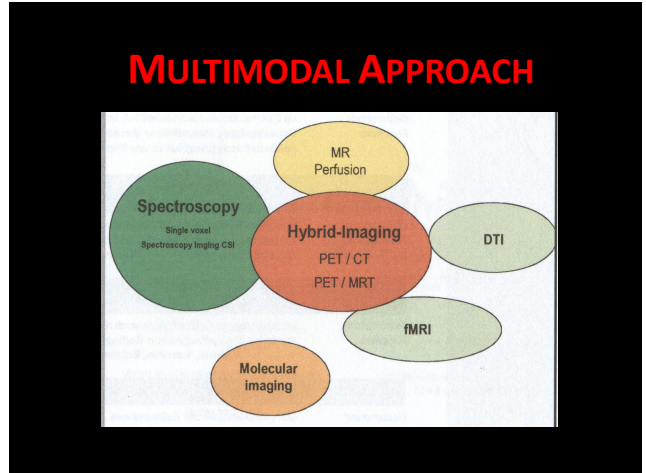



  
**ΙΑΤΡΙΚΗ ΣΧΟΛΗ**  
 Εθνικό και Καποδιστριακό  
 Πανεπιστήμιο Αθηνών

## MULTIMODAL IMAGING OF BRAIN TUMORS

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 Department of Neurosurgery, Medical School, University of Athens,  
 Evangelismos Hospital, Athens, Greece



- ### Outline
- Conventional MRI Role
  - Physiology based MRI
    - Diffusion/Tractography
    - Perfusion
    - MRS
    - fMRI
  - Clinical Challenges for MR Imaging

- ### Classification of Brain Tumors
- CNS consists of : **neurons**  
**neuroglia**  
*(astrocytes, oligodendrocytes, microglia, ependyma, choroid epithelium)*
- the majority of brain tumors arise from the neuroglia and are included under the broad term of **gliomas** ( 40-50% of all primary and metastatic intracranial tumors)
  - primary CNS lymphoma
  - metastatic disease
  - benign cystic masses (*arachnoid, epidermoid, dermoid, colloid*)

### Intracranial Tumors

- ✓ **Primary neoplasms** : 1/3  
astrocytoma, oligodendroglioma, GBM
- ✓ **Metastases** : 1/3  
lung, breast, melanoma
- ✓ **Non-glial tumors** : 1/3  
meningioma, lymphoma, pineal tumors

### Diagnostic Process

Traditional criteria to establish the diagnosis

- ✓ **Age** : \* adults - children
- ✓ **Location** : \* intra-, extra-axial  
\* supra-, infra-tentorial
- ✓ **Morphology - (CT-MRI)** :
  - \* margins
  - \* edema
  - \* hemorrhage
  - \* vascularity
  - \* pattern of enhancement
  - \* intratumoral cyst
  - \* calcifications
  - \* cellularity
  - \* necrosis
  - \* melanin
  - \* fat

### Supratentorial Intra-axial Neoplasms

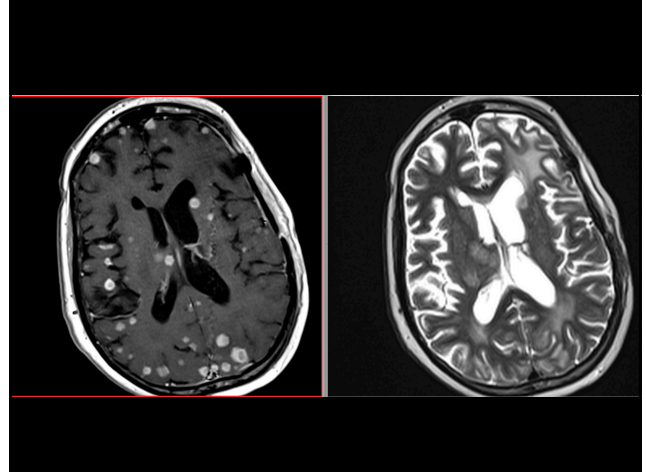
Adults	Children
✓ metastases	✓ ganglioglioma/cytoma
✓ gliomas	✓ DNET
✓ lymphoma	✓ neuroblastoma (PNET)
✓ sarcoma	✓ pilocytic astrocytoma

### Infratentorial Intra-axial Neoplasms

Adults	Children
✓ metastases	✓ astrocytoma
✓ hemangioblastoma	✓ medulloblastoma
✓ gliomas	✓ ependymoma
	✓ brain stem glioma

### Metastatic disease

- 30-40% of intracranial tumors  
*(lung - breast - melanoma - GI tract)*
- hematogenous spread - multiple lesions
- corticomedullary junction
- surrounding vasogenic edema
- enhancement : ↑ dose of contrast  
Magnetization Transfer (MT)



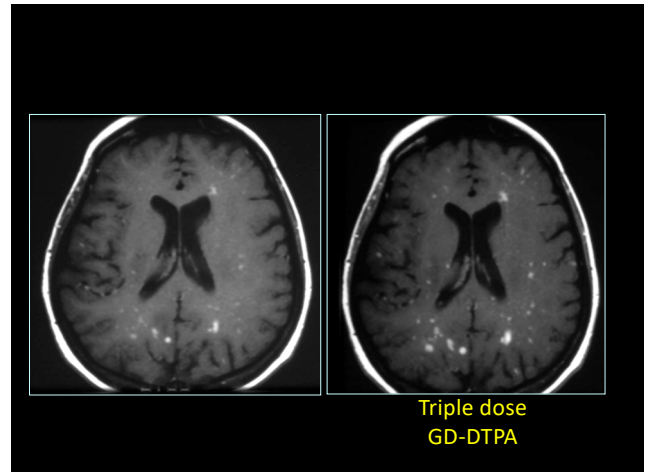
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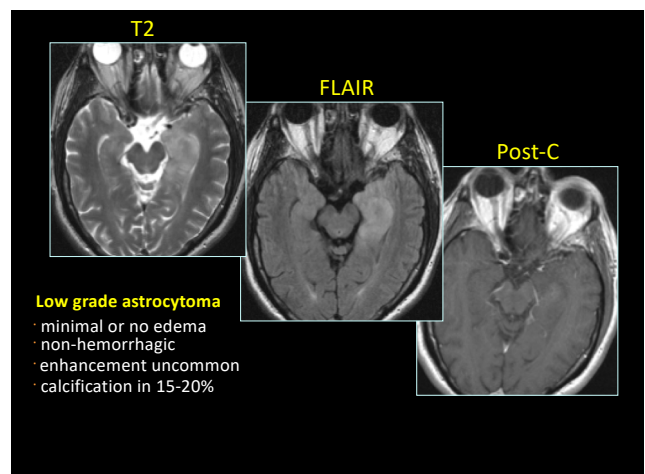
## Metastatic disease

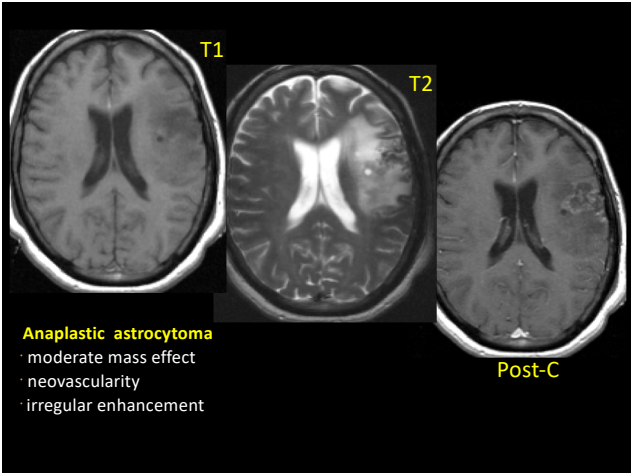
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*(lung - breast - melanoma - GI tract)*
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- corticomedullary junction
- surrounding vasogenic edema
- enhancement : ↑ dose of contrast  
*Magnetization Transfer (MT)*



## Gliomas

- heterogeneous group of tumors : astrocytoma (*pilocytic-anaplastic-GBM*), oligodendroglioma, ependymoma-subependymoma, choroid plexus papilloma
- 50% of solitary supratentorial masses
- middle age, male : female = 3:2
- ↓ grade astrocytomas (WHO grades I-II)
- ↑ grade astrocytomas (WHO grades III-IV)



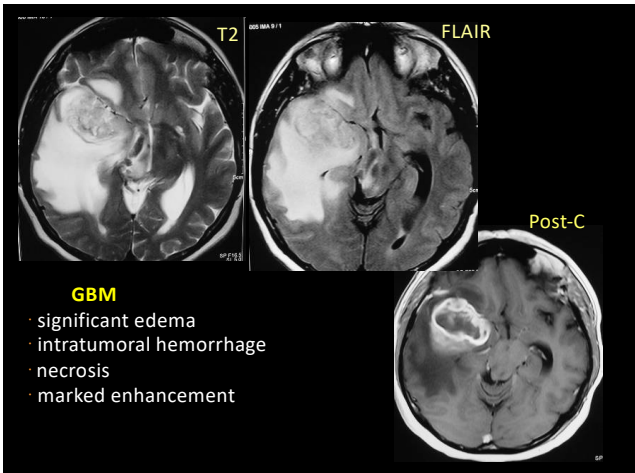


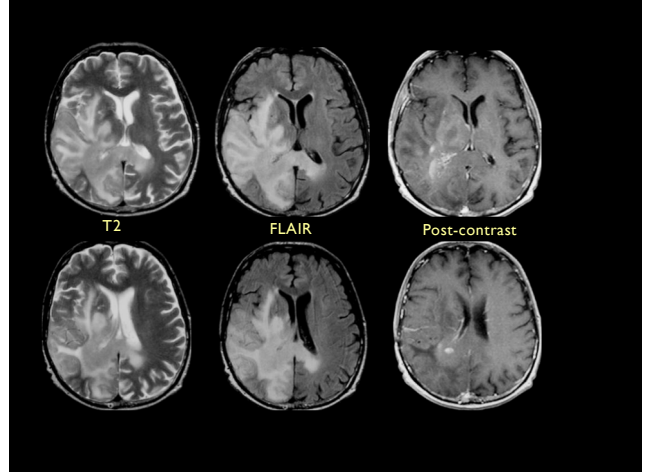
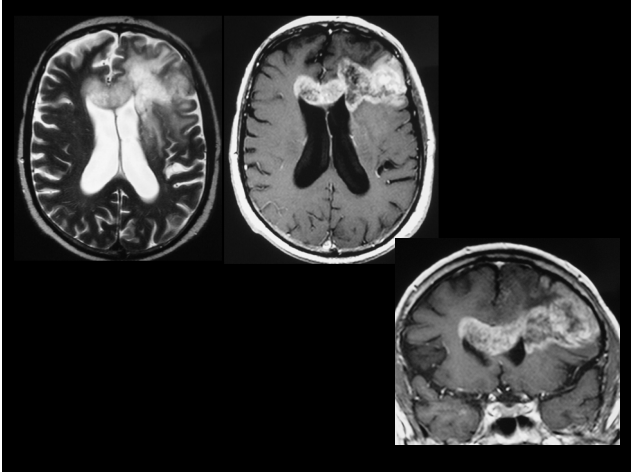
**Glioblastoma multiforme - GBM**

- the most common glioma (55%)
- dismal prognosis (optimal treatment  $\leq$  1 year)
- primary (de novo) or secondary GBM
- diffusively infiltrating tumor with various degree of enhancement
- butterfly or multi-centric appearance

**Imaging findings consistent with malignancy-aggressive behavior**

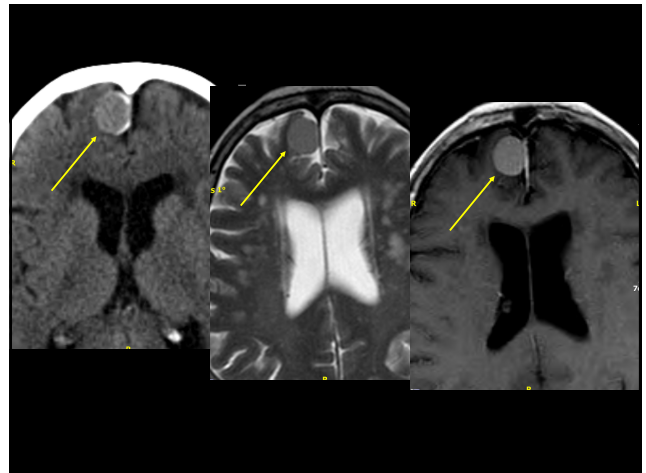
- significant peritumoral edema
- necrosis
- infiltrative pattern
- hemorrhage
- $\uparrow$  cellularity
- $\downarrow$  blood brain barrier

