

# ADVANCED NEUROIMAGING OF BRAIN TUMORS

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# Disclosures:

- I do not have financial interest in this presentation.
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# Neuroimaging in Neuro-oncology

## *Indications:*

- 1) Tumor diagnosis
- 2) Preoperative treatment planning
- 3) Intraoperative imaging
- 4) Postoperative care and treatment response.

# CURRENT PROBLEMS WITH ANATOMIC IMAGING

Highly sensitive but nonspecific

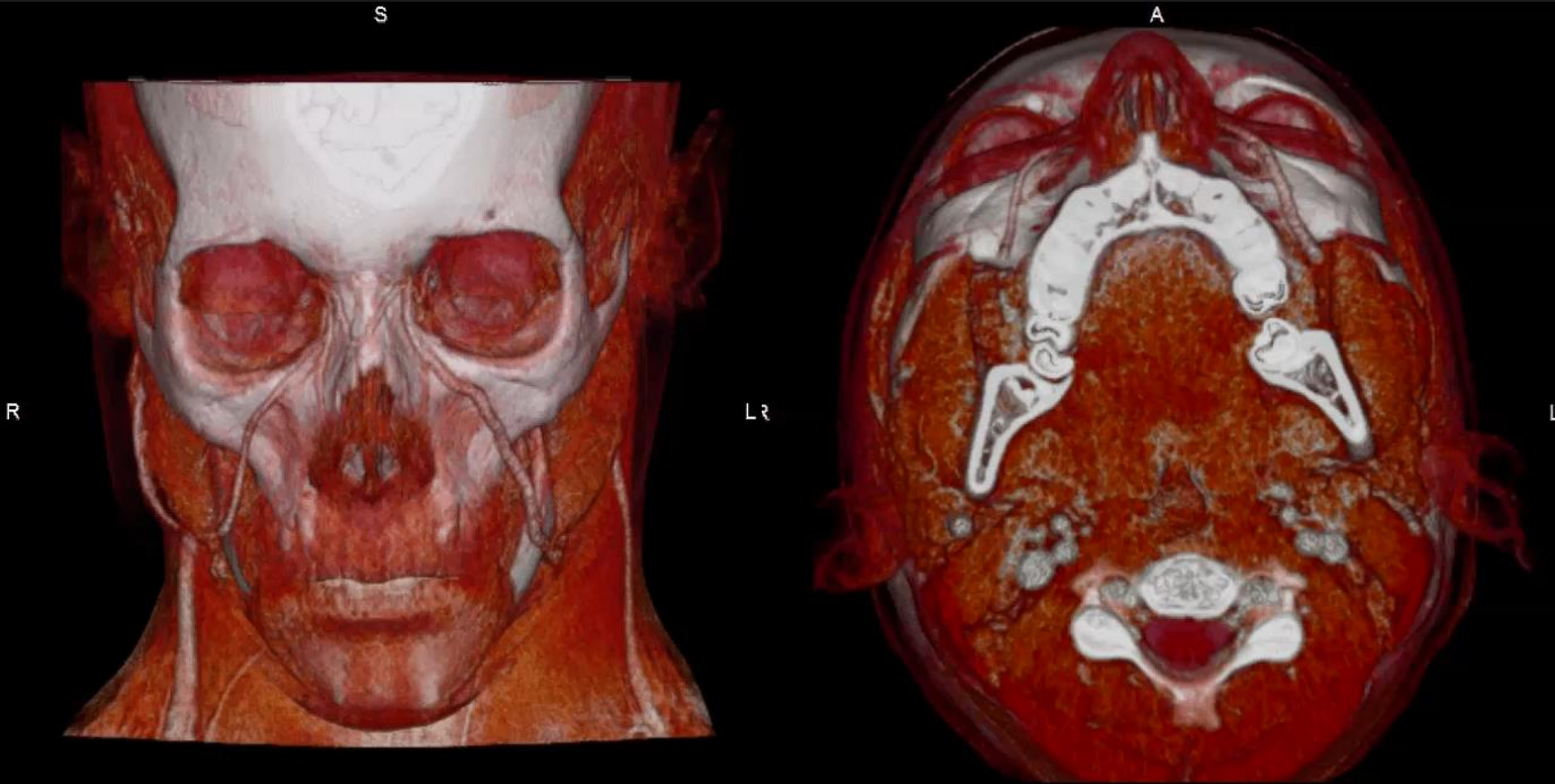
Cannot reliably differentiate tumor and treatment effects

Unable to guide specific targeted therapy

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Cannot assess early therapy failure & predict clinical outcome

# SKULL BASE MASS - PED



# IMAGING HAS TO DO A BETTER JOB IN....

- Characterizing brain tumor biology

Guiding therapy

Assessing therapeutic response

Detecting early treatment failure

Distinguishing tumor progression & treatment effects

Predicting clinical outcome

# ROUTINE ANATOMIC MRI SEQUENCES

- T1W.....anatomy
- T2W.....pathology
- FLAIR...more pathology
- STIR....fat vs blood
- GE/SWI...blood,calcium,flowing blood
- MRA/MRCV...vasculature
- DWI....acute stroke, hypercellularity

TUMOR PATHOLOGY ON MRI IS MOST OFTEN  
SEEN AS:

*Long T1*

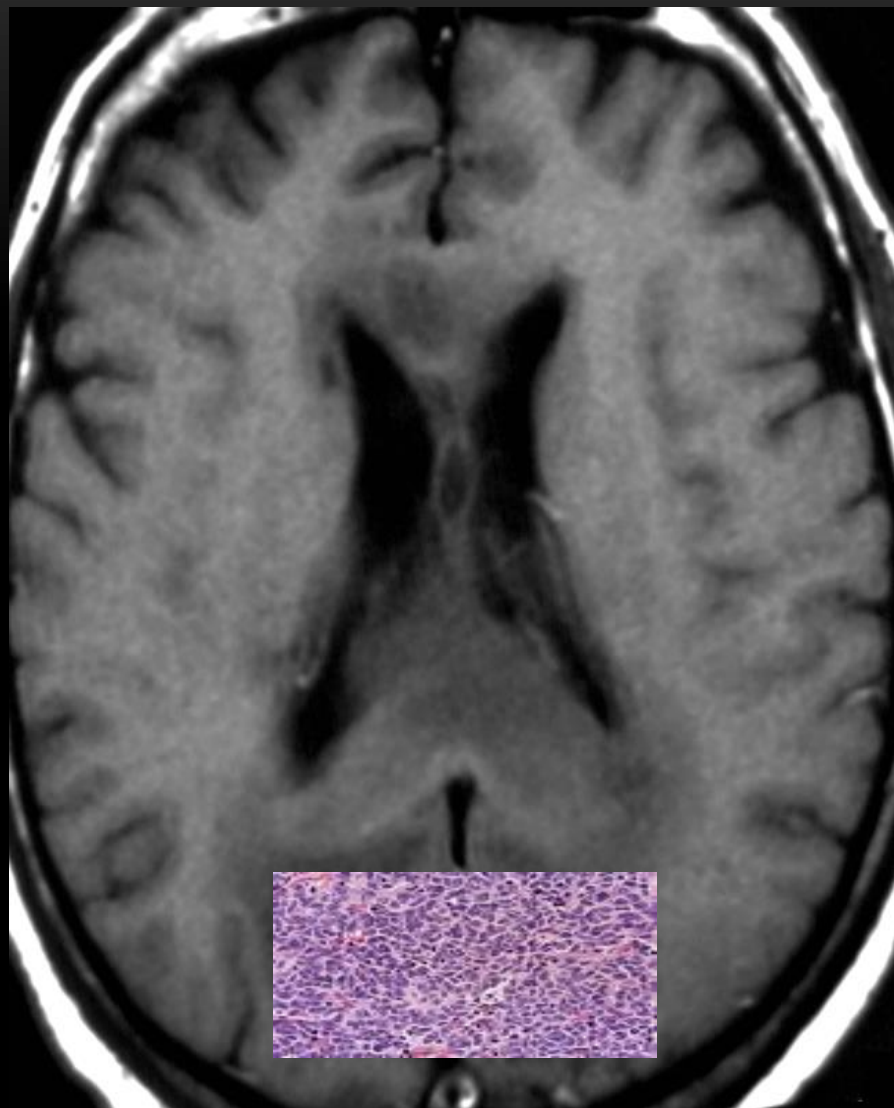
*and*

*Long T2*

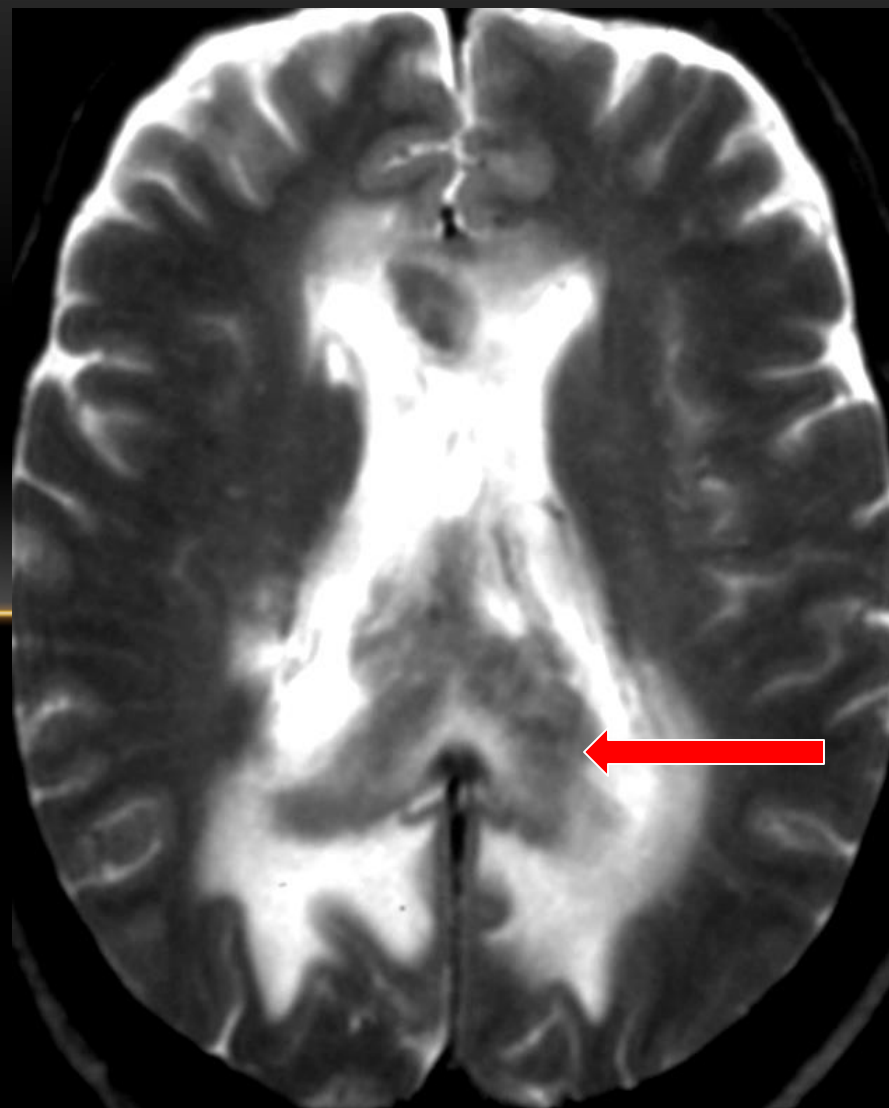




# PCNSL: IMMUNOCOMPETENT

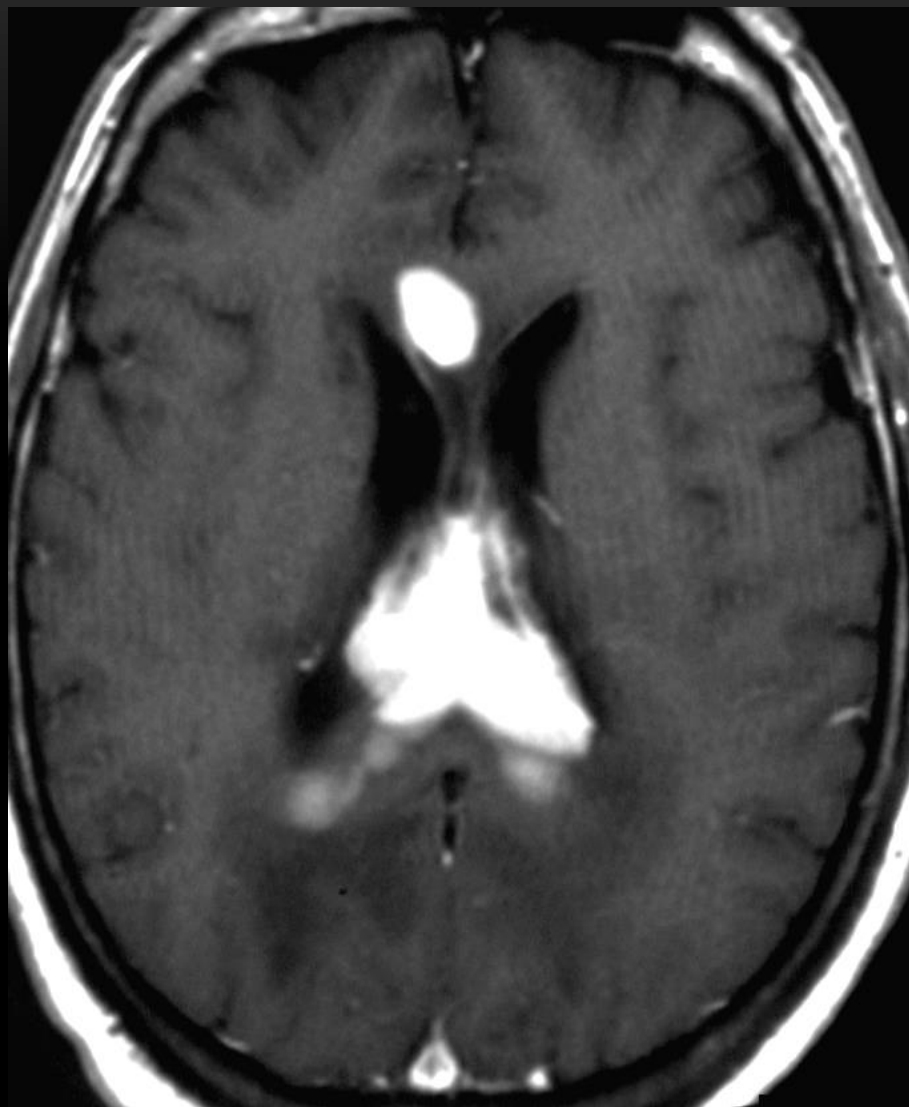


T1-non



T2

# PCNSL: IMMUNOCOMPETENT



T1-gad



T1-gad

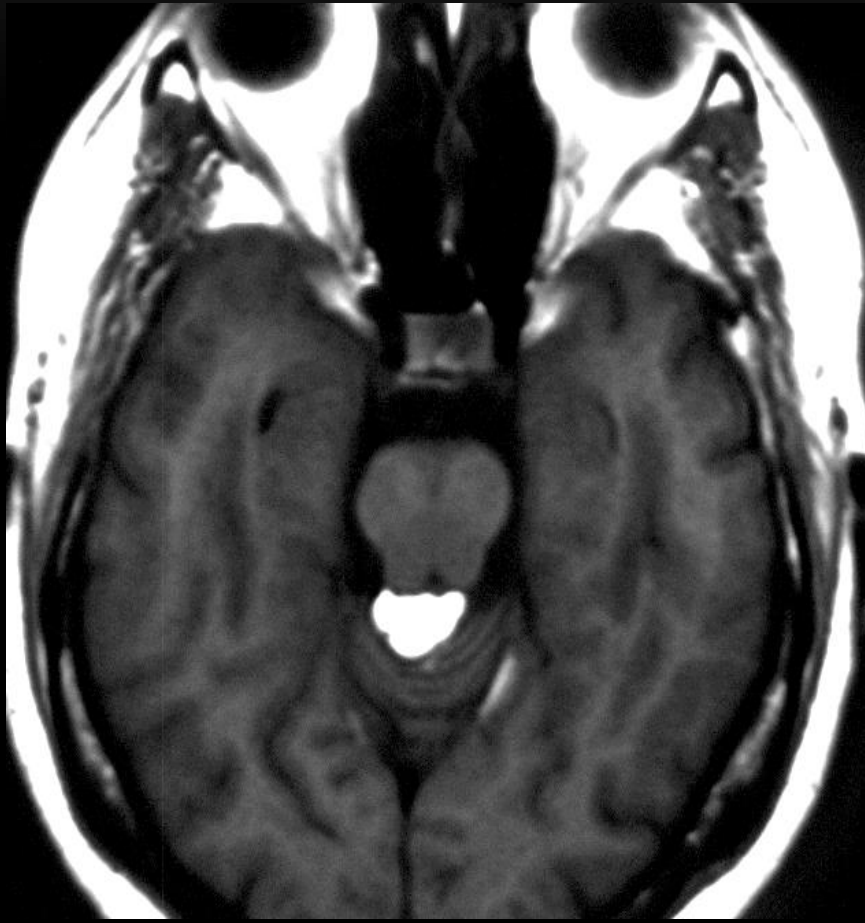
# SHORT T2 (HYPOINTENSITY)

Iron within necrosis  
Hemosiderin (chronic bleed)  
Deoxyhemoglobin (acute bleed)  
Melanin  
Ferritin  
Calcification  
High nucleus:cytoplasm ratio (PNET,  
lymphoma)  
Dense cellularity  
Macromolecule content  
Fibrocollagenous stroma  
Mucin (colon carcinoma)  
High protein content (Craniopharyngeoma)  
Fast flowing blood (Hemangioblastoma, GBM)  
Air

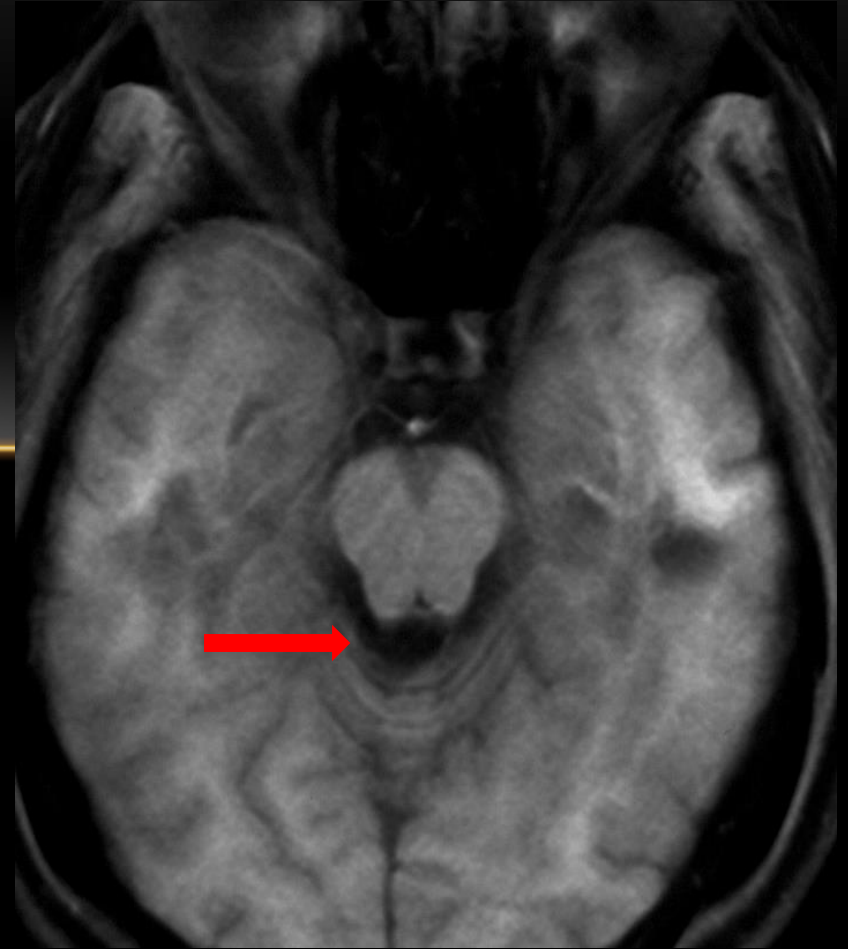
# SHORT T1 (HYPERINTENSITY)

Melanin  
Manganese  
Iron  
Calcium  
Copper  
High protein (colloid cyst)  
Methemoglobin (subacute blood)  
Fat (lipoma, dermoid)  
Cholesterol  
Paramagnetic agent (gadolinium)  
Flow-related enhancement  
in tumor vessel

