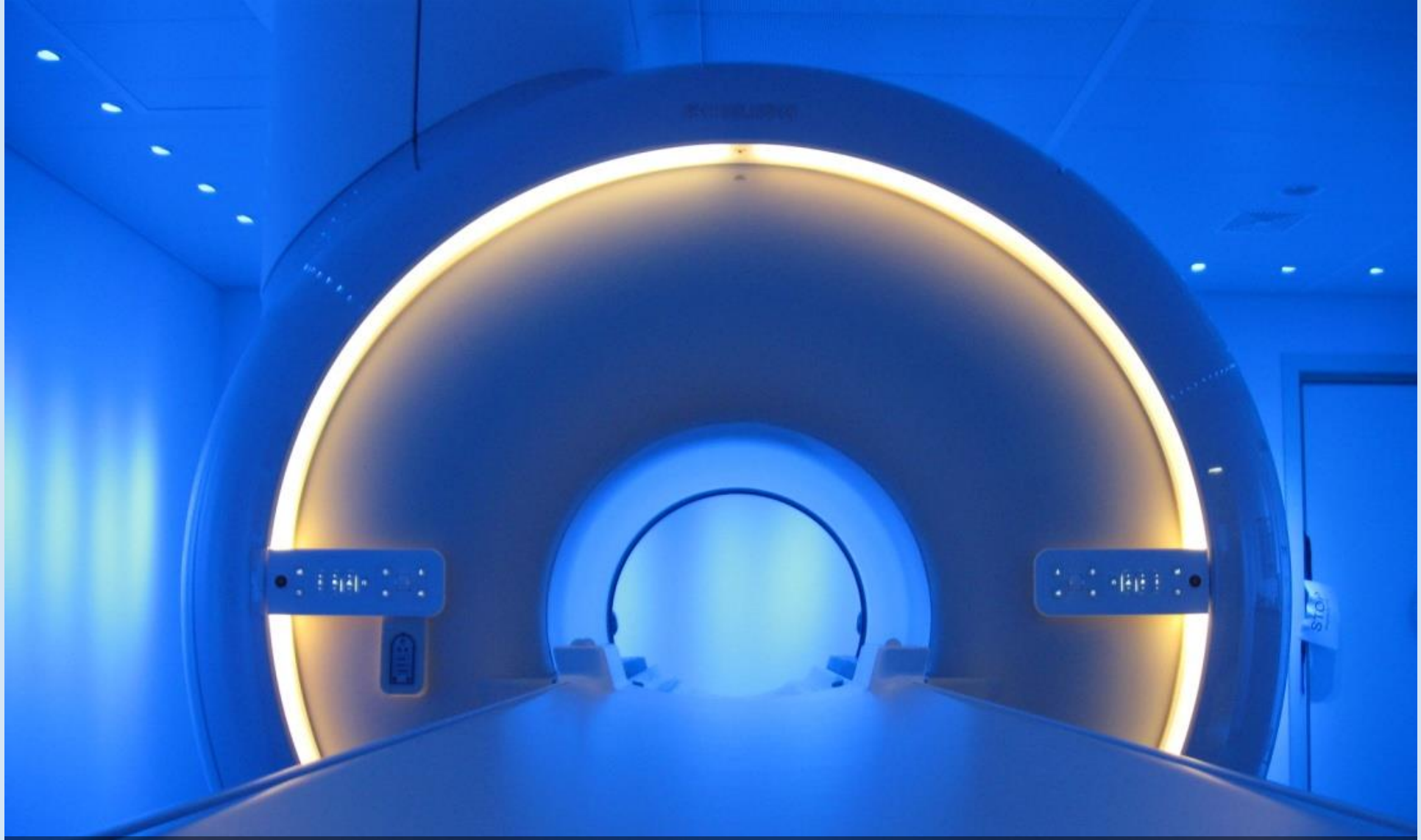


Advanced Neuroimaging Aspect of Brain Tumor

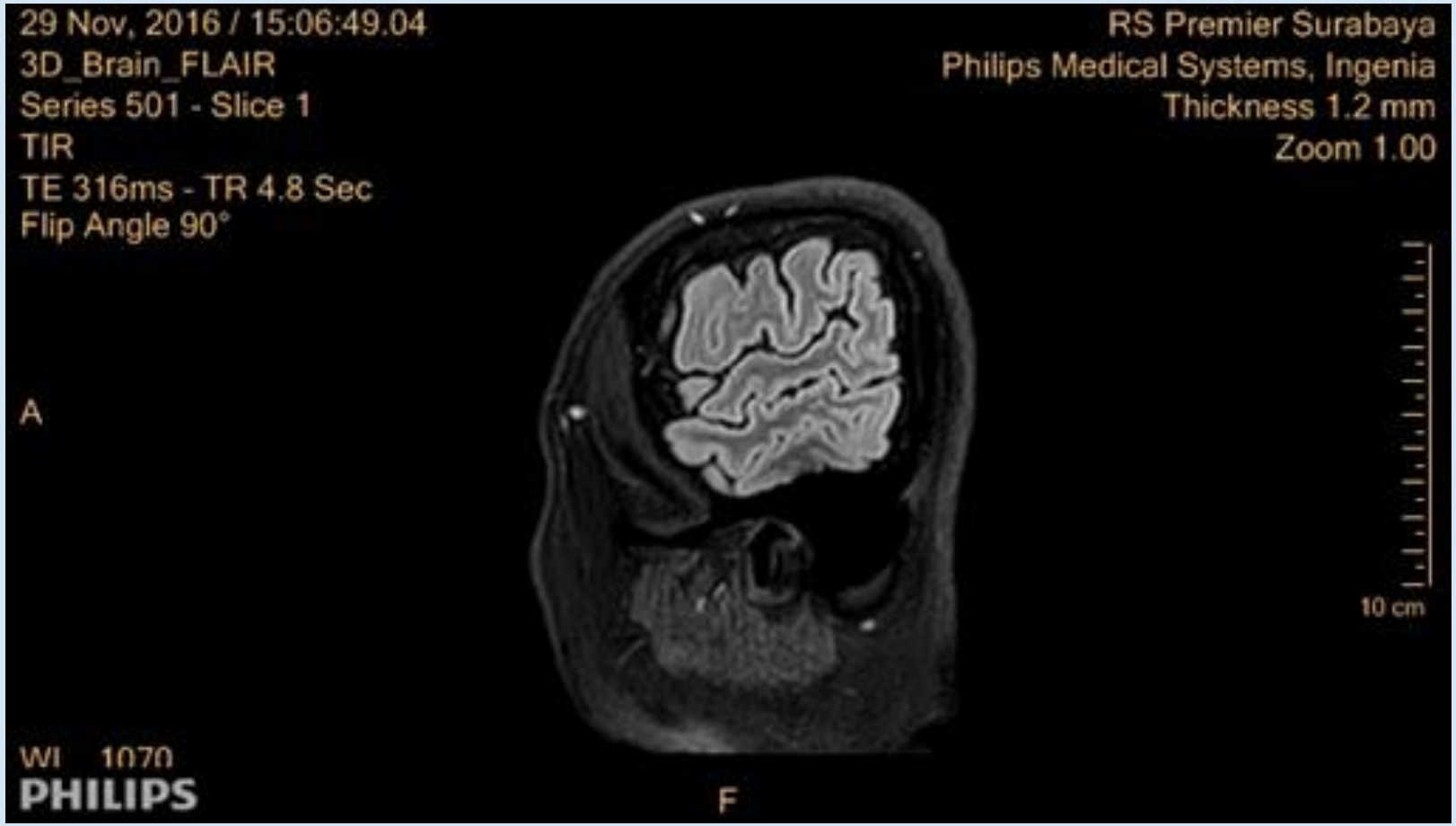
Dr. Cindy Sadikin, Sp.Rad(K)
RS Premier Surabaya

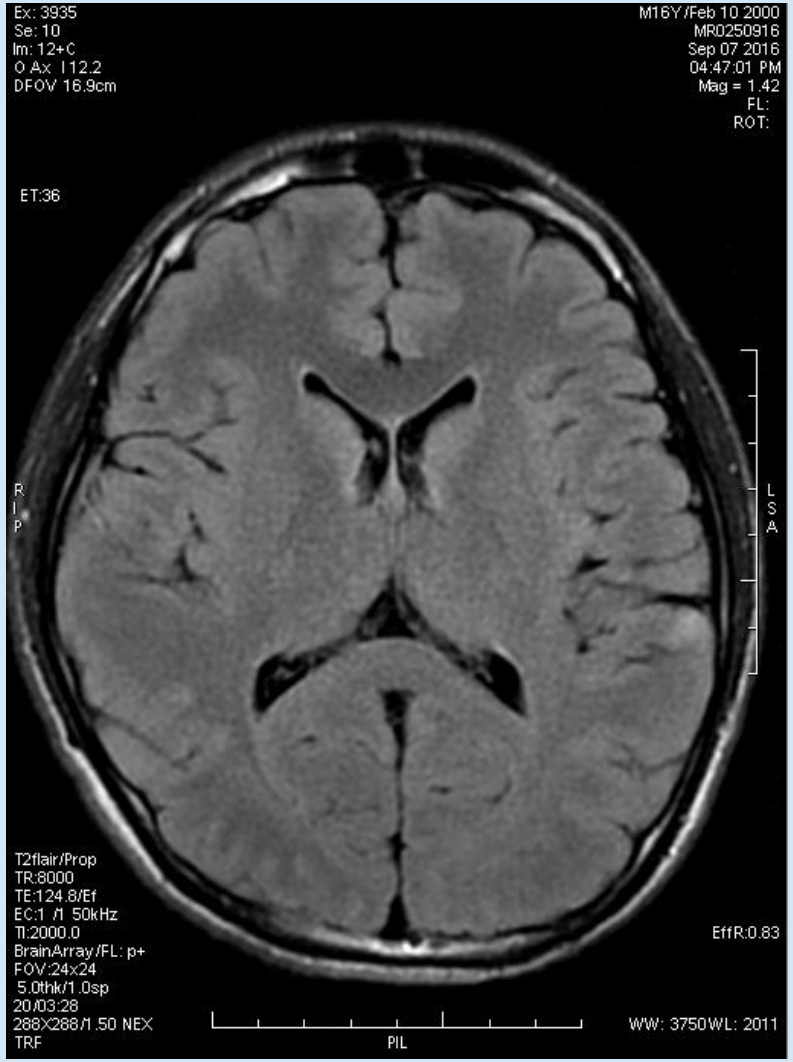
OVERVIEW

Advanced MR imaging techniques available for neurosurgical planning and their role in brain tumors assessment.

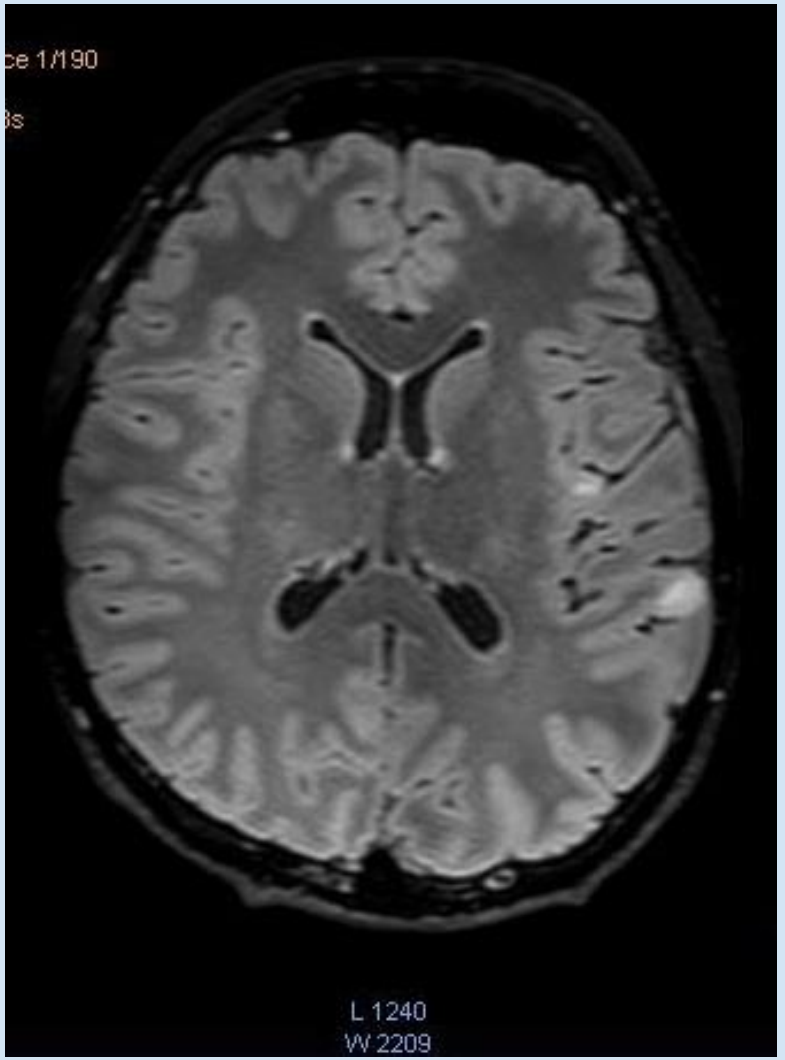
- **Functional MRI**
- **Perfusion-Weighted imaging**
- **Diffusion-Weighted imaging + Diffusion-Tensor imaging**
- **MR Spectroscopy**

