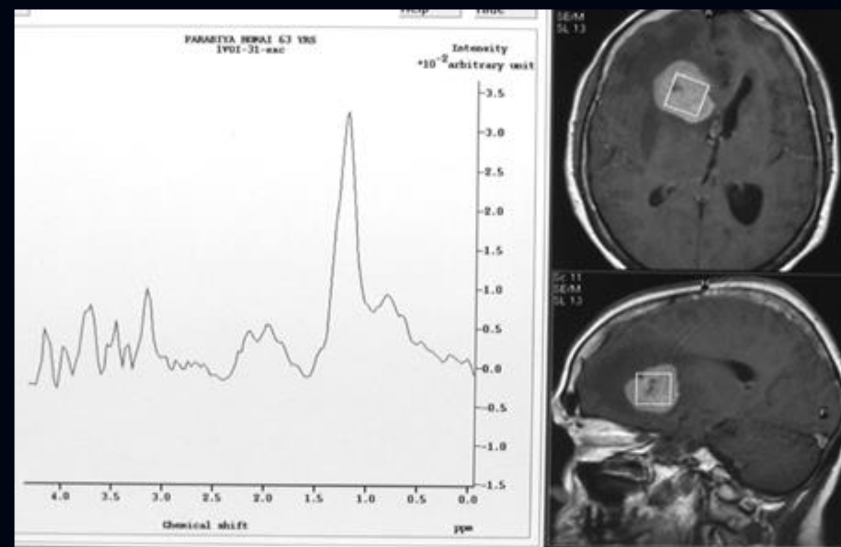
RADIATION NECROSIS








Intensity
*10-2 arbitrary unit
Chemical shift
ppm


Intensity
*10-2 arbitrary unit
Chemical shift
ppm

Lymphoma

LIMITATIONS OF SPECTROSCOPY

- Always needs to be interpreted with the conventional MR images.
- Small lesions, peripheral lesions.
- Voxel size.
- Hemorrhagic lesions
- System requirements.

MR PERFUSION

MR Perfusion

MR angiography → Bulk vessel flow

Perfusion MR → Microscopic tissue-level blood flow

MR Perfusion

- Perfusion is the steady-state delivery of blood to tissues through the capillaries.

- Perfusion imaging is thus an anatomical and physiological study to assess capillary level hemodynamics

MR Perfusion

- CBF: Amount of blood moving through a given amount of tissue per unit time (ml/100g/min)

- CBV: Amount of blood in a given amount of tissue at any time (ml/100gm)

- MTT: The amount of time required for contrast to flow from arterial to venous side

Normal adults

Parameter	Values in Gray matter
CBF	About 50 ml/100g/min
CBV	About 4ml/100ml of tissue
MTT	About 5 seconds

White matter values are approximately half

Techniques of MR perfusion

- Contrast(Exogenous) or Non-contrast(Endogenous)

- Contrast based techniques : Dynamic I.V. administration of *MR susceptibility contrast agent - usually Gadolinium DTPA*

- Non Contrast techniques : Arterial spin labelling(ASL) may allow flow quantification but their use is limited due to poor SNR

Contrast MR Perfusion

- These methods use a model that assumes the tracer is restricted to the intravascular compartment and does not diffuse into the extracellular space

- Gadolinium – Paramagnetic – high conc – heterogeneity of magnetic field – change in signal of surr tissues

- These signal changes are measured & signal-time course data are converted to relative tracer concentration-time course data

Indications

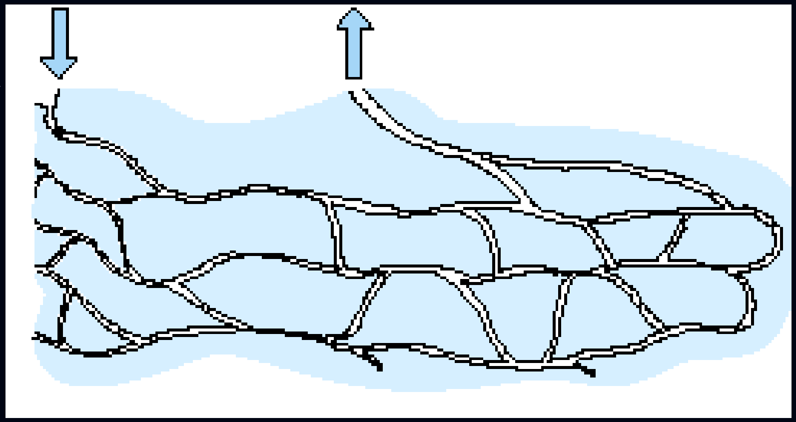
- Stroke
- Tumour imaging

Contrast MR Perfusion

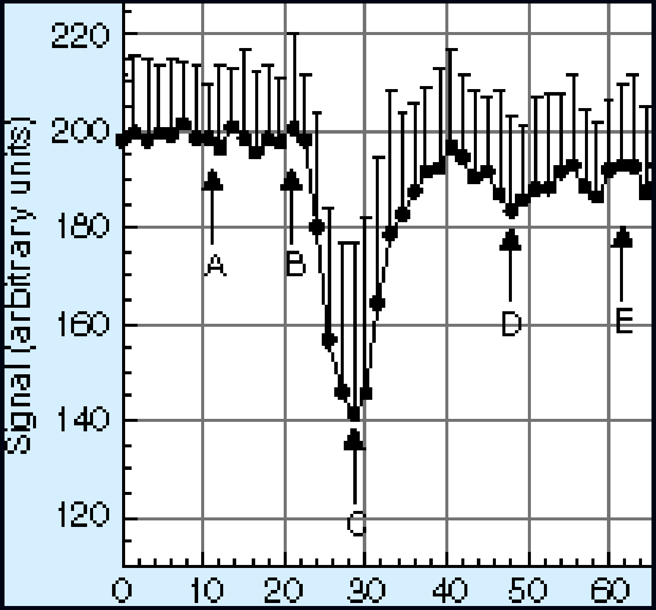
- T1W or T2W techniques used
- T2-W (spin echo) or $T2^*$-W (gradient echo) seqns mainly used
- Signal drop due to spin dephasing from susceptibility effect
- The time density curve is thus inverted, since there is signal loss

Dynamic passage of paramagnetic agent

Capillary bed



Spin dephasing from susceptibility effect



Signal drop

Used to compute relative perfusion

Tumour imaging

- Grading of brain tumours
- Stereotactic biopsy guidance
- Radiation necrosis vs recurrence
- Monitoring response to treatment

Tumour imaging

- Tumour growth is dependent on angiogenesis (neovascularisation)
- Microvascular changes in angiogenesis are detected as increased perfusion
- Generally, high grade tumours demonstrate increased angiogenesis and heterogeneity
- Hence, perfusion imaging can assess the grade of tumours. rCBV maps are used for evaluation