# INTRACRANIAL LIPOMA VS. BLEED FAST MRI

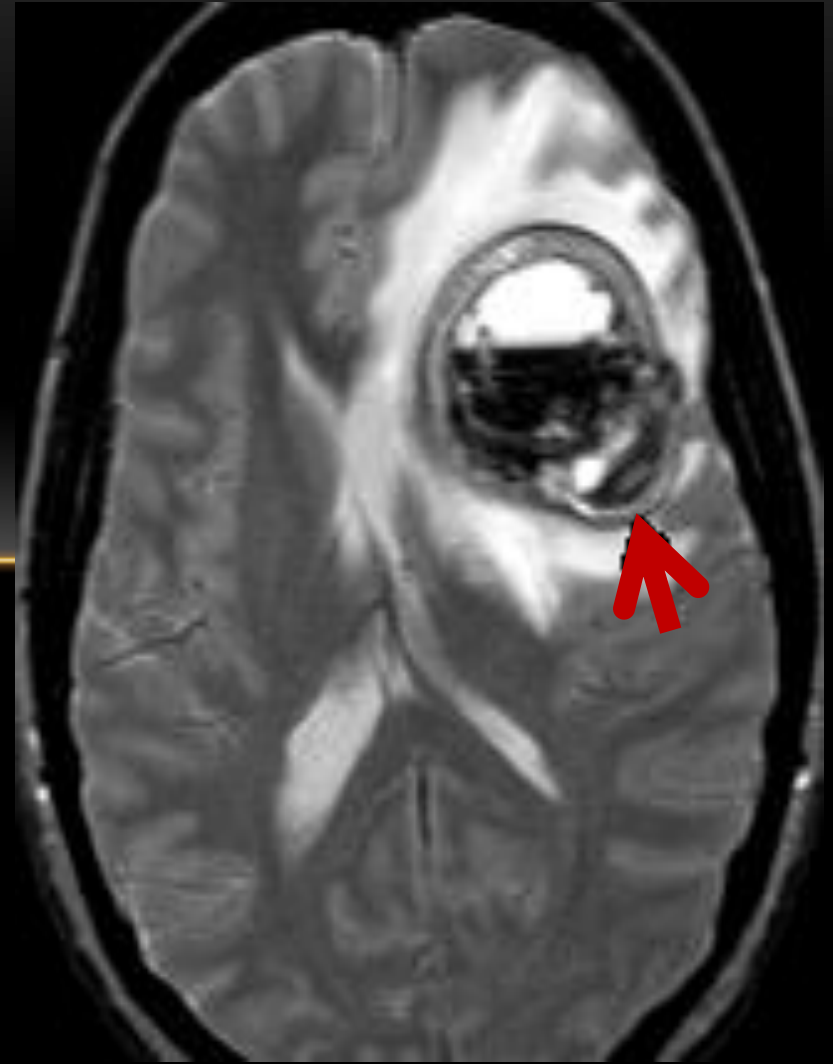


T1-non



T1-fatsat

# BRAIN METASTASES: MELANOMA



## Transition from

**Anatomy → Physiology → Biology**

# ADVANCED NEUROIMAGING

- **Diffusion-weighted imaging / DTI**

**Proton MR Spectroscopy**

**Functional MRI**

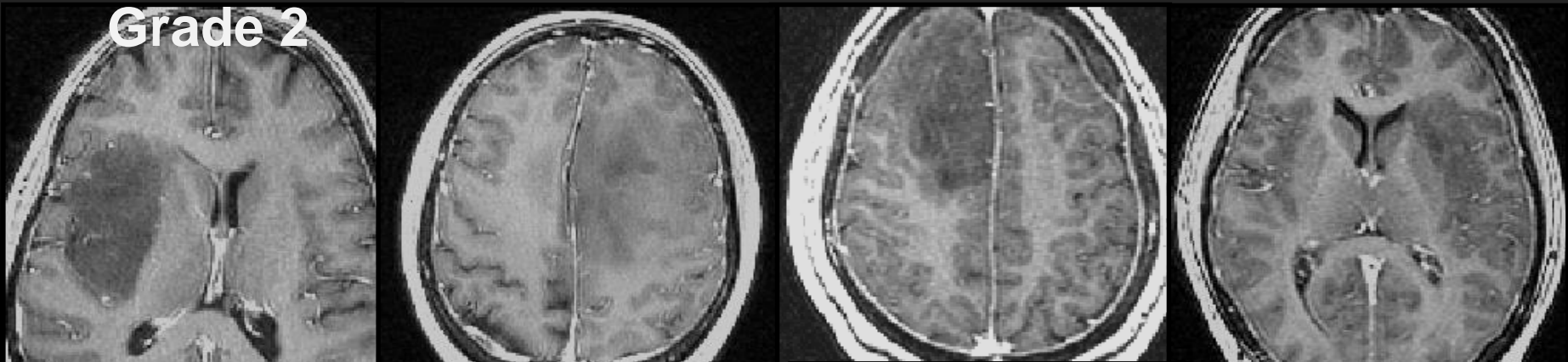
**Perfusion-weighted imaging**

**Intraoperative MRI**

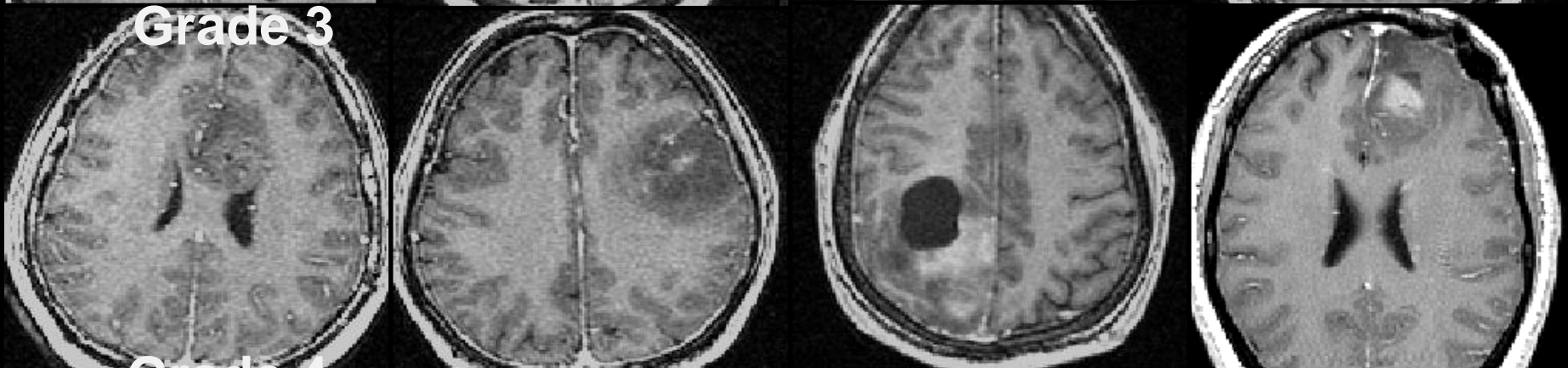
**Ultra-high field MRI**

# HETEROGENEITY OF GLIOMAS ON MRI

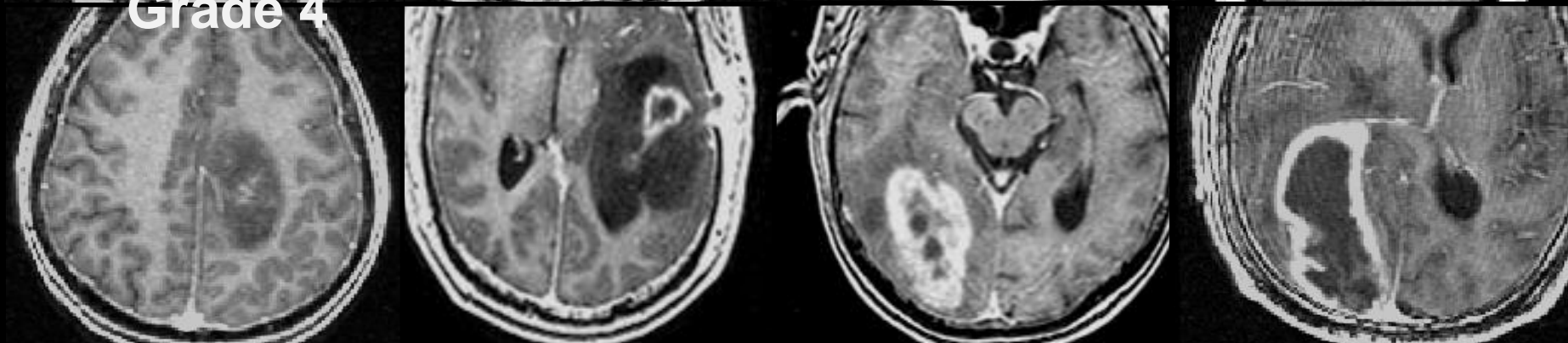
Grade 2



Grade 3

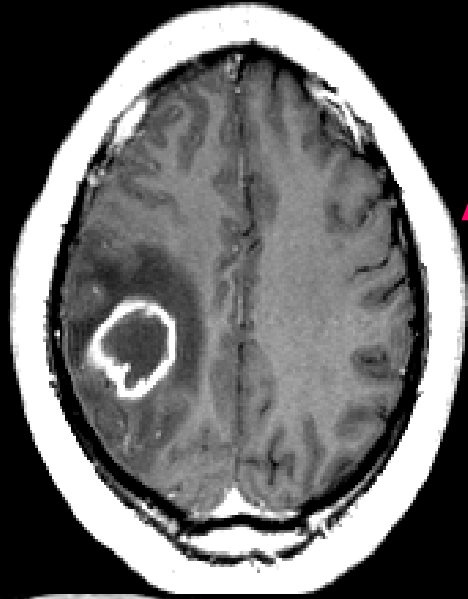


Grade 4



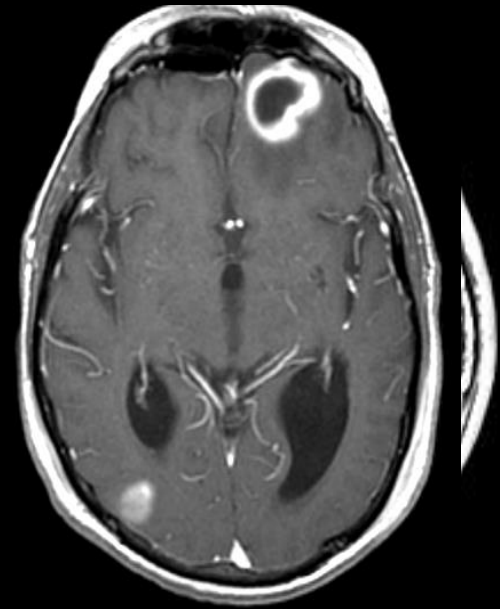


# CONTRAST ENHANCEMENT ON MRI IS NONSPECIFIC!

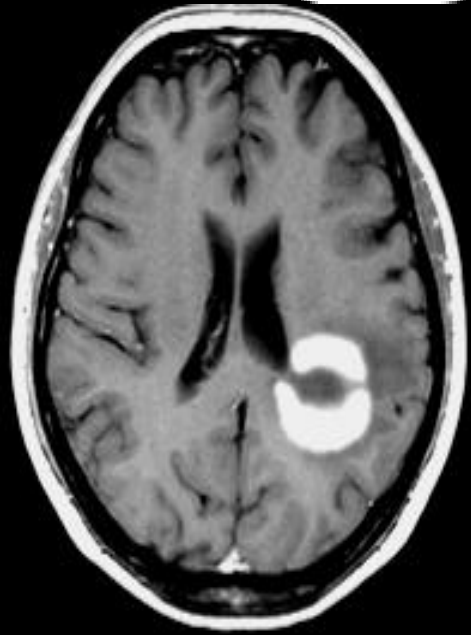


Abscess

Glioblastoma ?

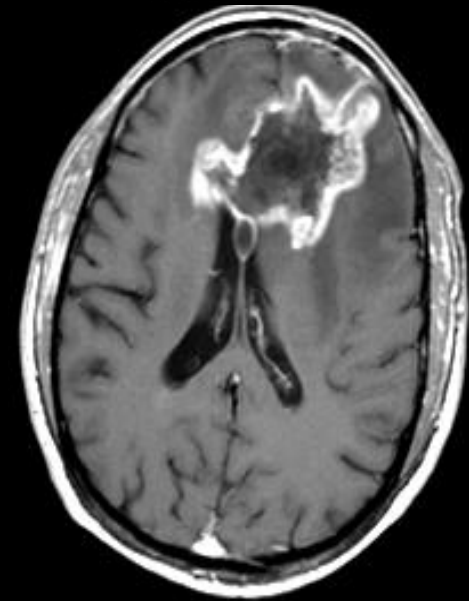


TB

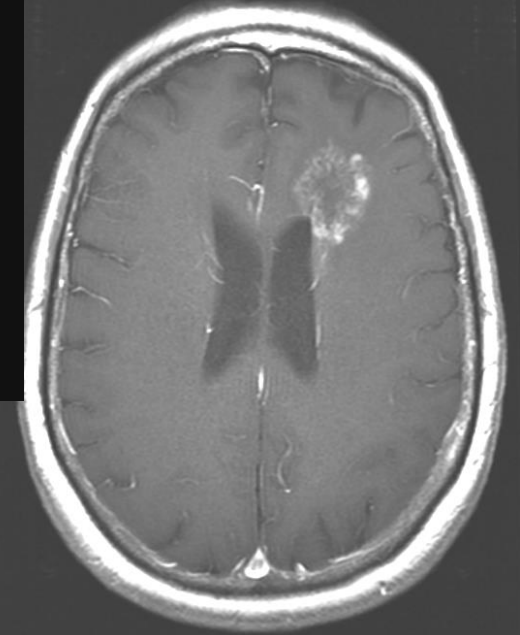
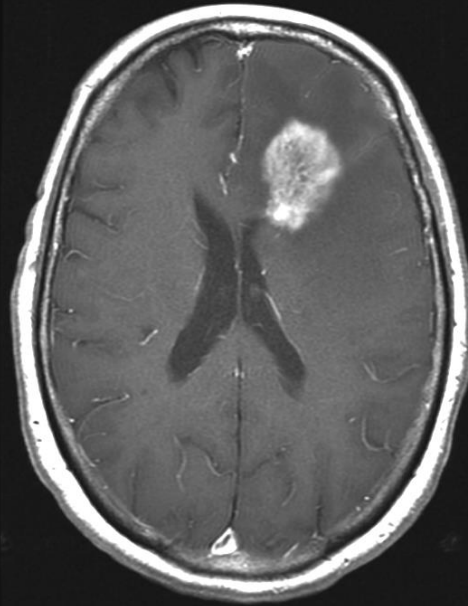


Demyelinating lesion

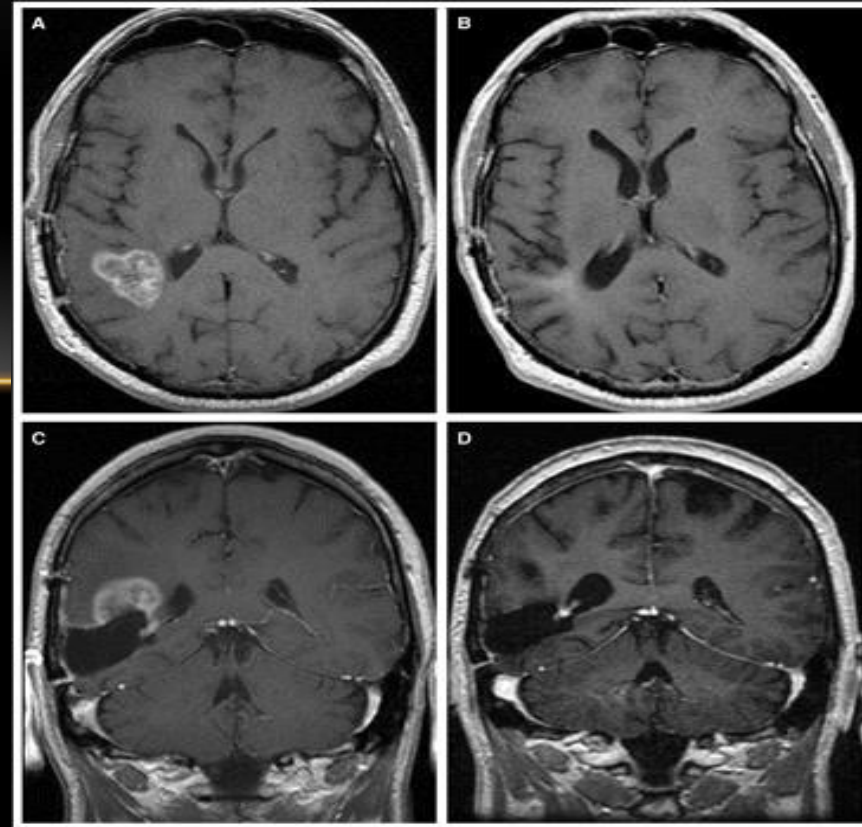
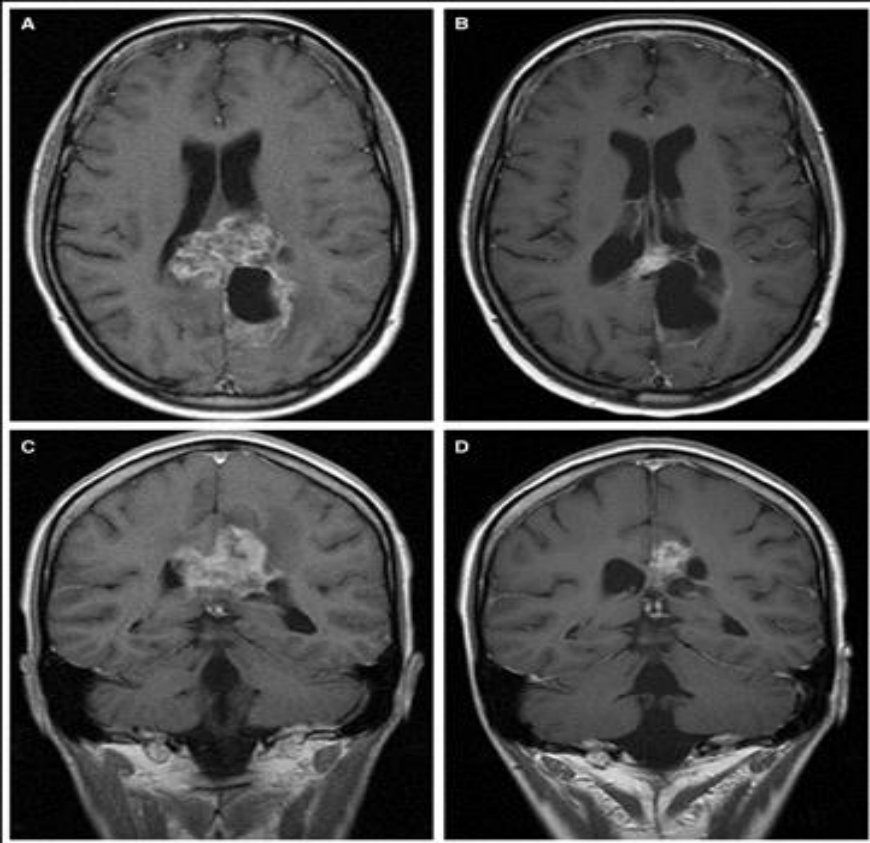
radiation necrosis



# PSEUDOPROGRESSION POST CHEMORADIOOTHERAPY



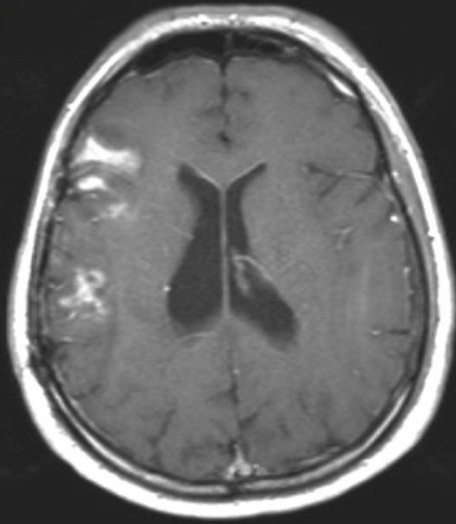
# BEVACIZUMAB + IRINOTECAN FOR RECURRENT GLIOBLASTOMA



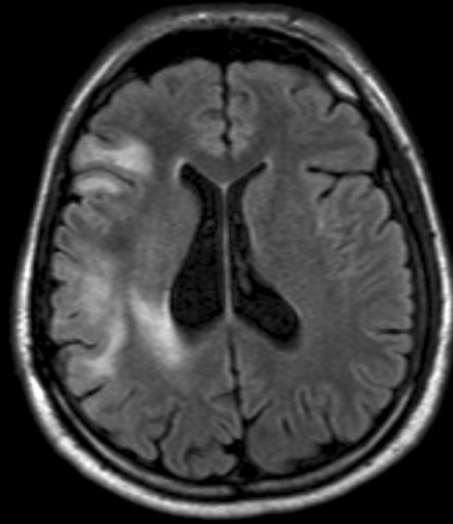
T1-Gd response

# PSEUDO-NORMALIZATION

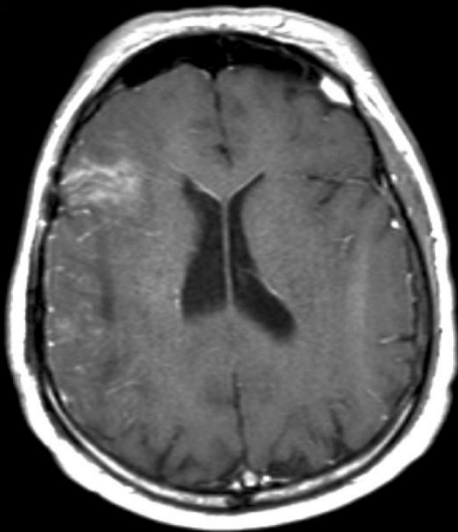
**A**



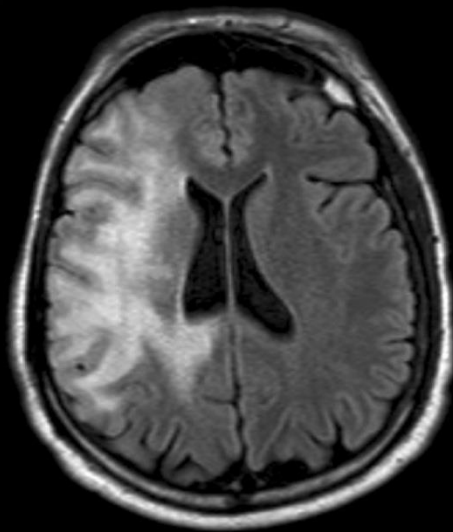
**B**



**C**



**D**



# 55 Y/O WITH PROGRESSIVE QUADRAPLEGIA AND LETHARGY

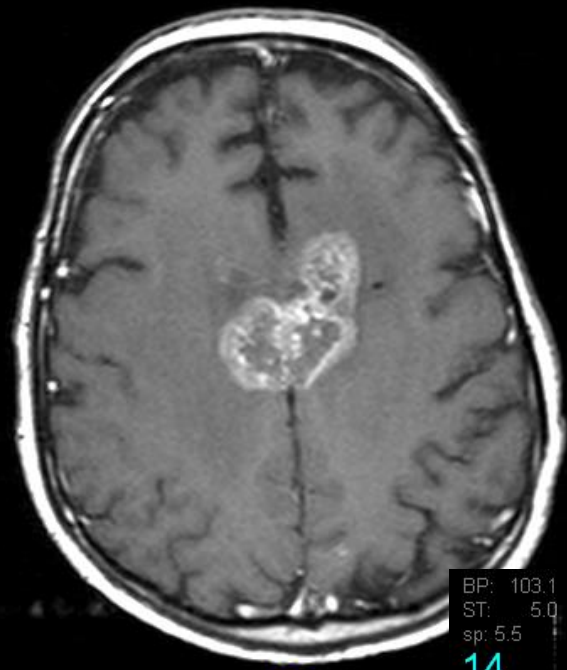
BP: 36.8  
ST: 5.0  
sp: 5.5  
17

TR: 575.2  
TE: 13.0  
FA: 90.0  
512x512  
NEX: 1.0

BP: 36.1  
ST: 5.0  
sp: 5.5  
17

TR: 8000.0  
TE: 120.0  
TI: 2300.0  
FA: 90.0  
512x512  
NEX: 2.0

R

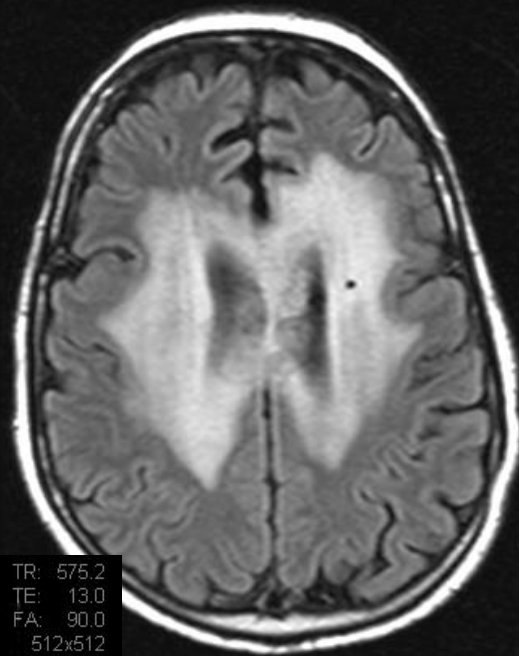


Lossy 1:9  
11:17  
Zoom:1.0

BP: 103.1  
ST: 5.0  
sp: 5.5  
14

L

R



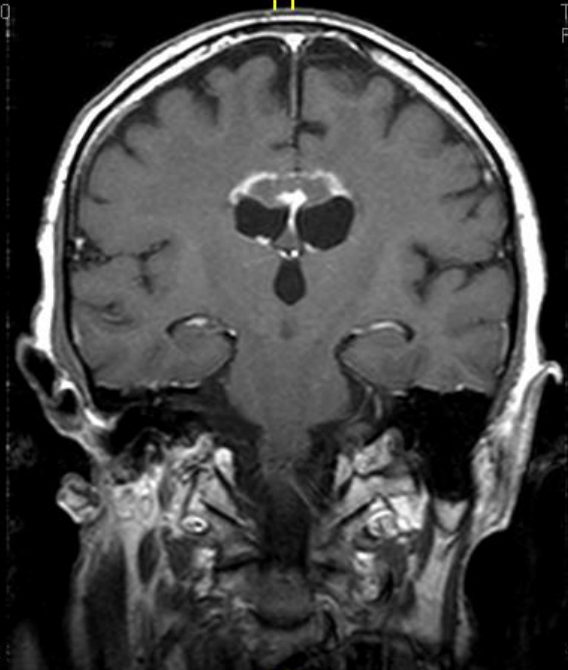
W: 1837  
C: 816  
Fast Brain \*FLAIR AX\*