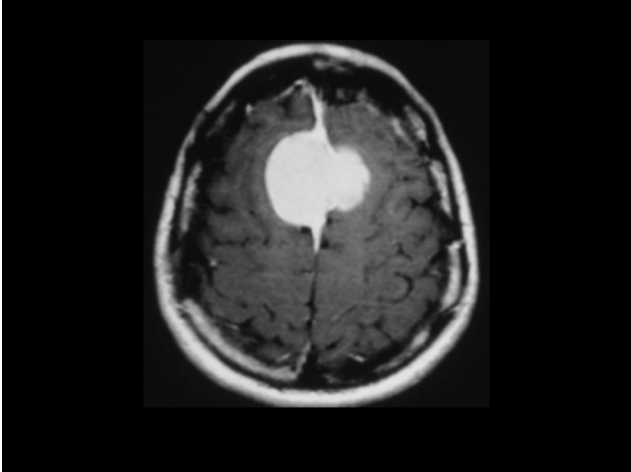




## Meningioma

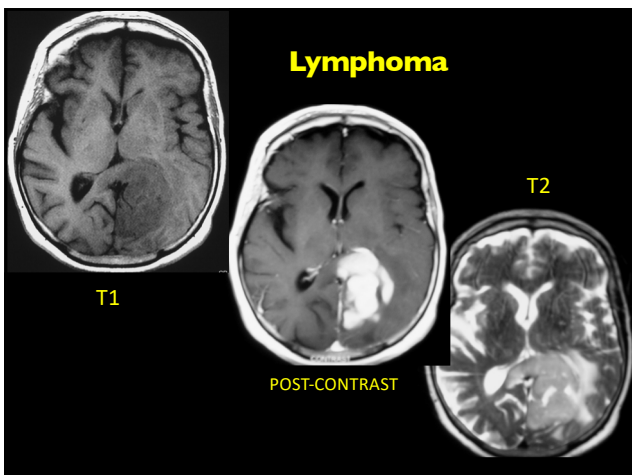
- ✓ falx, sphenoid wings, parasellar region, olfactory groove, CP angle
- ✓ calcifications (20-50%)
- ✓ hyperostosis (20%)
- ✓ "dural tail" sign
- ✓ women 40-70 yrs





## Lymphoma

- ✓ B-cell, non Hodgkin
- ✓ formerly rare, with increasing frequency in the era of immunosuppression and AIDS (10%)
- ✓ deep - subependymal location, corpus callosum
- ✓ highly cellular tumor : ↑ CT, ↓ T2 and ADC



## Limitations of Conventional MRI

- ✓ exact limits of tumor extension
- ✓ tumor behavior - grading
- ✓ DDx
  - ✓ primary tumor from metastasis
  - ✓ residual or recurrent tumor vs radiation necrosis
  - ✓ Neoplastic versus non - neoplastic lesions

### Physiology Based MR Techniques

- Diffusion Imaging
- Perfusion Imaging
- MR Spectroscopy
- Functional MRI

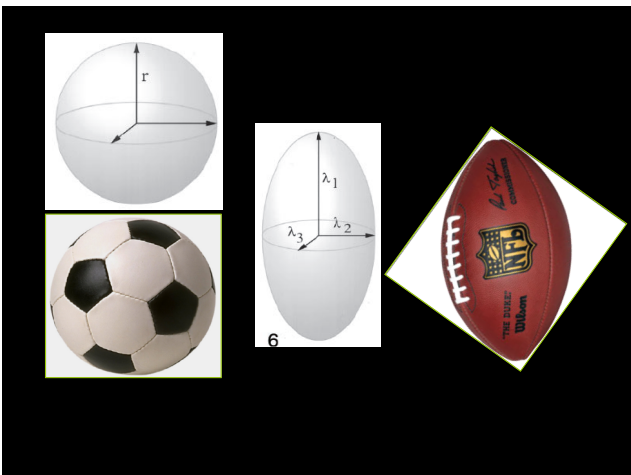
### Diffusion Imaging

*Microstructural information*

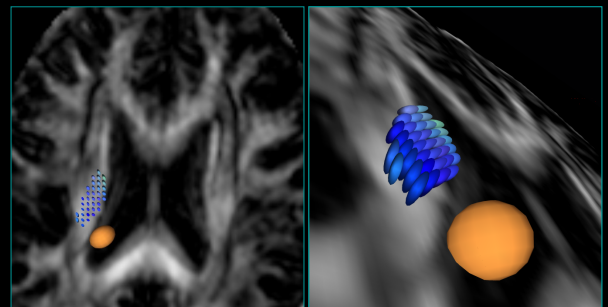
- ✓ DDX : · non neoplastic lesions (*abscess - epidermoid*)
- ✓ Tumor types or grades ( ↓ADC in ↑ grade tumors)  
*inverse correlation between diffusivity and tumor cellularity*
- ✓ Tumor extension : · *vasogenic edema-tumor infiltration*

#### Diffusion Tensor Imaging (DTI - Fiber Tractography) :

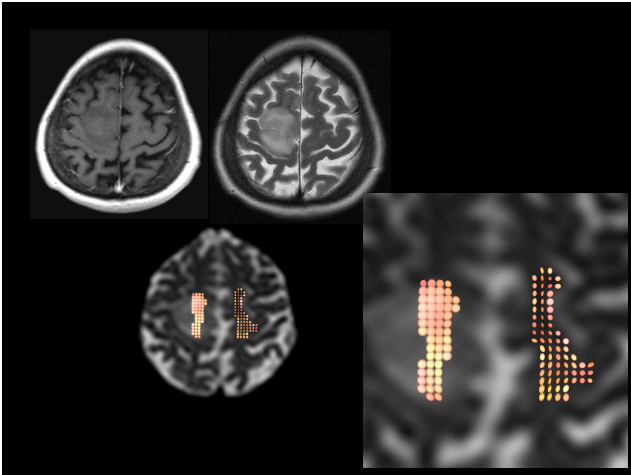
- *WM tracts - presurgical planning*  
( *deformation - displacement - infiltration* )



### DIFFUSION MODELS IN TISSUES

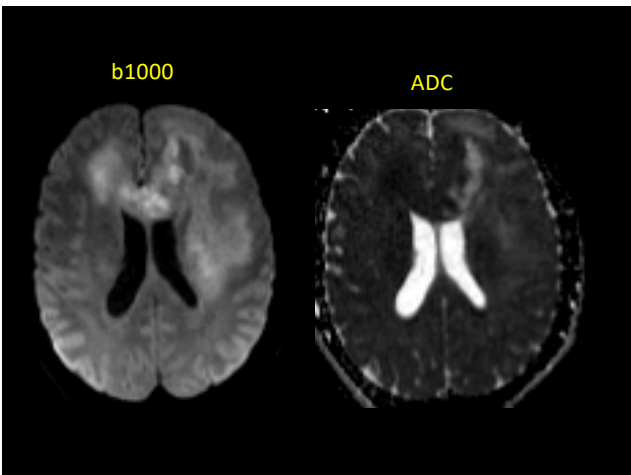




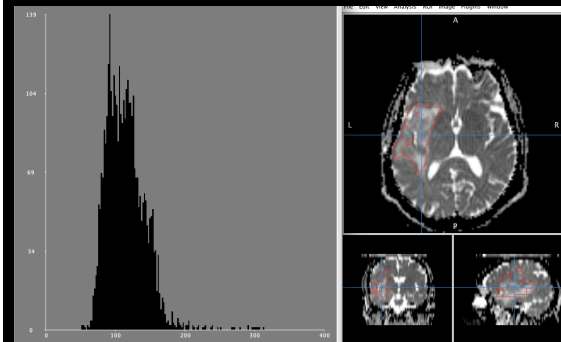


### Tumor Cellularity - DWI

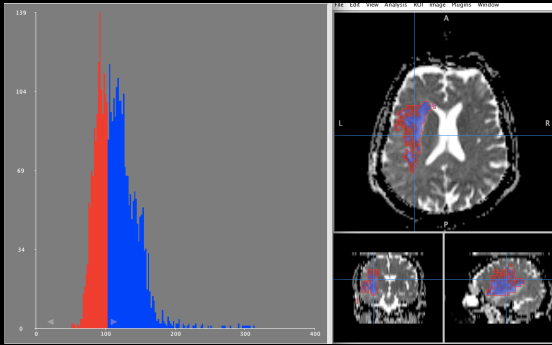
- ✓ Tissue cellularity or fluid with increased viscosity results in restricted diffusion pattern and presents with low ADC values
- ✓ Tissue necrosis, gliosis or free moving fluids results in elevated diffusion pattern and high ADC values
- ✓ High grade tumors are heterogeneous with areas of hypercellularity and areas of necrosis



### Whole Tumor ADC Histograms



### Whole Tumor ADC Histograms



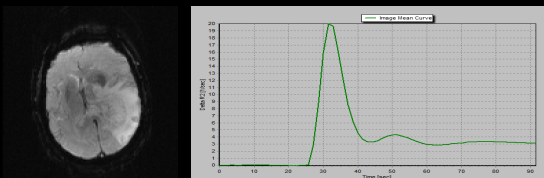
### Perfusion Imaging

Microvascularity - angiogenesis

- ✓ Tumor margins (rCBV, CBF, MTT)
- ✓ ↑ rCBV correlates with ↑ grade of malignancy
- ✓ Guidance stereotactic biopsy
- ✓ DDX :
  - solitary meta vs glioma
  - lymphoma vs toxoplasmosis (AIDS)
  - non neoplastic lesions (MS- abscess)
- ✓ Monitoring follow-up:
  - recurrent tumor vs radiation necrosis
  - antiangiogenic treatment

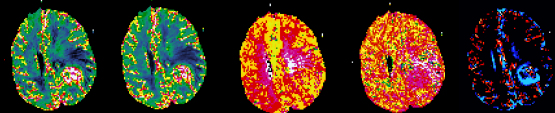
### Dynamic susceptibility contrast (DSC) MRI

- Perfusion is the delivery nutrients and oxygen via blood to the brain tissue
- An intravenous bolus injection of gadolinium-based contrast agent is given while the patient is in the scanner and the scan is running
- This bolus gives a strong susceptibility effect on the MR signal



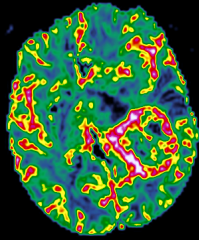
### Dynamic susceptibility contrast (DSC) MRI

- ✓ Parameters that can be estimated include
  - Relative blood volume and blood flow, rBV and rBF.
  - Time to peak (TTP), mean transit time (MMTT) and leakage.
- ✓ Pathology changes the perfusion in the affected areas,
  - Tumors typically have increased blood volume.

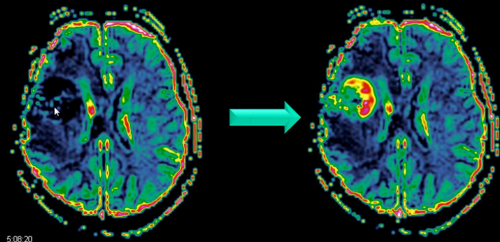


### Dynamic susceptibility contrast (DSC) MRI

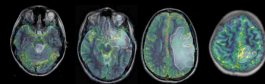
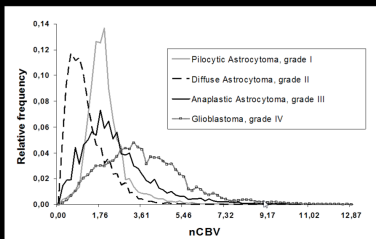
- Cerebral blood volume the most used parameter for tumor evaluation
- Need to normalize the CBV values
- Normalize to CBV in unaffected brain tissue



### Dynamic susceptibility contrast (DSC) MRI Leakage Correction

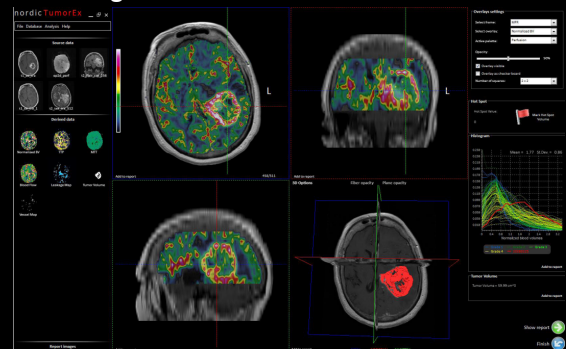


### Dynamic susceptibility contrast (DSC) MRI nBV Histograms



\*Emblem et al. Radiology 2008

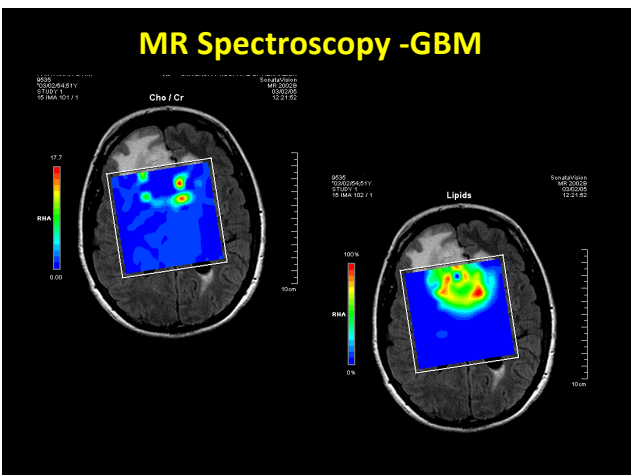
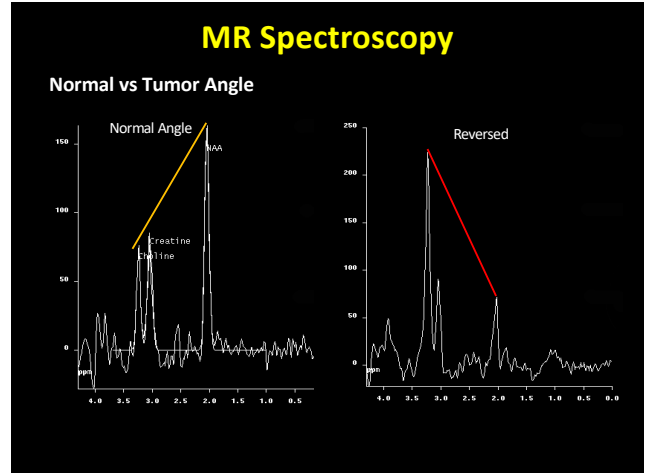
### Dynamic susceptibility contrast (DSC) MRI nBV Histograms