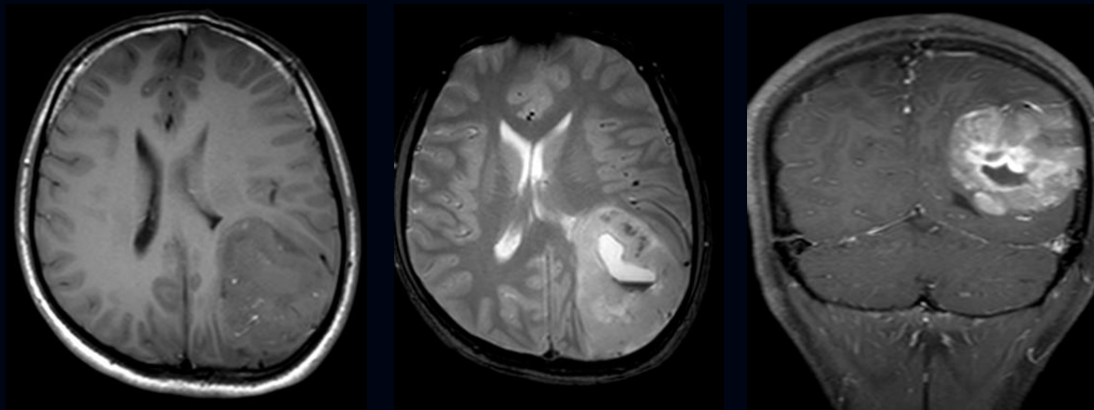
Tumour imaging

- In a large heterogeneous tumour, the area with maximum rCBV is of the highest grade. This is most useful for planning “targetted” biopsies

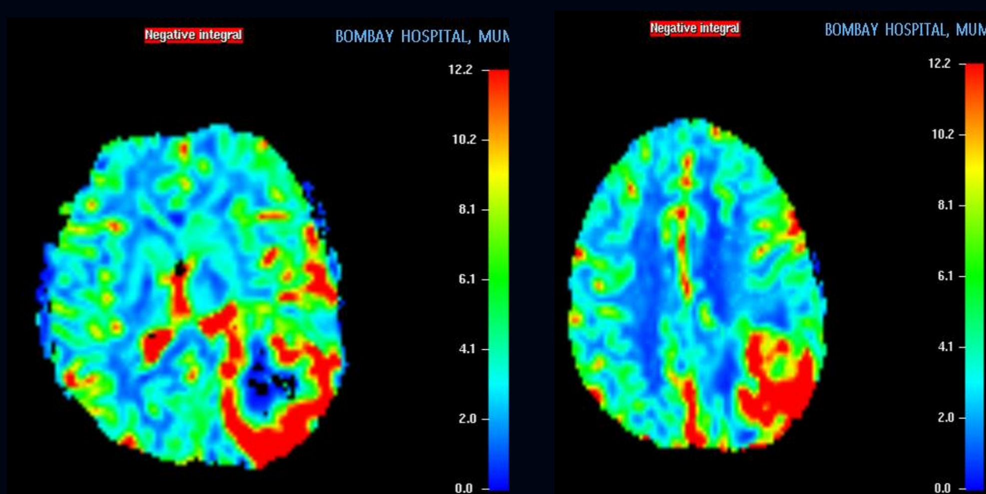
- **High rCBV:**
  - High grade astrocytoma
  - Meningioma
  - Vascular mets
  - Oligodendroglioma

- **Low rCBV:**
  - Low grade astrocytoma
  - Medulloblastoma
  - Lymphoma

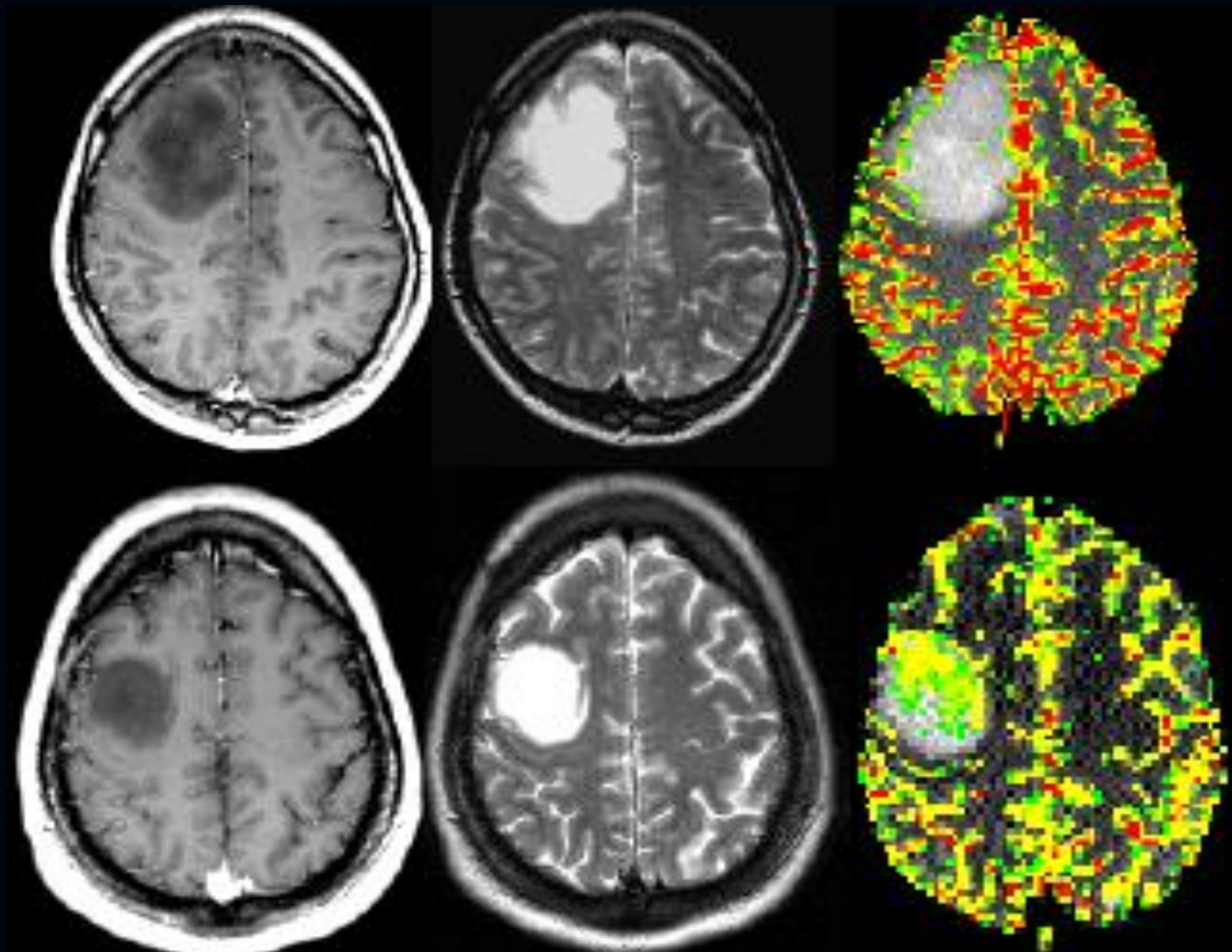
GLIOBLASTOMA



T1, T2 and contrast MRI of a high grade glioma.