P

H

R

L



Lossy 1:9  
11:18  
Zoom:1.0

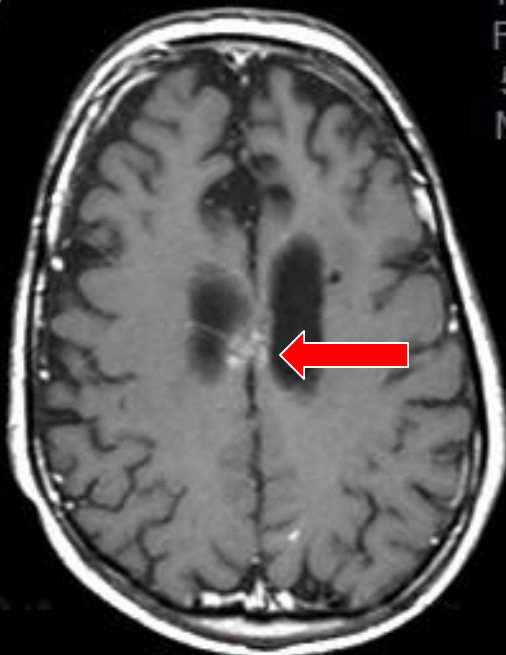
W: 1277  
C: 893  
Fast Brain \*T1 COR\*CE

F

BP:39.0  
ST: 5.0  
sp: 5.5

18

R



L

10:21  
Zoom:0.6

P

Fast Brain \*T1 AX CE

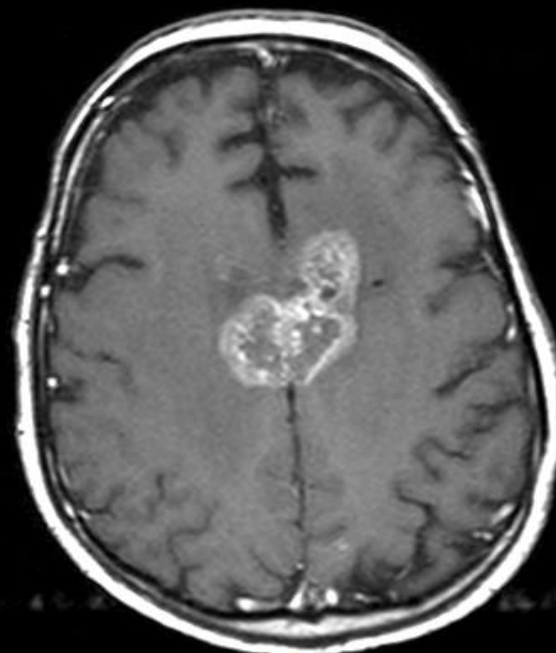
W:999  
C: 585

TR:642.7  
TE: 13.5  
FA: 90.0  
512x512  
NEX: 1.0

BP: 36.8  
ST: 5.0  
sp: 5.5

17

R



L

9 Lossy 1:9  
11:17  
J Zoom:1.0

P

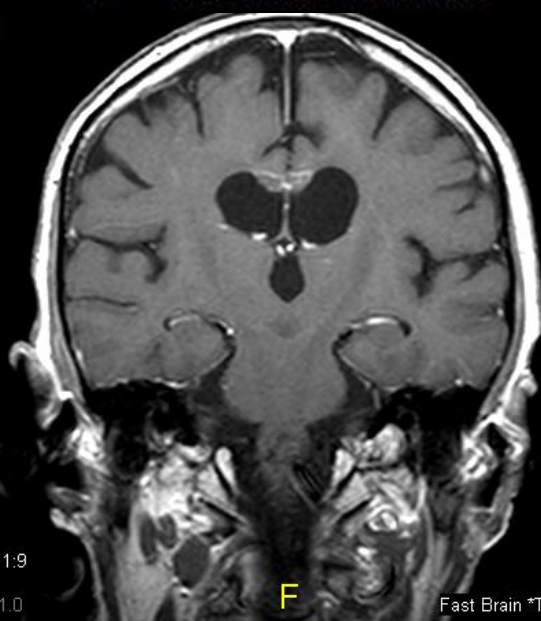
Fast Brain \*T1 AXIAL\*CE

W: 1198  
C: 636

TR: 575.2  
TE: 13.0  
FA: 90.0  
512x512  
NEX: 1.0

14

R



L

Lossy 1:9  
10:05  
Zoom:1.0

F

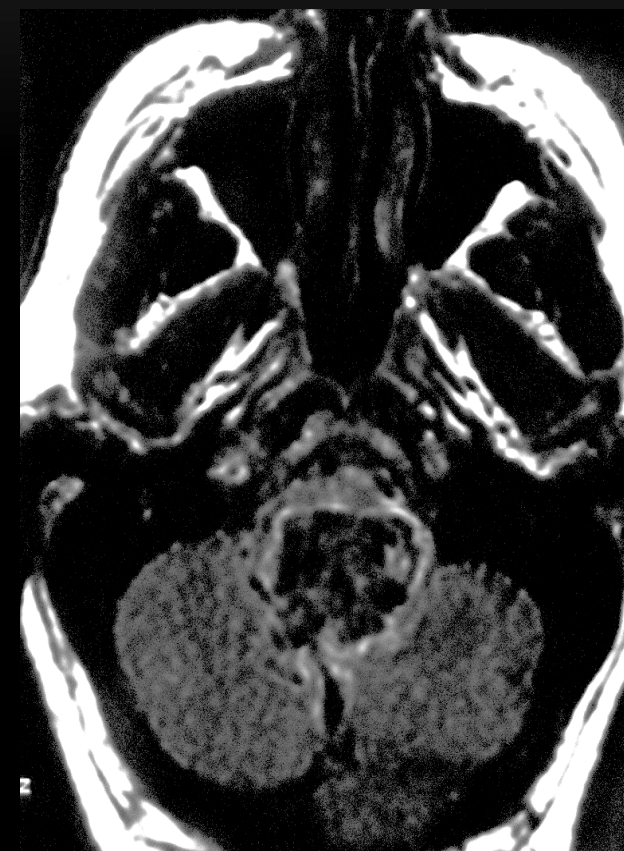
W: 1049  
C: 603  
Fast Brain \*T1 COR\*CE

# Pre-bevacizumab

# DWI IN NEURO-ONCOLOGY

- **tumor differential diagnosis**
- **tumor grade and cellularity**
- **postoperative injury**
- **integrity of white matter tracks**

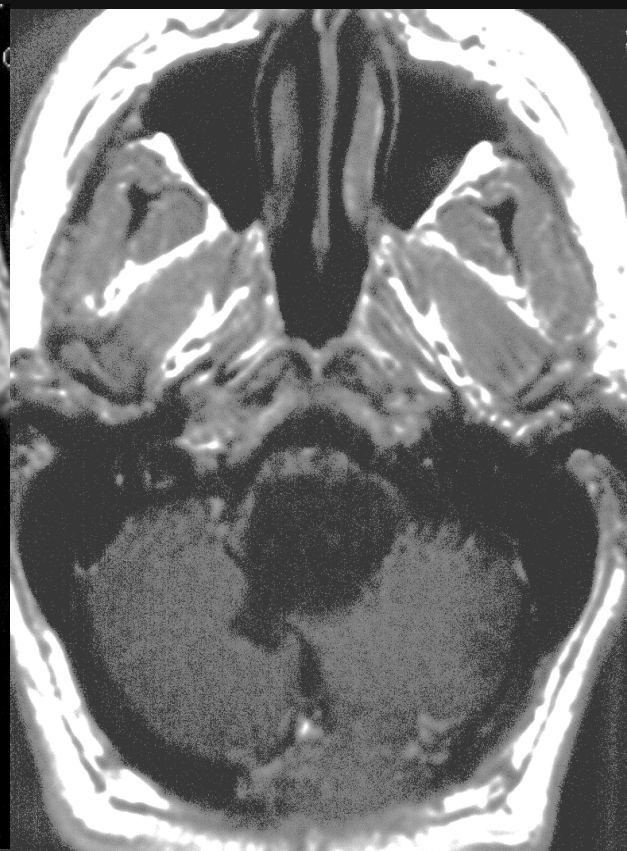
# EPIDERMOID CYST



**FLAIR**



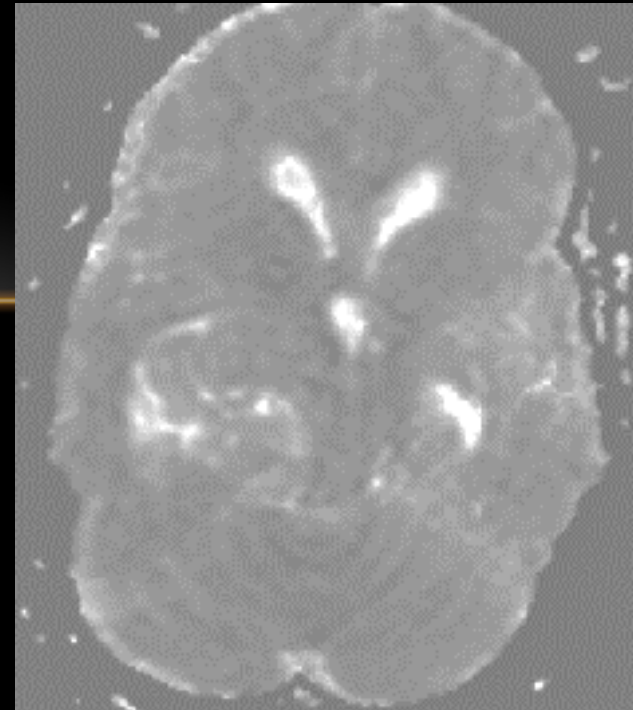
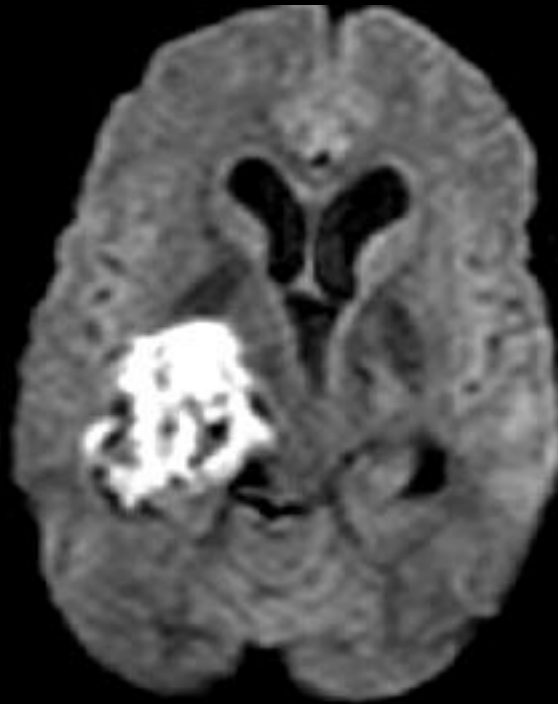
**T2**



**T1-gad**



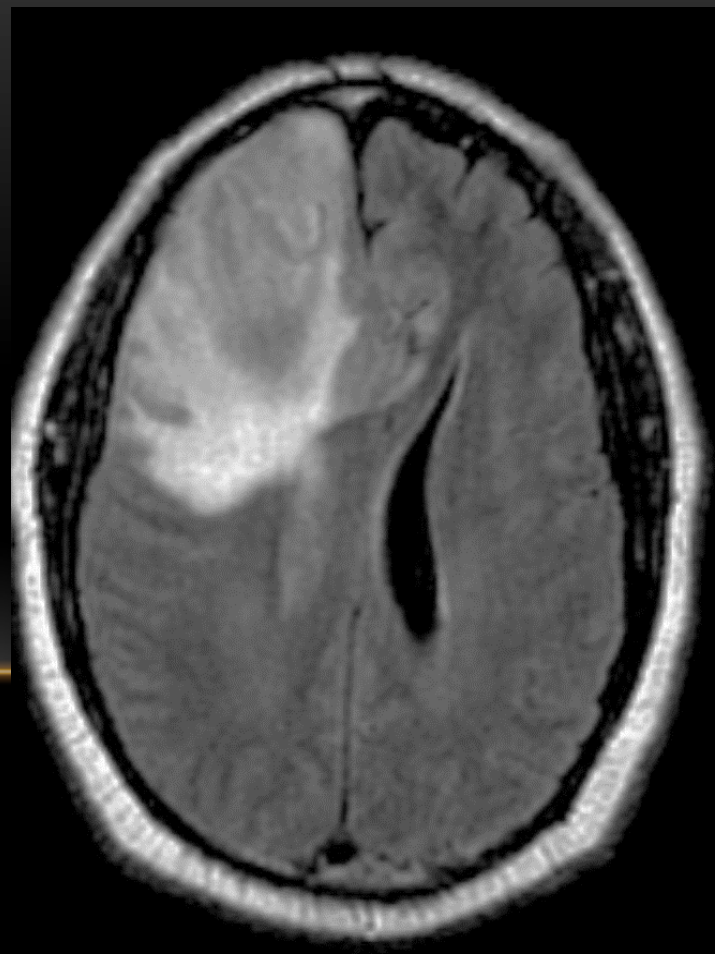
# EPIDERMOID CYST! DECREASED WATER DIFFUSION



TUMOR?



T1-post

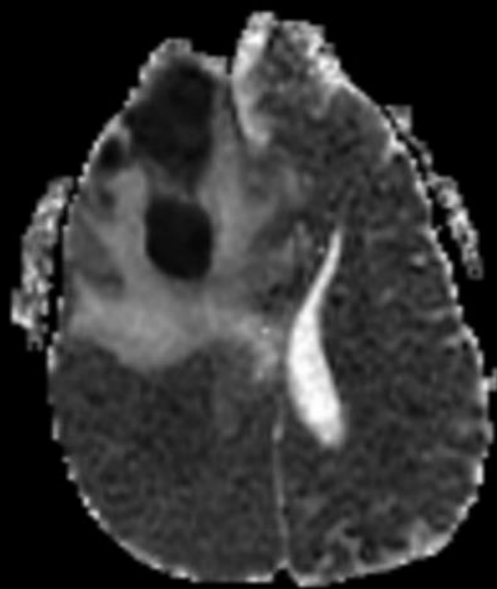
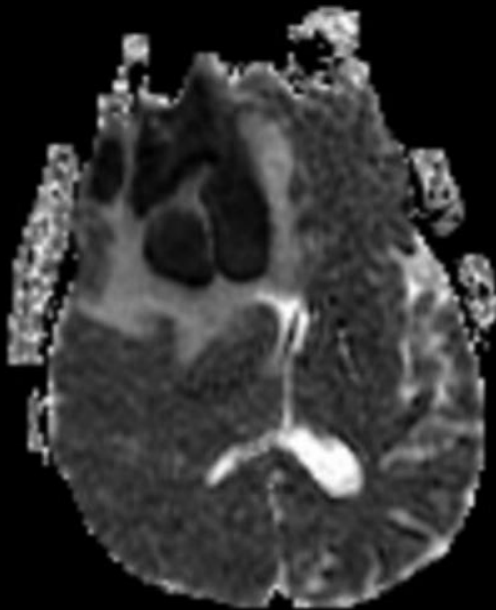
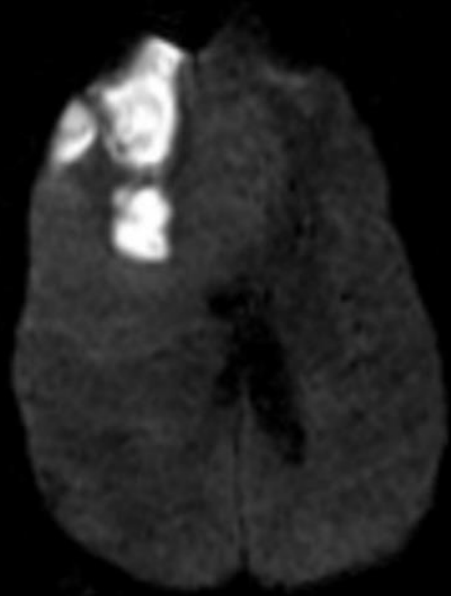
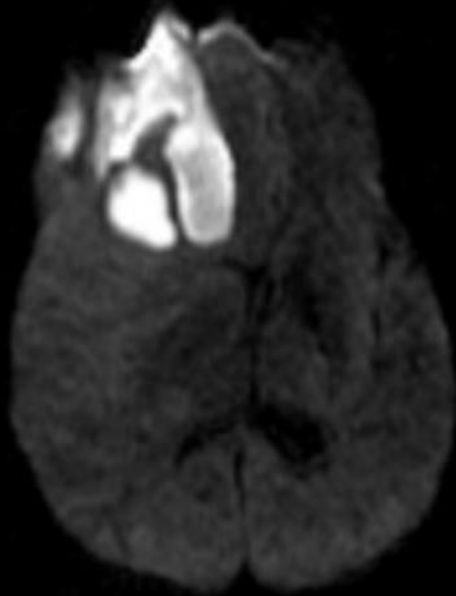


FLAIR

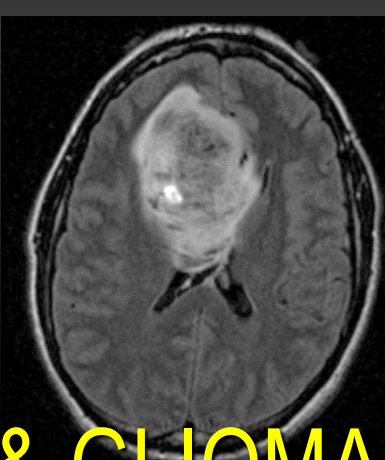
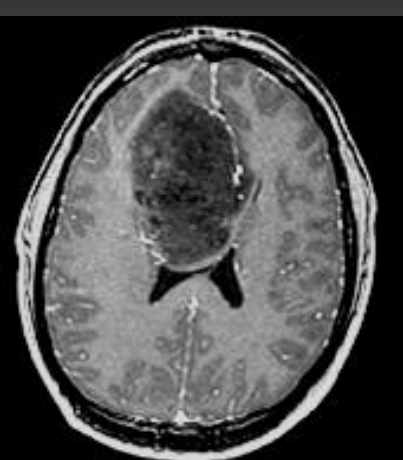
DWI

ABSCCESS

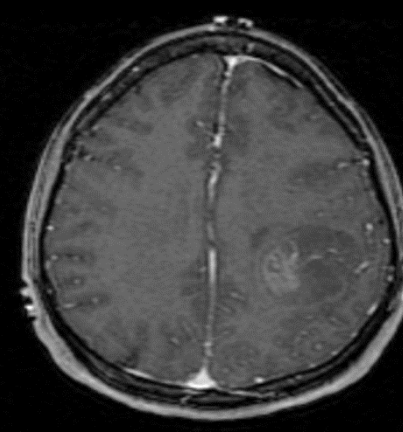
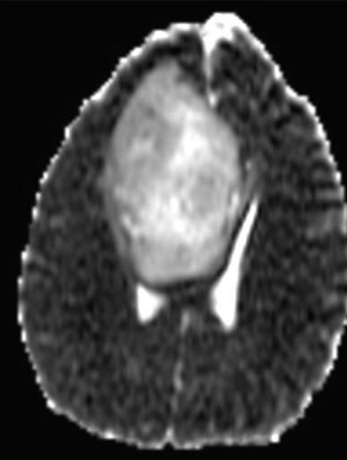
ADC



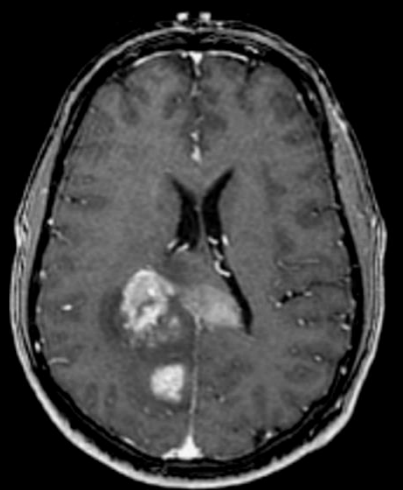
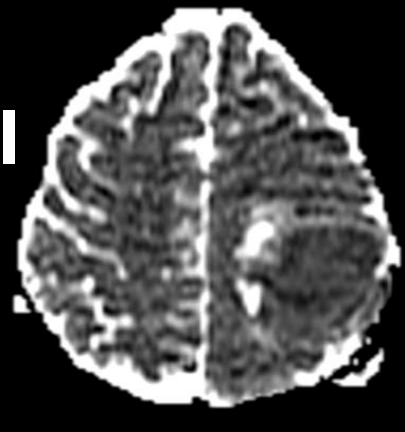
# ADC & GLIOMA GRADE