### MR Spectroscopy

Biochemistry - metabolism

- ✓ Grading of tumor : (  $\uparrow$  Cho  $\downarrow$  NAA =  $\uparrow$  grade)
- ✓ Guide stereotactic biopsy
- ✓ DDX :
  - tumor
  - necrosis
  - edema
- ✓ Monitoring follow-up:
  - recurrent tumor vs radiation necrosis



### fMRI

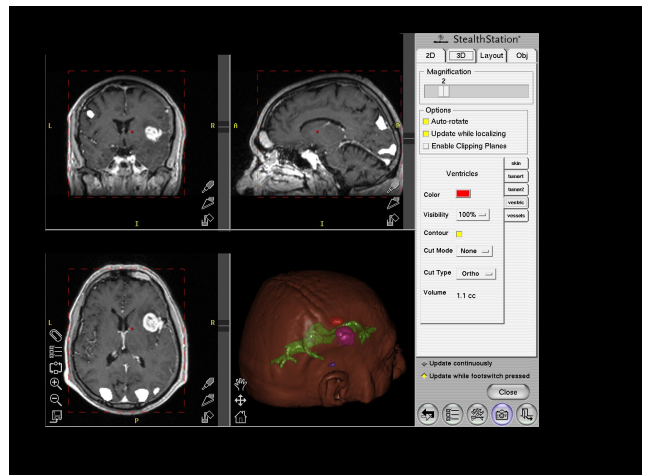
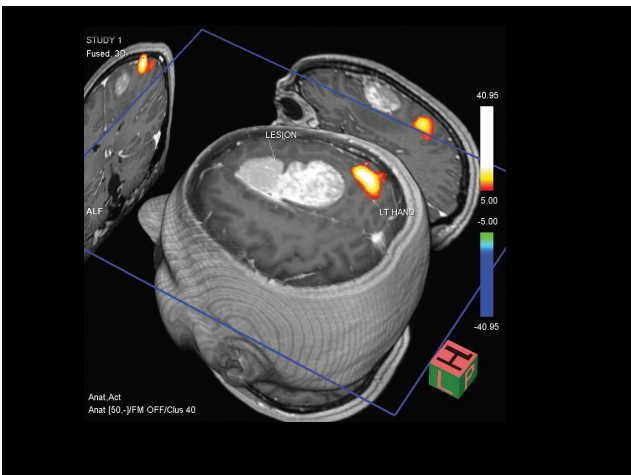
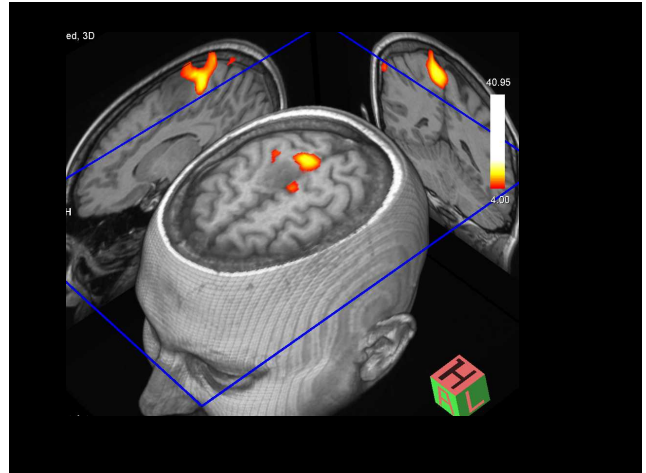
**BOLD: Blood Oxygen Level Dependent**

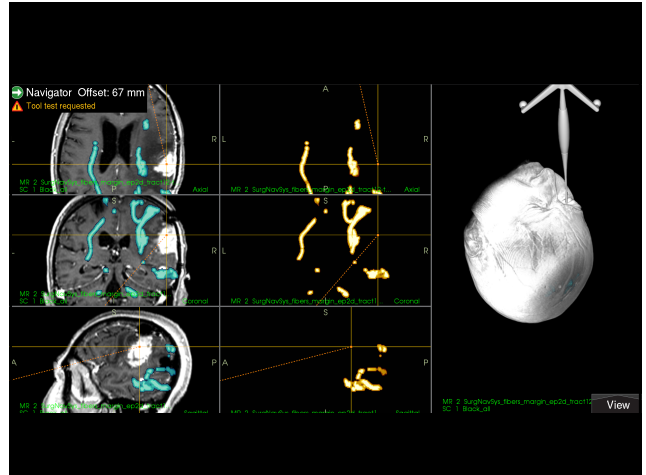
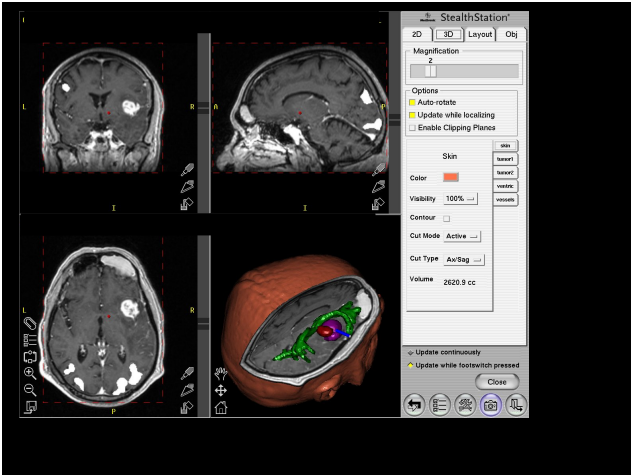
Increased Neuronal Activity  $\Rightarrow$  Increased Metabolism  $\Rightarrow$  Increase Blood Flow

The number of red blood cells carrying oxygen (oxyhaemoglobin) increases in the small blood vessels of the brain  $\Rightarrow$  increase of the T2\* constant

### fMRI Basic Aspects

- ✓ Monitor T2\* contrast during cognitive task  
e.g. acquire 20-40 slices every 5 seconds
- ✓ Design experiment to have alternating blocks (epochs) of task and control condition
- ✓ Look for statistically significant signal intensity changes correlated with task blocks





### Clinical Challenges

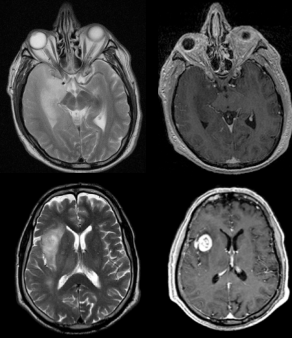
- ✓ Detection, Localization, Morphology
- ✓ Characterization – Grading – Progression
- ✓ Differential Diagnosis
- ✓ Preoperative Mapping
  - ✓ Surgical excision planning – margins
  - ✓ Tumor relationship with adjacent structures
- ✓ Stereotactic Biopsy Guidance
- ✓ Assessment of therapeutic response
  - ✓ Post chemoradiation therapy evaluation
  - ✓ Dd radiation necrosis from tumor recurrence

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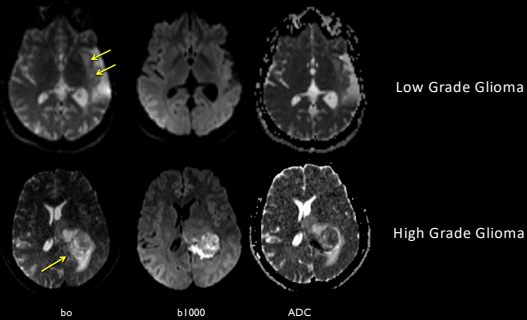
- ✓ Detection
- ✓ Localization
- ✓ Morphology
  - Margins
  - Edema
  - Intratumoral cyst
  - Necrosis
  - Hemorrhage
  - Calcifications
  - Melanin
  - Fat
  - Pattern of enhancement



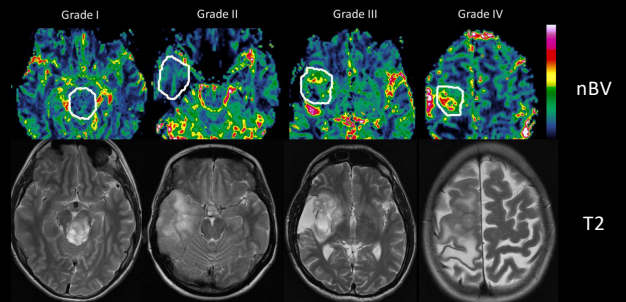
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### Tumor Grading: Cellularity