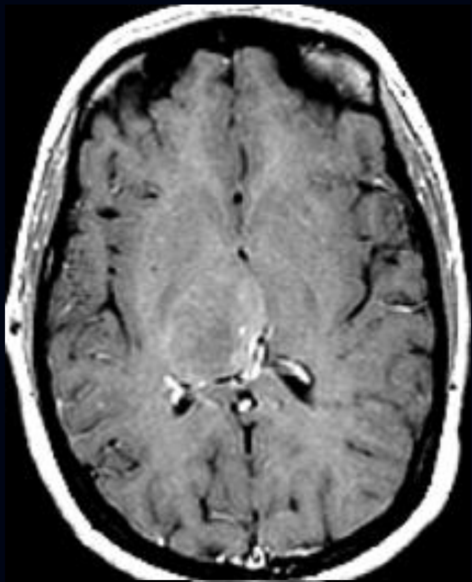
Perfusion Imaging showing hyperperfusion in tumor



Non enhancing tumour but hyper perfusion suggesting higher grade.

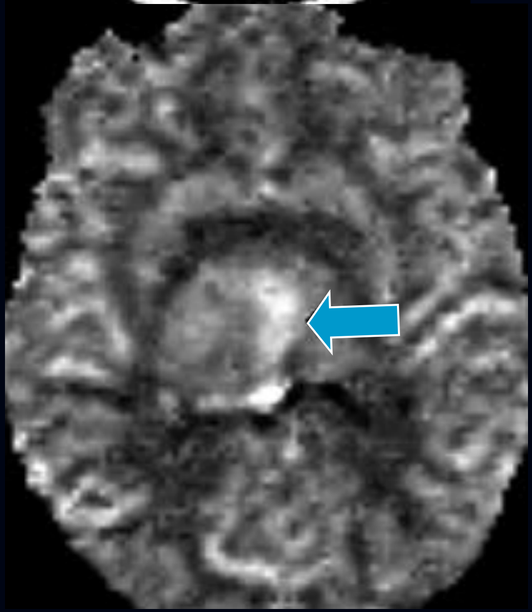
Follow-up of treated tumors

- To identify aggressive foci in the treated tumor bed (after cytoreduction by Sx or RT)
- Radionecrosis (low rCBV) vs tumor
- Effect of anti-angiogenetic drugs

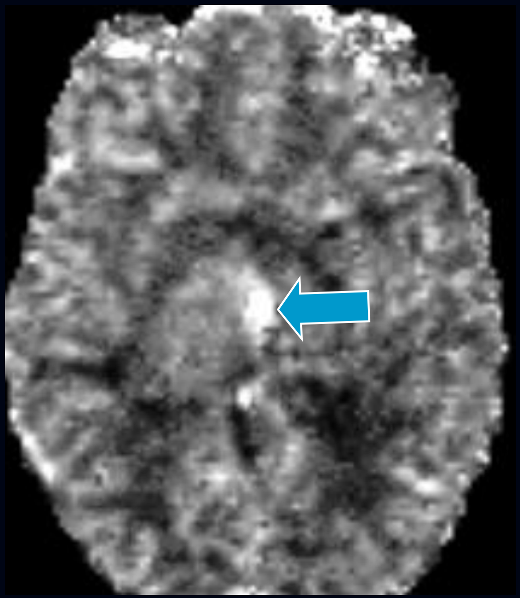


Post RT follow up

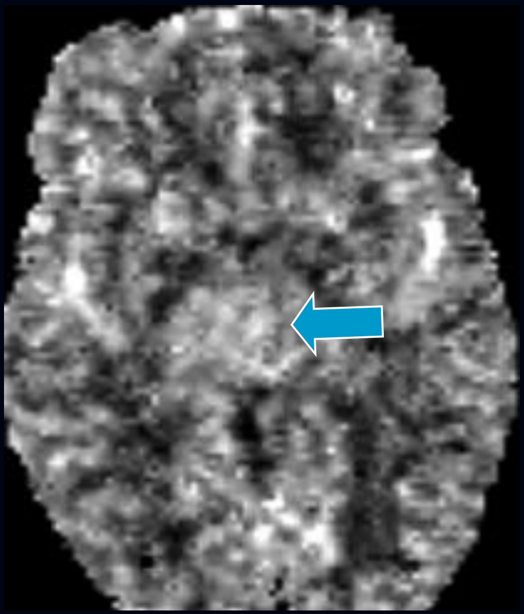
Gradual reduction in rCBV with time (radiation effect on microvasculature)