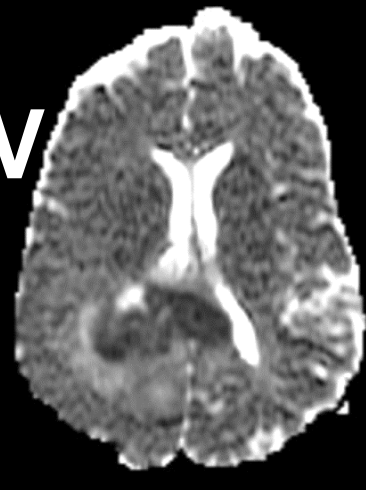
II



III



IV



PRE-OP

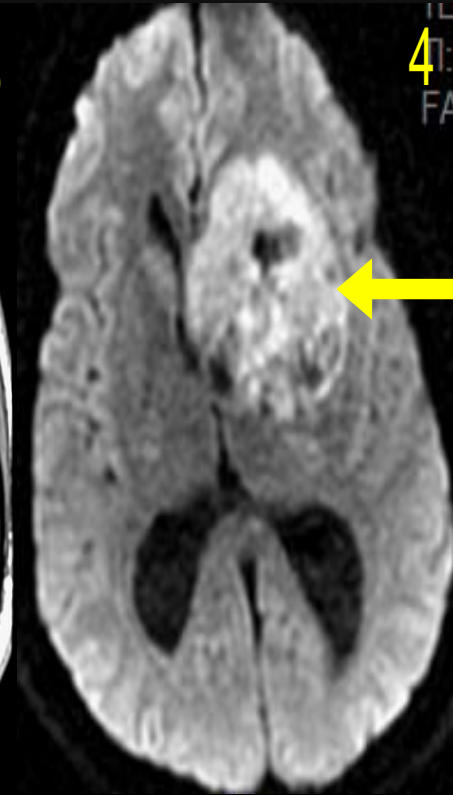
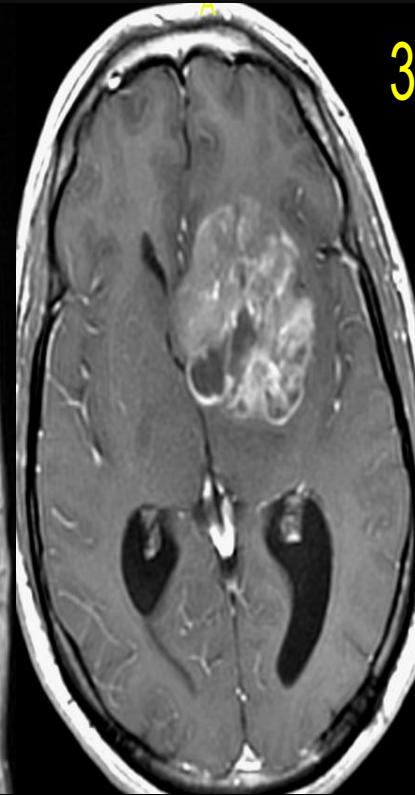
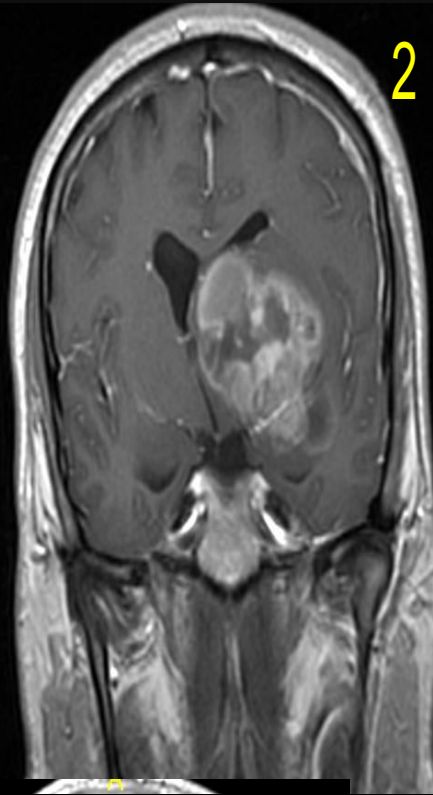
25 Y/O MAN PRESENTING WITH RIGHT SIDED WEAKNESS

MRA

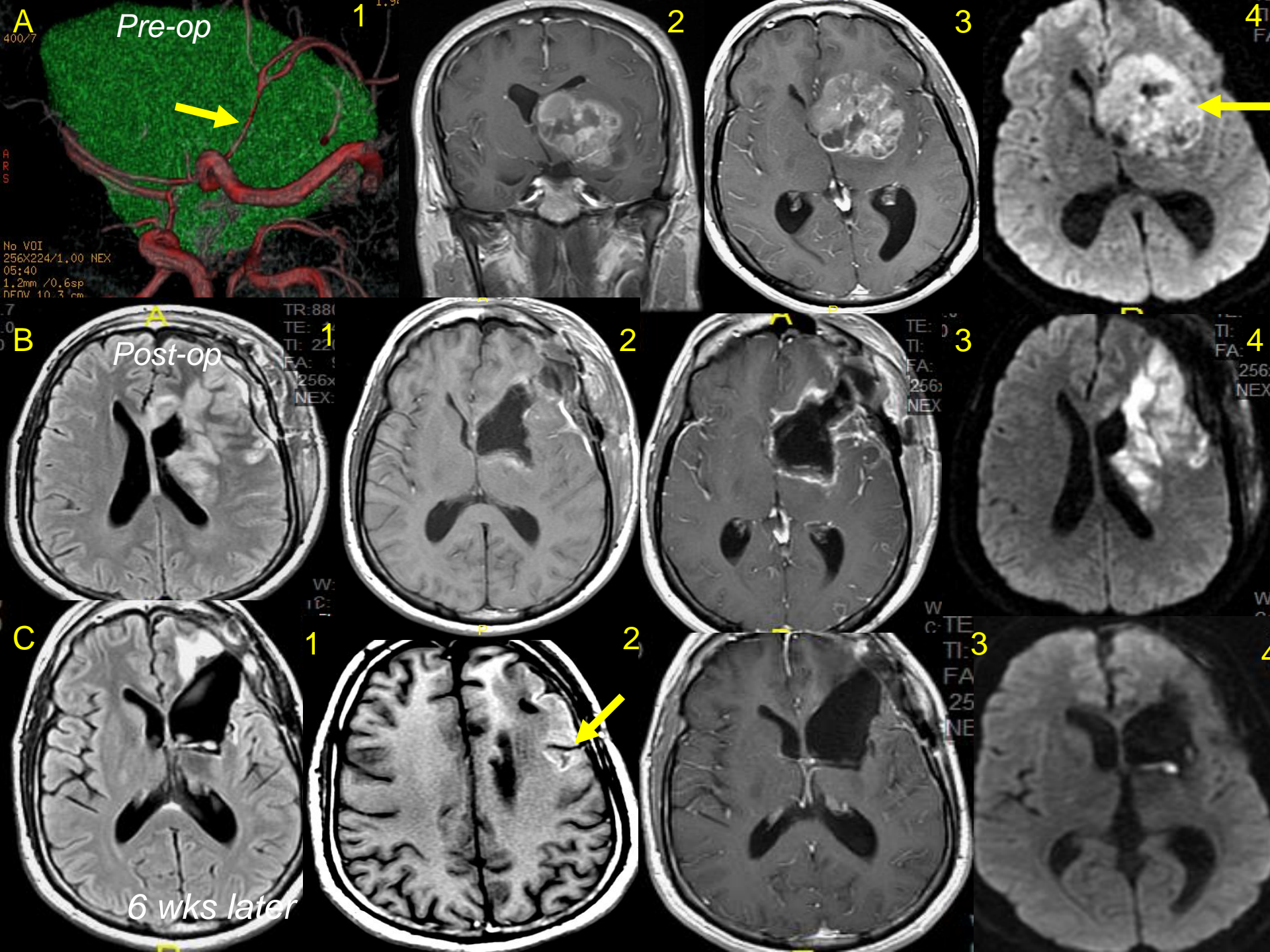
T1W coronal gd+

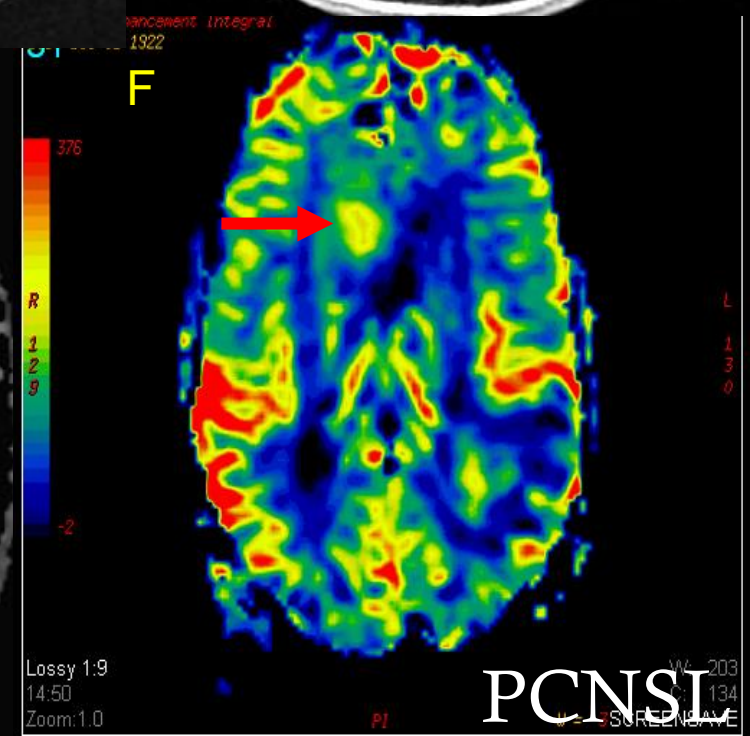
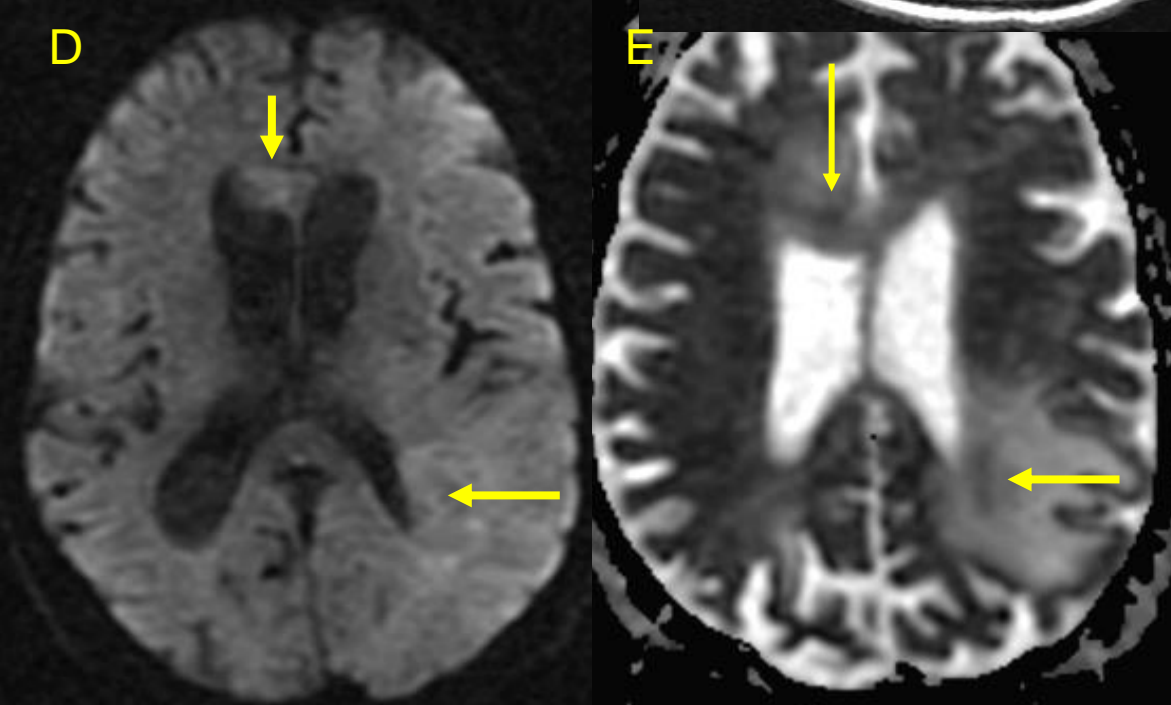
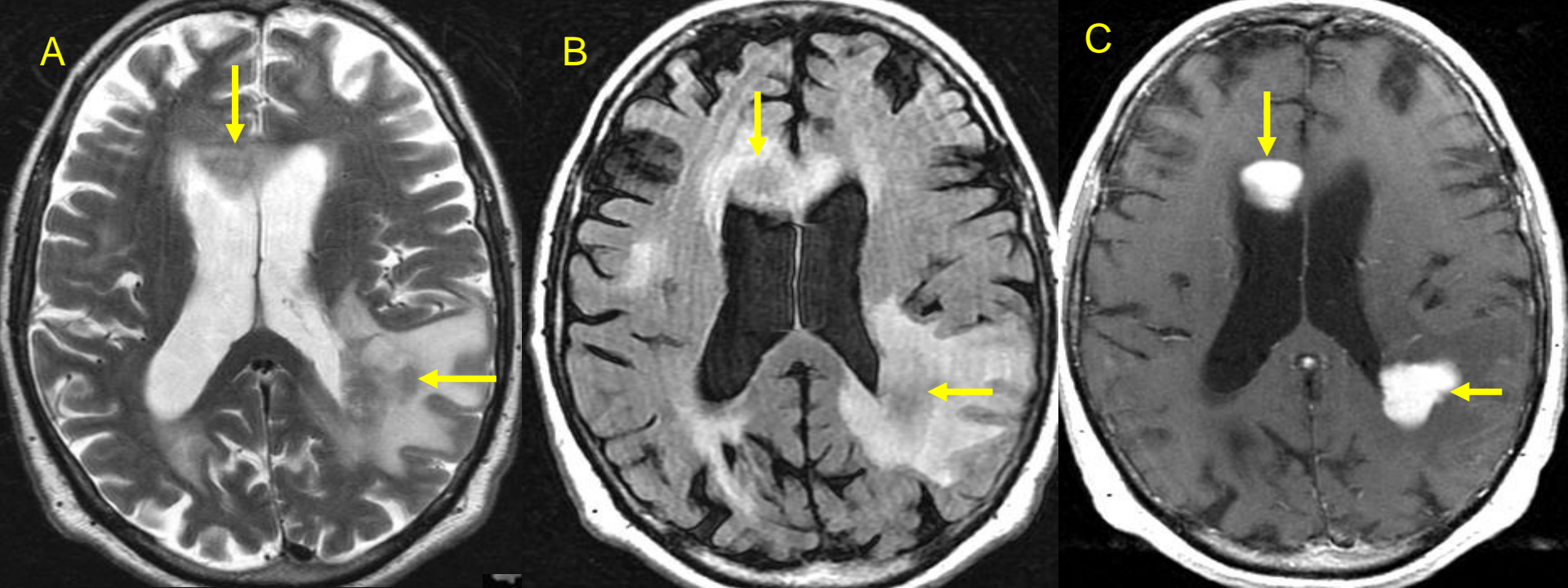
T1W axial gd+