32 Channel Sense Head Coil
3D VISTA FLAIR with 3T MRI





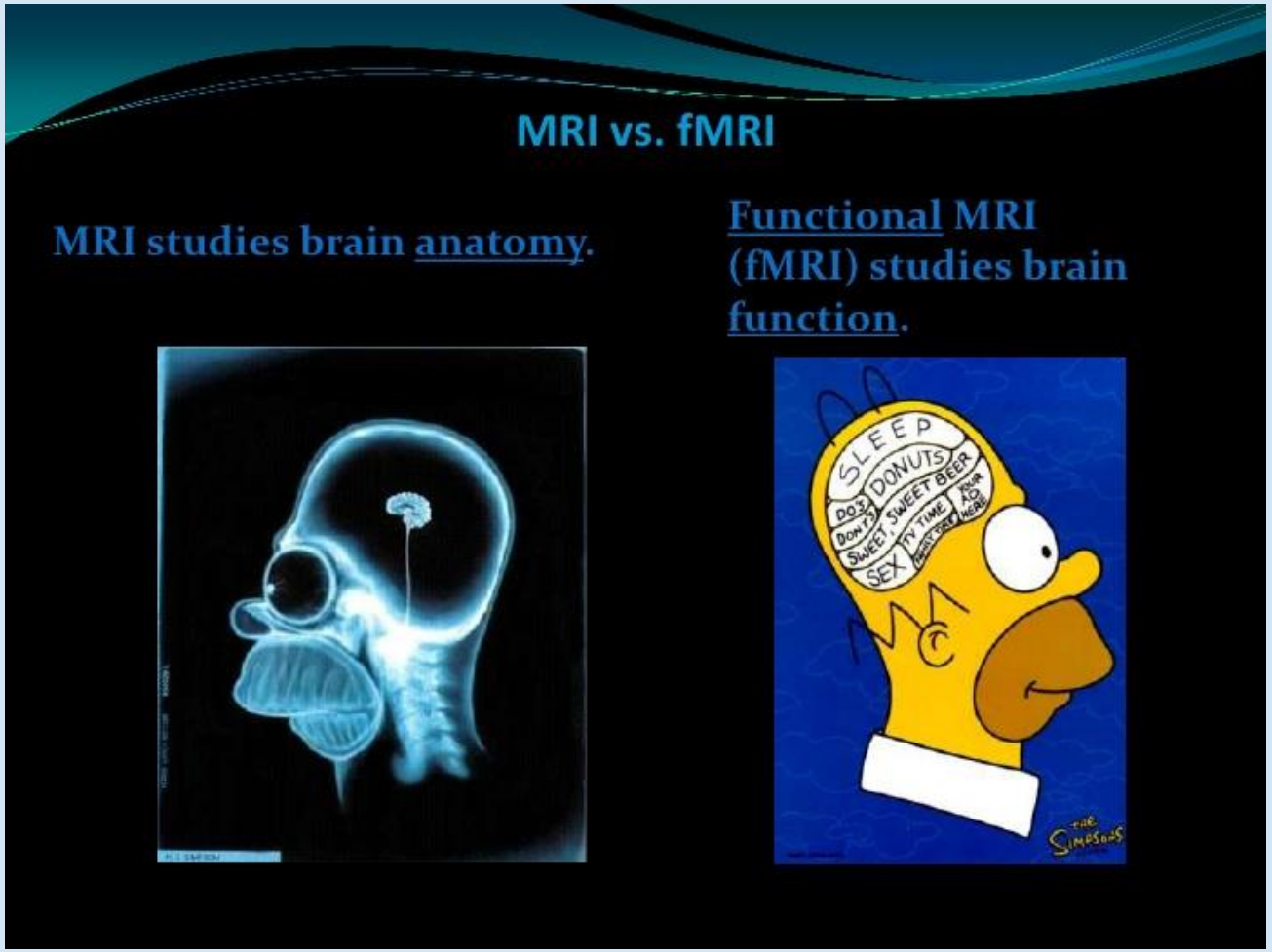
1.5T MRI



3.0 T Ingenia MRI

Functional MRI (fMRI)

Functional MRI (fMRI)



fMRI

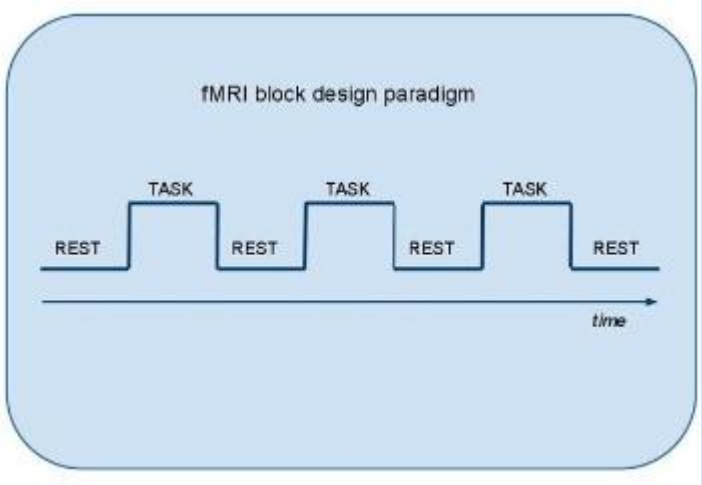
- Obtain functional information by visualising cortical activity
- fMRI detects subtle alteration in blood flow in response to stimuli or actions.
- It is used in two broad ways: clinical practice & research
- Technically challenging to perform as the techniques used to visualise cortical activity (typically **BOLD imaging**) rely on minute changes in a low **signal-to-noise ratio (SNR)** environment.

Blood oxygenation level dependent (BOLD) imaging

- A task → a specific region of the cortex increases its activity → the extraction fraction of oxygen from the local capillaries leads to an initial ↓ in oxyHb and an ↑in local CO_2 and deoxyHb.
- Following a lag of 2-6 seconds, cerebral blood flow (CBF) increases, delivering a surplus of oxyHb, washing away deoxyHb.
- It is this large rebound in local tissue oxygenation which is imaged.
- The reason fMRI is able to detect this change is due to a fundamental difference in the paramagnetic properties of oxyHb and deoxyHb.

fMRI study design

- block design
- event-related design



Block design uses repeated blocks of activity (paradigm) separated by blocks of inactivity or alternative activity. This is by far the most frequently used study design in clinical fMRI.

Event-related design involves individual events rather than blocks, and can be randomly distributed during the study.

32 Channel Sense Head Coil

Comparison with 8 channel Sense Head Coil

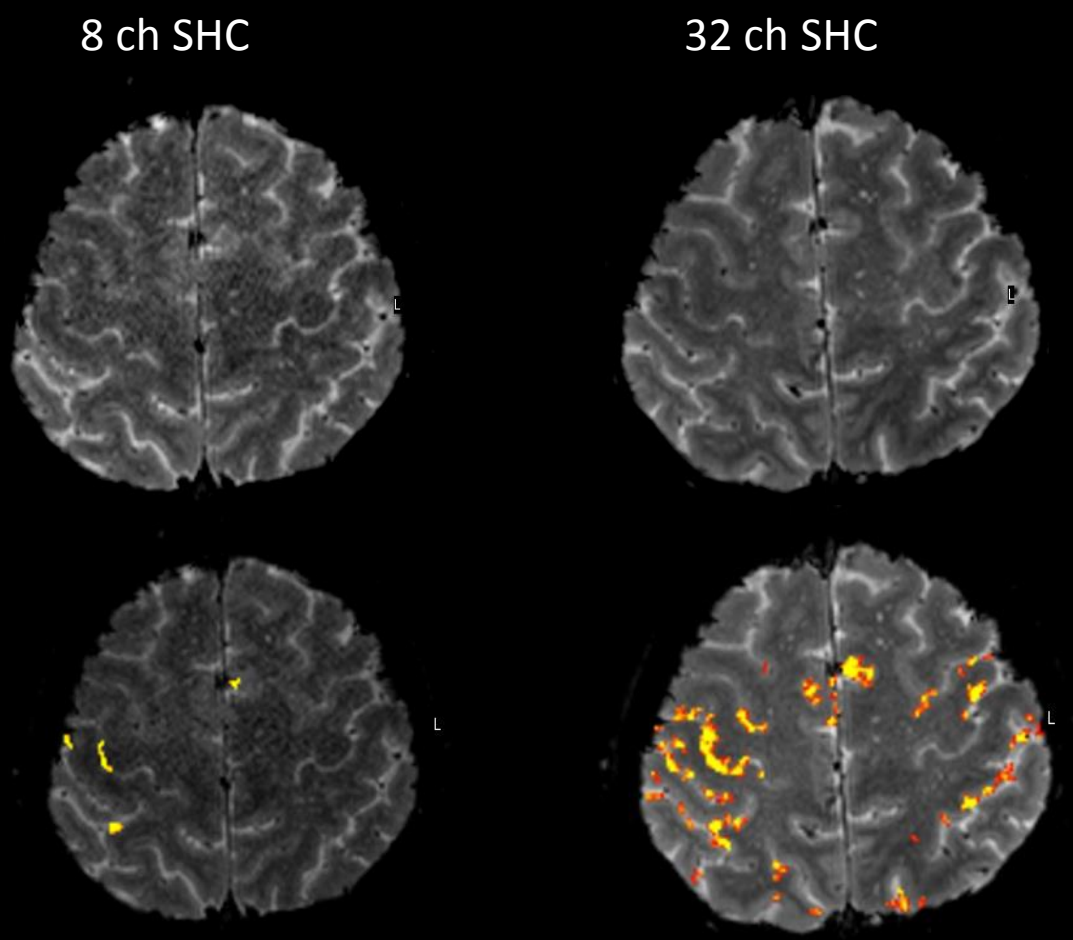
fMRI

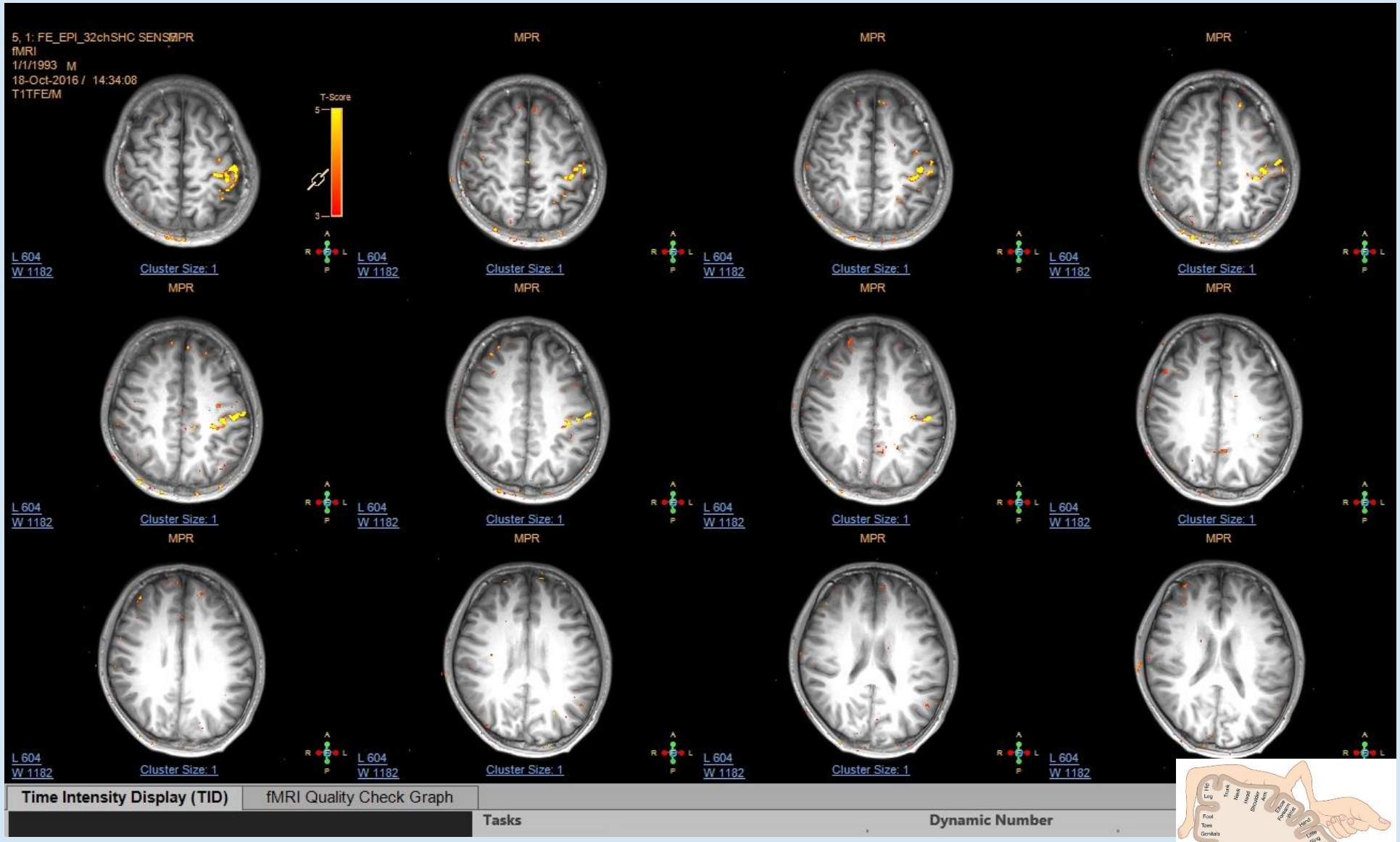
FFE EPI
TR/TE 3000/30
SENSE 3.5
1.0 x 1.0 x 2.0 mm^3