rCBV : Pre RT



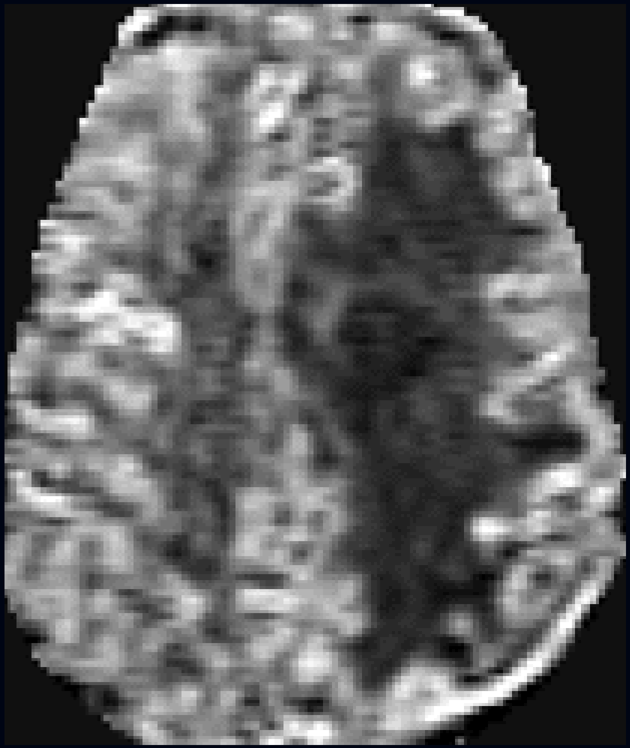
6 week map



5 month map

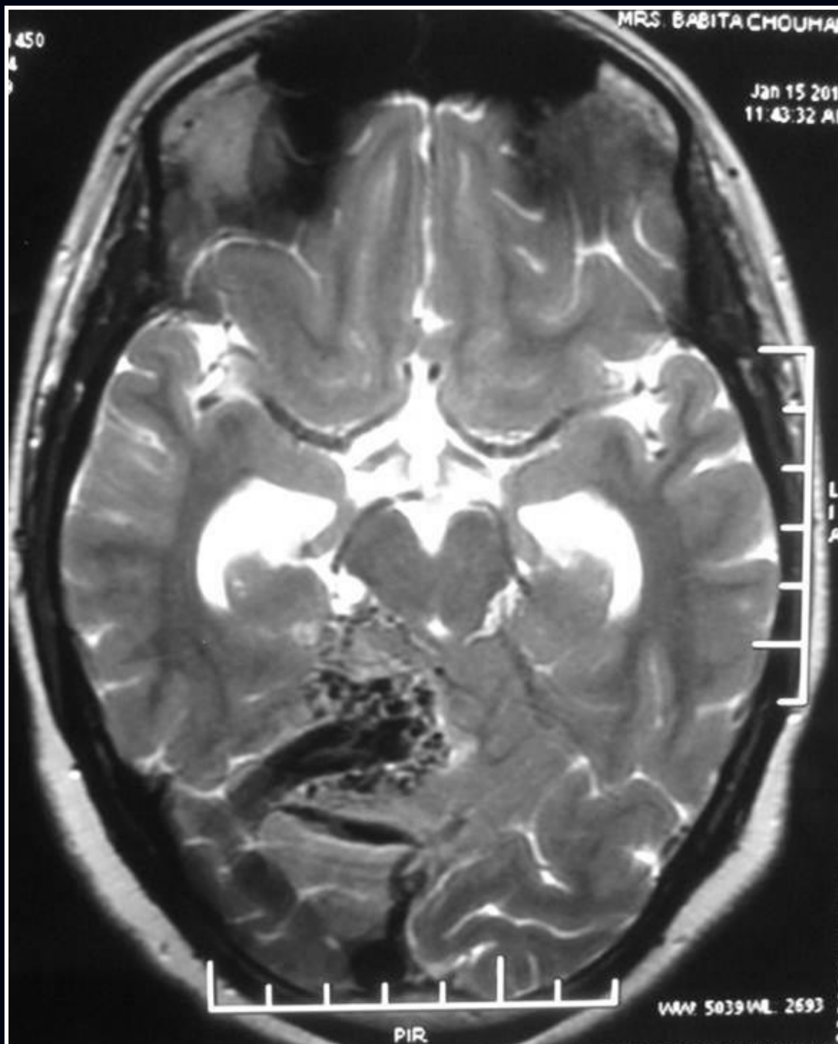
Radiation Necrosis

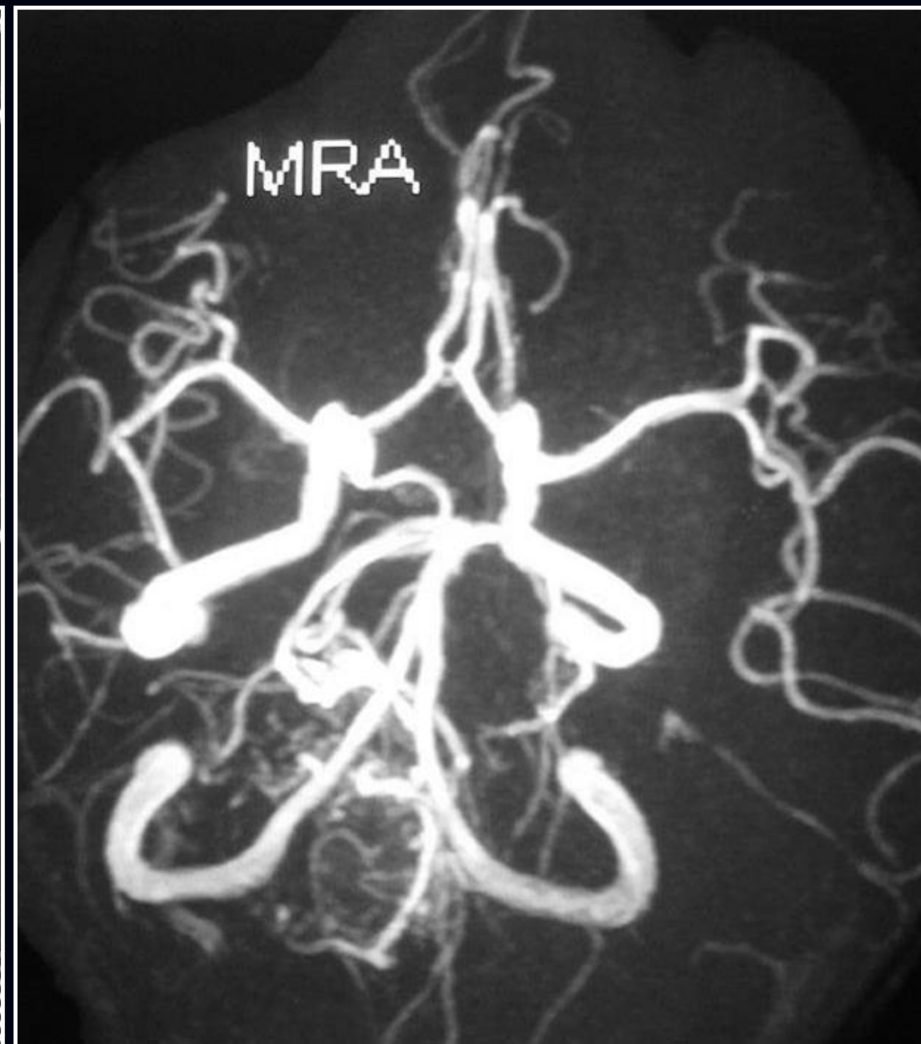
?Necrosis/tumor

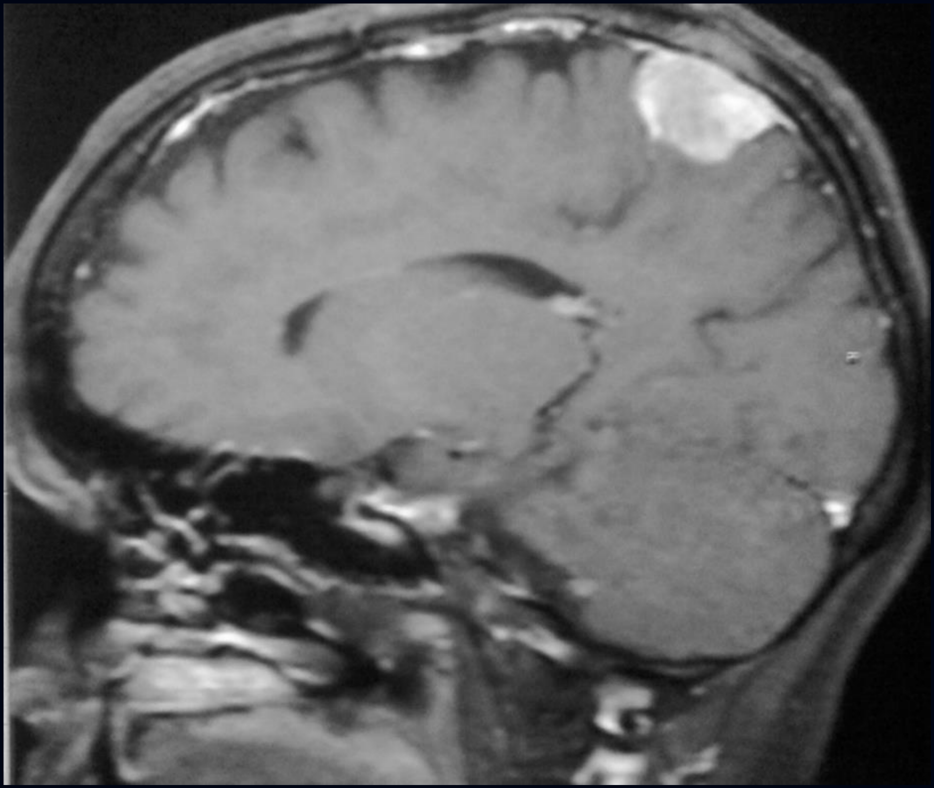


rCBV : No increase in CBV seen. RT effect more likely

MRAngio


MRS. BABITA CHOUHA
450
Jan 15 201
11:43:32 A
WW 5039 WL 2693
PIR


MRA



M
R
V

fMRI

functional Magnetic Resonance Imaging

Mechanism of BOLD Functional MRI

Brain activity ↑

Oxygen consumption ↑

Cerebral blood flow ↑↑

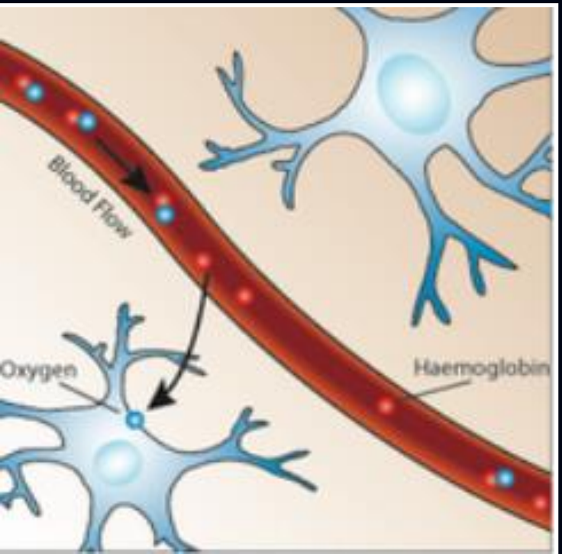
Oxyhemoglobin ↑
Deoxyhemoglobin ↓

DeoxyHb paramagnetic

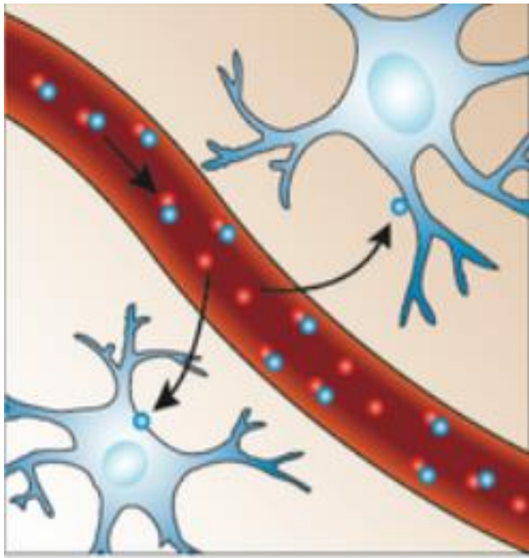
T2* ↑

MRI signal intensity ↑

Resting



Activated



Practical Setup

- Echoplanar imaging – common imaging seqn

- Subject performs a task that shifts brain activity between two or more well-defined states while in MRI Scanner

- Signal time course in each voxel of the slice stack is correlated with the known time course of different activities

- Voxel indentified which show significant changes associated with particular brain function under consideration

- Superimposition of these statistical images on high resolution anatomic images

Applications

"Clinical applications of functional MRI using neurosensorial stimulation algorithms"