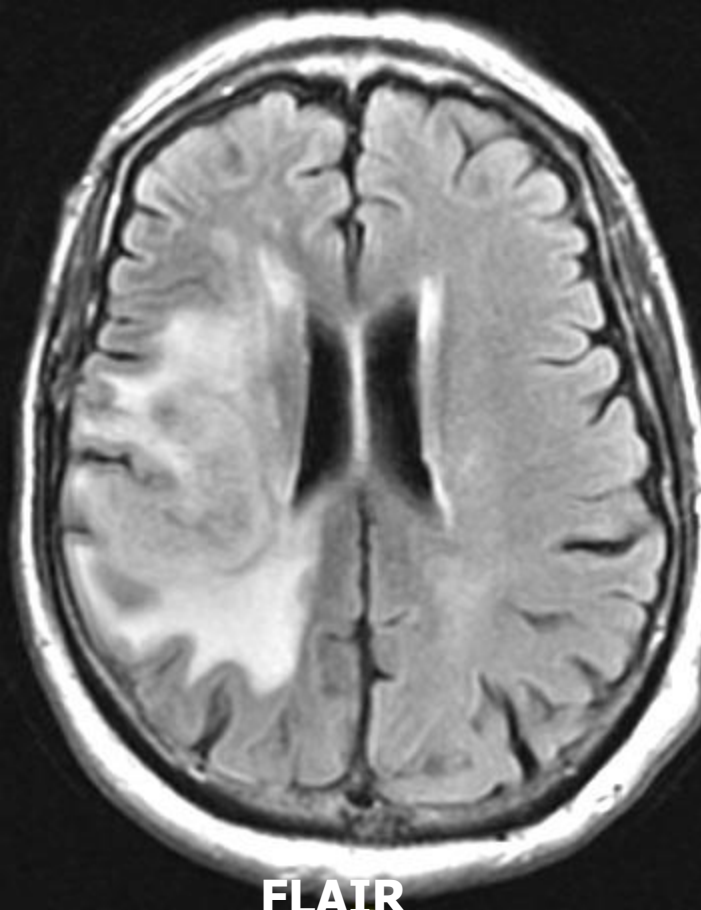
DWI



GBM



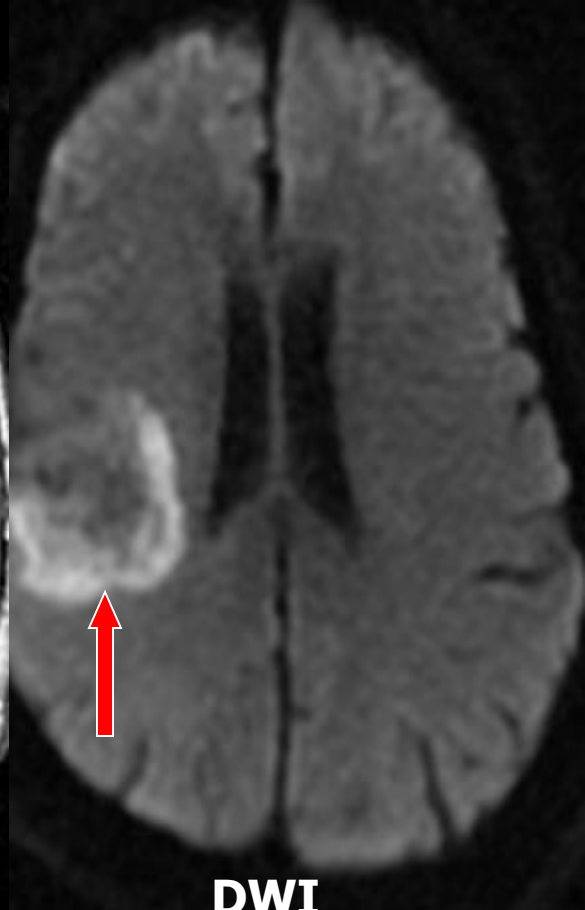




FLAIR

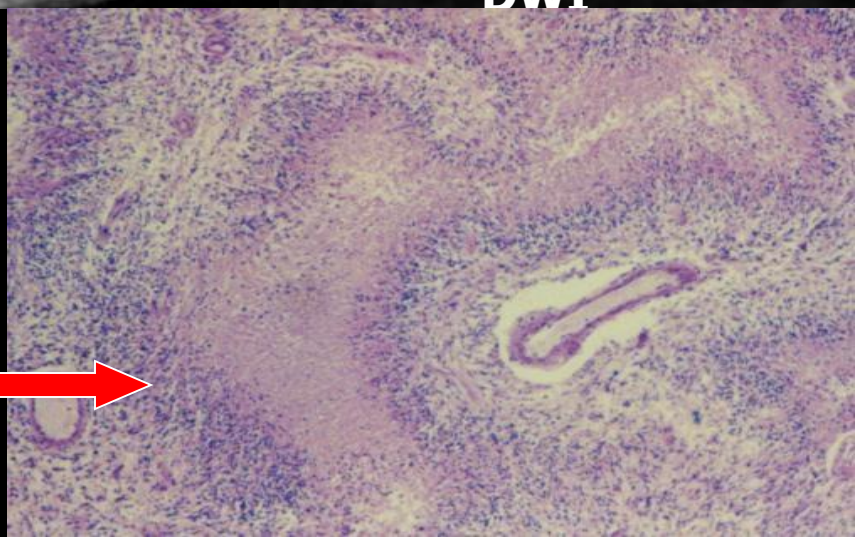


T2

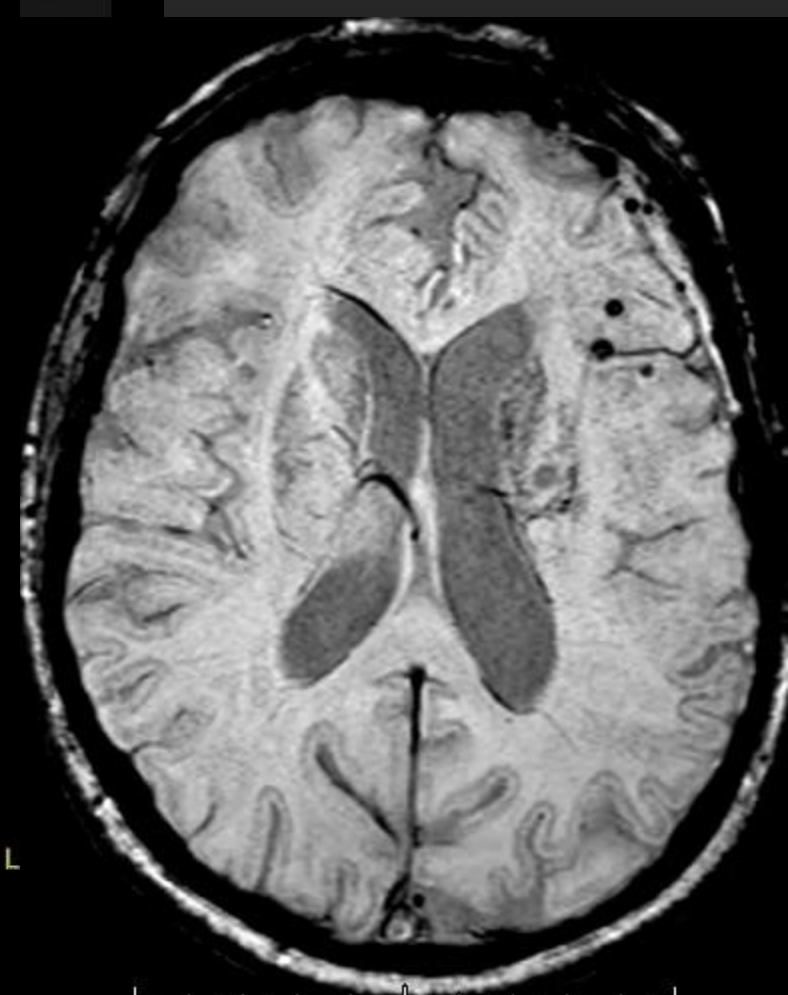


DWI

Recurrent GBM

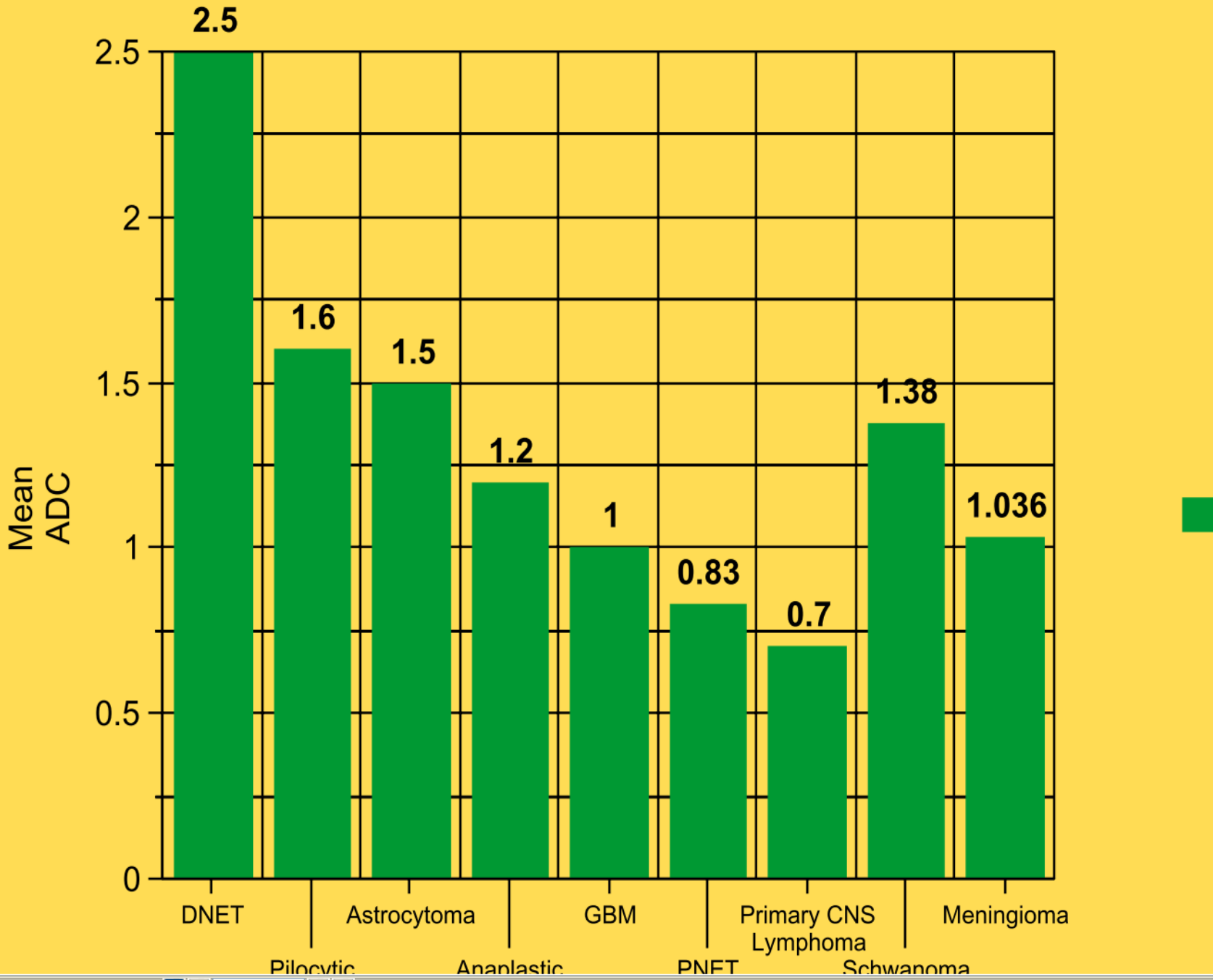




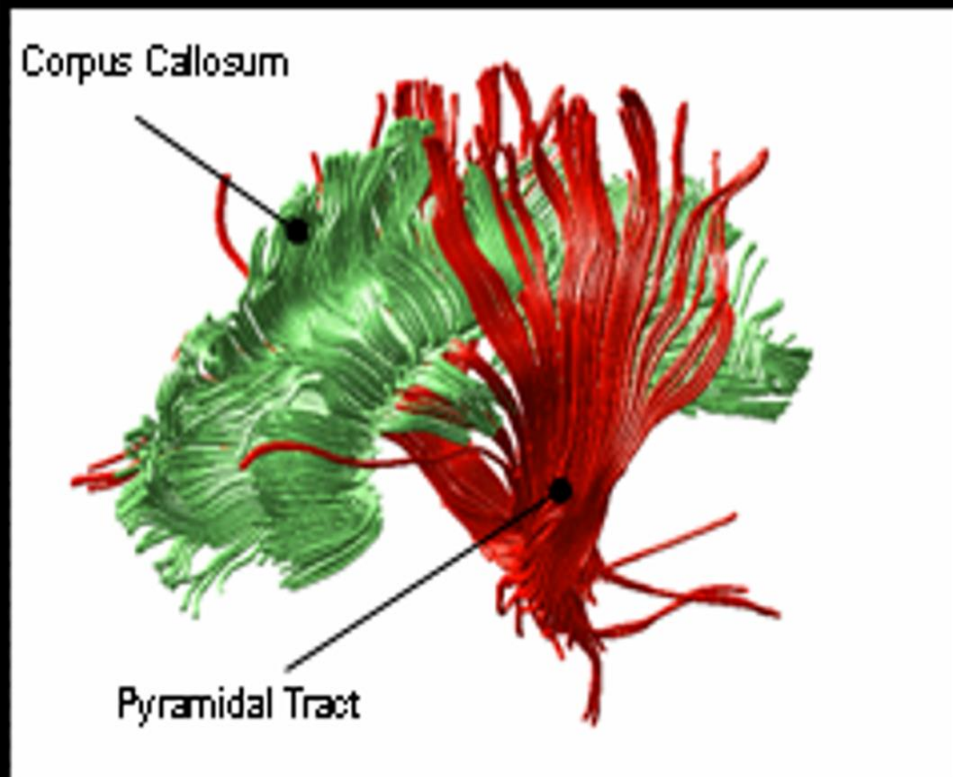


# SUSCEPTIBILITY WEIGHTED IMAGING

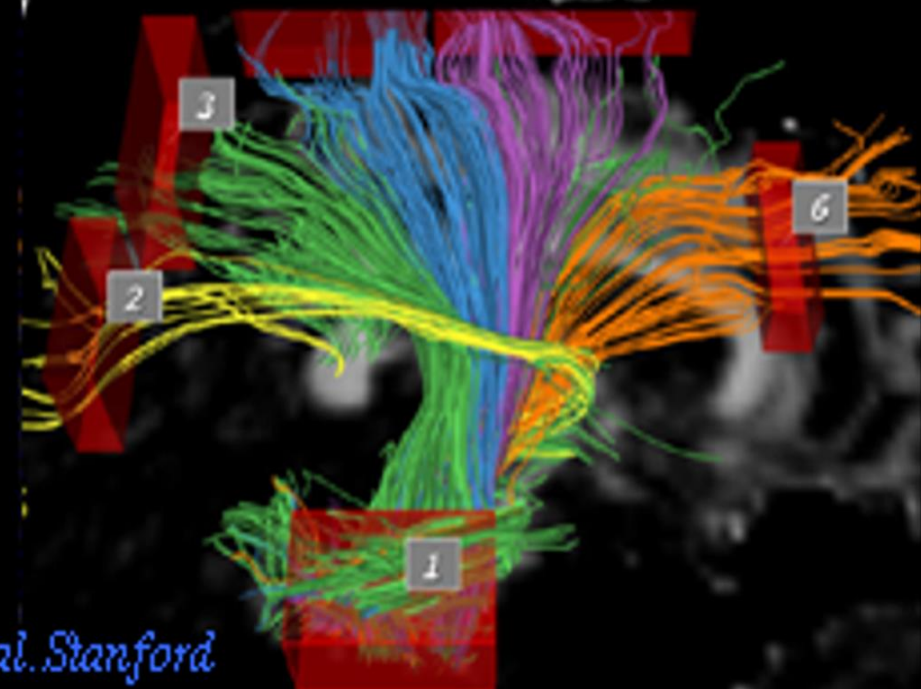
# Apparent Diffusion Coefficient



# Fiber Tracking- Visualization of WM Tracts by DTI



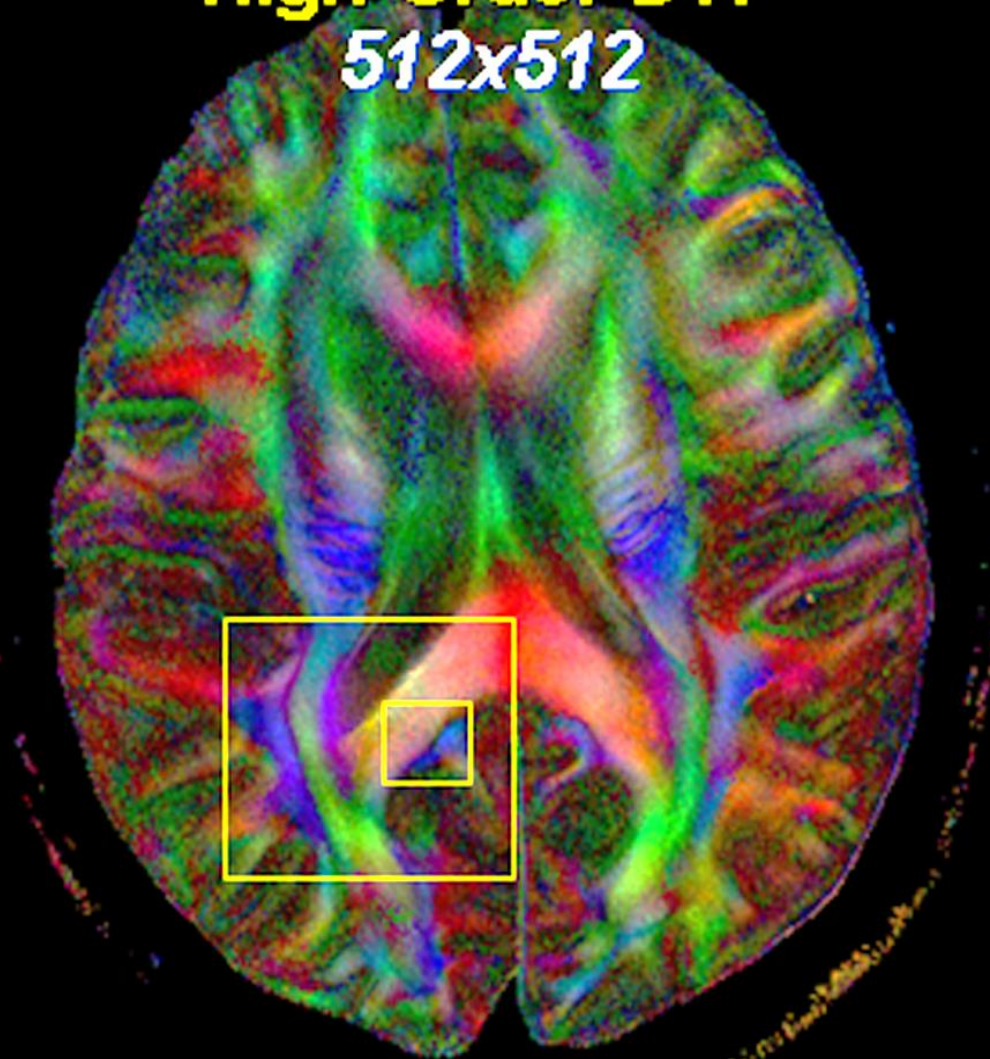
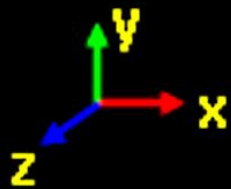
*Stanford DT Toolbox*



*T. Sherbondy, et al. Stanford*

# DIFFUSION TENSOR IMAGING (DTI)

**High-Order DTI**  
**512x512**



11:52:39 AM  
15 IMA 13 / 1

RFA

MF 1.00

TR 475.0  
TE 9.4  
TA 01:58  
BW 140.0  
MWD

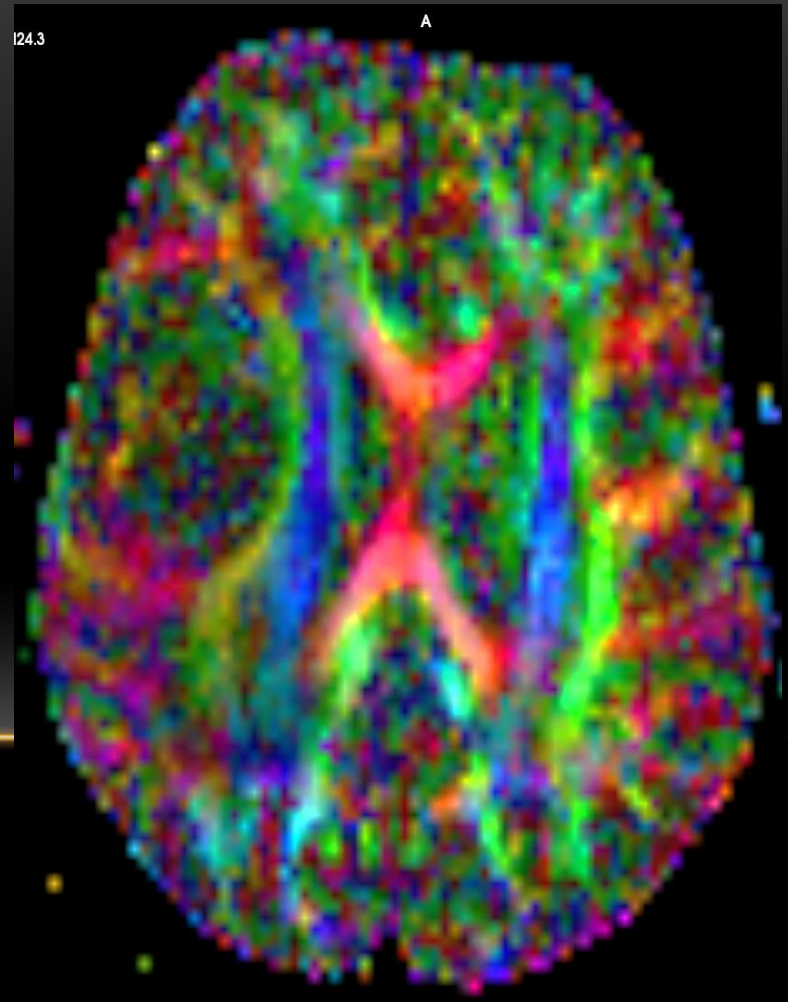
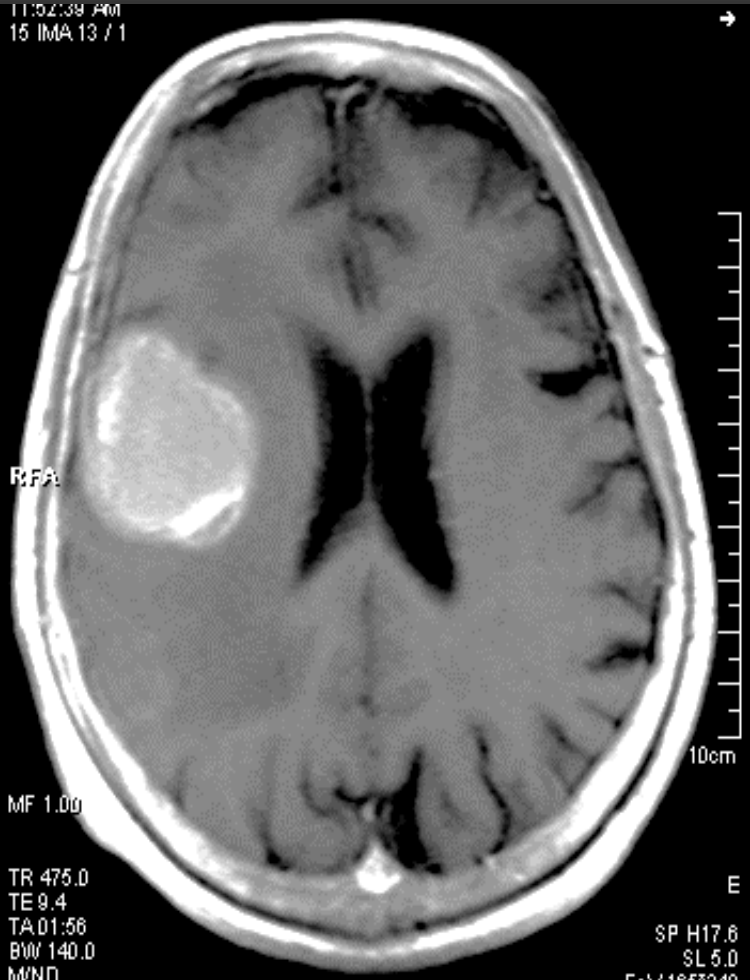
E  
SP H17.6  
SL 5.0  
FoV 165\*240

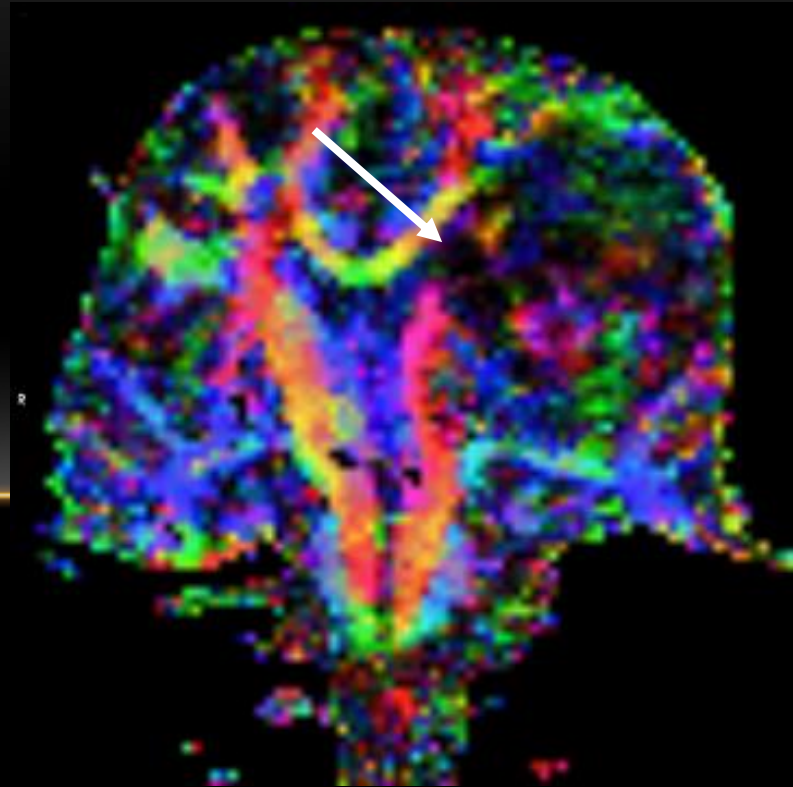
10cm

124.3

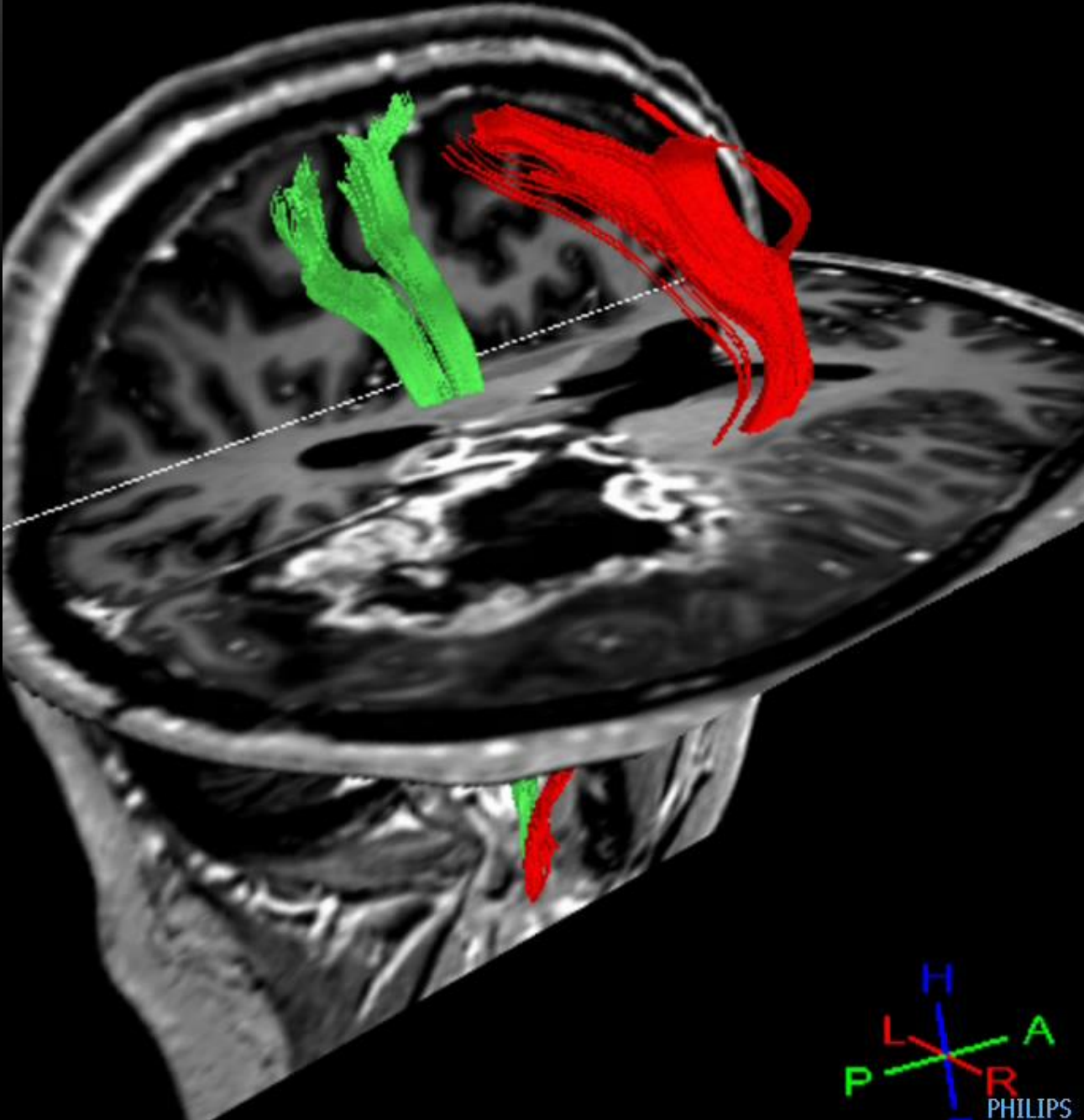
A

# METASTASIS WITHOUT INVASION OF CORTICOSPINAL TRACT





**GBM WITH INVASION OF CORTICOSPINAL TRACT**



DTI



# MRS IN NEURO-ONCOLOGY

## Preoperative

1. Differentiate high grade from low-grade gliomas
2. Differentiate GBM-related “edema” from metastases-related “edema”
3. refinement of pre-operative differential diagnosis
  - a. abscess
  - b. tuberculoma
  - c. tumefactive demyelinating lesion
4. diagnose meningioma
5. diagnose PCNSL