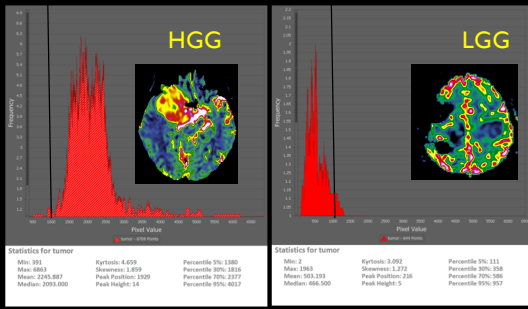
### Tumor Grading: Neovascularity





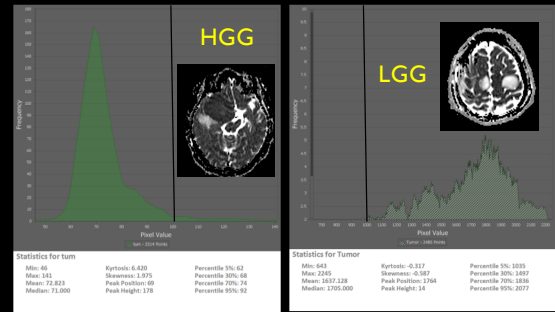


### Tumor Grading: Histogram Analysis



nBV

### Tumor Grading: Histogram Analysis

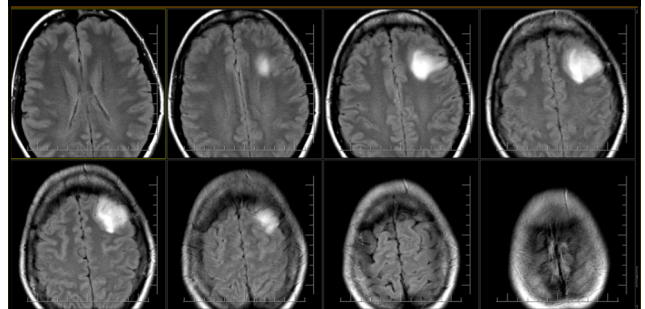


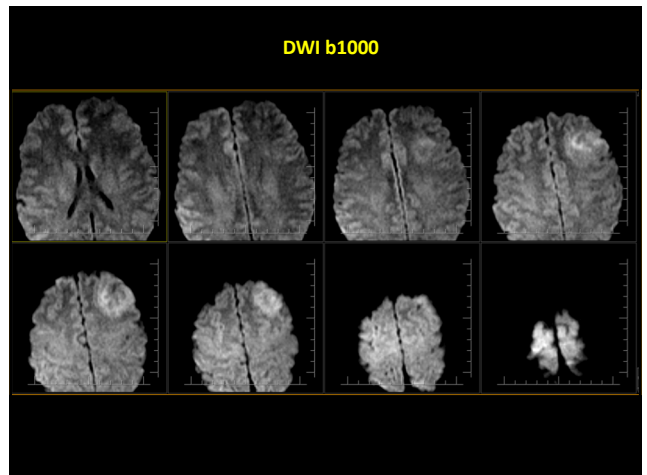
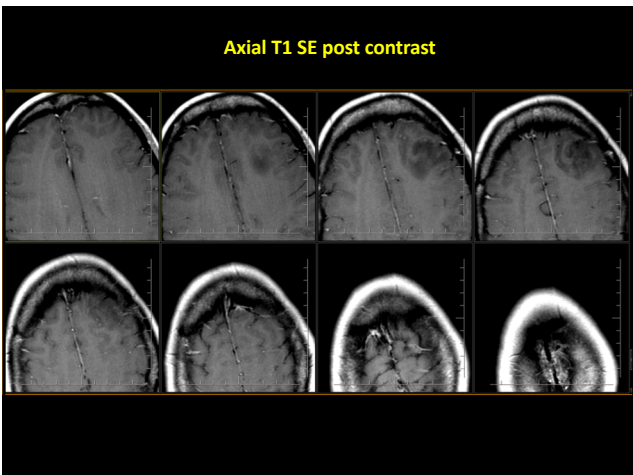
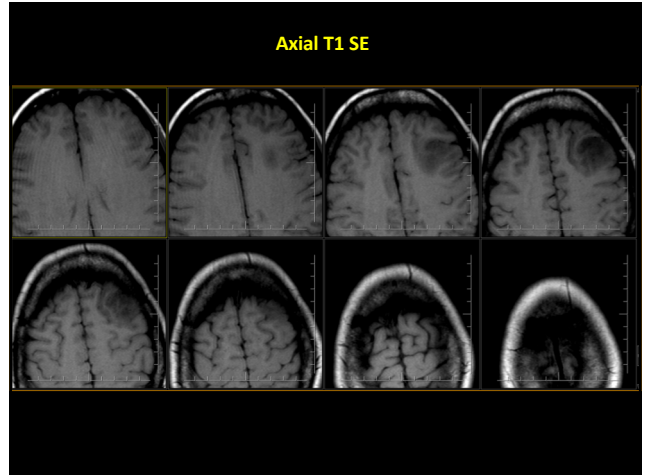
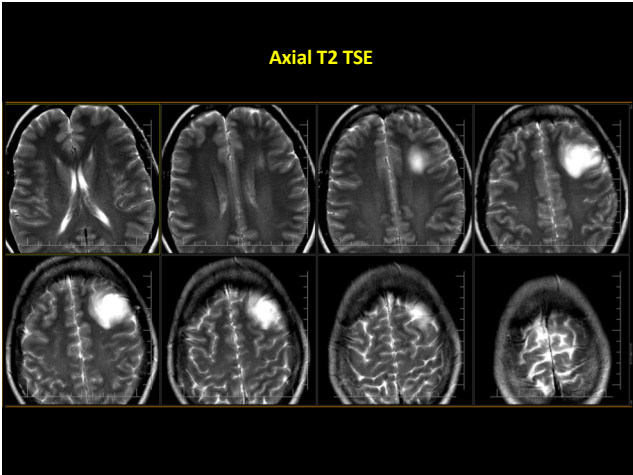
ADC

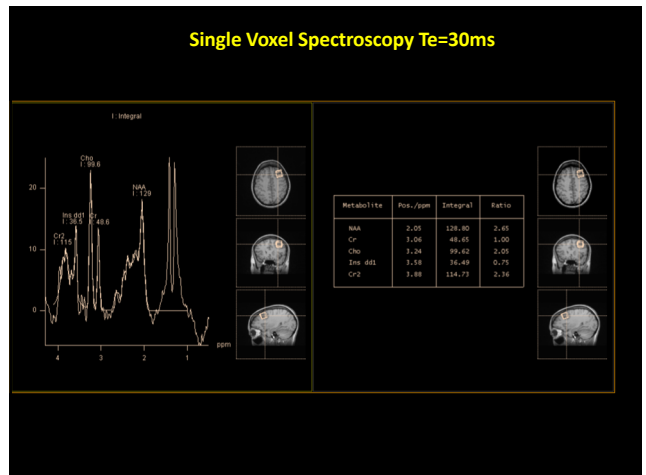
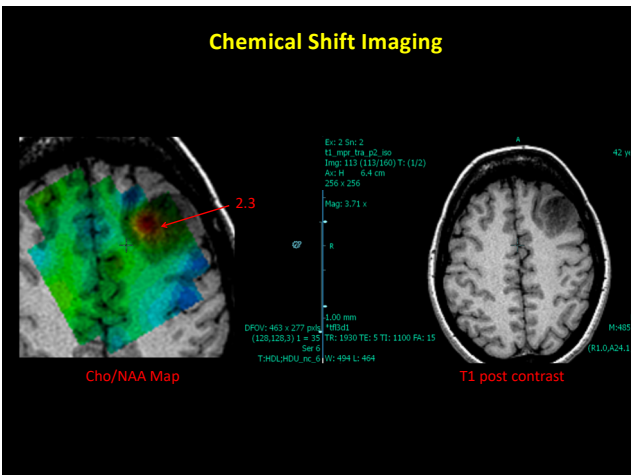
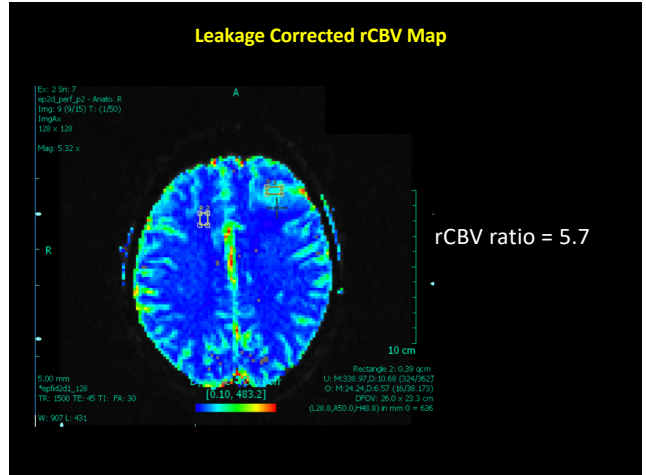
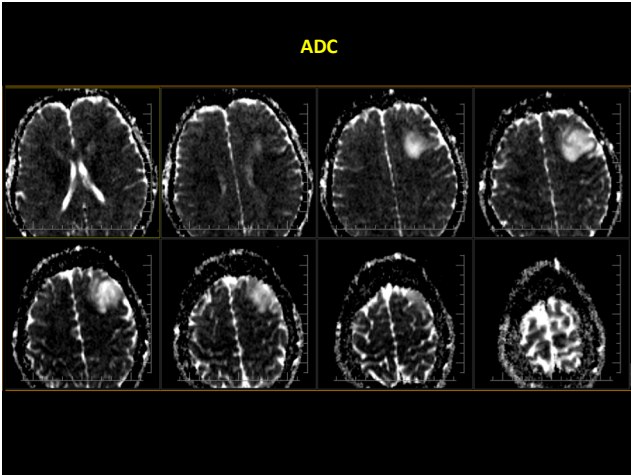
### Tumor Grading: Metabolic Profile

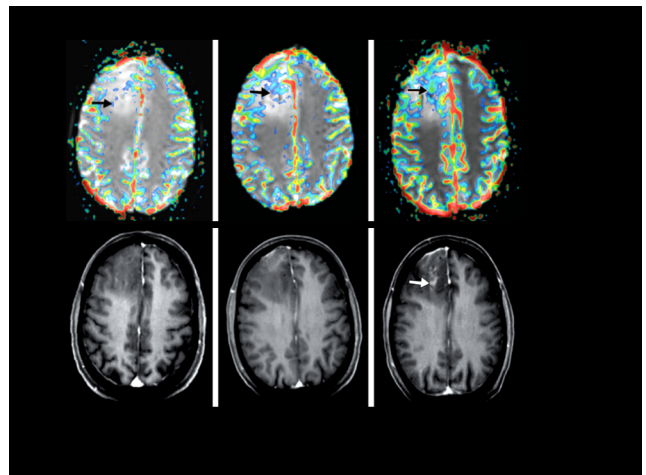
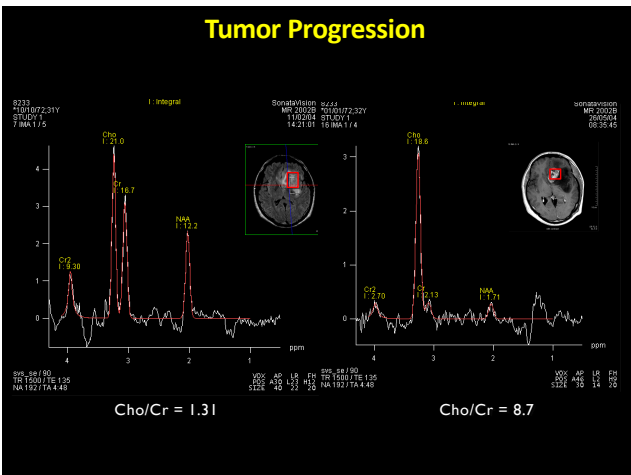
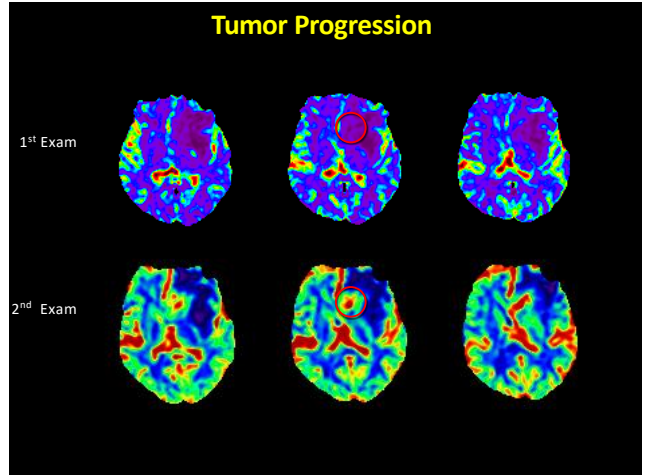
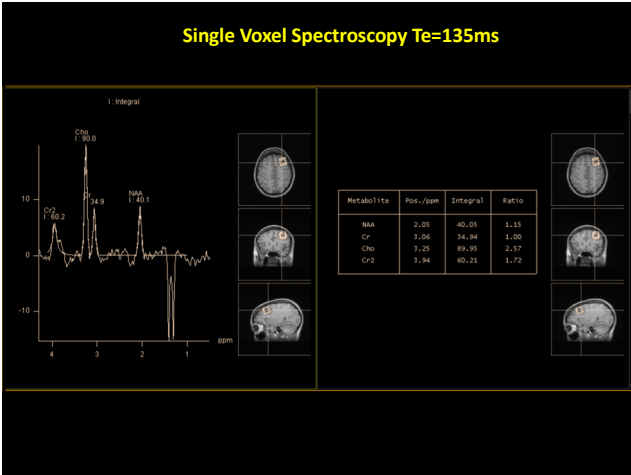
- Cho/Cr, Cho/NAA increases with tumor grade
  - Moderate TE is better than short TE (due to longer Cho T2 of tumors)
- ml is typically increased in LG gliomas
- Lipid concentrations in short TE increase with grade and if present at long TE may indicate HG gliomas
- High Cho/Cr ratio and elevated lipid levels are also a characteristic of malignant meningiomas and mets
- Peritumoral Cho/Cr ratios are higher in HG tumors than mets

### Axial FLAIR







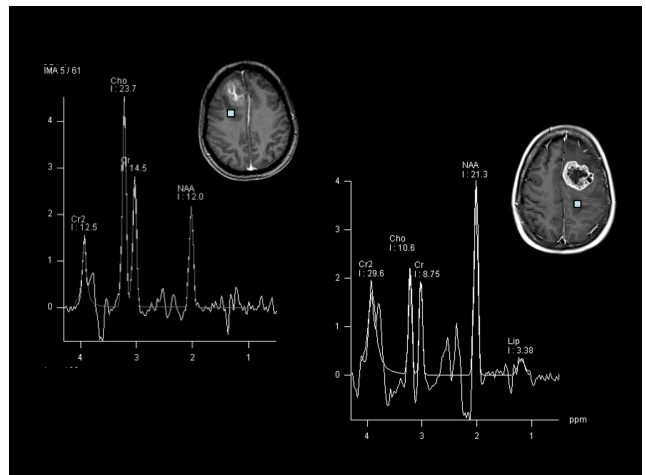
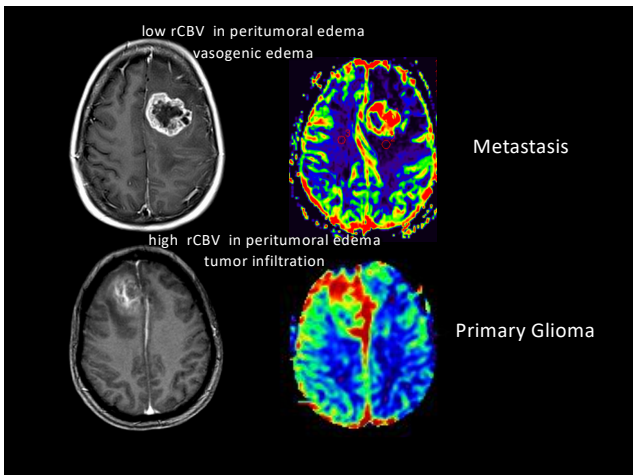