Motor paradigms

Tactile paradigms

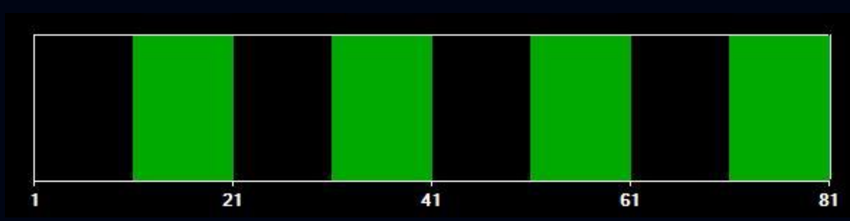
Auditory paradigms

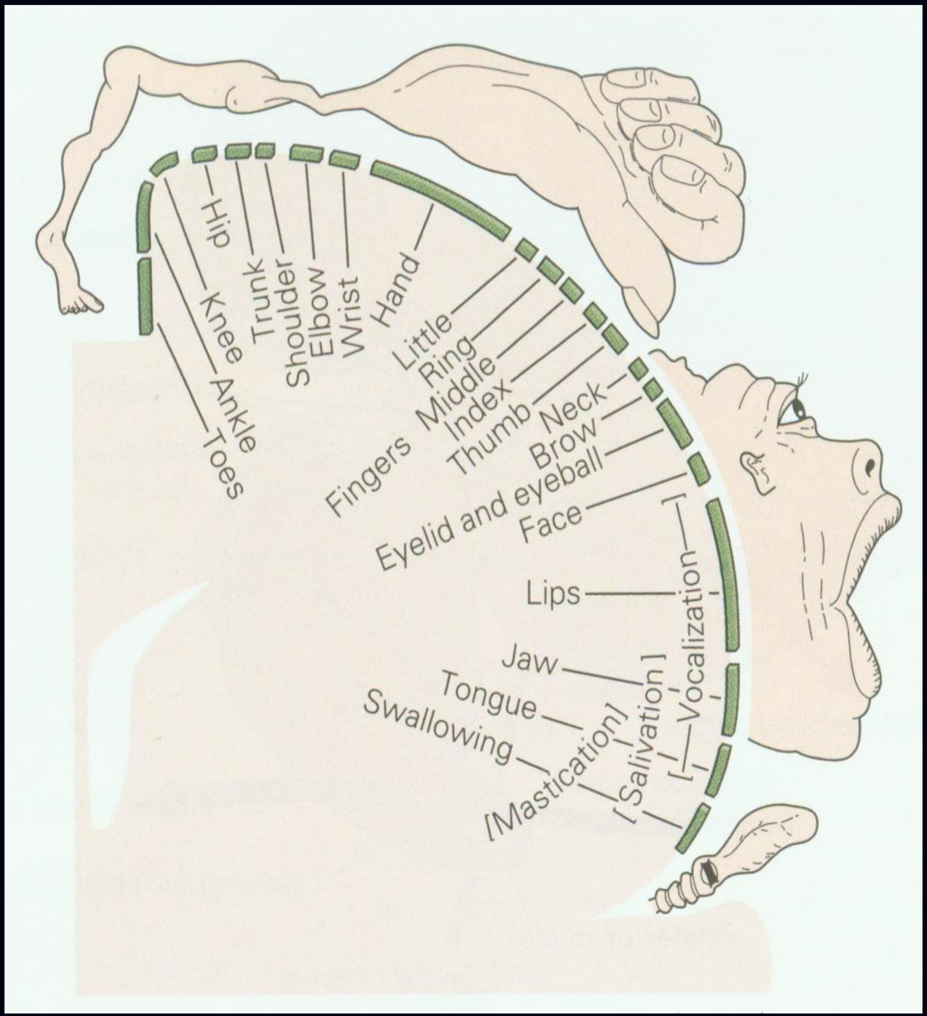
Visual paradigms

1. Motor paradigms:

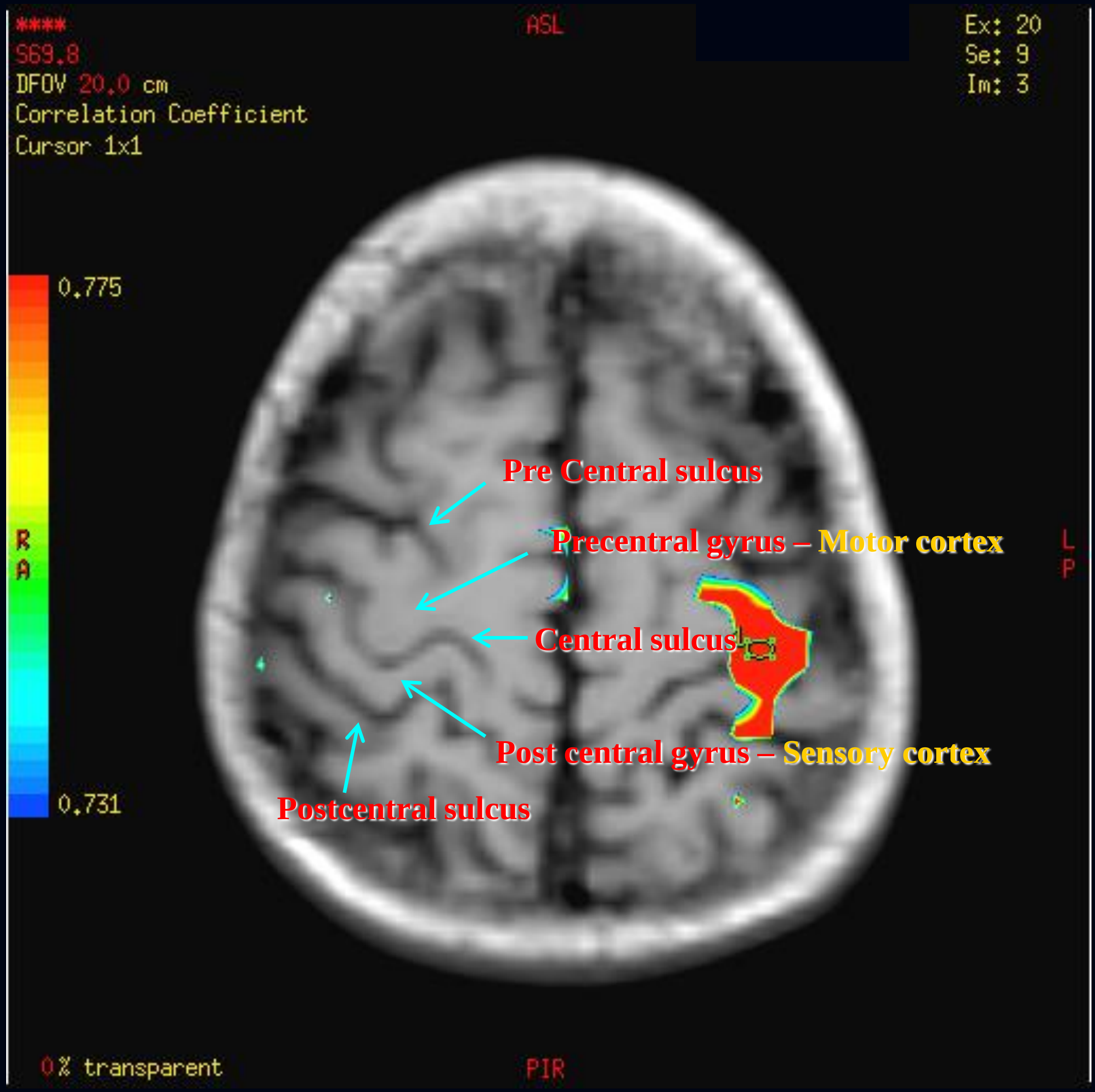
- Based on Pennfield’s homunculus
- Block design
- Externally paced at 2 Hz
- Can be replaced by imaginary motor performance

eg. Fingertapping, lip-touting,...