## Perioperative

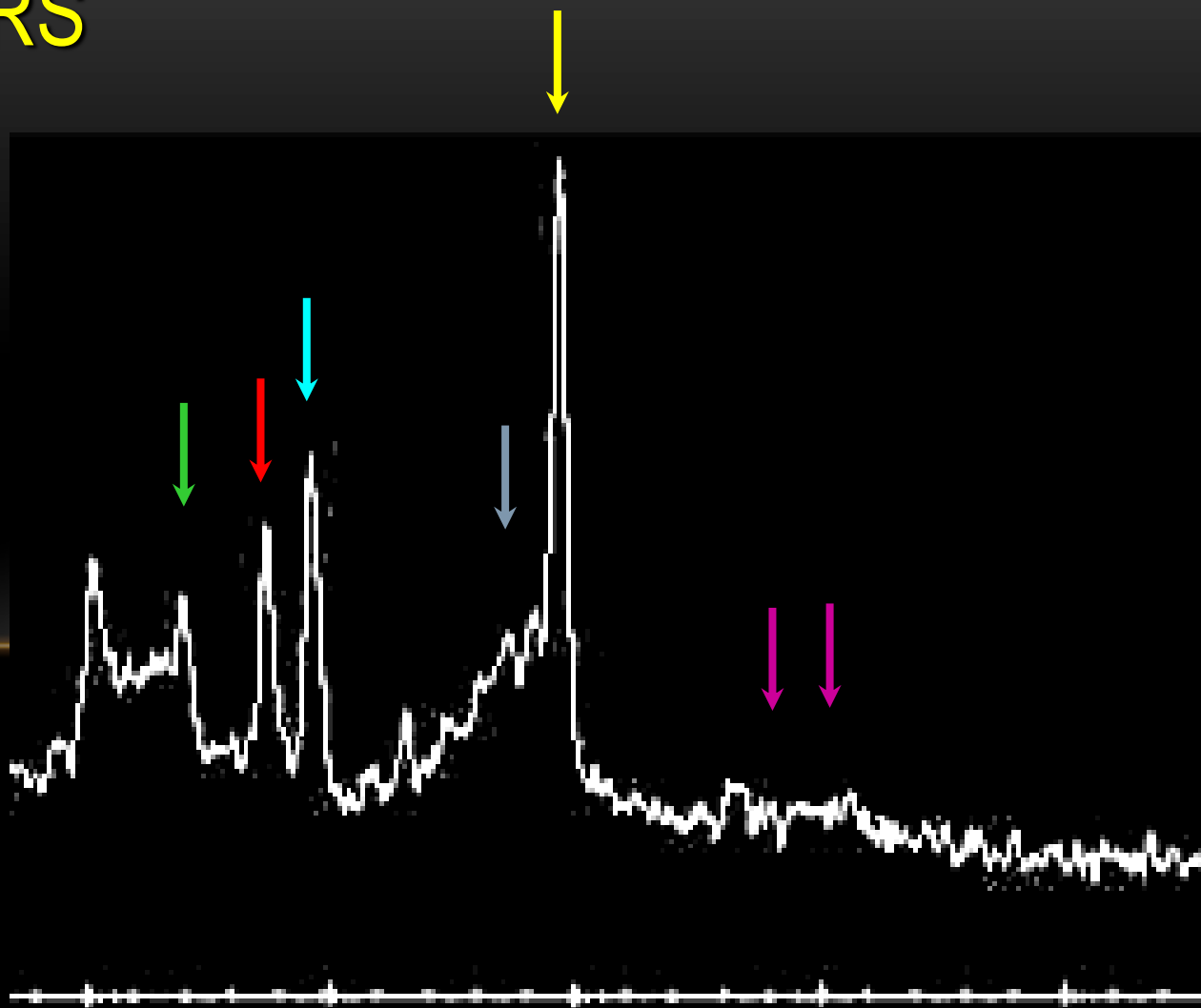
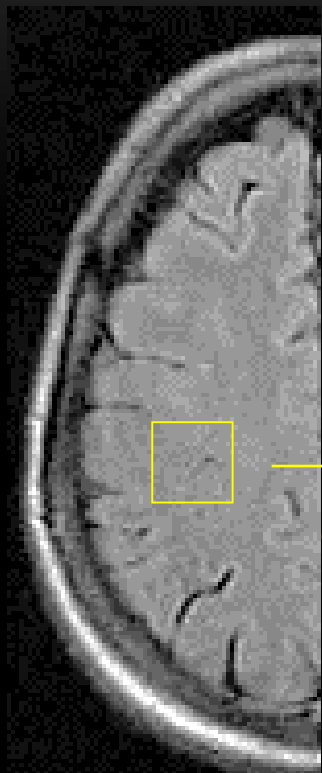
1. Localize for stereotactic biopsy
2. determination of extent of resection
3. Multivoxel MRS to predict radiotherapy volumes

## Postoperative

1. monitor malignant transformation of low grade tumors
2. monitoring of response to treatment
3. Differentiating recurrent GBM from radiation necrosis



# NORMAL MRS

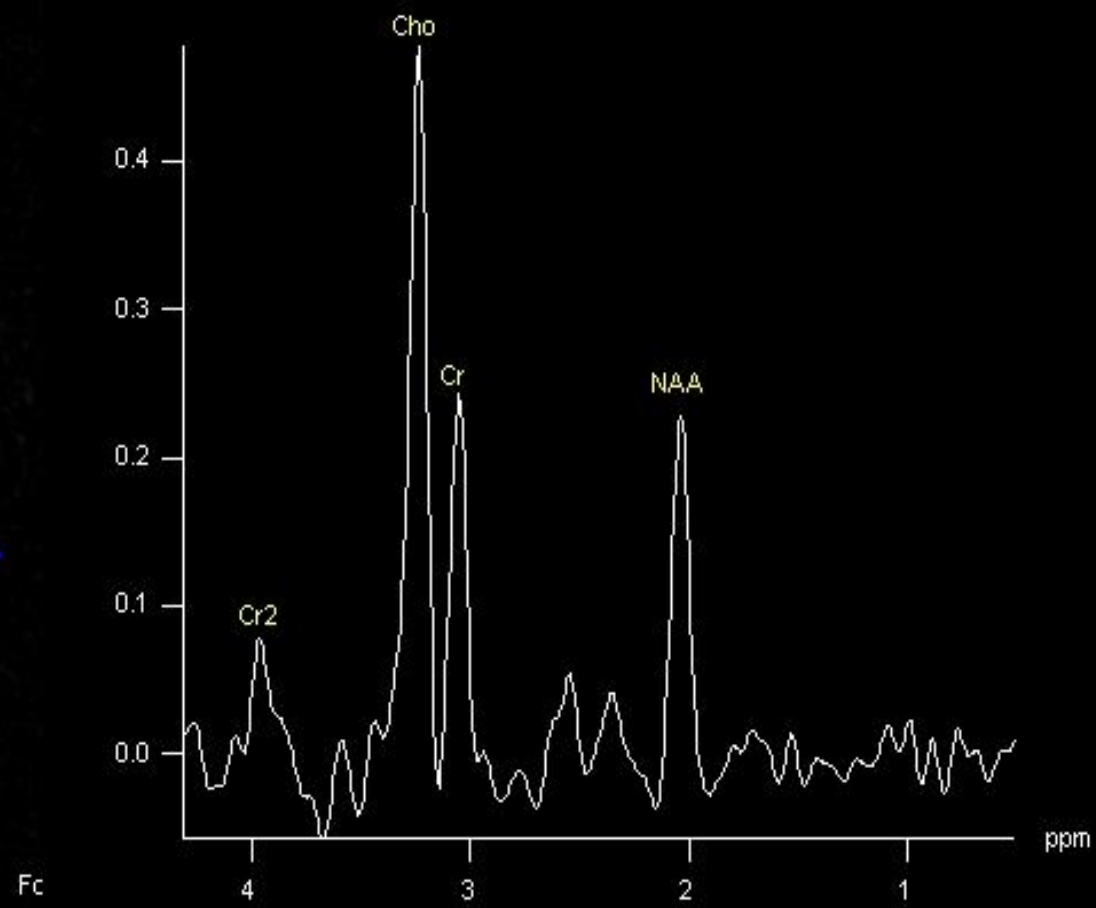
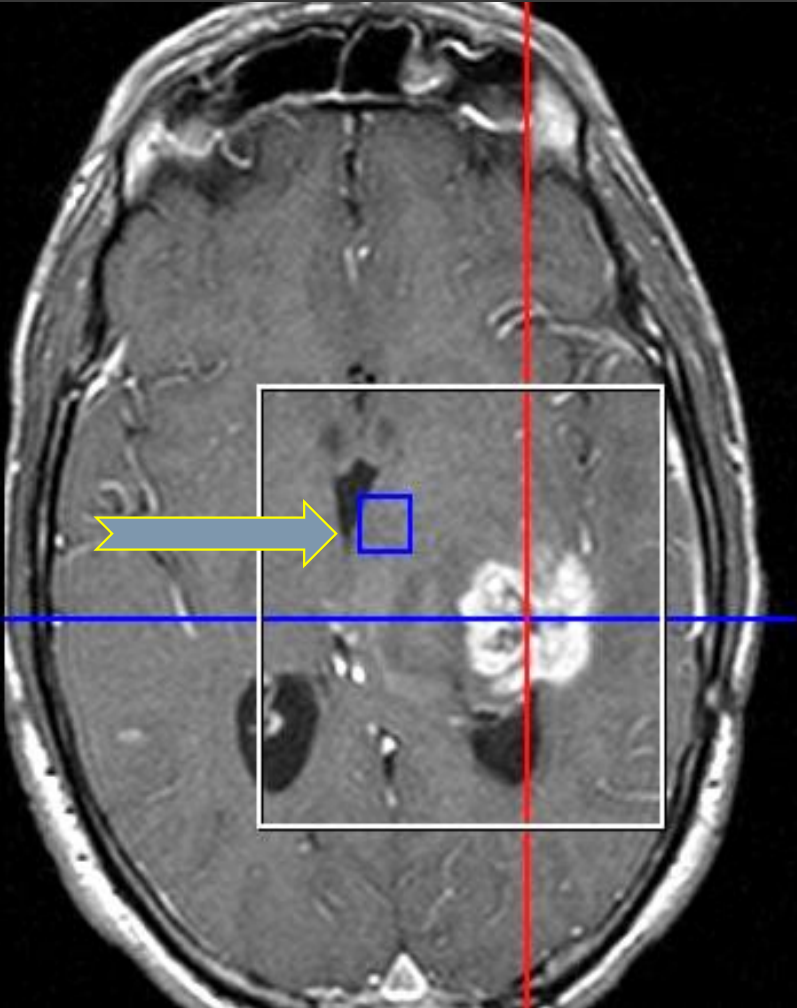


Myoinositol Choline Creatine Glutamine/glutamate N-acetyl aspartate Lipids/lactate

- **Decreased NAA** signal in neoplasms is from reduced or absent production of these metabolites because normal neurons have been destroyed or displaced by the neoplastic process

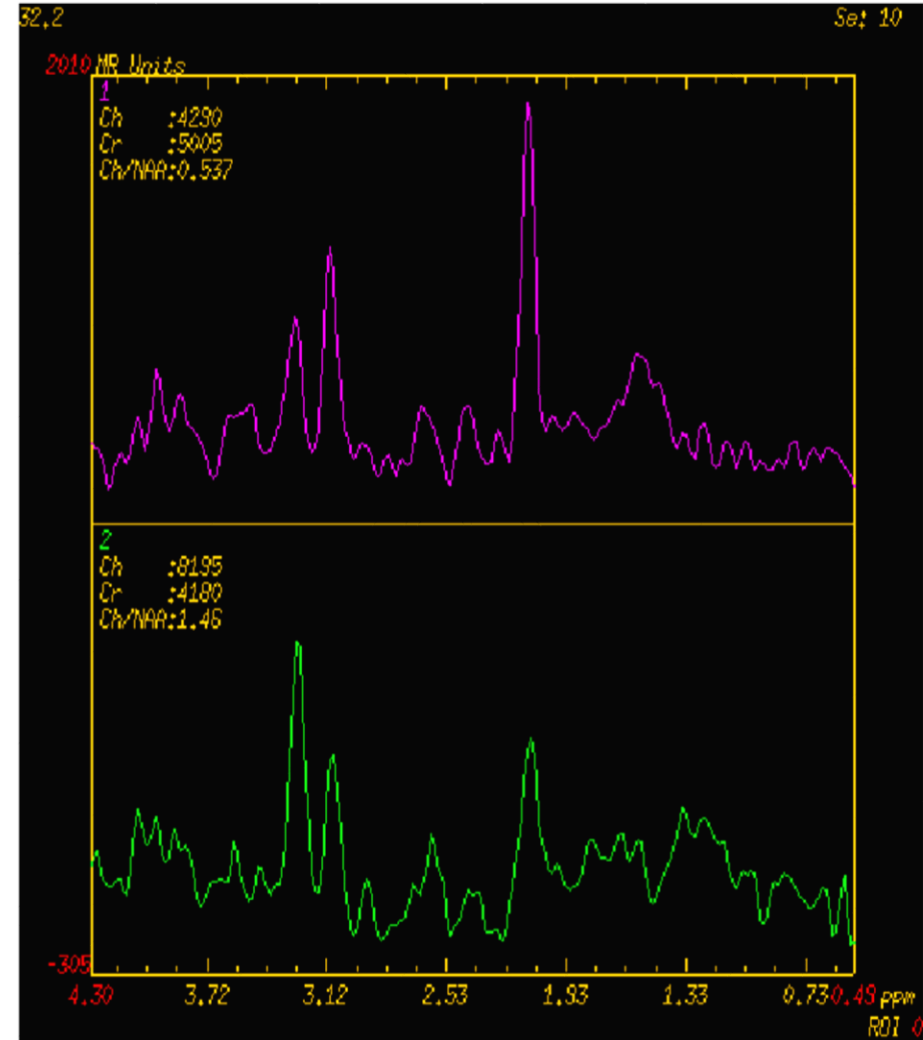
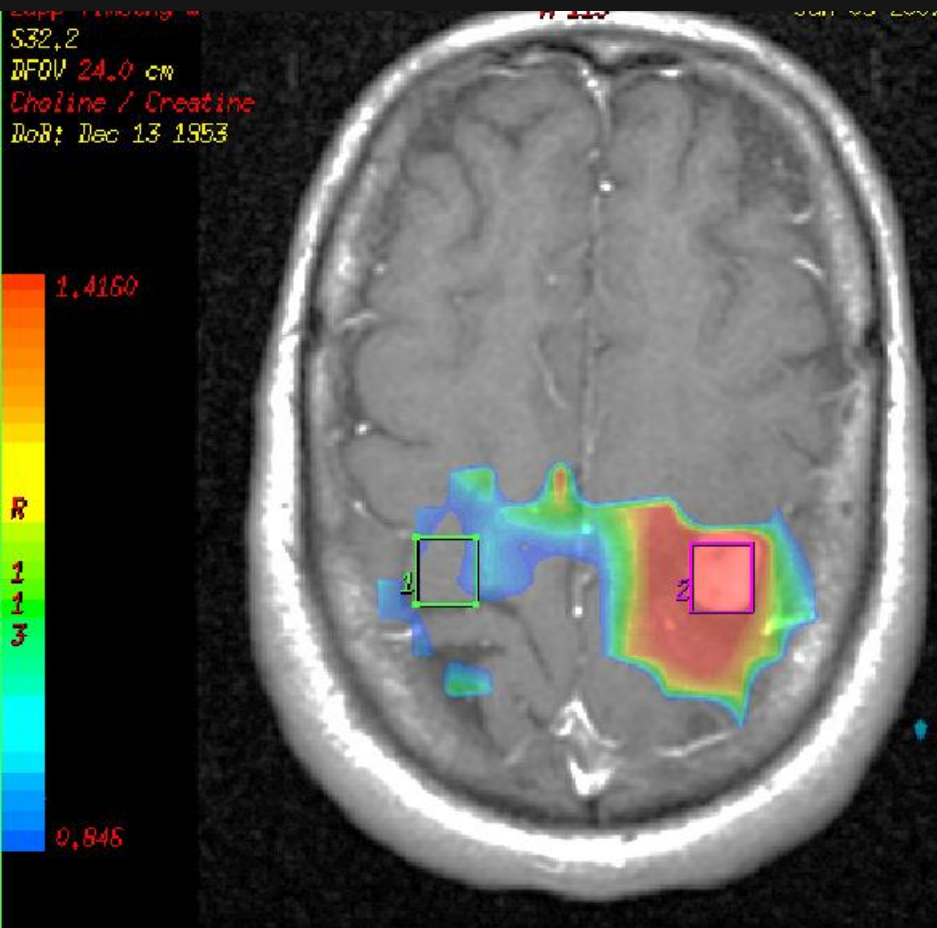
**Elevated choline** peak is a surrogate marker of increased cell membrane turnover caused by tumor growth or normal cell destruction or may at least in part be elevated because of increased production through phospholipase upregulation.

The relative anaerobic environment of many neoplasms and derangements in glucose metabolism result in incomplete glucose breakdown and likely account for the **elevated lactate signal**

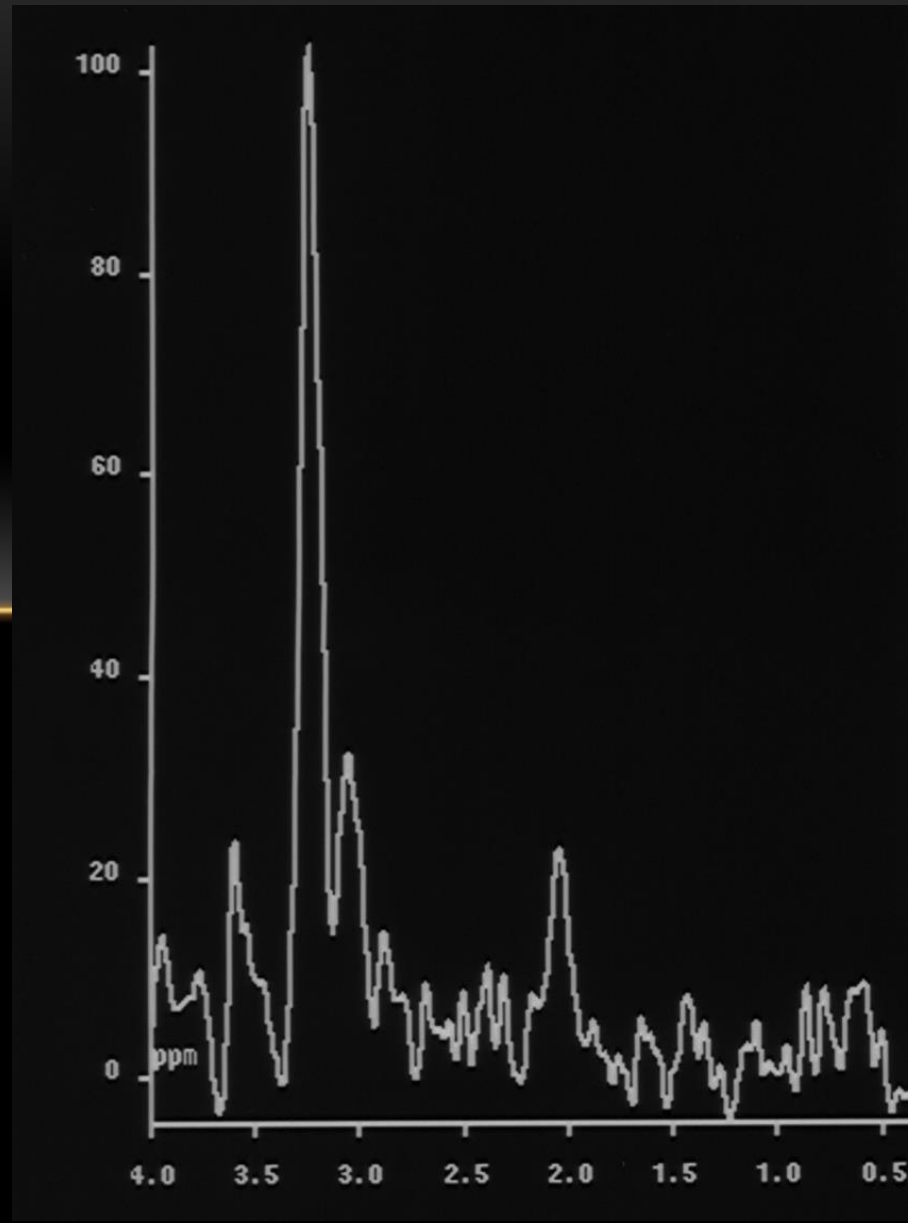
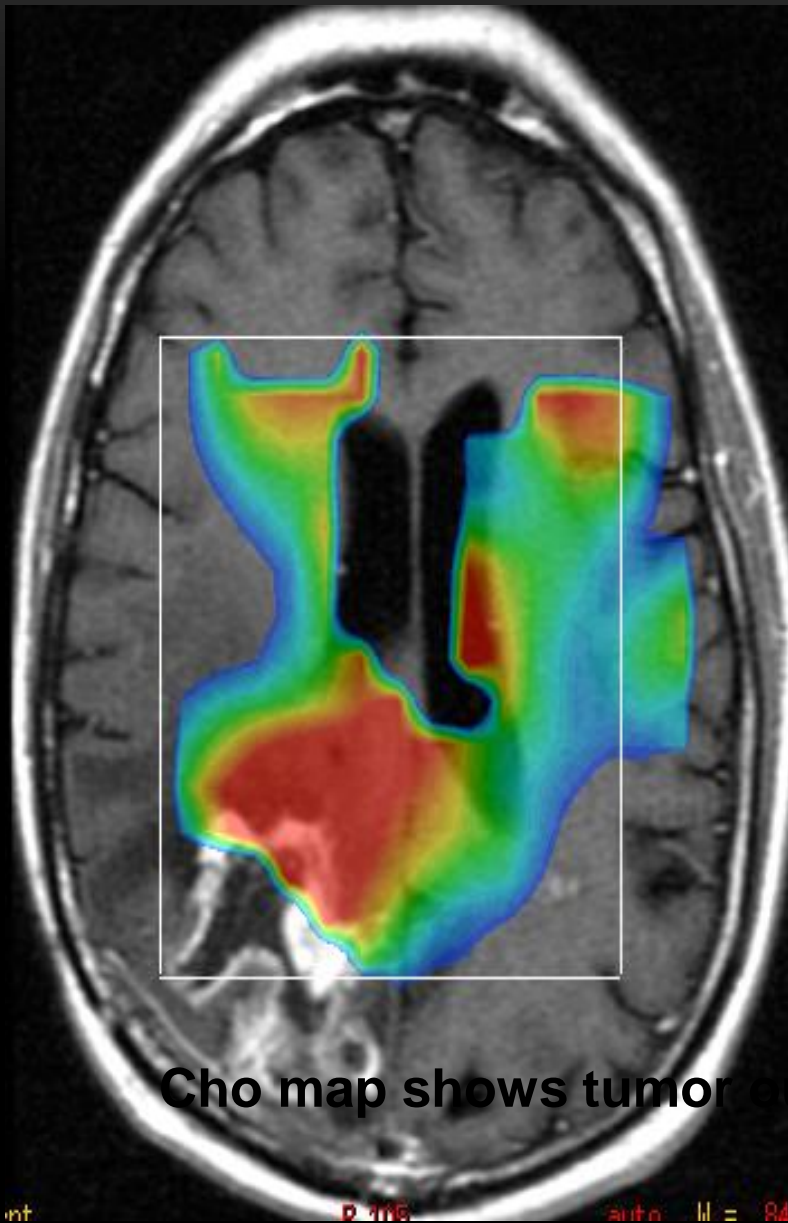