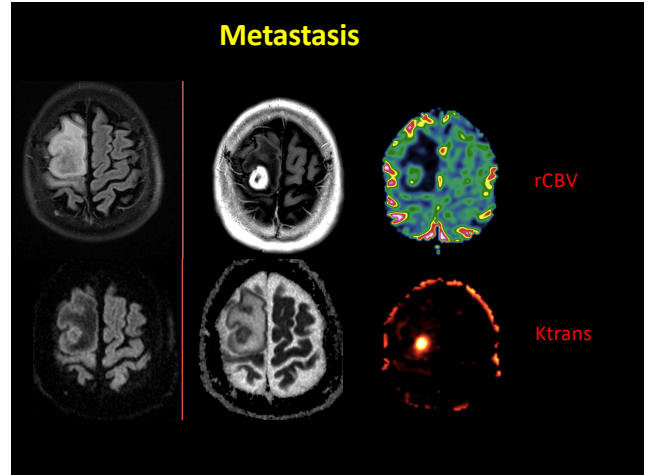
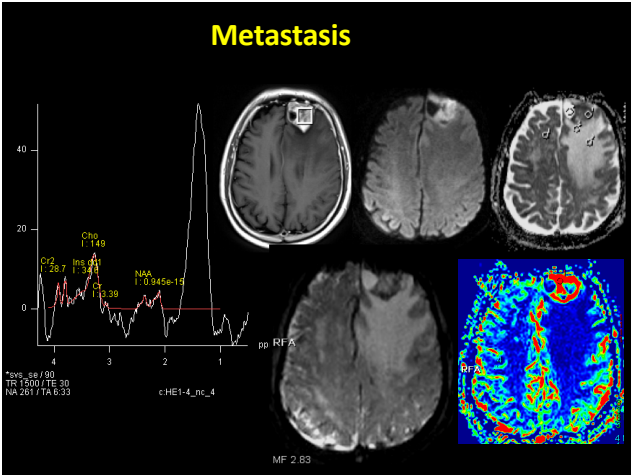
## Clinical Challenges

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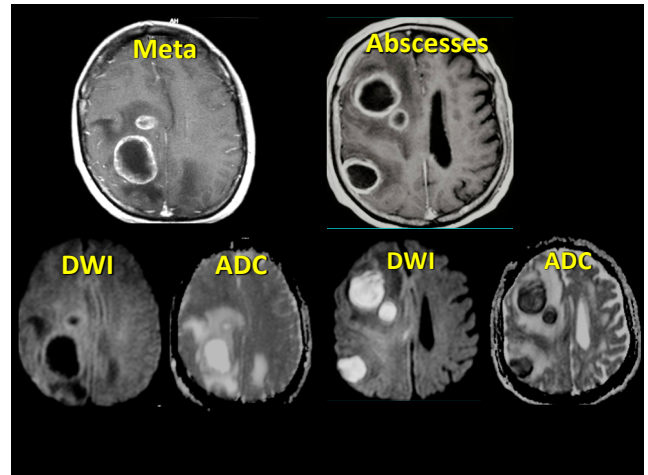
## Differential Diagnosis Primary from Secondary Tumors

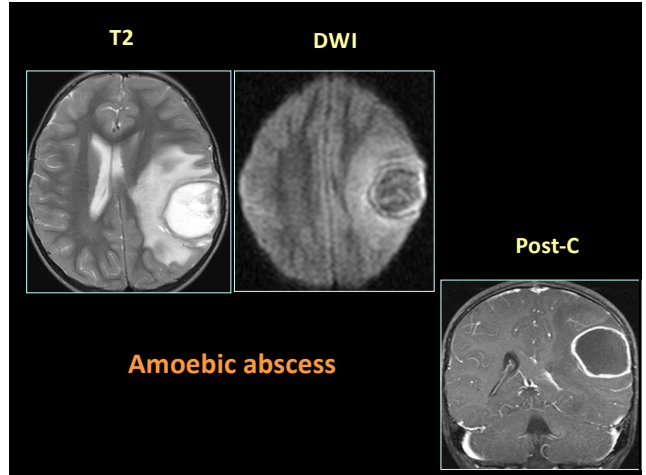
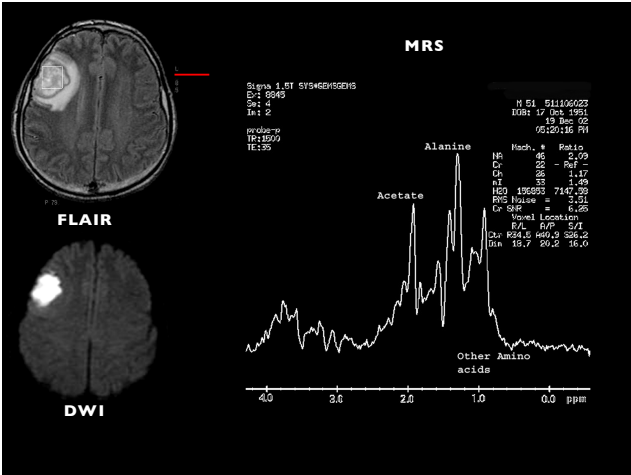
- ✓ Vasogenic peritumoral edema presents with low rCBV and low Cho/Cr, Cho/NAA, while malignant edema from primary tumors presents with high rCBV and Cho/Cr, Cho/NAA due to tumors infiltration
- ✓ Metastasis have typical lipid peaks due to necrosis



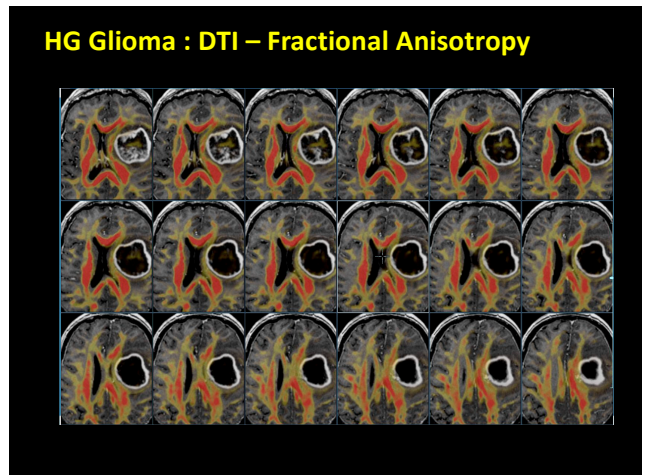


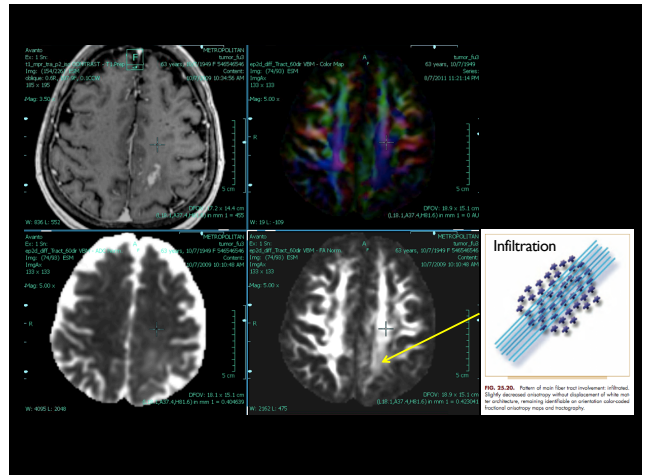
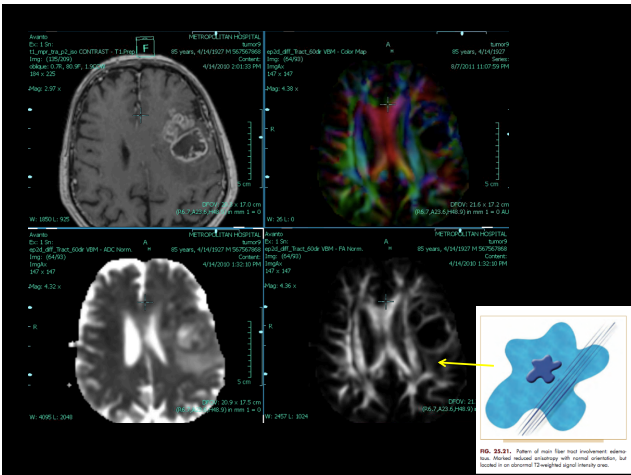
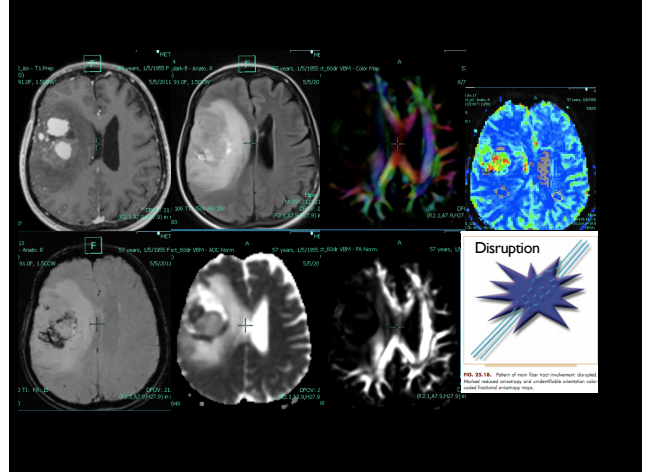
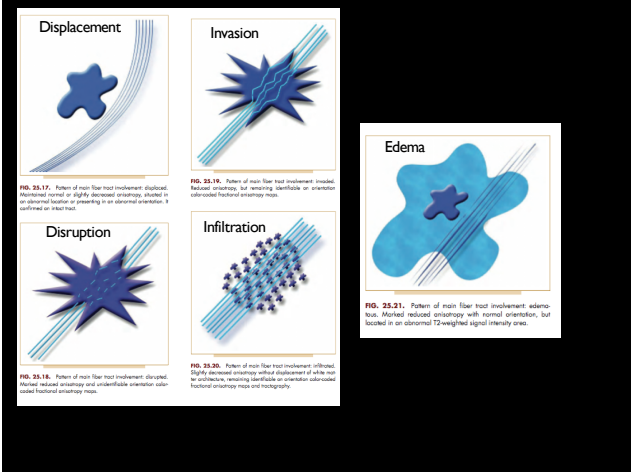
- ### Differential Diagnosis Tumor - mimicking lesions
- ✓ gray matter heterotopia
  - ✓ brain infarct
  - ✓ brain abscess
  - ✓ demyelinating diseases ( MS - ADEM )
  - ✓ vascular lesions - aneurysms
  - ✓ hematoma



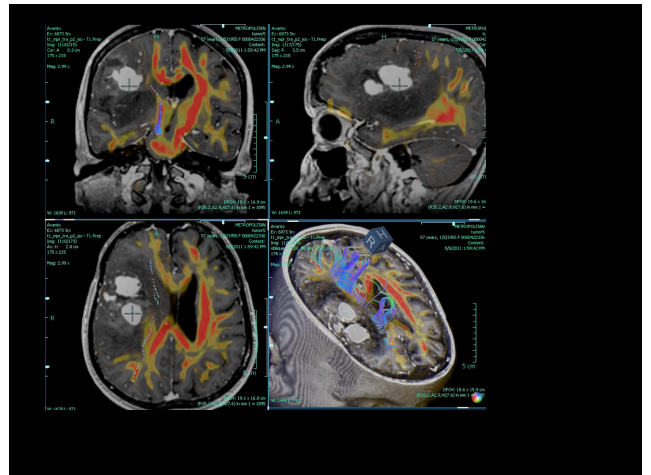
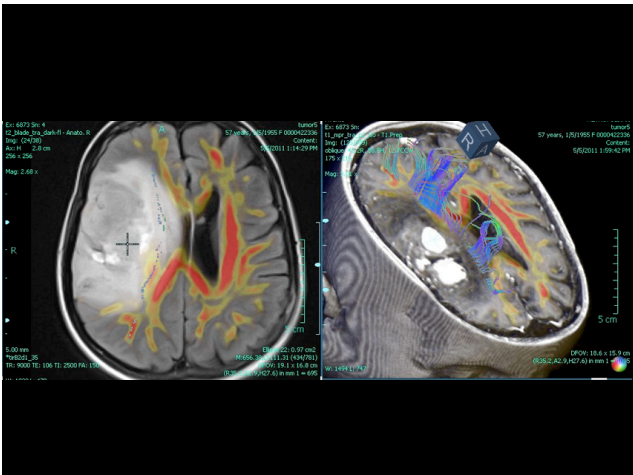
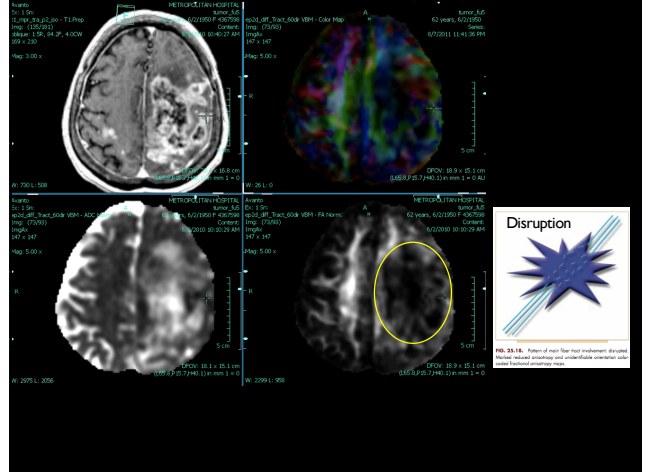
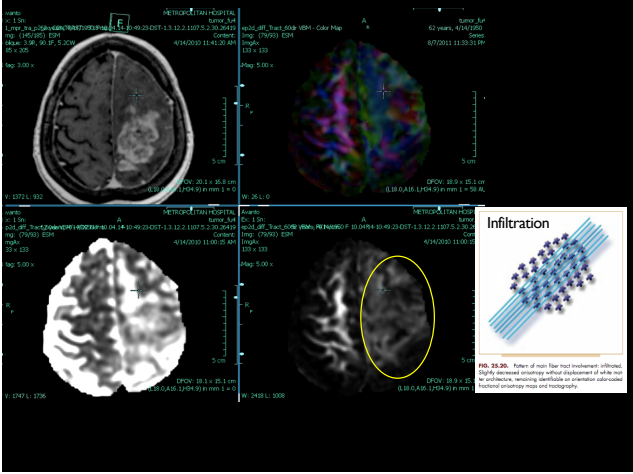