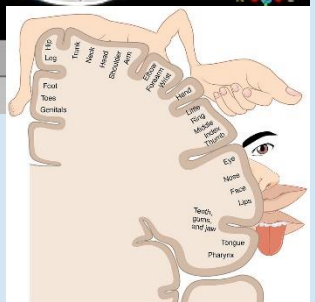
15s rest, 15s motor
4 activation blocks

Controlled for cluster size & t-test values

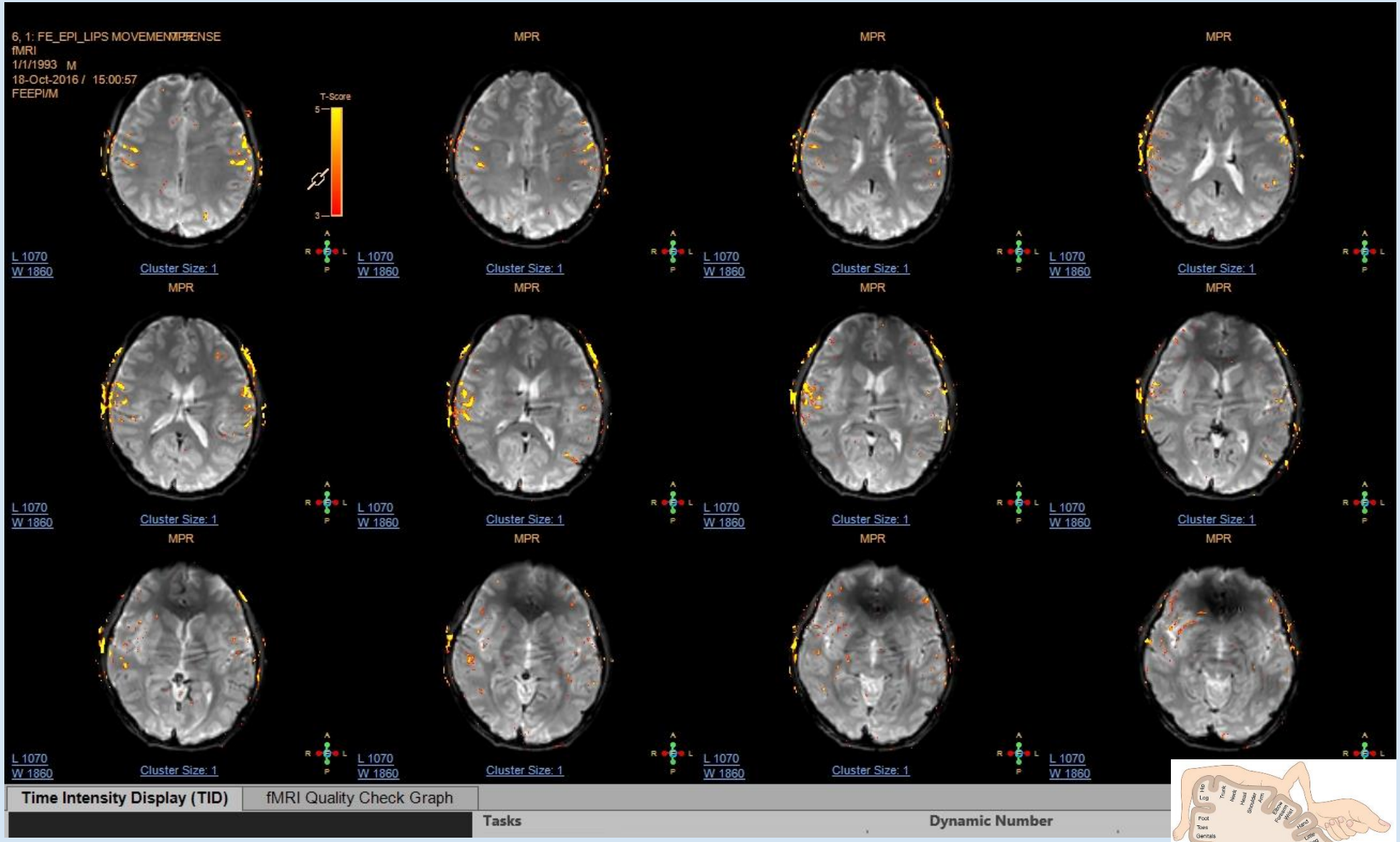
Better BOLD sensitivity

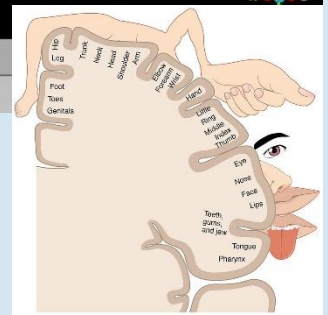






FUNCTIONAL MRI – RIGHT HAND MOVEMENT





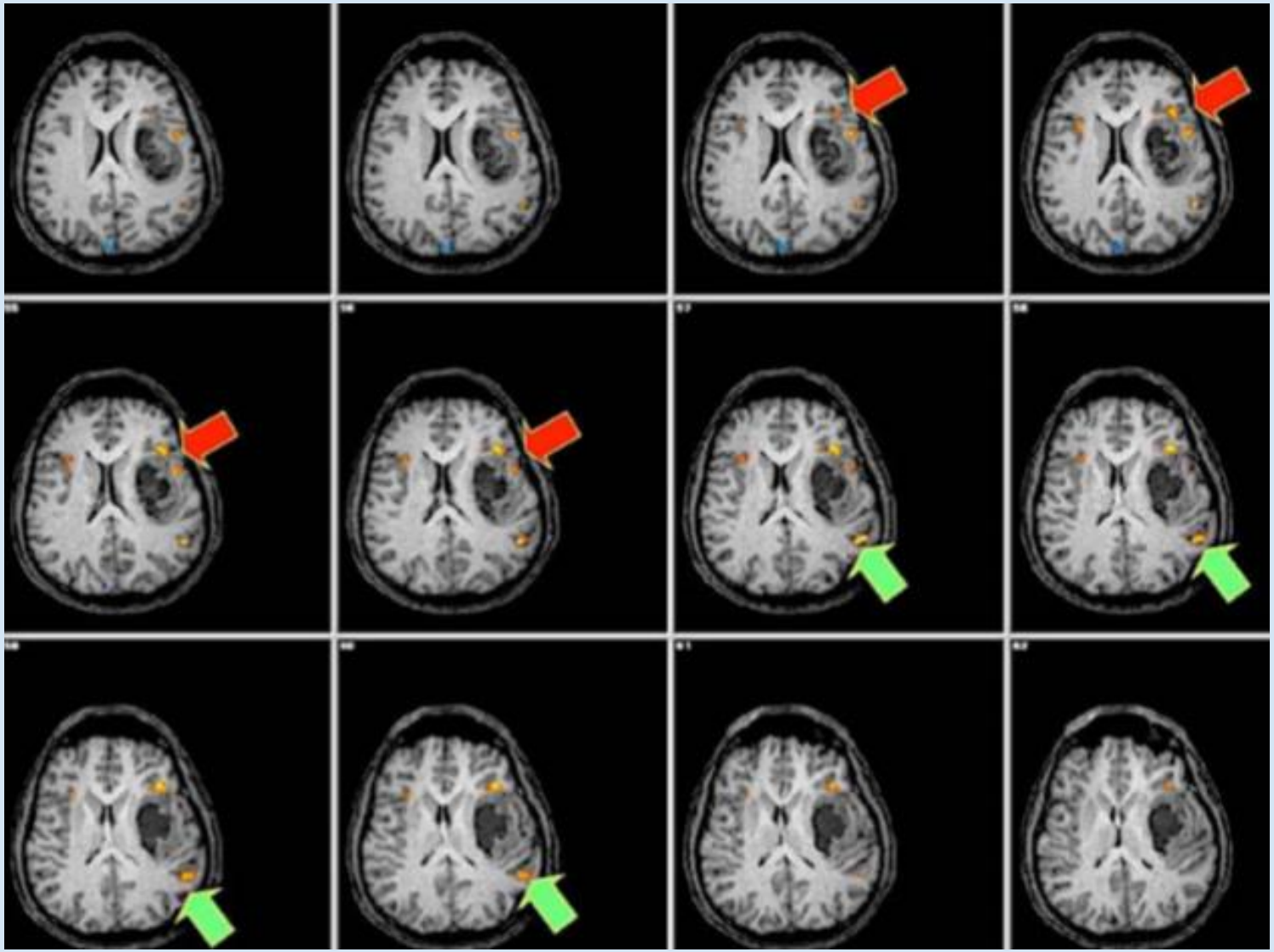
FUNCTIONAL MRI – LIPS MOVEMENT

fMRI in Brain Tumors

Main goals of presurgical functional MRI:

- determine the risk for eventual neurological deficits, by identifying the distance between the margin of planned tumour resection and the eloquent/essential functional areas → 10mm or more (lower risk) Håberg et al. Preoperative blood oxygen level-dependent func- tional magnetic resonance imaging in patients with primary brain tumors: Clinical application and outcome. Neurosurgery, 54, 2004

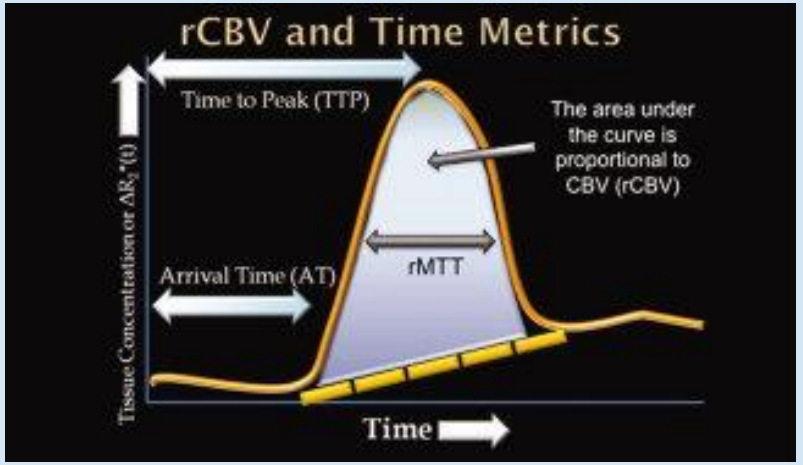
Patient cooperation is essential and pre-fMRI training is very important.