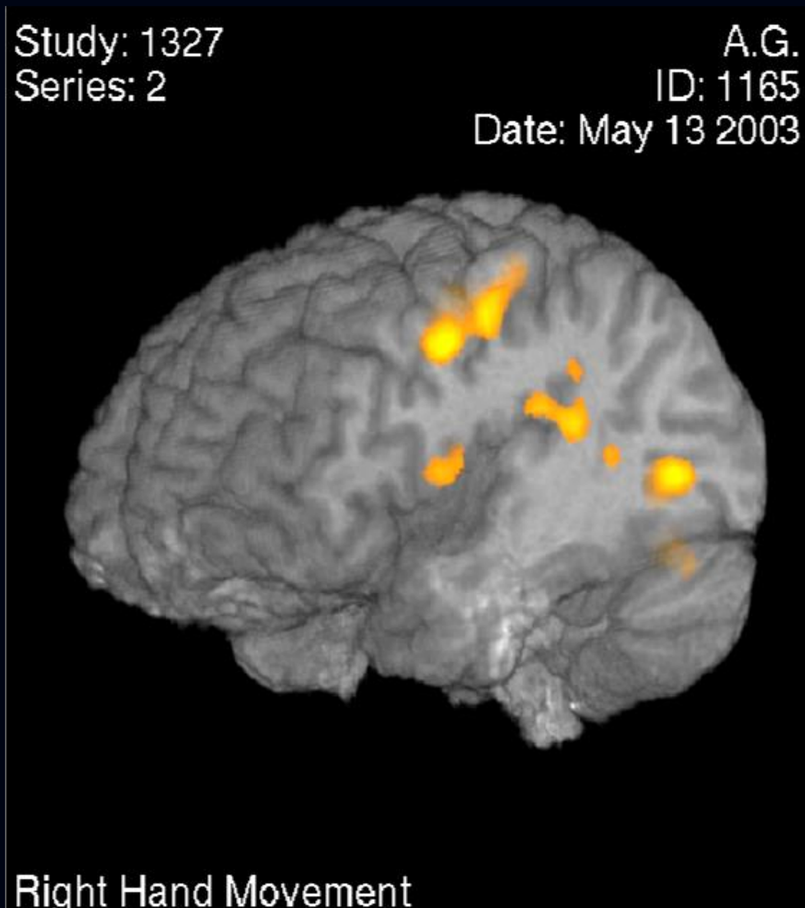


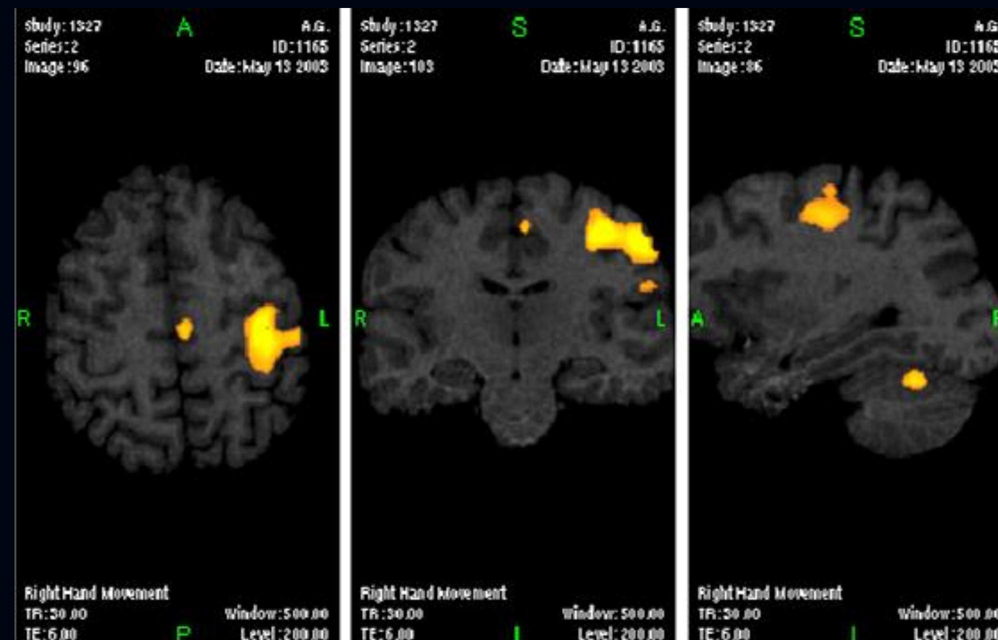


Normal anatomical location of Motor & Sensory cortex



BOLD Imaging





Potential Applications of fMRI

- Mapping the eloquent cortex pre-operatively

- Lateralization of language and memory functions in surgical treatment of epilepsy

- Differential diagnosis of neuropsychiatry disorders

ELOQUENT AREA SURGERY

RECENT ADVANCES
FACILITATING SURGERY

BETTER IMAGING

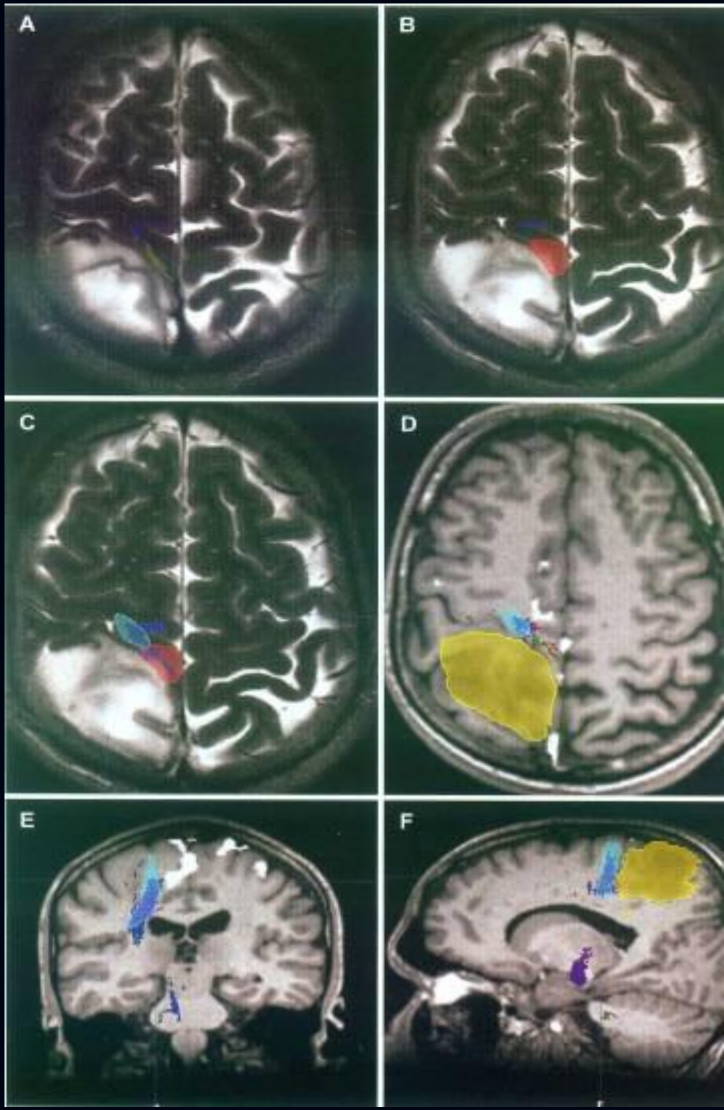
CT

MRI (DIFFUSION, PERFUSION, TENSOR)