- ### Clinical Challenges
- ✓ Detection, Localization, Morphology
  - ✓ Characterization – Grading
  - ✓ Differential Diagnosis
  - ✓ Preoperative Mapping
    - ✓ Surgical excision planning – margins
    - ✓ Tumor relationship with adjacent structures
  - ✓ Stereotactic Biopsy Guidance
  - ✓ Assessment of therapeutic response
    - ✓ Post chemoradiation therapy evaluation
    - ✓ Dd radiation necrosis from tumor recurrence

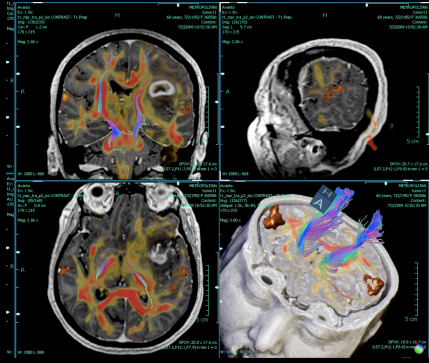




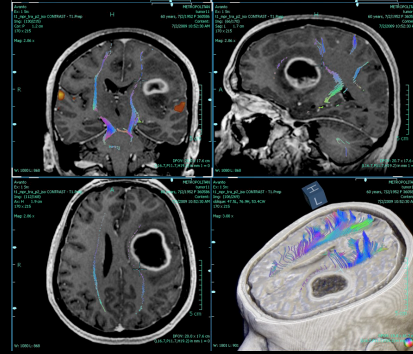




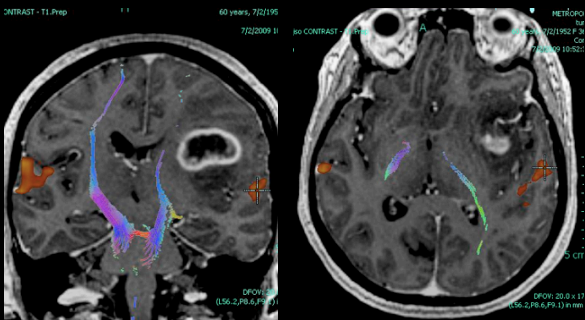
**HG Glioma : DTI – Fiber Tracking**



**HG Glioma : DTI – Fiber Tracking - fMRI**

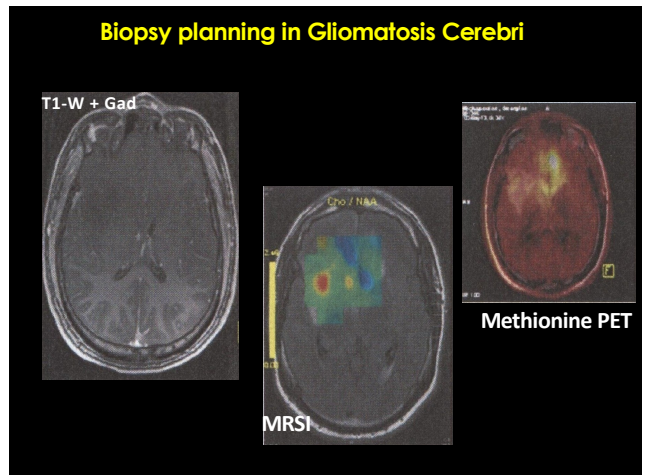
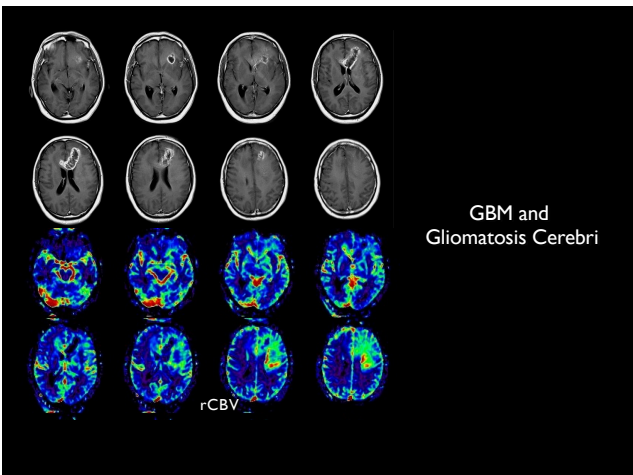
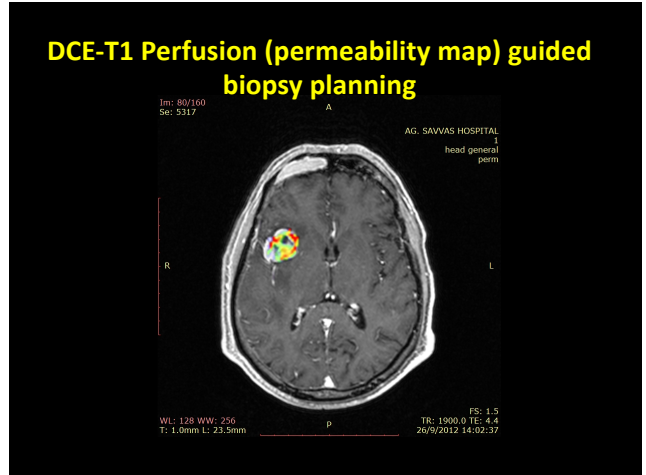
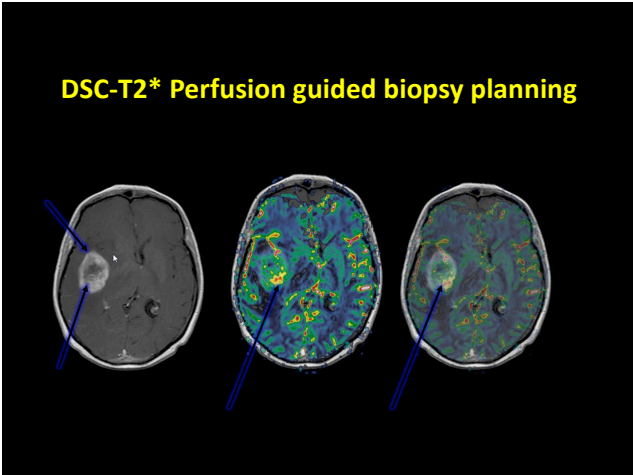


**HG Glioma : Fiber Tracking - fMRI**



**Clinical Challenges**

- ✓ Detection, Localization, Morphology
- ✓ Characterization – Grading – Progression
- ✓ Differential Diagnosis
- ✓ Preoperative Mapping
  - ✓ Surgical excision planning – margins
  - ✓ Tumor relationship with adjacent structures
- ✓ Stereotactic Biopsy Guidance
- ✓ Assessment of therapeutic response
  - ✓ Post chemoradiation therapy evaluation
  - ✓ Dd radiation necrosis from tumor recurrence

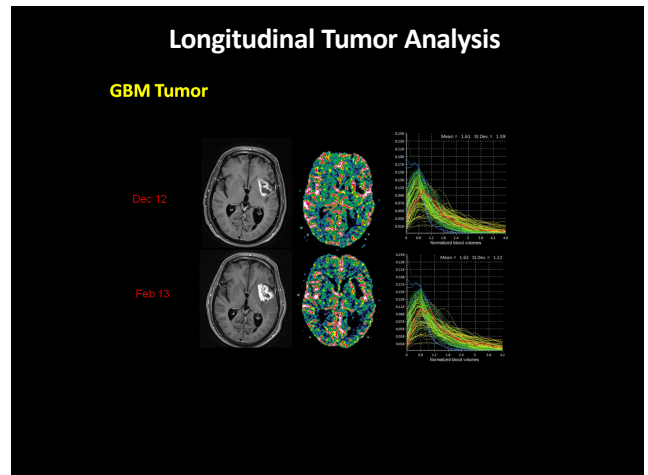
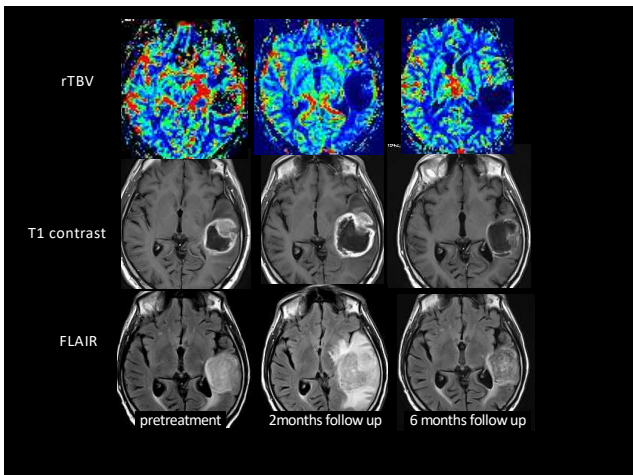


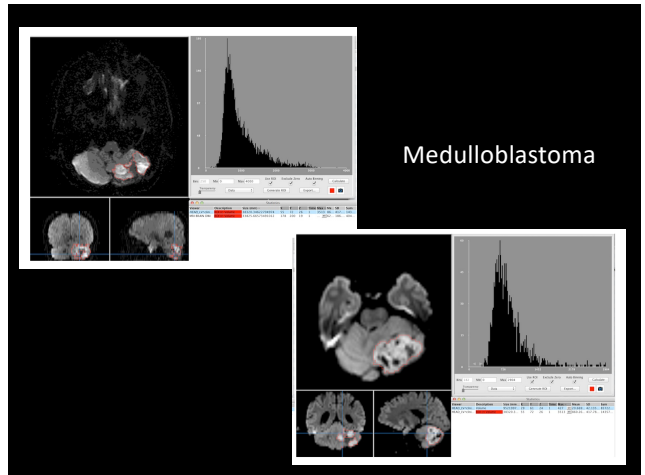
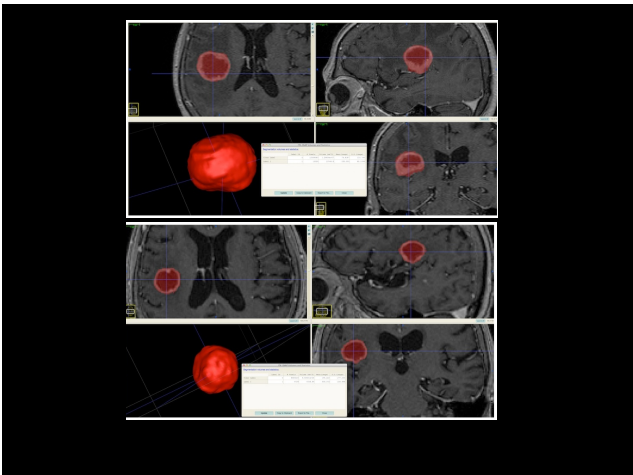
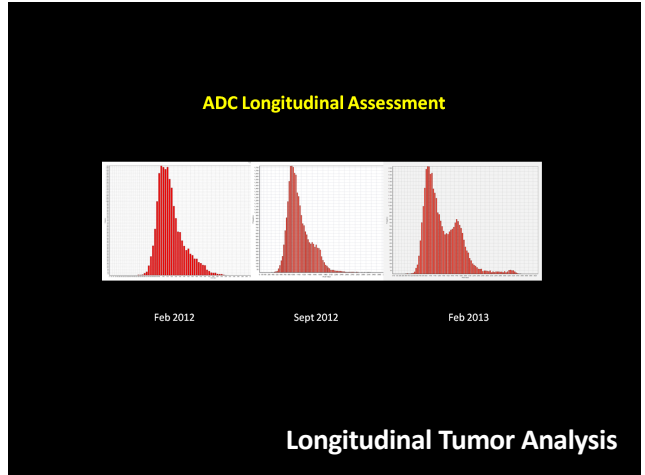
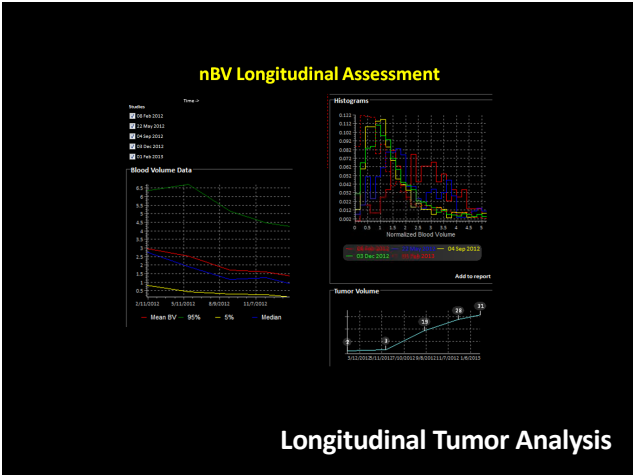
## Clinical Challenges