High grade glioma involving left frontal and temporal lobe

Perfusion Weighted Imaging (PWI)

Perfusion Weighted Imaging

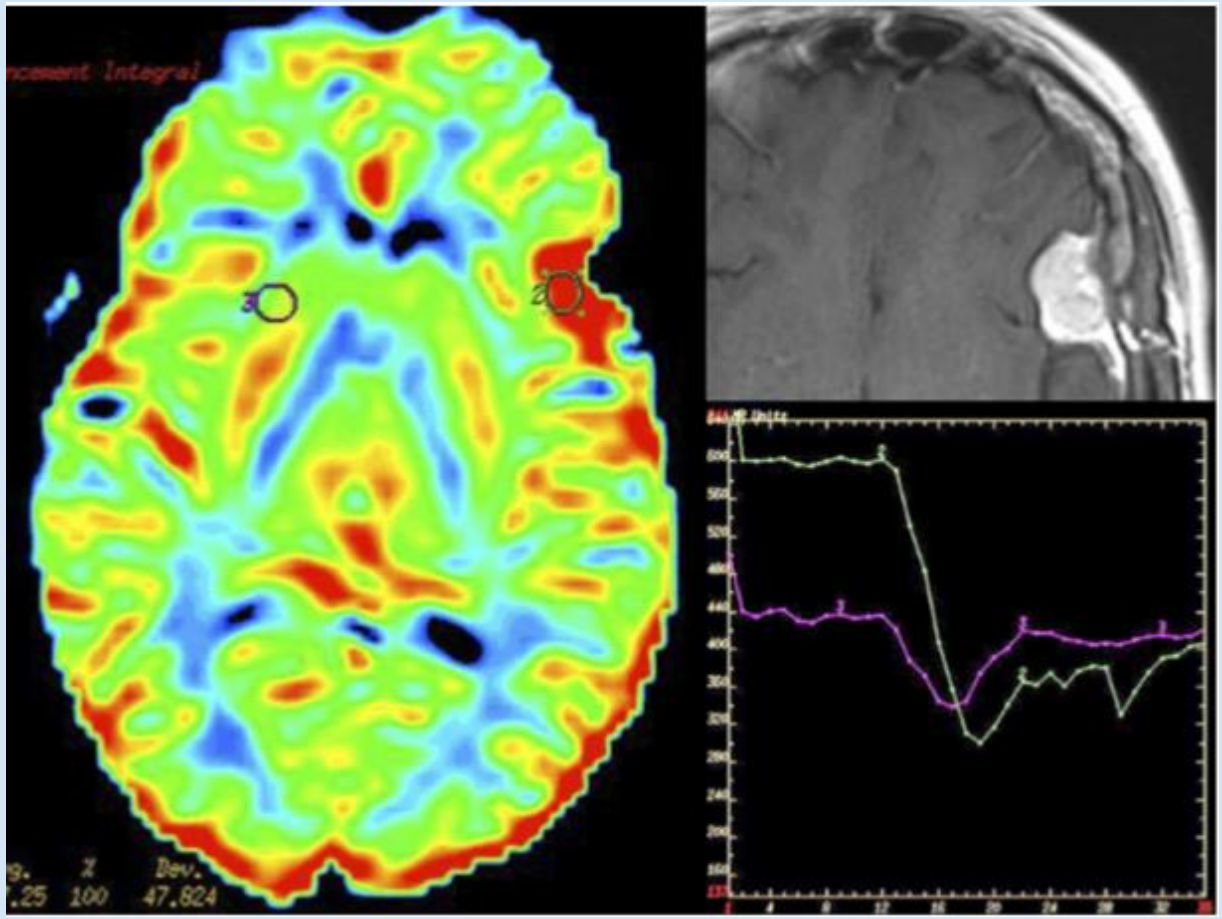


- PWI provides hemodynamic status of the brain tissue
- Techniques: Arterial spin labelling (ASL), **Dynamic susceptibility contrast (DSC)**, Dynamic Contrast Enhancement (DCE)
- Parameters:
  - Mean Transit Time (MTT): average time spent by blood in cerebral vascular bed
  - Time To Peak (TTP): time from the start of bolus injection to the maximum signal intenisity
  - relative Cerebral Blood Flow (rCBF): volume of blood passing through a given amount of brain tissue per unit of time
  - **relative Cerebral Blood Volume (rCBV)** → represents tumour angiogenesis.

PWI in Brain Tumor

- PWI allows better estimates of biological activity and aggressiveness in brain tumours
- Strong positive correlation between tumour rCBV and astrocytoma grading.
- Higher rCBV ratios were present in both solid portions and peri-tumoural regions of anaplastic gliomas, but not in low grade gliomas
- PWI should be integrated in the diagnostic work-up of non-enhancing gliomas in order to predict grading

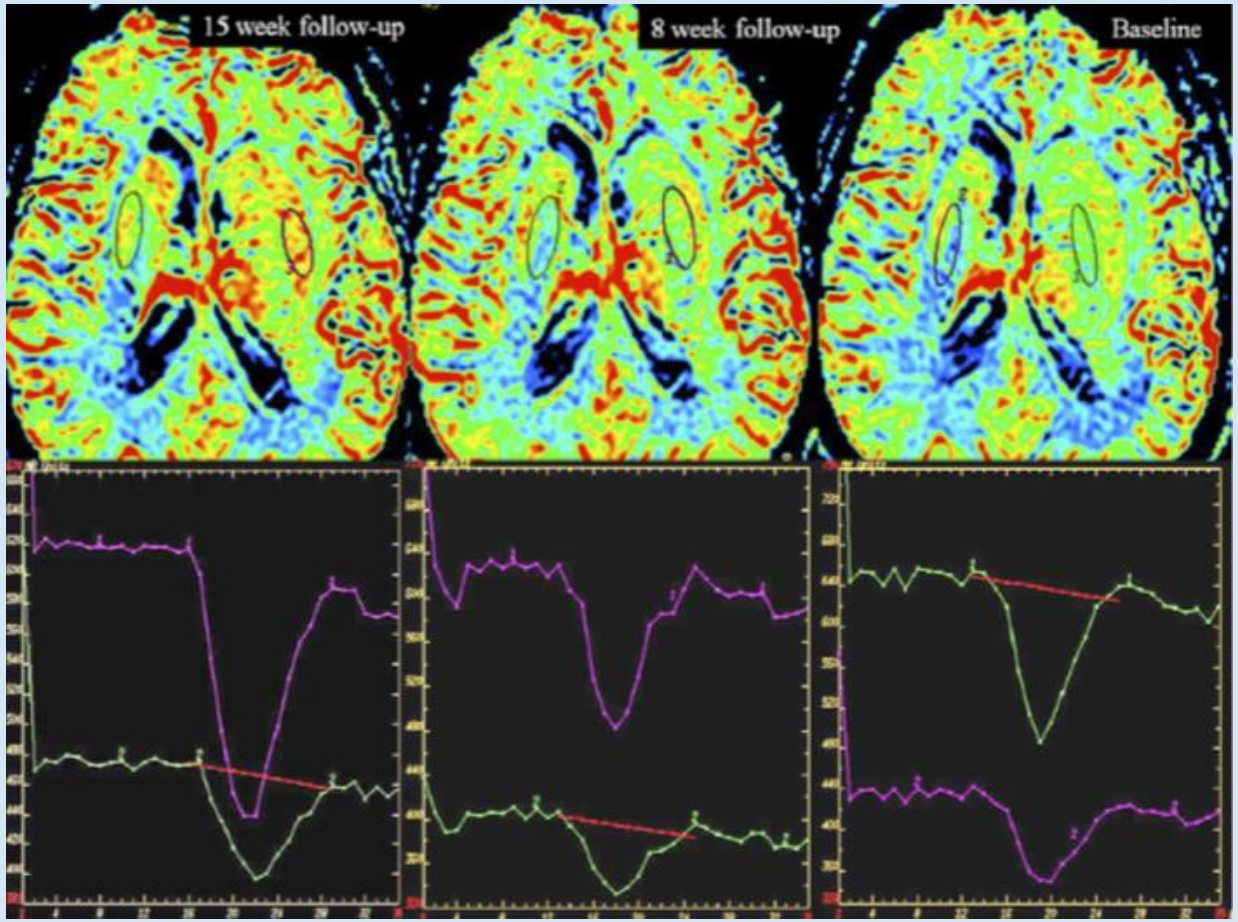
PWI in Extra axial Mass



Tumors of extra axial and non glial origin do not form a BBB, so very large fraction of bolus leaks into extravascular space during first pass

Glioma microvessels form a BBB that is impaired but not absent, the TIC curve returns significantly toward baseline although not as much as normal brain

PWI in High Grade Glioma

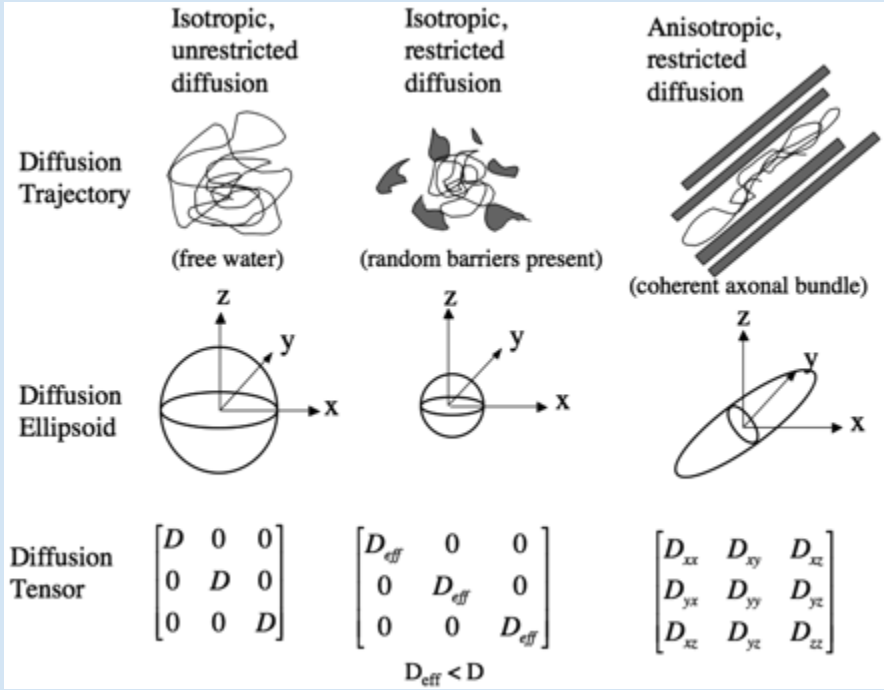


Serial FU from rCBV maps and TIC of left subinsular recurrent WHO grade III to IV Glioma.

Alhough conventional MRI shows no significant changes, the ROI data shows definite new hypervascularity 2.5-3 times contralateral basal ganglia → progressive recurrence

DWI and DTI

DWI and DTI



Diffusion or Brownian movement, denotes the random motion of molecules.

Displacement of water molecules → 3 different types:

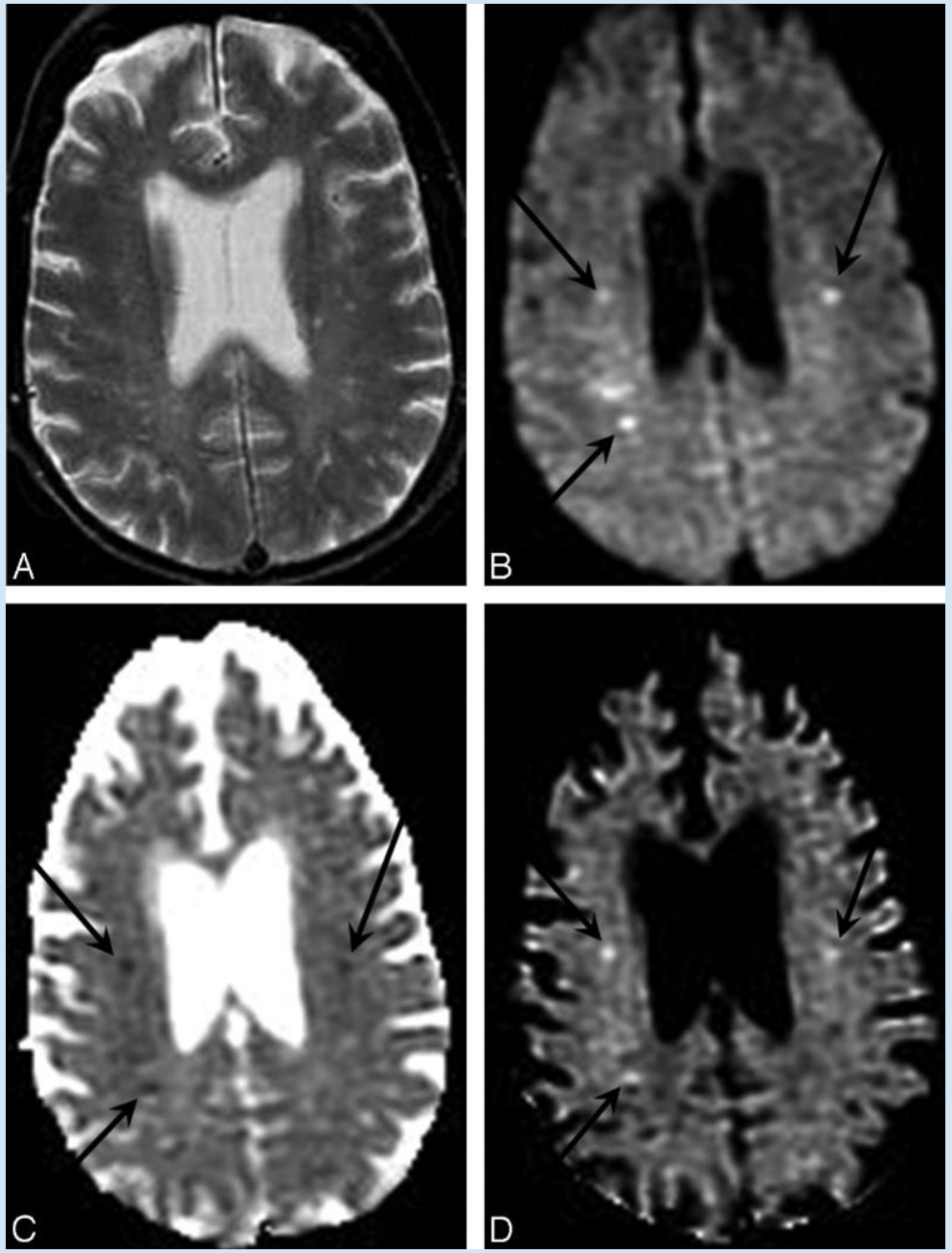
- **Free diffusion**: displace freely in all spatial directions, ex: CSF
- **Restricted isotropic diffusion**: displacement is restricted, in whatever spatial direction, by numerous obstacles (proteins, cells), ex: abscess, tumor
- **Restricted anisoptropic diffusion**: certain structured tissues create obstacles that orientate the motion of the water molecules (tendency to displace themselves in one or several particular directions). Ex: nerve fibers