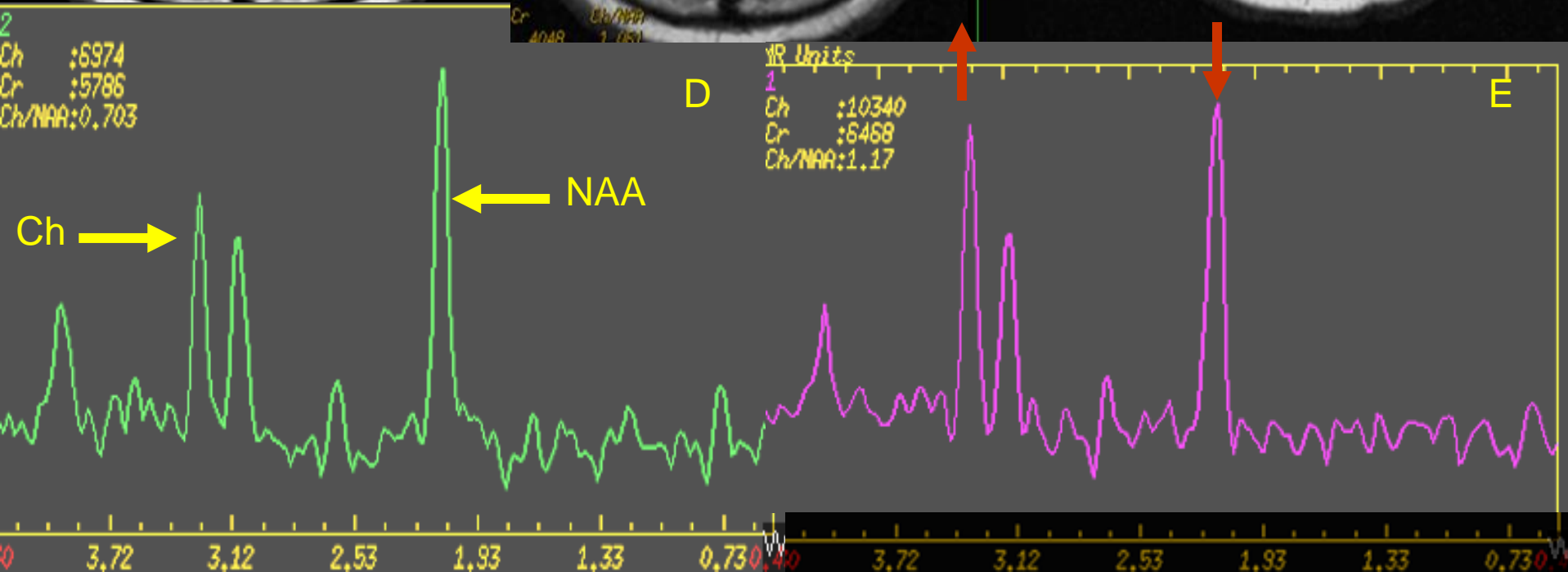
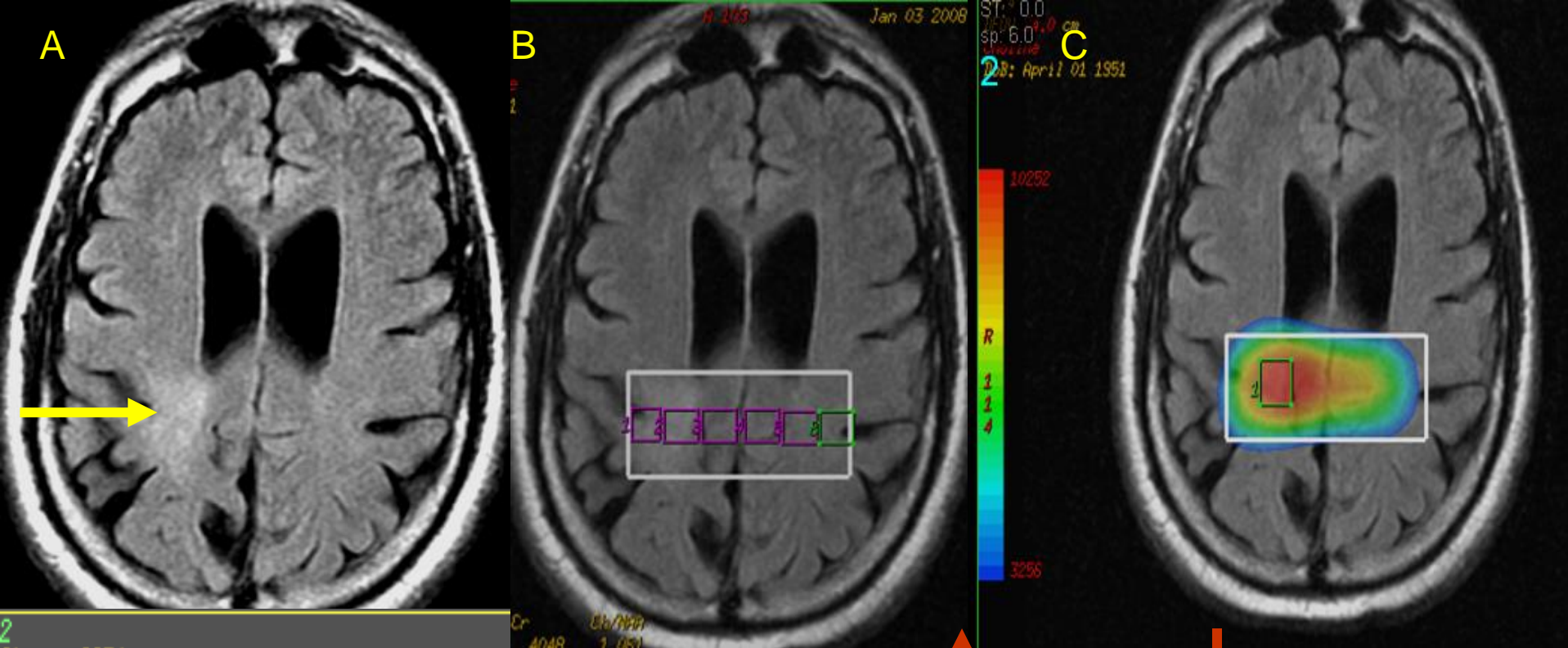
**GBM, TUMOR EXTENSION BEYOND ENHANCEMENT**

# MULTI VOXEL MRS



**MAPS HAVE IMPLICATIONS FOR PROGNOSIS AND RT PLANNING**





# PERFUSION MRI: CLINICAL APPLICATIONS

Glioma grading (astrocytomas only)

Image-guided biopsy

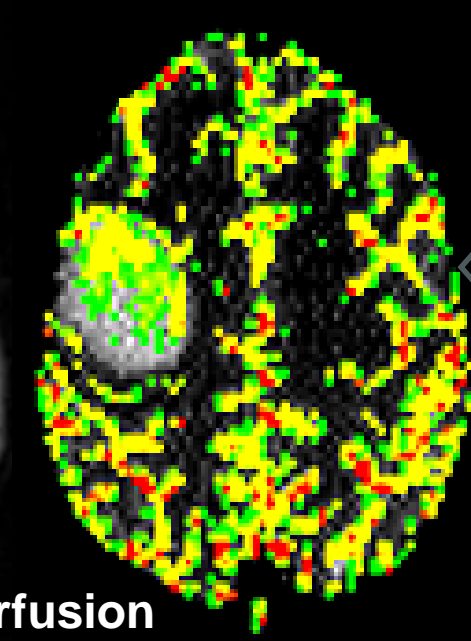
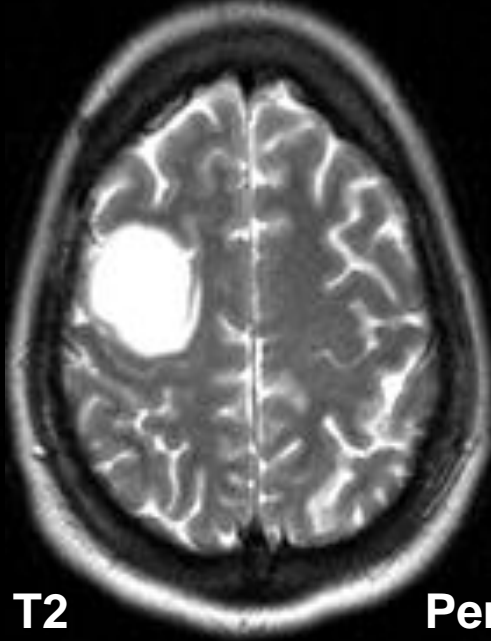
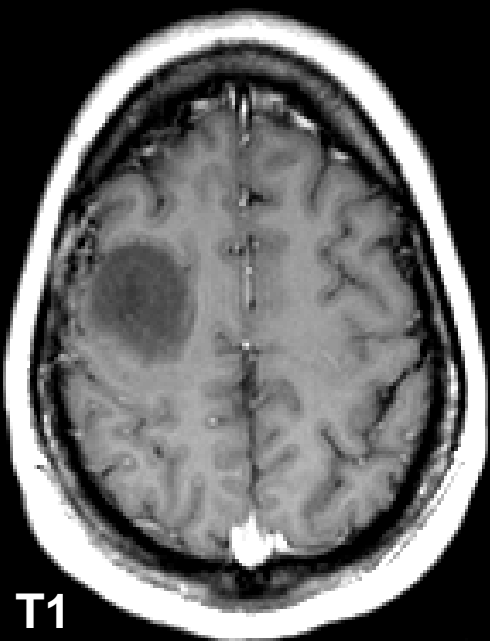
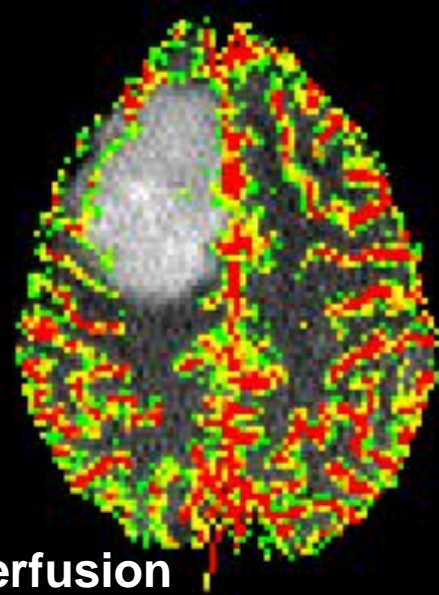
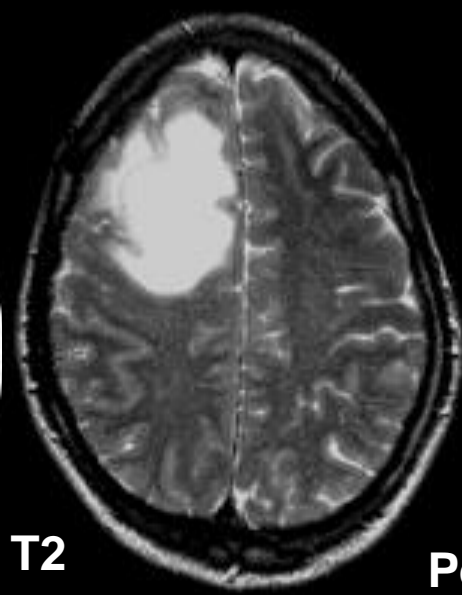
Primary vs Secondary brain tumor

Tumor vs Treatment effect

Tumor-mimicking lesions

**Perfusion MR**

**Grade 2 astro**



**Grade 3 astro**



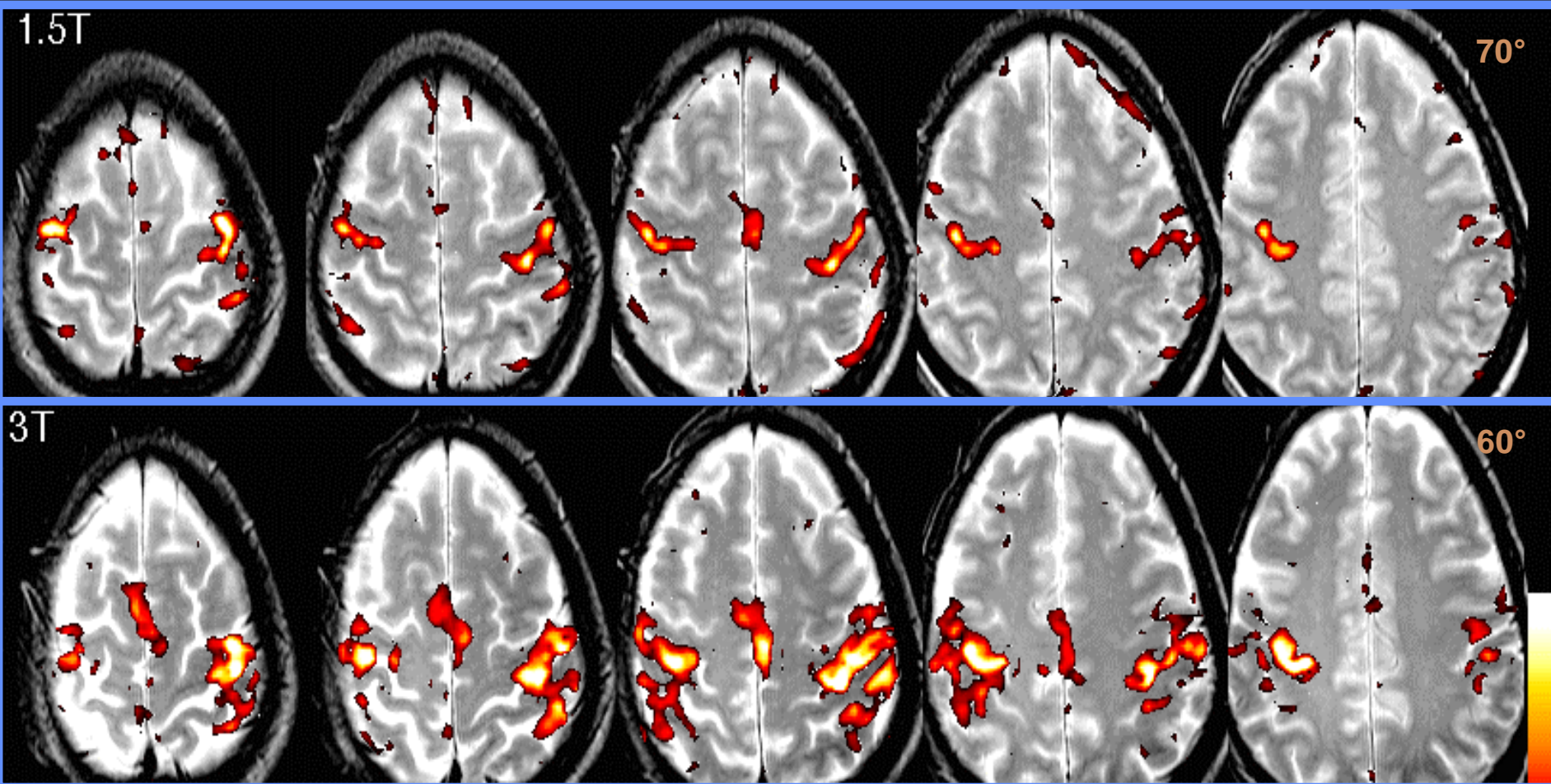
# THREE GOALS OF PRESURGICAL FUNCTIONAL MRI INCLUDE:

to determine the feasibility of surgical treatment and risk for inducing neurologic deficits,

to select patients for intraoperative cortical stimulation, which would be indicated when a functional area is included within the lesion or at the radiological boundary

to provide guidance for functional neuronavigation based on preoperatively acquired structural information using MRI

# 1.5T VS. 3.0T MOTOR TASK FINGER APPPOSITION



3T 60°; 1.5T 70° ( $T_1$ ) @ 3T:  $T_1@1.5T\sim 900ms$ ;  $T_1@3.0T\sim 1400ms$   
20cm FOV, 5mm/skip 0, 90x90, 6 slices

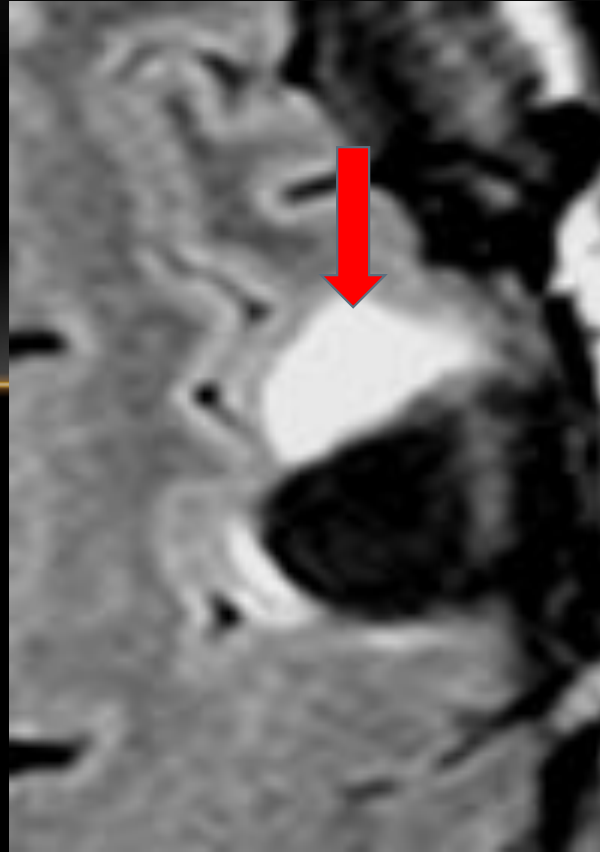
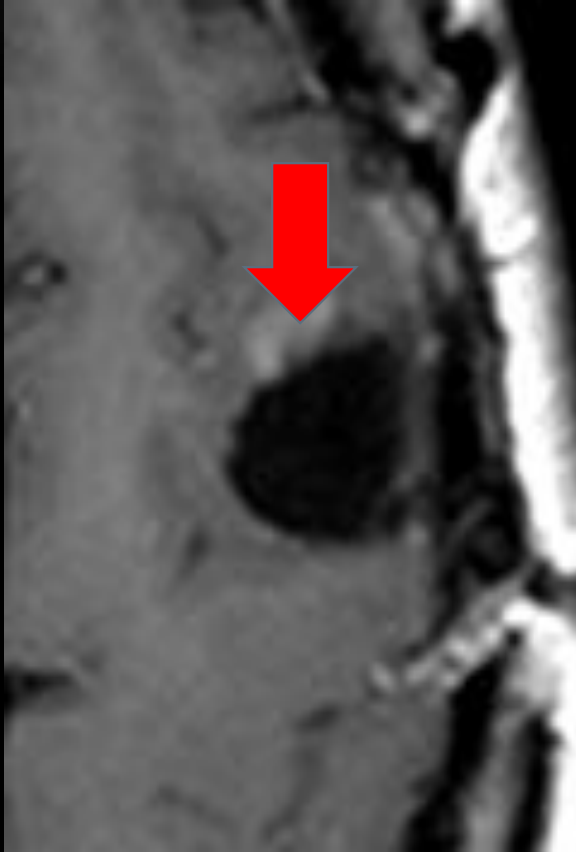
# THREE GOALS OF PRESURGICAL FUNCTIONAL MRI INCLUDE:

to determine the feasibility of surgical treatment and risk for inducing neurologic deficits,

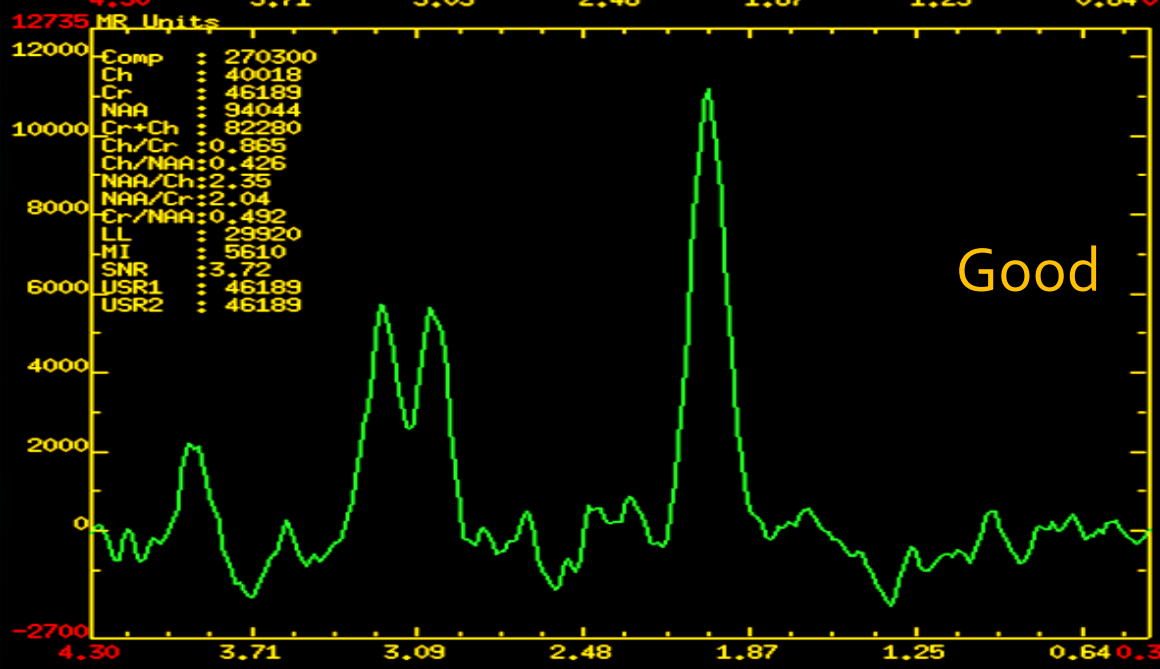
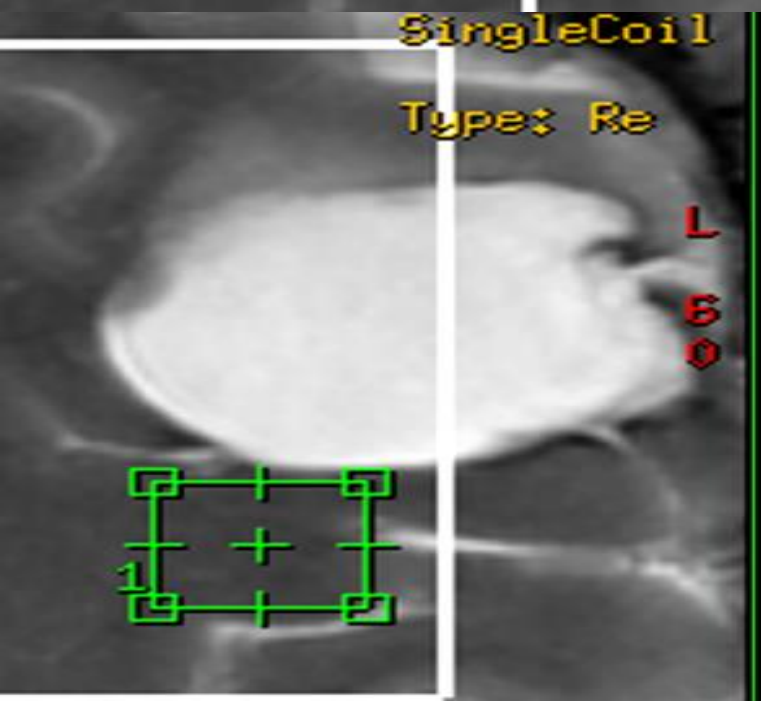
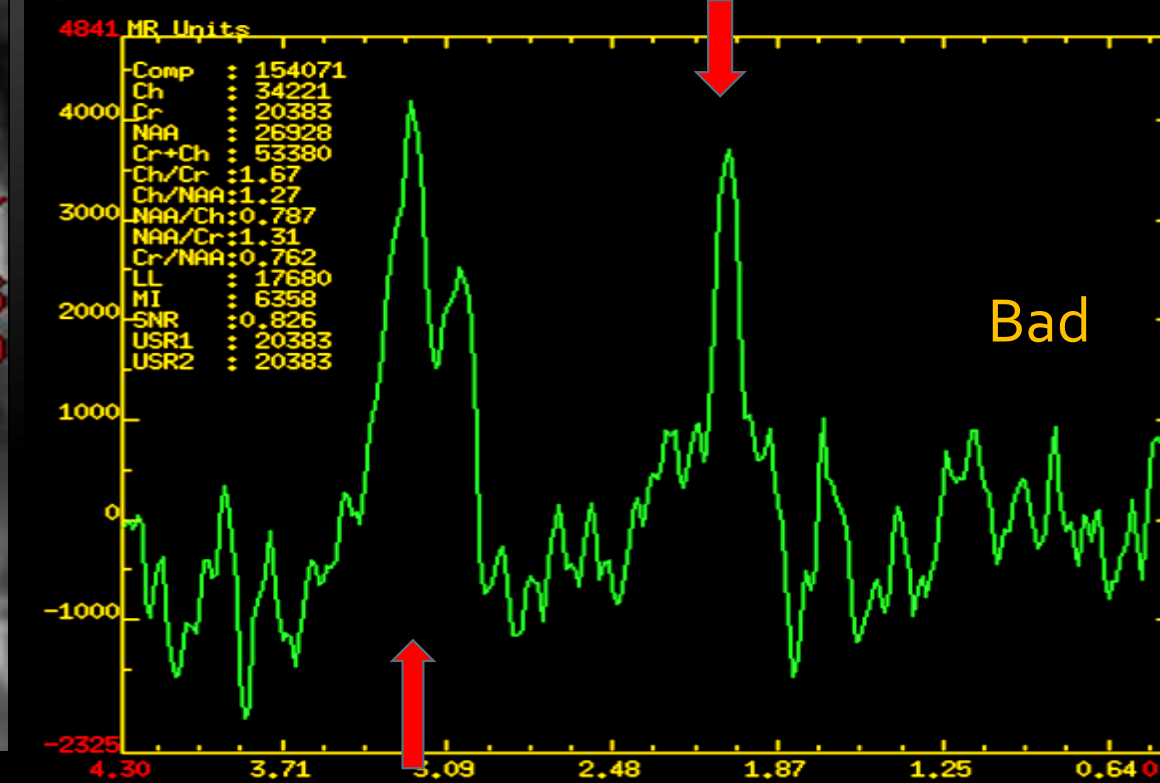
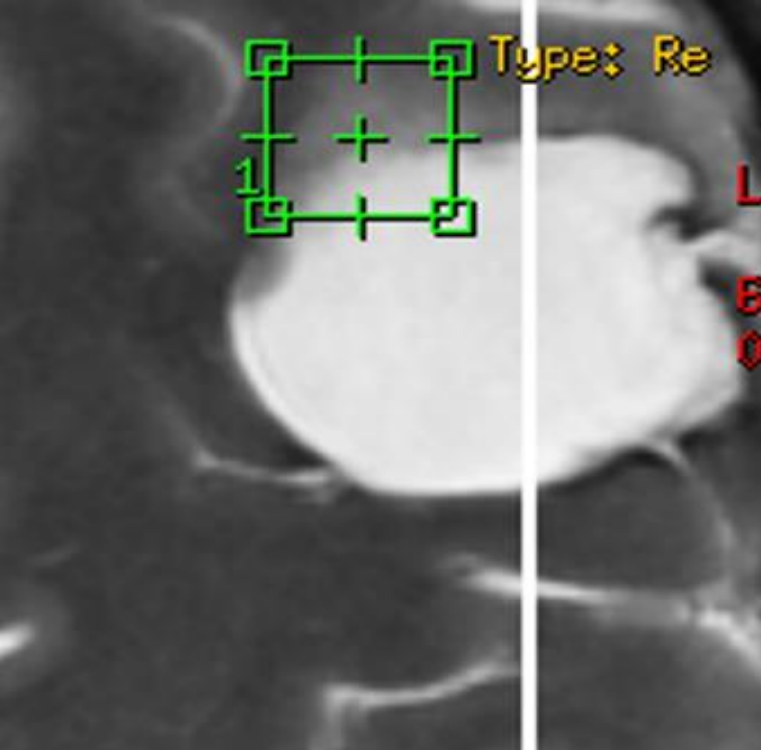
to select patients for intraoperative cortical stimulation, which would be indicated when a functional area is included within the lesion or at the radiological boundary