- ✓ Detection, Localization, Morphology
- ✓ Characterization – Grading – Progression
- ✓ Differential Diagnosis
- ✓ Preoperative Mapping
  - ✓ *Surgical excision planning – margins*
  - ✓ *Tumor relationship with adjacent structures*
- ✓ Radiotherapy Planning
- ✓ Stereotactic Biopsy Guidance
- ✓ Assessment of therapeutic response
  - ✓ *Post chemoradiation therapy evaluation*
  - ✓ *Dd radiation necrosis from tumor recurrence*

## Assessment of therapeutic response

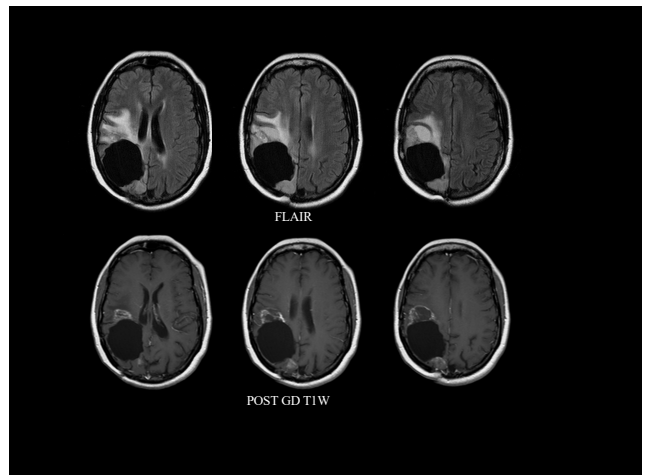
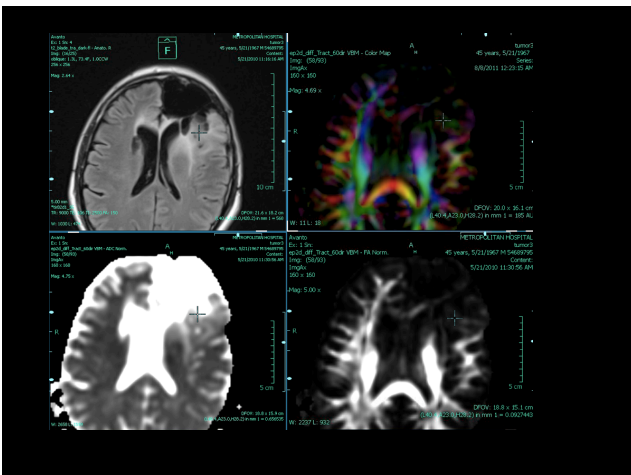
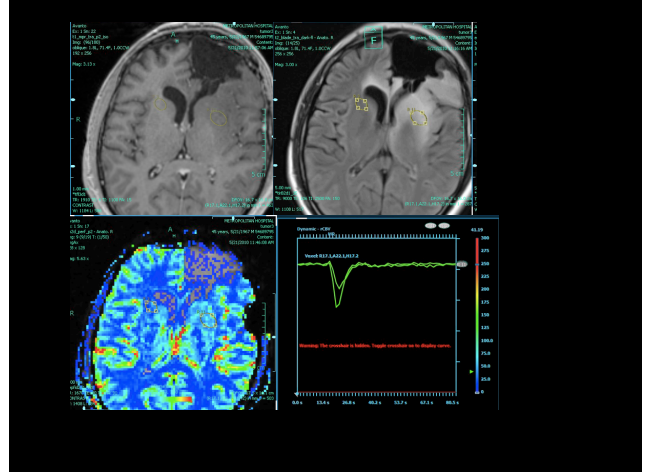
- ✓ Perfusion and DWI are providing insights into tumor behavior that are not available from conventional MRI and will likely be more important for assessment of tumor response to therapy
- ✓ T1 DCE Perfusion (Ktrans, Kep) can be used to assess therapeutic response
- ✓ Whole tumor histograms on ADC and rCBV are essential for therapeutic response assessment

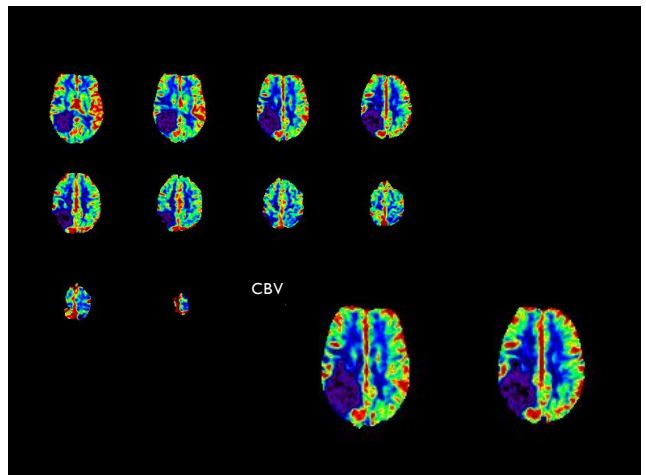
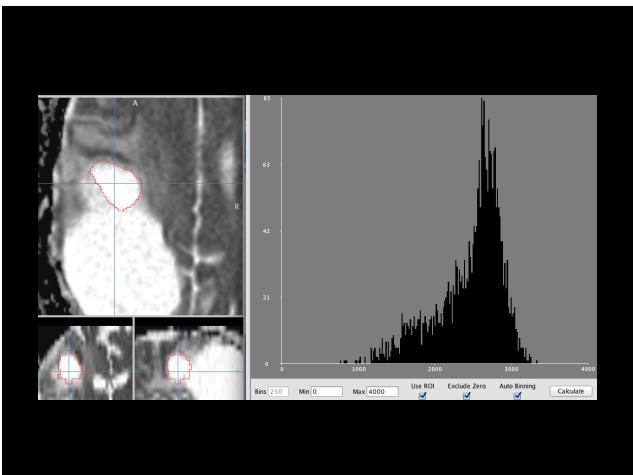
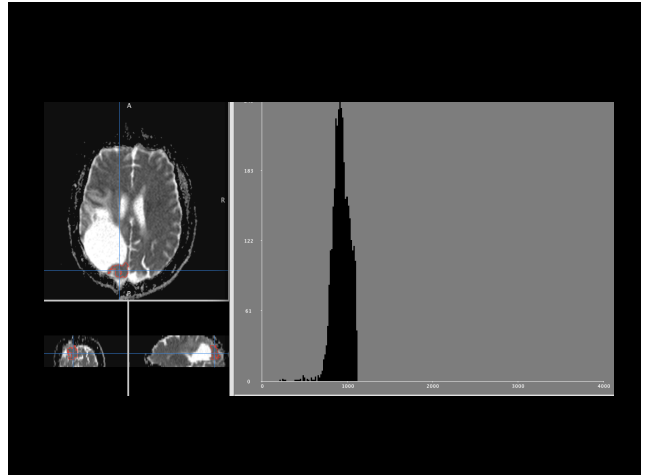
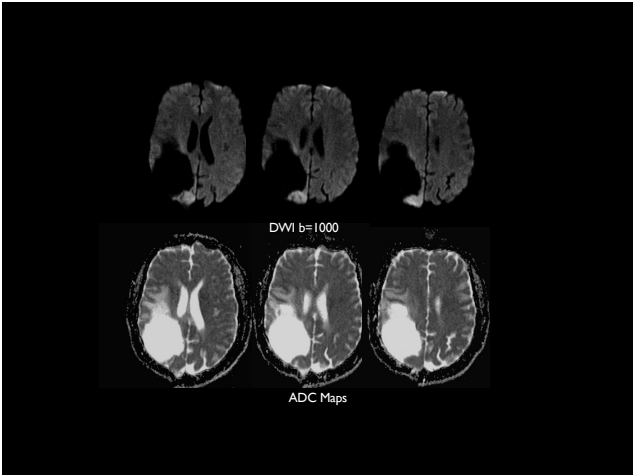


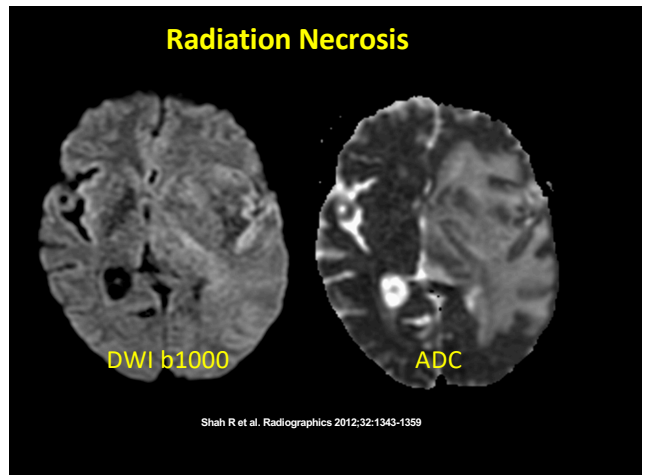
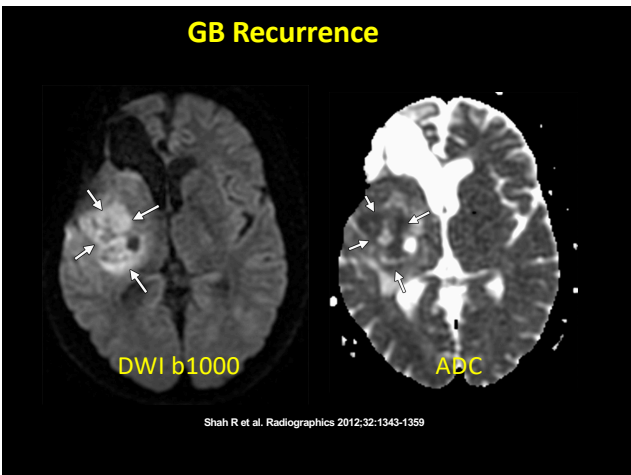
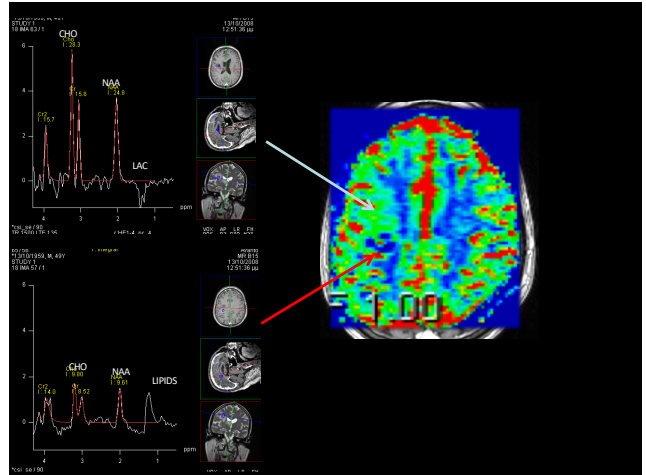
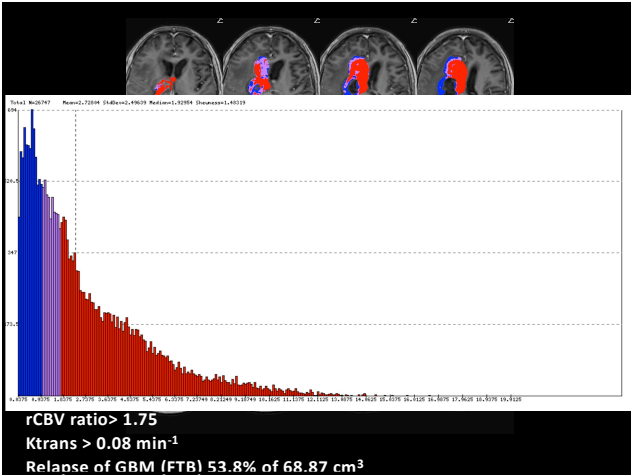