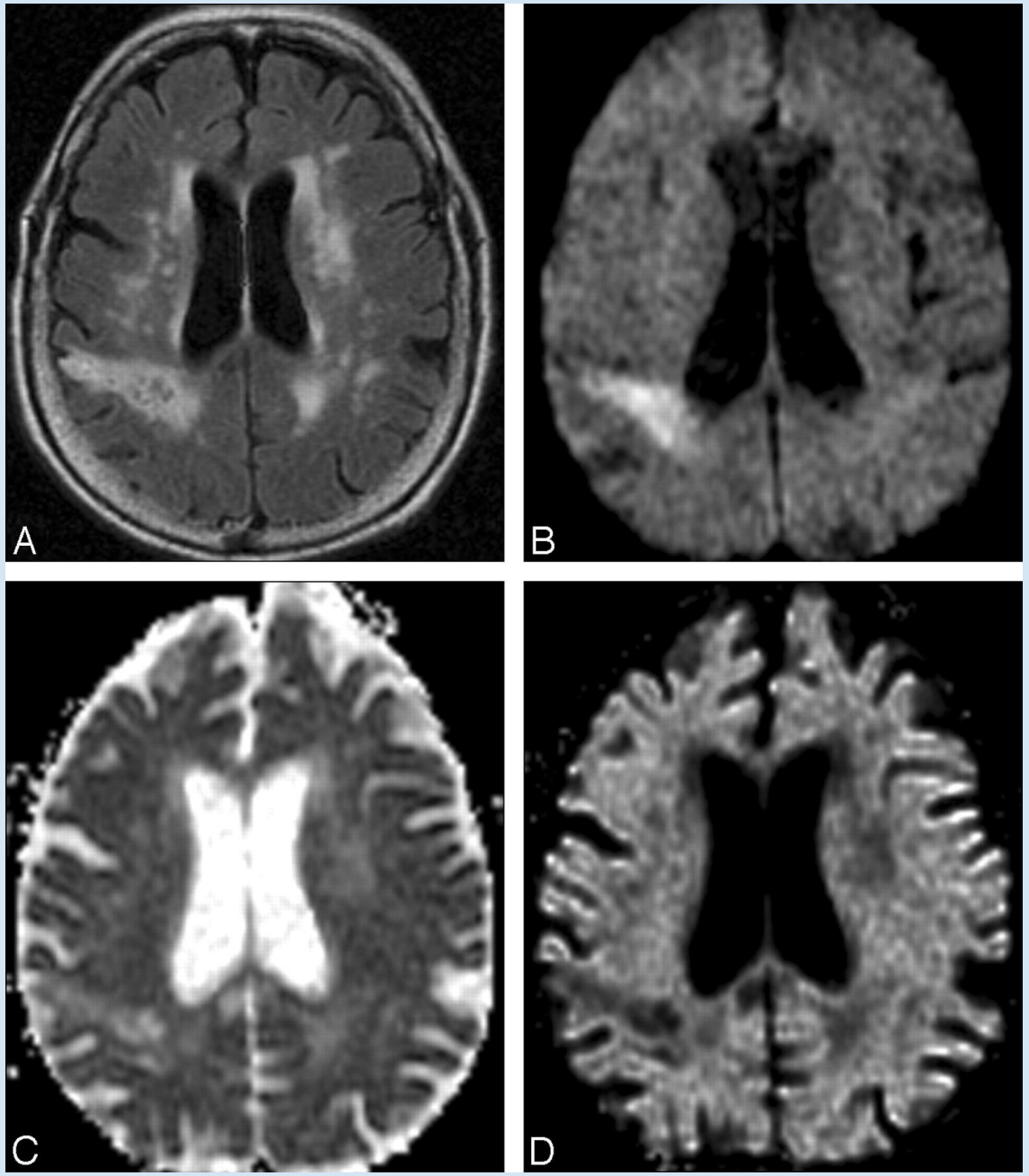
Diffusion measurements parameter

- **Apparent diffusion coefficient (ADC):** measure the magnitude of molecular motion
- **Fractional anisotropy (FA):** measure the directionality of the molecular motion of water
- Relative anisotropy (RA), or the ratio between anisotropic and isotropic portions of the diffusion tensor
- Volume ratio (VR): expresses the relationship between the diffusion ellipsoid volume and that of a sphere, the radius of which is the averaged diffusivity

DWI and ADC

- Mean diffusivities in adult brain: 0.67–0.83 × 10^{-3} mm^2/s for gray matter and 0.64–0.71 × 10^{-3} mm^2/s for white matter
- Most types of pathology in the human brain cause increases of ADC values
- **Reduced ADC** in the human brain are less numerous → specific diagnosis. The most common ones are **acute cerebral ischemia** and other causes of cytotoxic edema, such as status epilepticus and hypoglycemia.
- Why reduced ADC: energetic failure leads to membrane permeability changes, resulting in cellular swelling, decreased volume and increased tortuosity of the extracellular (controversial)


A
B
C
D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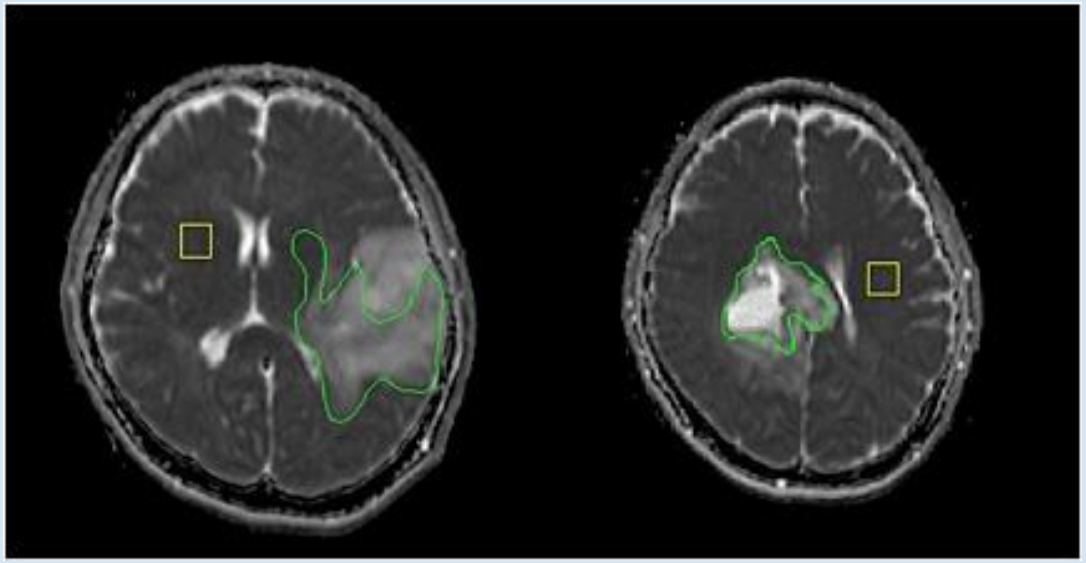
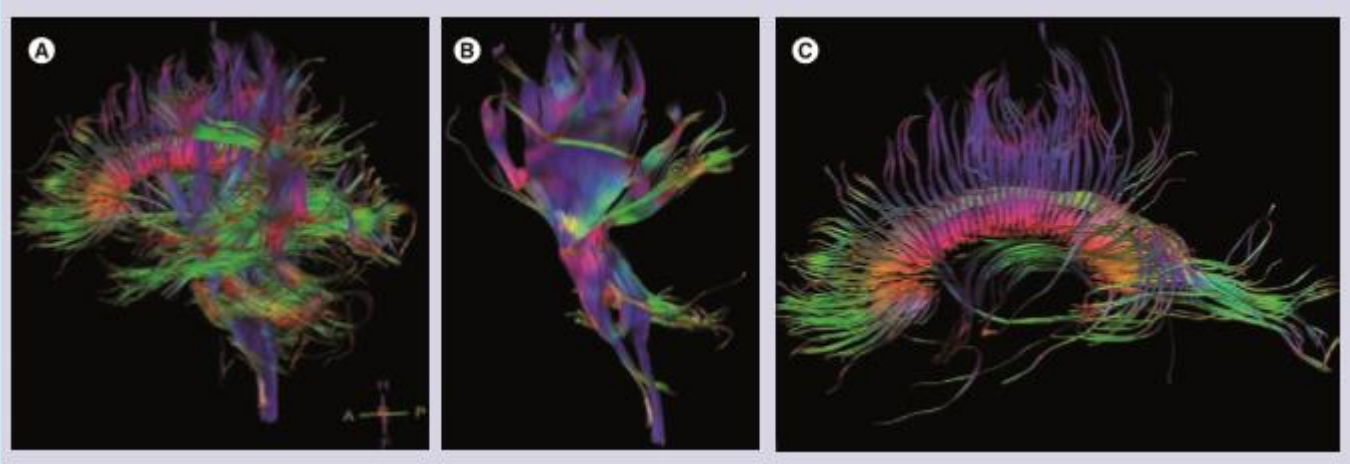
DWI and ADC in Brain Tumor



- Low-grade gliomas tend to have a higher ADC compared with high-grade lesions
- ADC value → inversely related to tumour cellularity and grading
- Characterize highly cellular versus low cellular components

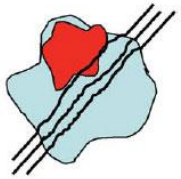
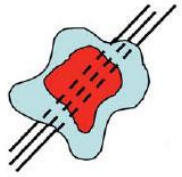
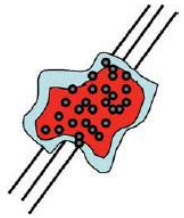
DTI in Brain Tumor

- Tractography allowed visualization of **white matter tracts** by means of diffusion anisotropy maps
- Tractography potentially solves a problem in neurosurgical planning → minimizing functional damage and determining the extent of diffuse infiltration of pathologic tissue to minimize residual tumor volume.



DTI White matter tracts in Brain Tumor

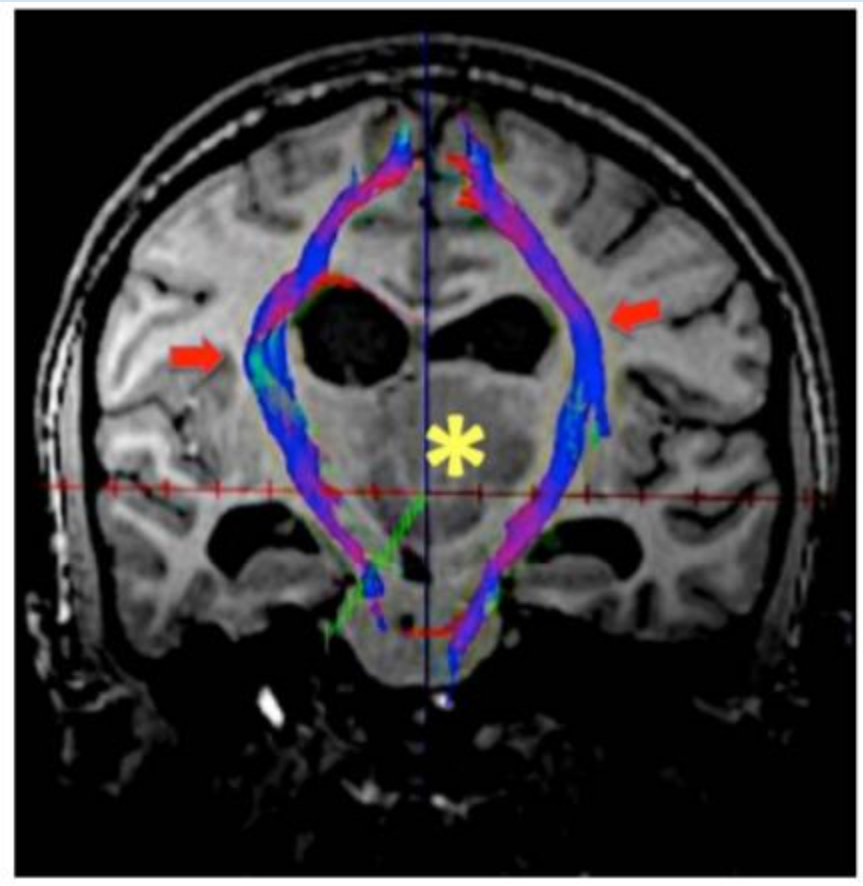
Table 1 DTI patterns seen in patients with brain tumors.