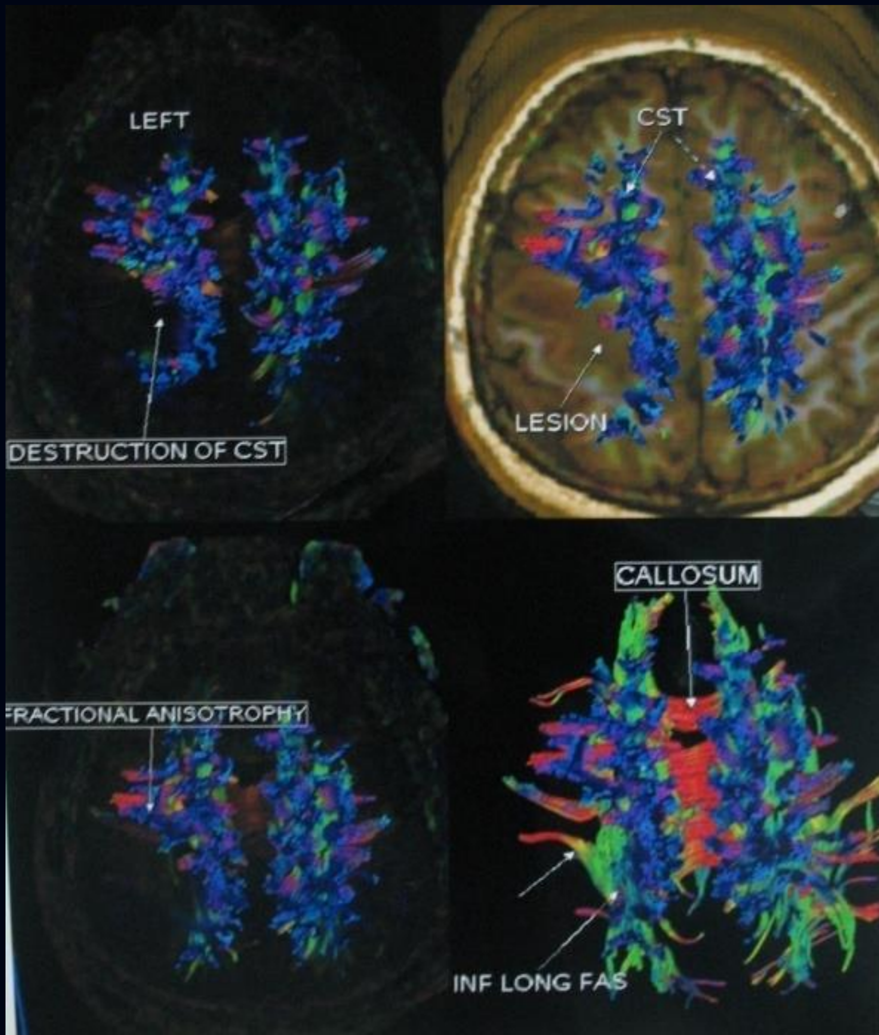
PET

SPECT

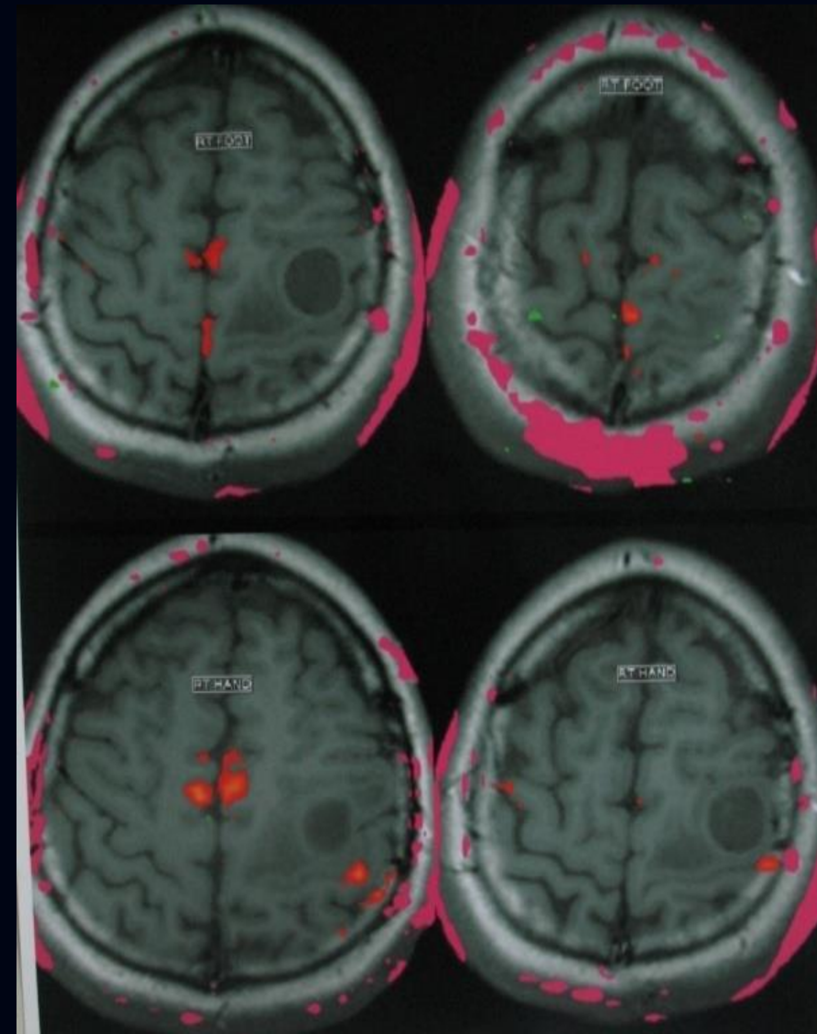
FUNCTIONAL IMAGING



DTI



Diffusion tensor imaging (DTI) with tractography showing destruction of tracts due to tumour



Functional MRI using BOLD technique in case of left frontal glioma showing its relationship with motor cortex.


THANK YOU