### Assessment of therapeutic response

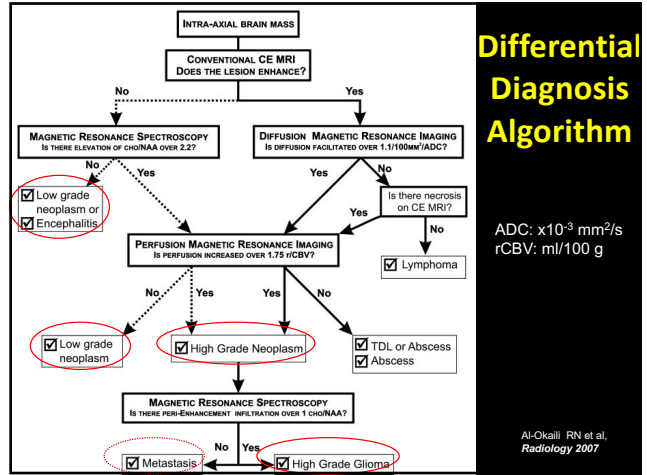
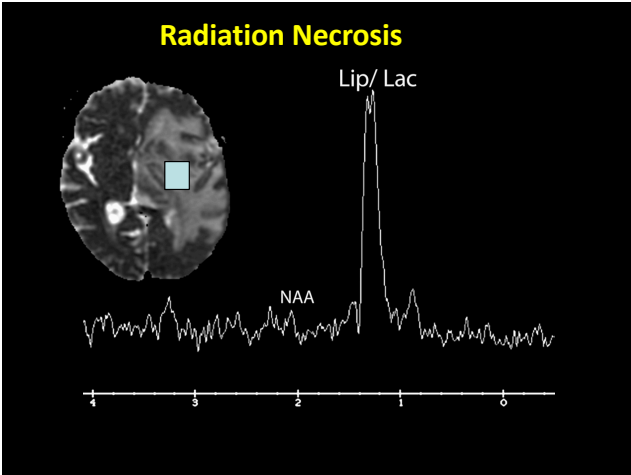
- ✓ Differentiation of radiation necrosis from recurrent disease may be based on low rCBV and absence of NAA and Cho peaks found on perfusion and MRS
- ✓ Low ADC indicates tumor recurrence while high ADC is present in radiation necrosis
- ✓ The significant reduction of FA with loss of color in diffusion directional maps is indicative of tumor recurrence





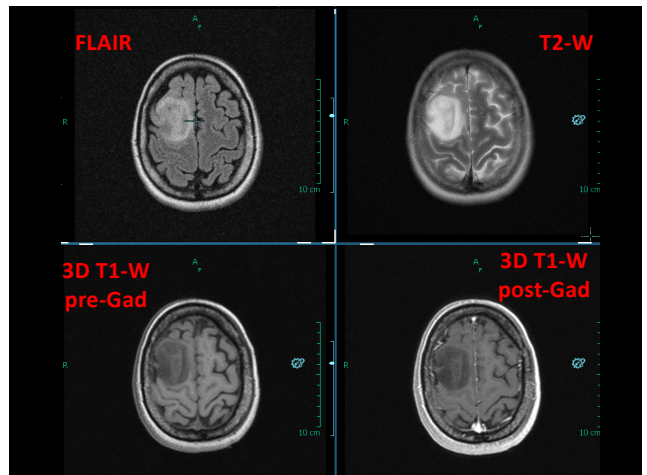


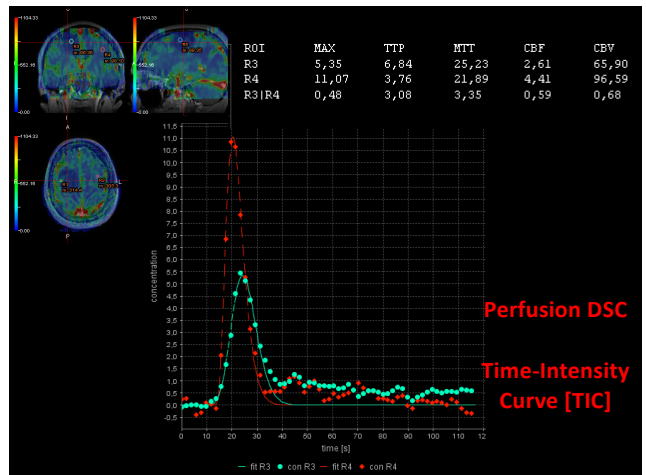
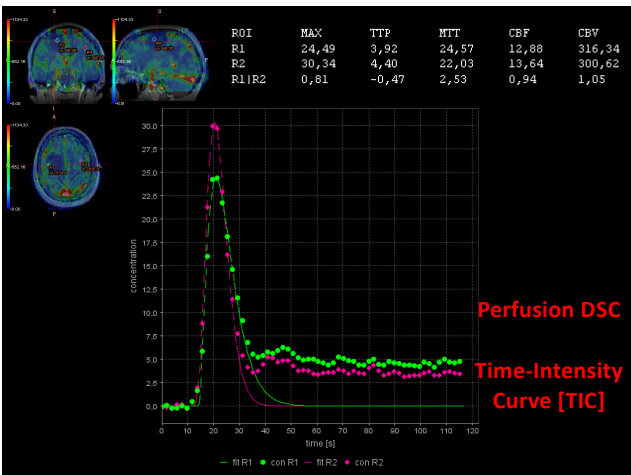
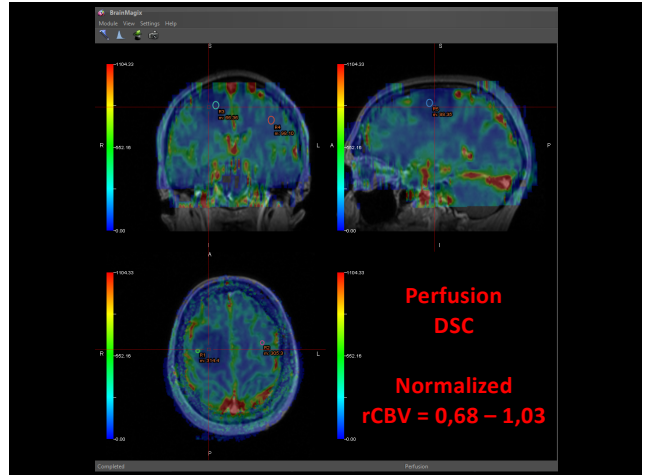
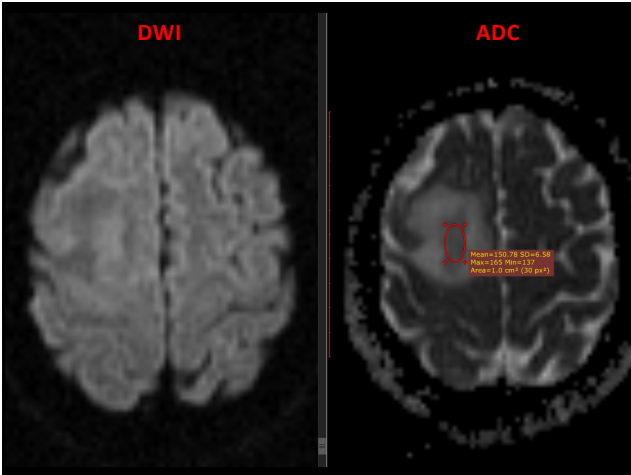


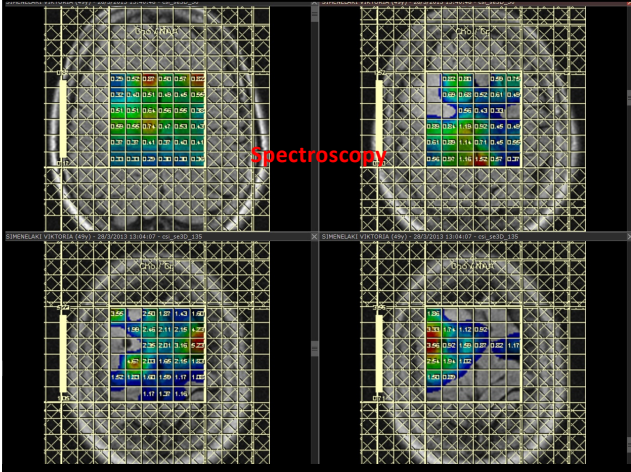


**49 years old female patient**

**Fibrillary Astrocytoma Grade II of the right frontal lobe with focal motion seizures of the left hand**







**C 1980 Protocol combining advanced and functional MRI with neuropsychological evaluation for patient-tailored therapy decision and treatment of brain masses**

**Poster No. C1980**

**Types:** Scientific Exhibit

**Keywords:** MRI, Neuroimaging, Brain, Oncology, MR-Diffusion/Perfusion, MR-Functional Imaging, MR-Gastroenterology, Physiological Studies, Surgery, Diagnostic Analysis, Radiotherapy, Cancer Care, Image Registration, Radiation

**Authors:** V. K. Katarova, S. Bostof, A. Katarova, E. Louca, N. Papanikolaou, G. Stroganov, T. Sabanovic, T. Zambanovic, T. Jussan, C. Vercelac

**DOI:** 10.1594/ncr2014/C-1980

**Section Results:**

- 63 patients were excluded from the study either due to inadequate cooperation and motion artifacts, which resulted in poor image quality, or because of other pathology.
- The remaining 236 patients included:
  - 82 high-grade gliomas (9 anaplastic astrocytomas),
  - 37 cases with low-grade gliomas,
  - 47 meningiomas,
  - 43 metastases,
  - 8 cavernomas/ arteriovenous malformations,
  - 7 lymphomas,
  - 3 inflammation,
  - 2 DNET,
  - 2 colloid cysts,
  - 2 epidermoids,
  - 3 developmental venous anomaly,
  - 1 DNET and
  - 1 post-infectious angli.

**Sidebar:**

Release of a DNET from its generating area.

21-year-old patient with a large aneurysm.

Based on the previously published algorithm (Figure 13) for brain tumors as seen above, to establish the correct diagnosis in 236/236 patients (98.3%) (10).

In respect of patients (60%) the combination of neuroanatomical and neurophysiological evaluation showed that gross total excision was possible, thus we proceeded with surgery instead of biopsy.

80% and DTI-FI were used for demonstration of the border of eloquent cortex activation and the metabolic delineation of the border of the brain, and not to define the tumor excision borders.

The imaging-based surgery in 143/152 (94%) of the patients achieved gross total excision, especially in the groups of low-grade gliomas and meningiomas.

In the rest 18 operations partial excision/biopsy or biopsy was performed.

In the 73 patients which were initially considered to be operated, radiotherapy or chemotherapy was applied.

23 of them could not be operated not because of the results of our combined protocol, but due to their bad clinical condition.

In 46 patients (19%), the final decision for surgical approach was based on the combination of the neuroimaging results and the neuropsychological evaluation, that supported the possibility of a wider post-surgical neurological deficit.

Concerning the pre- and post-surgical clinical condition of the patients 44 showed improvement, 2 deterioration, 20 mild or transient neurological deficit and 72 no direct change.

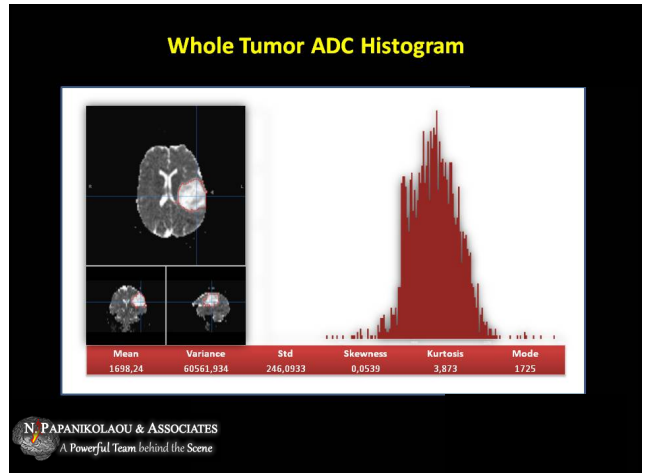
Protocol-based risk assessment before surgery had a high correlation with the clinical outcome achieved and compensated for 69% (153/220 patients) with only minimal deficits or no functional improvement (Figure 13).

**EPOS, ECR 2014**

**MULTIMODAL APPROACH**

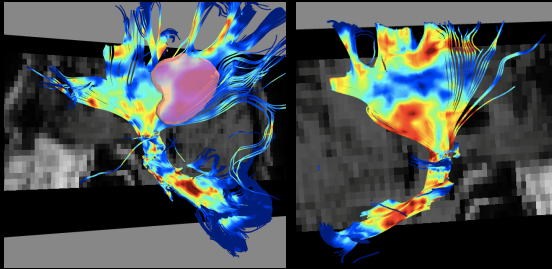
**ADVANCES / PERSPECTIVES of**

**ADVANCED MRI**





### DTI/DSI – Fiber Tracking



### Conclusions

#### MRI : Imaging modality of choice

Clinical Challenges	Conv MRI	DWI	DTI	Perfusion	MRS	fMRI
Detection, Localization, Morphology	++	++	-	-	-	-
Characterization – Grading	-	+++	+++	+++	+++	-
Differential Diagnosis	-	+++	-	+++	+++	-
Preoperative Mapping	+	-	+++	+++	++	+++
Radiotherapy Planning	-	-	+++	+++	+++	-
Stereotactic Biopsy Guidance	-	-	-	+++	+++	+++
Assessment of therapeutic response	-	+++	-	+++	++	-



Thank you very much for your attention !!!