DTI patterns	FA	Location / orientation (FA color coded maps)	Illustration	Diagnosis
Displaced	Normal / slightly decreased	Abnormal (intact tracts)		• Low grade gliomas • Anaplastic astrocytomas • Glioblastoma multiforme • Metastasis
Edematous	Decreased	Normal		• Metastasis
Infiltrated	Decreased	Fiber tracts remain identifiable		• Anaplastic astrocytomas • Glioblastoma multiforme
Disrupted	Markedly decreased (isotropic or near isotropic diffusion)	Non-identifiable fiber tracts		• Anaplastic astrocytomas • Glioblastoma multiforme

DTI, diffusion tensor imaging; FA, fractional anisotropy. (Adapted from Jellison et al.[10]).

- **Displaced:** normal anisotropy relative to corresponding contralateral tract but are locate in an abnormal location
- **Edematous**: reduced anisotropy, normal orientation, ↑intensity on T2
- **Infiltrated:** reduced anisotropy yet remain visible on the orientation maps
- **Disrupted:** marked reduced anisotropy (near isotropic), no identifiable tracts on the orientation maps

DTI Clinical in Brain Tumor



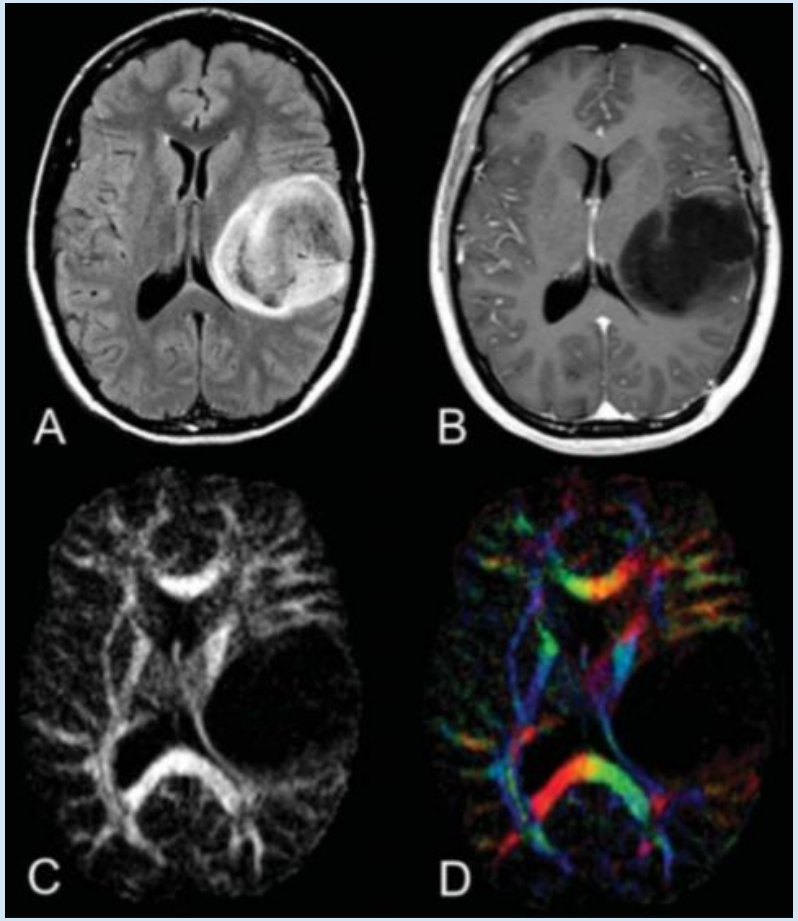
In presurgical sensory-motor planning:

- **cortico- spinal tract (M1)**
- **thalamo-cortical tracts (S1)**

In language mapping:

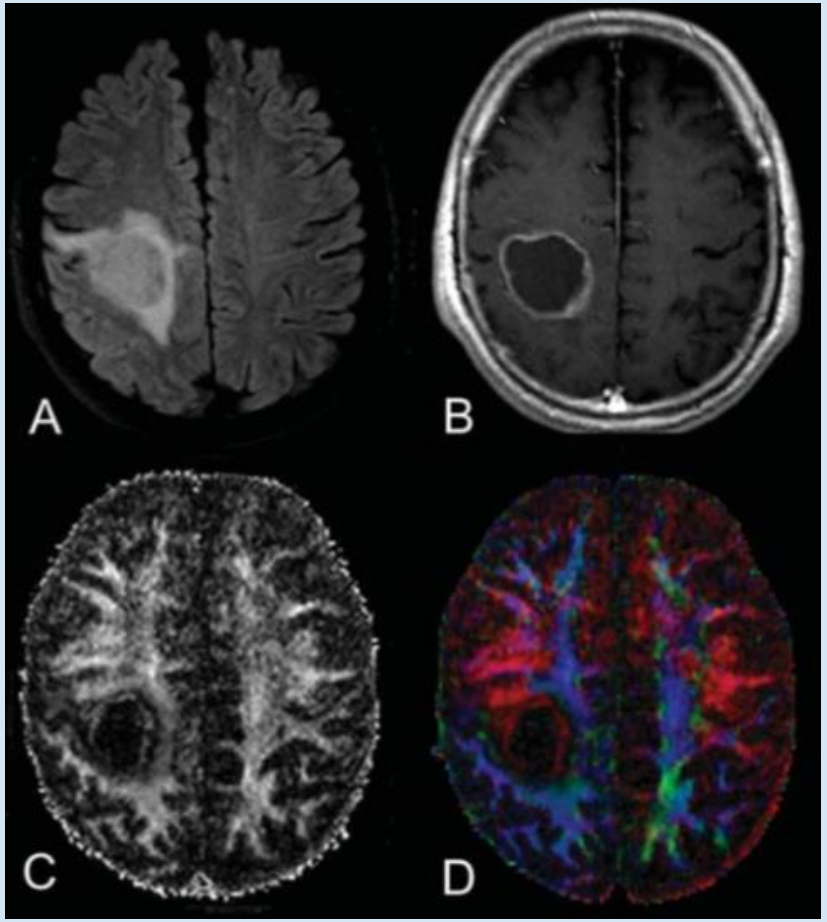
- **superior longitudinal fasciculus (SLF)**
- **arcuate fasciculus (AF)**
- **inferior fronto- occipital fasciculus (IFOF)**

LGG



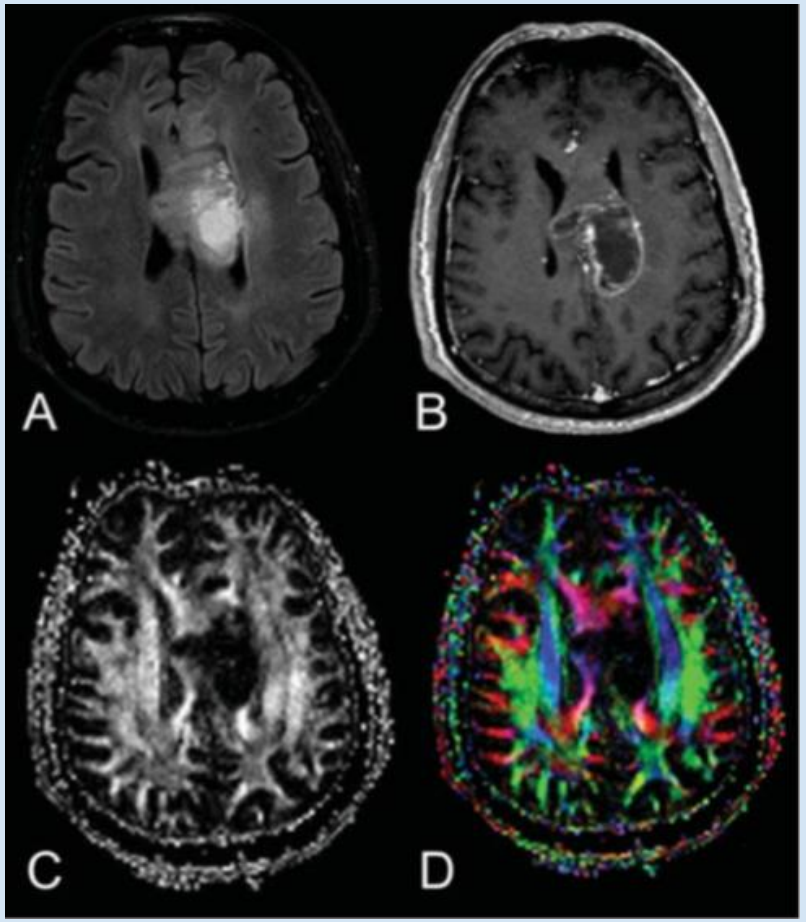
FA & color map: posterior limb of internal capsule medially displaced.

Lung Mets

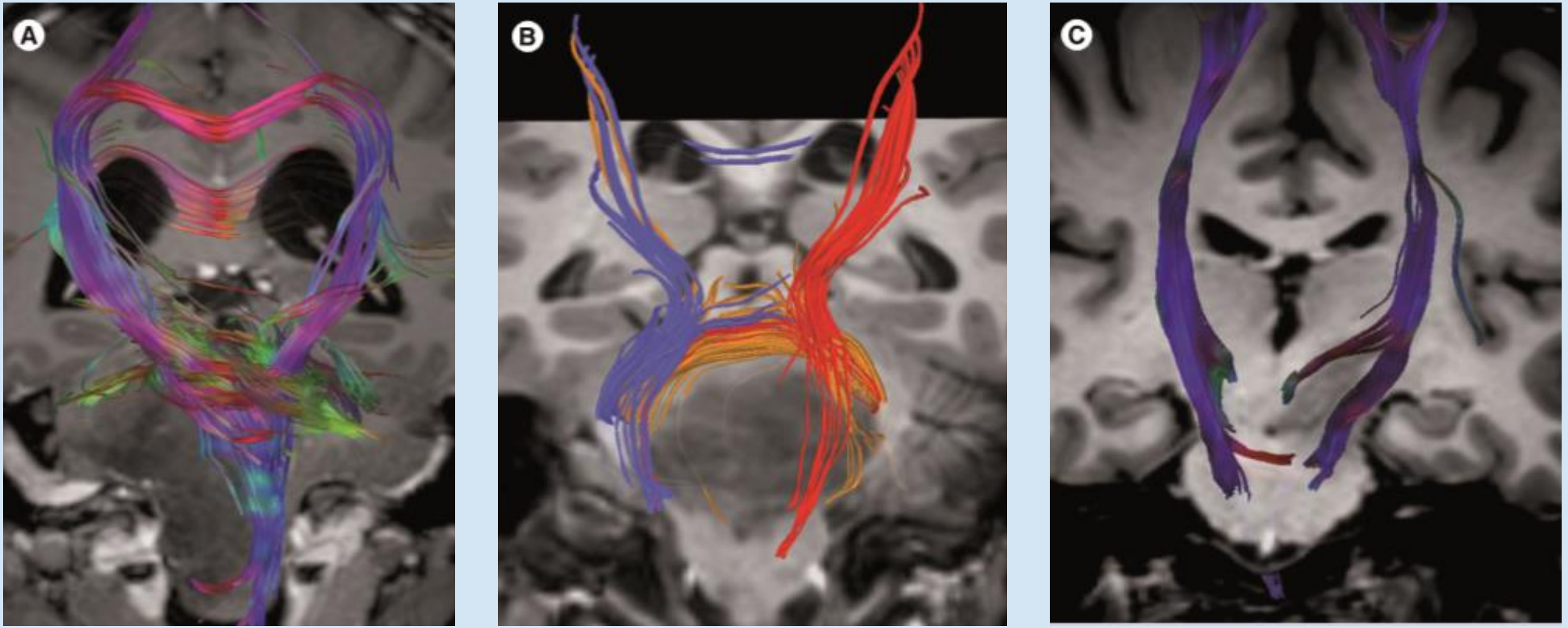


Decreased anisotropy in the white matter surrounding the tumor with edematous pattern & medial deviation of the corona radiata

Anaplastic Astro



Significant reduction + disrupted patern CC fibers with displaced left corona radiate
White matter tract infiltrated pattern


A
B
C

MR Spectroscopy

MR Spectroscopy (MRS)

- MRS displays brain metabolites in the form of spectra whose shape basically depends on metabolite concentration → used to measure chemical markers of neoplastic activity
- Single-voxel spectroscopy (SVS), multi-voxel 2D and 3D chemical shift imaging (2D and 3D CSI)
- Principal metabolites that can be analyzed: branch amino acids (0.9-1.0 ppm), lipid (0.9-1.5 ppm), lactate (1.3 ppm), alanine (1.5 ppm), n-acetyl aspartate (NAA, 2.0 ppm), choline (3.2 ppm), creatine (3.0 and 3.39 ppm) and myoinositol (3.6 ppm)

MRS

N Acetyl Aspartate: marker of neuronal number and function

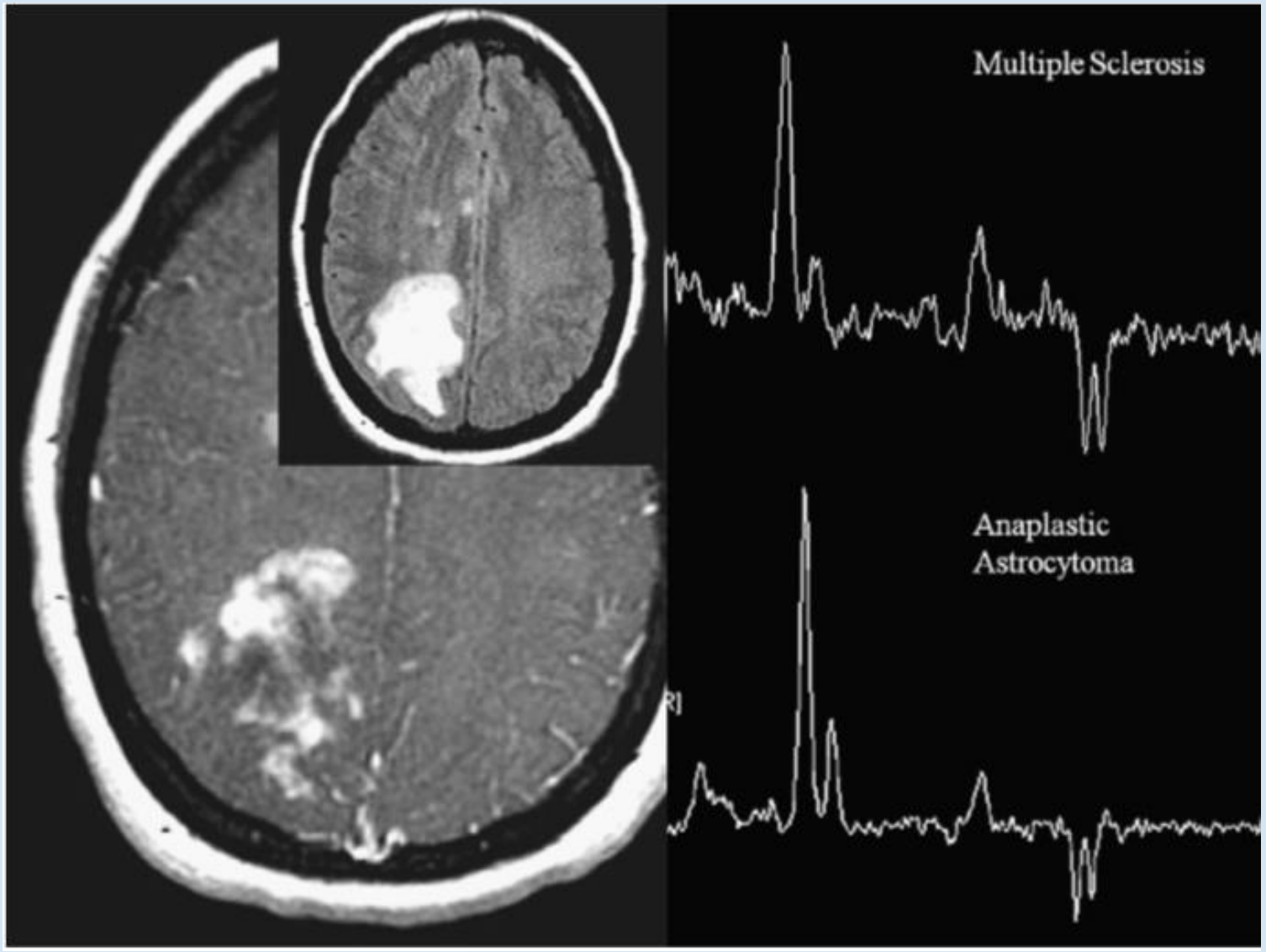
Creatine: marker of energy metabolism and store

Choline: marker of membrane synthesis and degradation (membrane turnover)

- Injury neurons ↓ NAA
- Injury glia or stimulate glial division ↑ Cho
- Disrupt aerobic glycolysis ↑ lactate
- Produce necrosis ↑ lipid and ↓ creatine

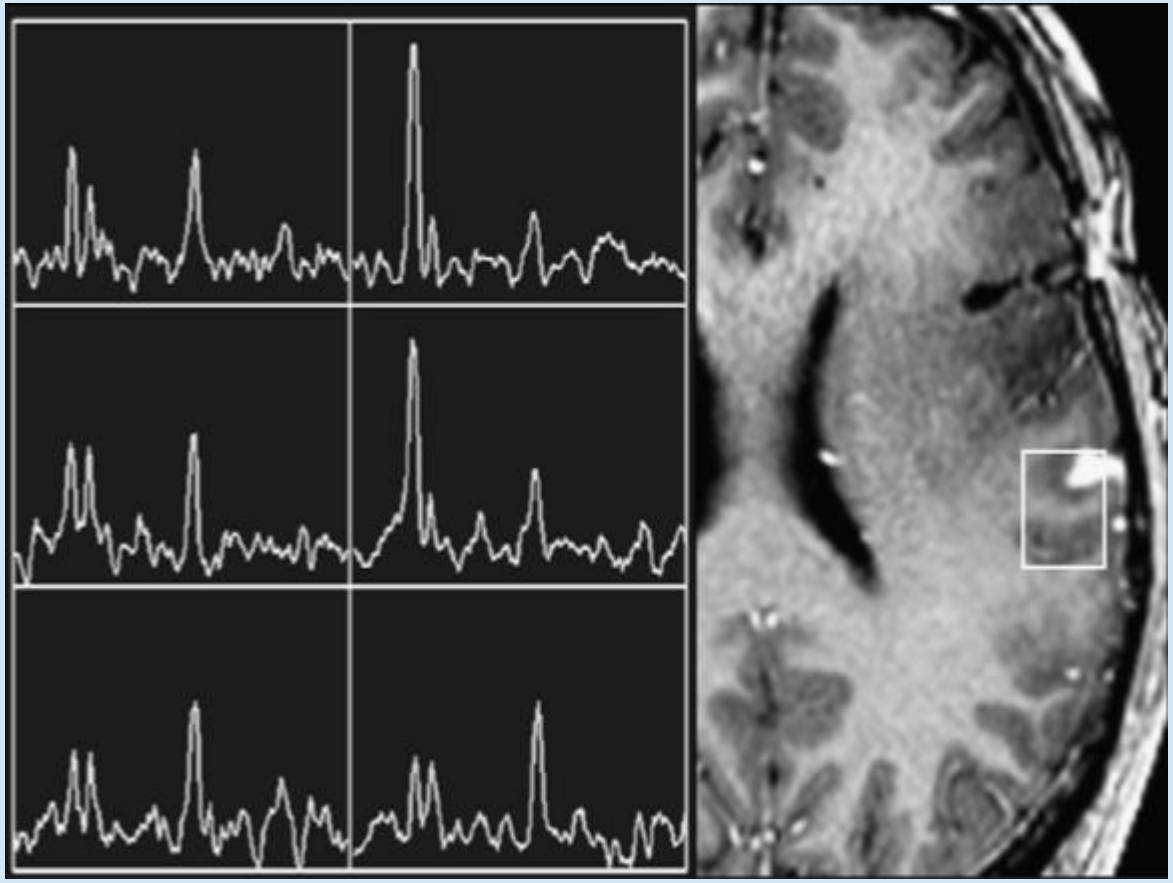
MRS in Brain Tumor

- Typical pattern of glioma: High choline, low or absent NAA peaks, lipid and lactate peak → often seen in GBM
- Extra axial tumors that do not arise from glial as meningioma, reveal very high choline and no NAA (because contain no neurons). Very high alanine peak in meningioma – not always
- **Lack of specificity of the principal MRS markers**
- Large Choline peak: increased membrane turnover (*neoplasia* with rapid membrane formation or *demyelination* or *ischemia* with rapid membrane breakdown). All three reduced NAA


Multiple Sclerosis
Anaplastic
Astrocytoma

MRI in Brain Tumor

- Pre op: Cho/NAA ratio > 1.5 – target biopsy and guide stereotactic radiosurgery
- Treatment response need serial MRS:
  - Complete absence NAA & choline peak + lactate/lipid peaks → delayed necrosis
  - Increase choline + increase cho/NAA ratio → tumor recurrence

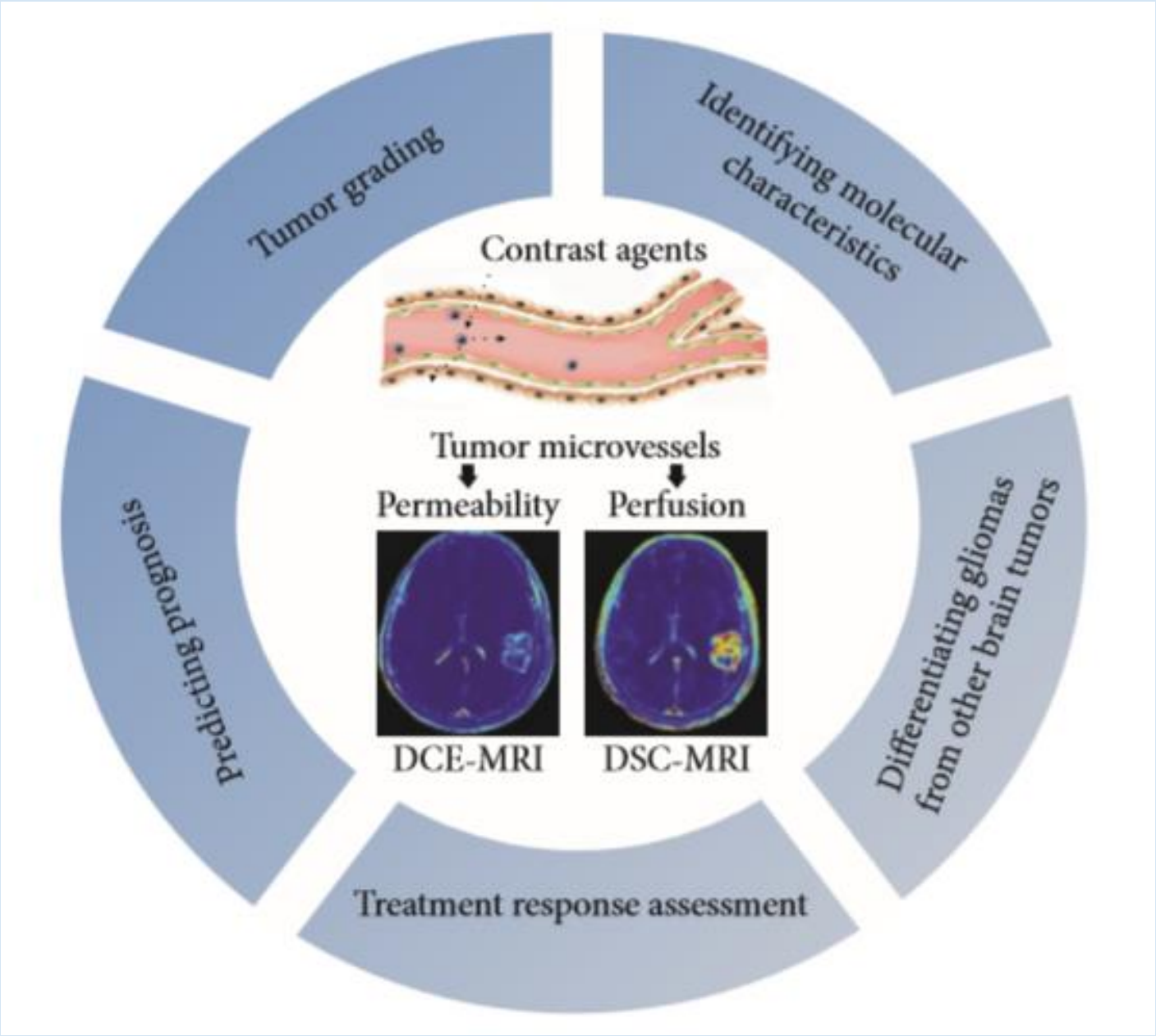


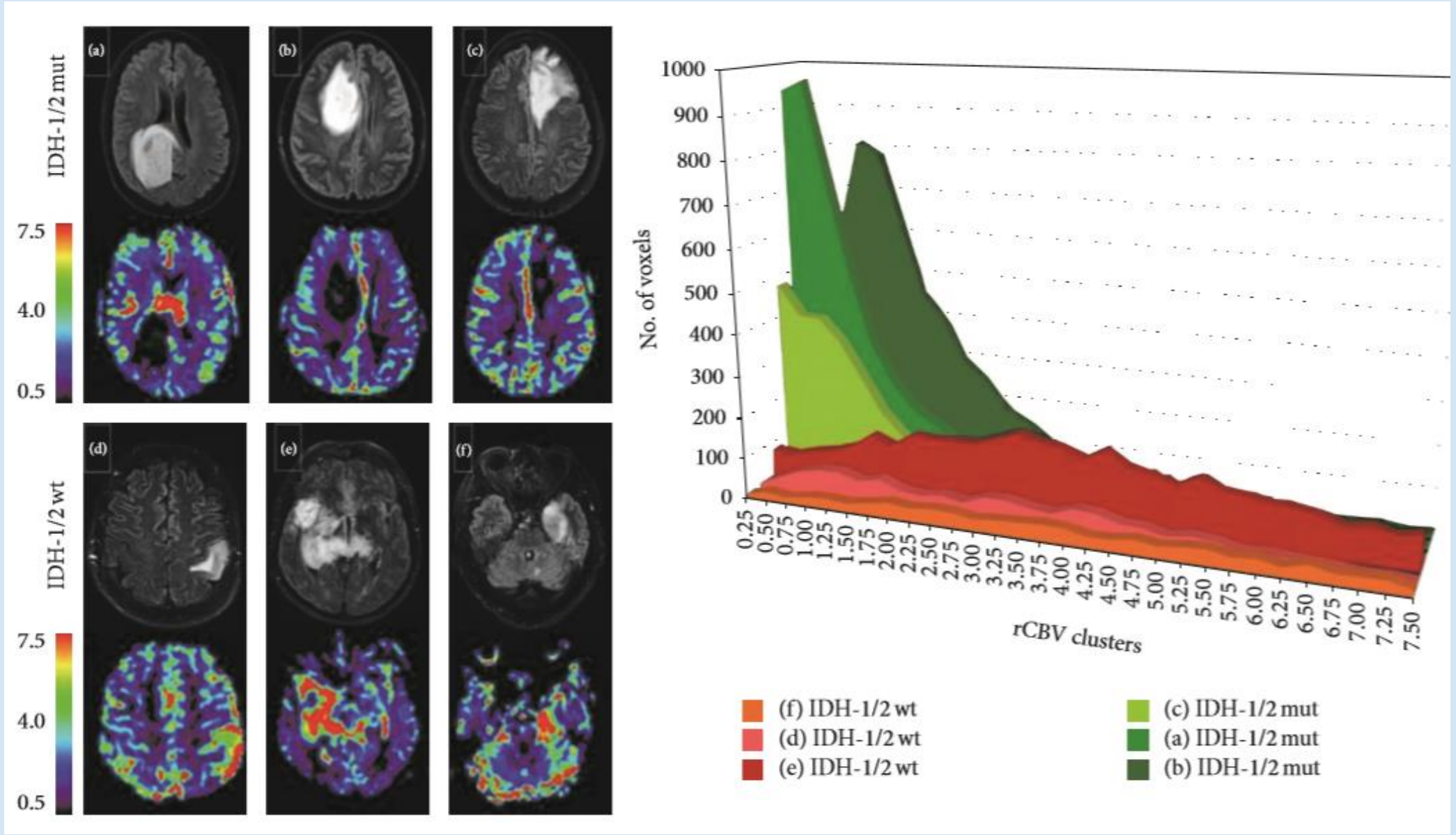
GBM Primary and Secondary

- 90% of glioblastomas develop rapidly de novo in elderly patients
- Secondary glioblastomas progress from low-grade diffuse astrocytoma/anaplastic astrocytoma. They manifest in younger patients, have a lesser degree of necrosis, are preferentially located in the **frontal lobe**, and carry a significantly better prognosis.
- Histologically, primary and secondary GBM are similar, but they differ in their genetic and epigenetic profiles.
- **Isocitrate dehydrogenase (IDH) gene mutations**: 50%–80% of grades II and III glioma and nearly all secondary GBM

GBM Primary and Secondary

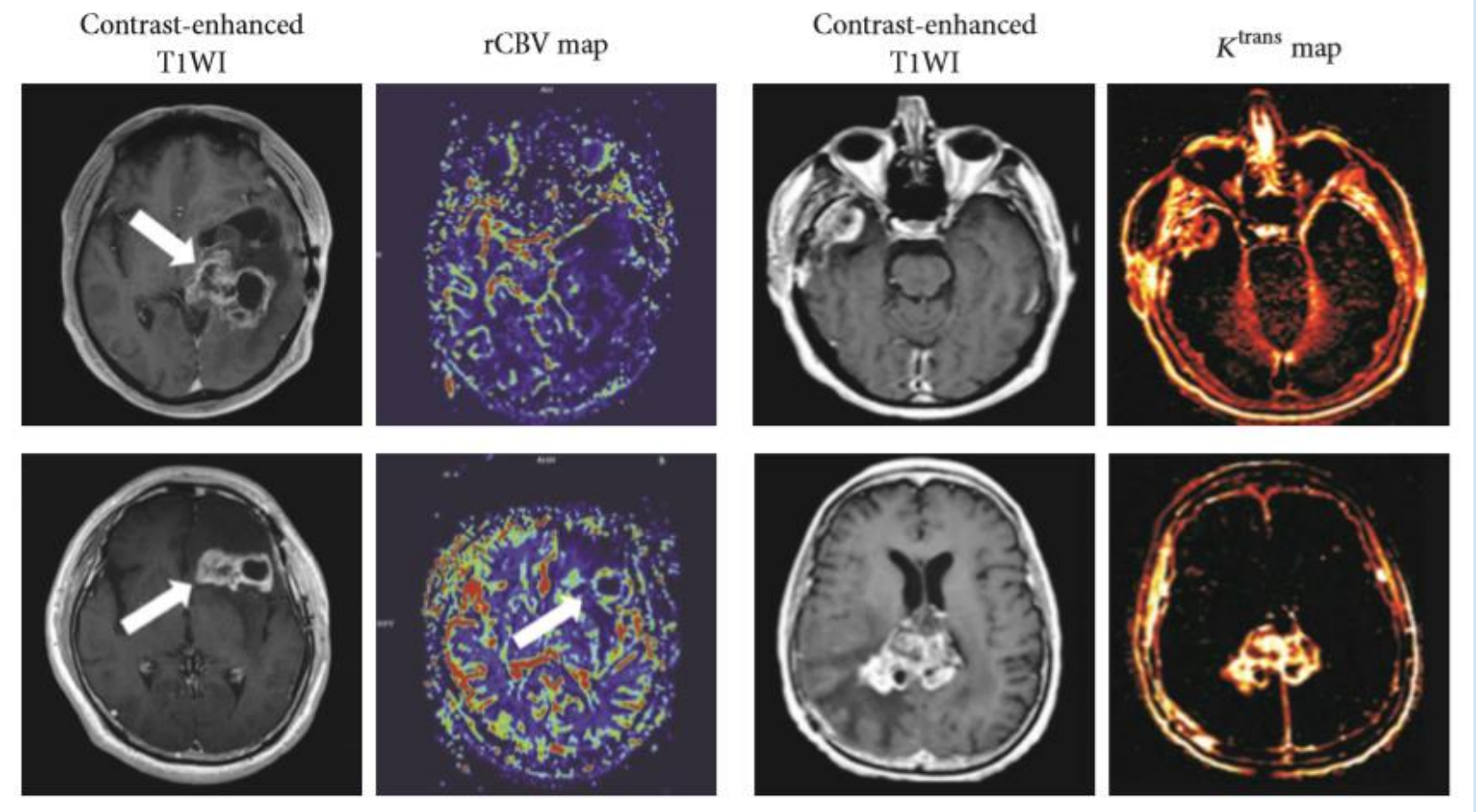
- MRS detected elevated 2-HG levels in gliomas with IDH1 mutations compared to those with wild-type IDH1 (P = 0.003) → But frequent false negative results (N.Bertolino et all,"Accuracyof2hydroxyglutaratequantificationbyshort-echoproton-MRSat3 T:aphantomstudy,"PhysicaMedica,vol.30,no.6, 2014)
- Considering that IDH mutation status is associated with hypoxia induced factor-1α,a driving factor in hypoxia-dependent angiogenesis, perfusion MRI may predict this genetic alteration indirectly.
- Potential of rCBV for predicting IDH mutation status in LGG and Anaplastic Glioma.


Tumor grading
Identifying molecular characteristics
Contrast agents
Tumor microvessels
Permeability
Perfusion
DCE-MRI
DSC-MRI
Predicting prognosis
Differentiating gliomas from other brain tumors
Treatment response assessment



P. Kickingereder et al., “IDH mutation status is associated with a distinct hypoxia/angiogenesis transcriptome signature which is non-invasively predictable with rCBV imaging in human glioma,” Scientific Reports, vol. 5,2016

Pseudo progression (PsP) vs Progressive disease (PD)

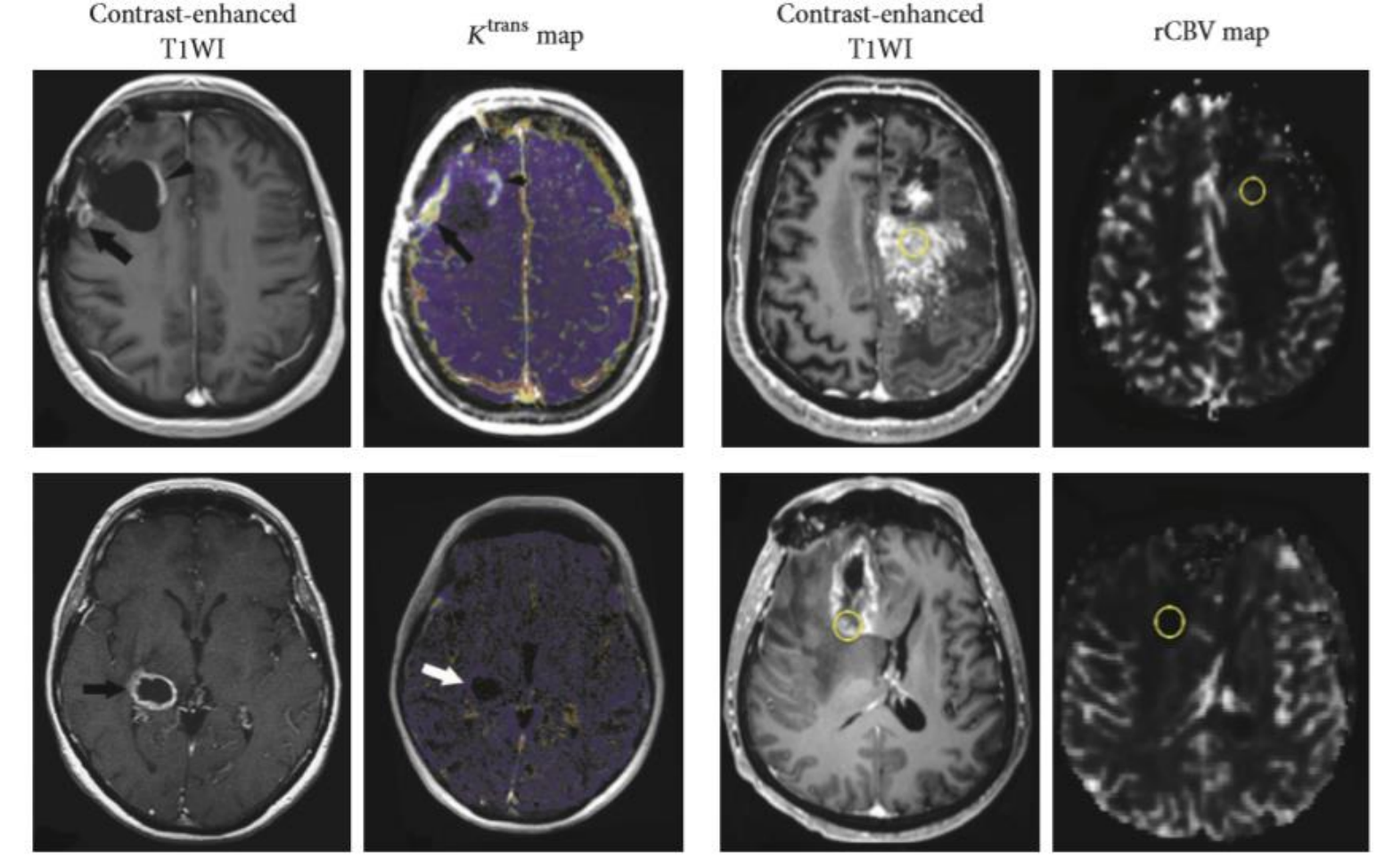


GBM treated with temozolomide demonstrates increased contrast enhancement suspicious for both PsP and PD

DSC–MRI: rCBV maps show low perfusion in PsP

DCE-MRI: Ktrans maps demonstrate decreased Ktrans value in PsP

Radiation Necrosis VS Reccurent GBM



Contrast-enhanced T1WI demonstrates similar contrast enhancement in recurrent glioblastoma and RN

Corresponding rCBV and Ktrans maps show significant difference between these two entities,with higher Ktrans and rCBV for recurrent tumor but low for RN

CONCLUSION

- Advance MRI is helpful in brain tumor assessment and neurosurgical planning
- Advance MRI consist of: fMRI, PWI, DWI - DTI and MRS
- At the moment none of the single techniques can be considered the golden standard.
- Only the integration of advanced and conventional MR imaging proves to be a reliable tool in the hands of the neuroradiologist; to help neurosurgeon in maximazing tumor resection and function preservation.

THANK YOU