to provide guidance for functional neuronavigation based on preoperatively acquired structural information using MRI

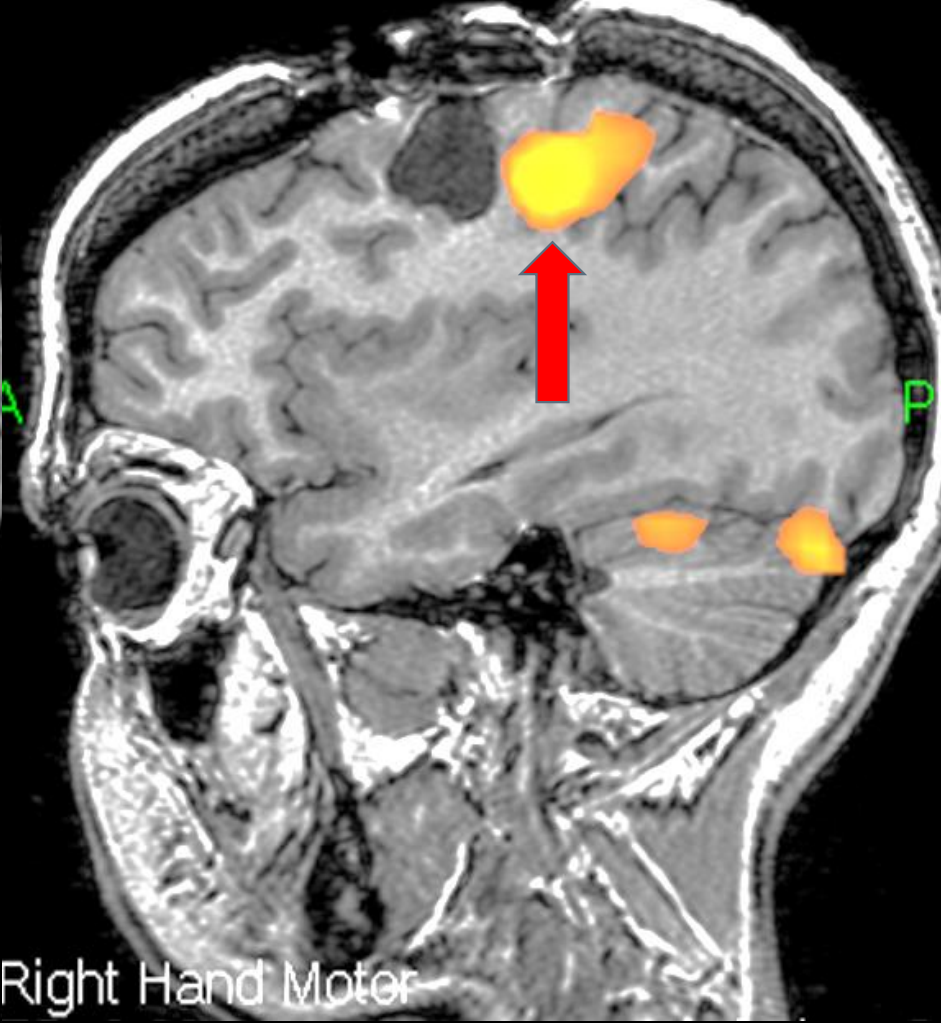
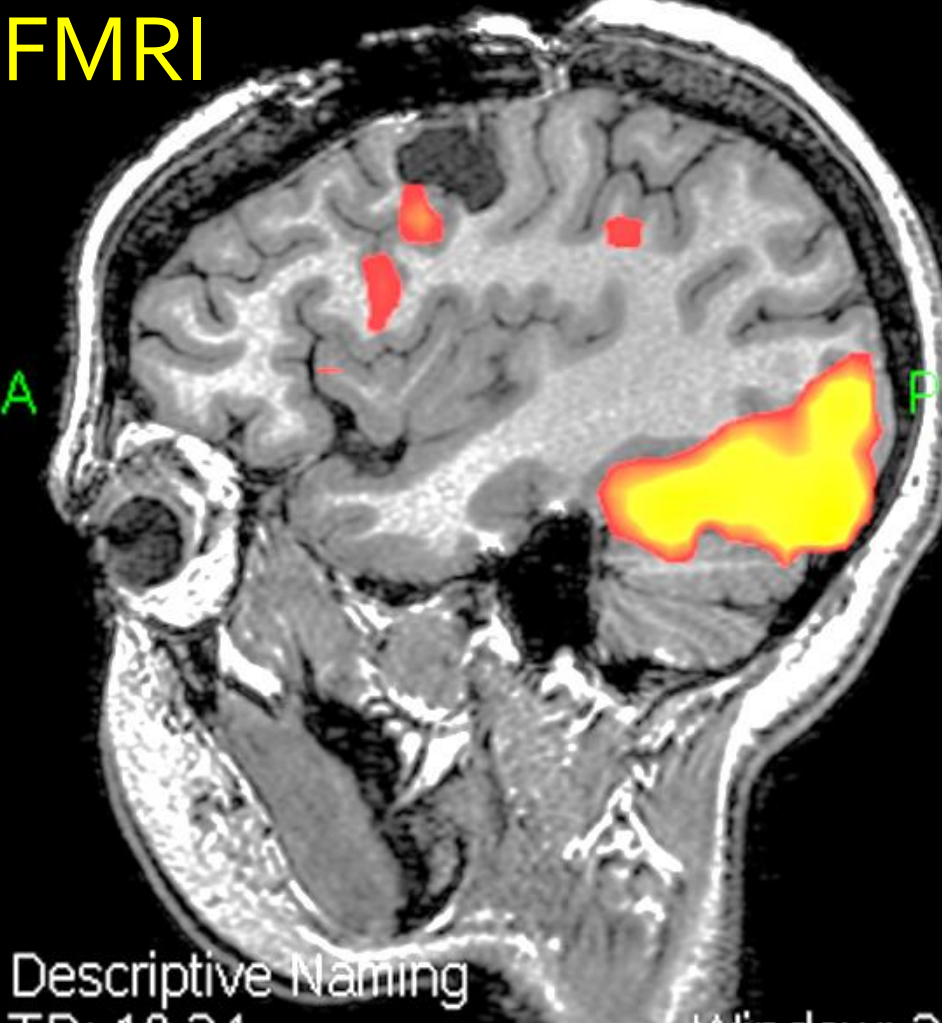
A 31-year-old women operated 1 year ago for a oligoastrocytoma located in the superior aspect of the left middle frontal gyrus. Asymptomatic



Arrows point to  
NEW lesion

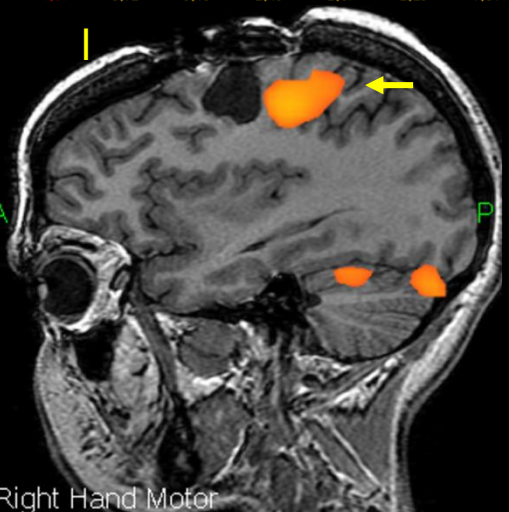
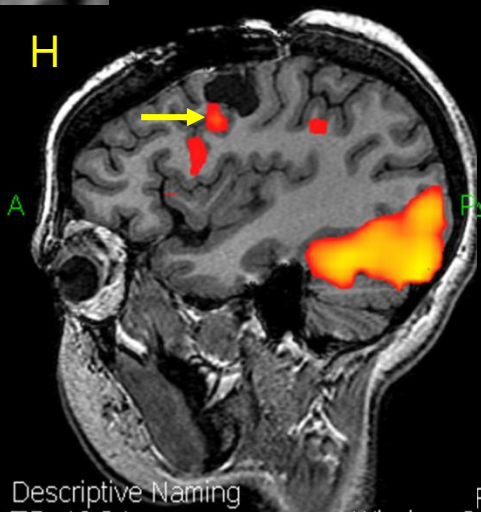
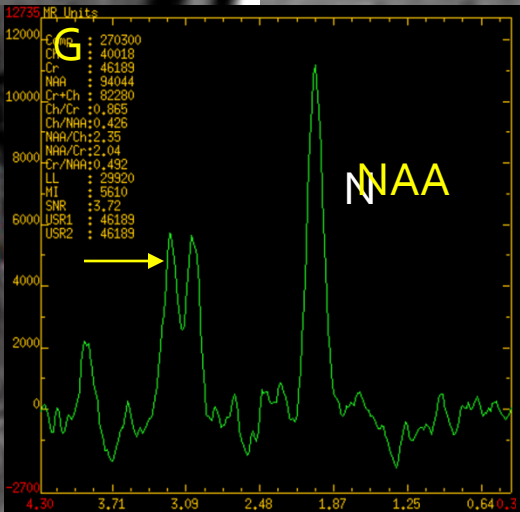
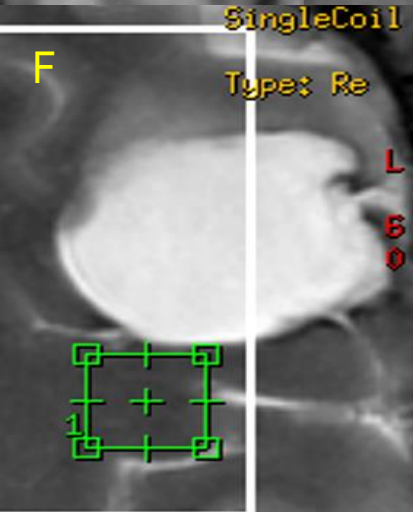
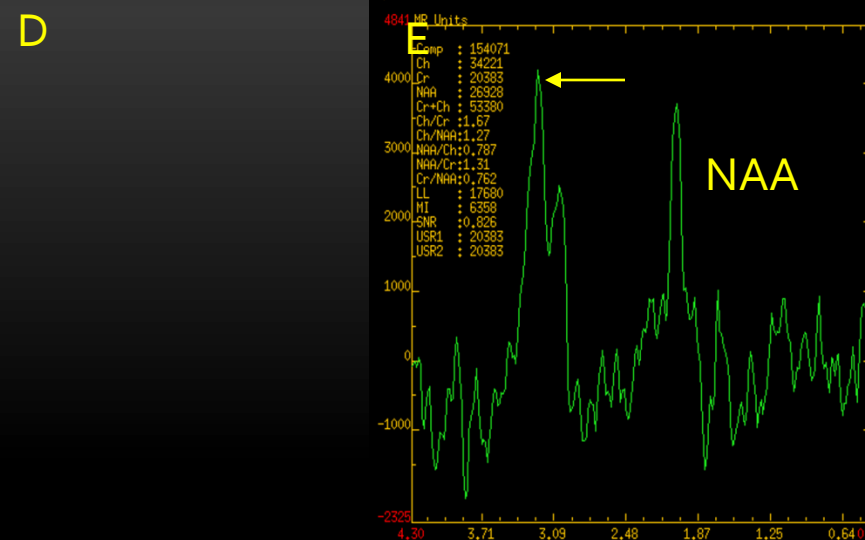
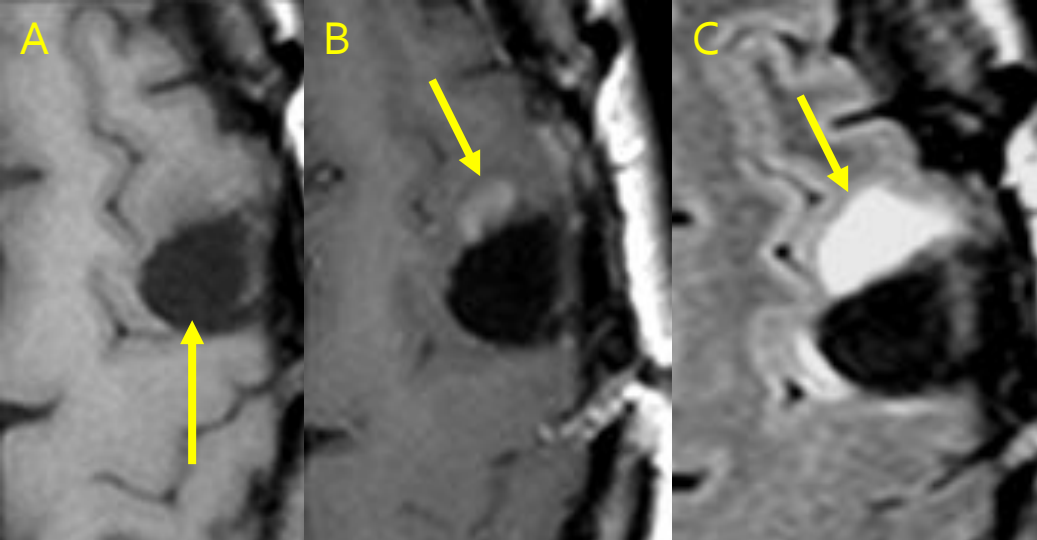


# FMRI



Functional MRI in the sagittal plane using descriptive naming (H) indicates activation in the left premotor cortex just below the enhancing lesion (arrow). For right hand activation (I) was found adjacent to the posterior margin of the post-op cyst, that was normal on MRS

OOPS  
!!!!!!!!!!!!!!



# IOMRI SYSTEMS

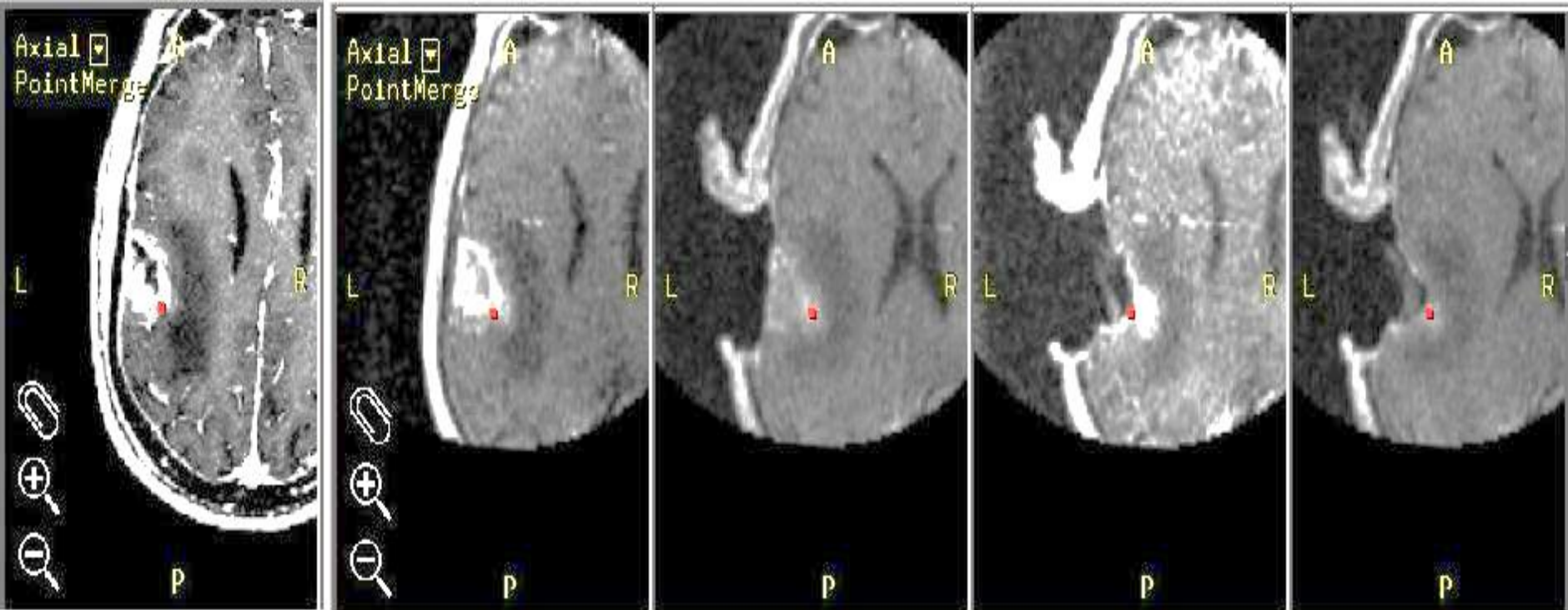


0.12 to 3T Tesla



# IOMRI

## GBM Operative Progression



Diagnostic Pre-Op Scan

Pre-Op

PoleStar® Intra-Op Scans  
with surgery progression

# IOMRI

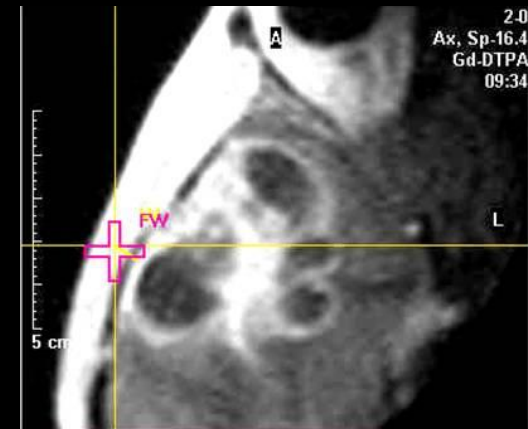
Resection control

Maintain navigational  
accuracy despite brain shift

Complication avoidance



1.5T pre-op image

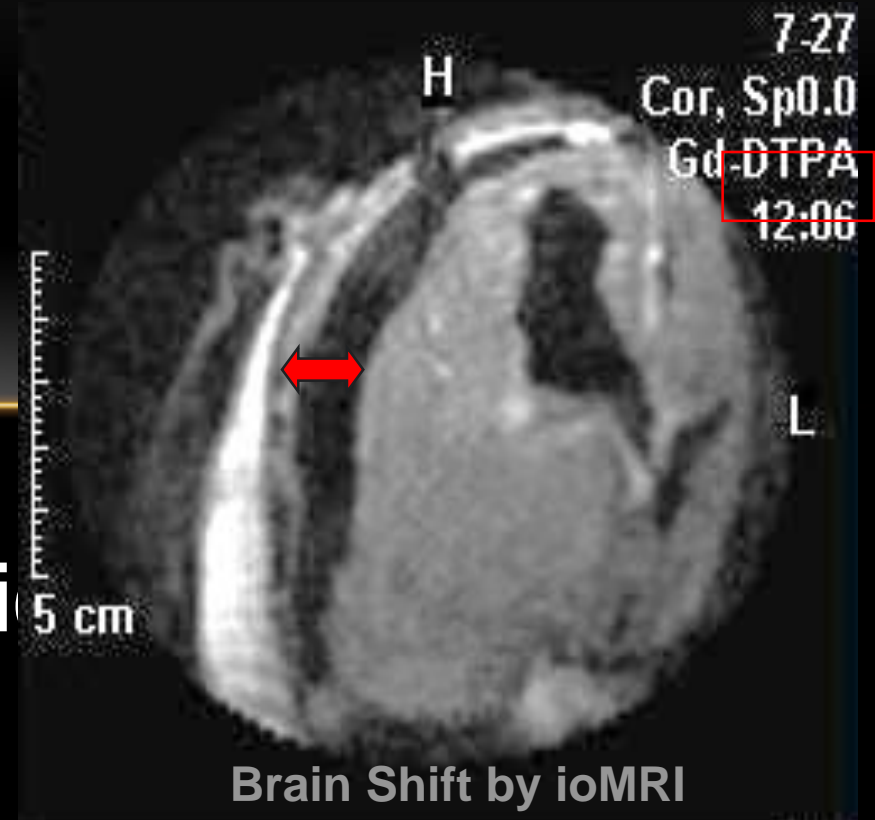


0.15T MRI taken in OR

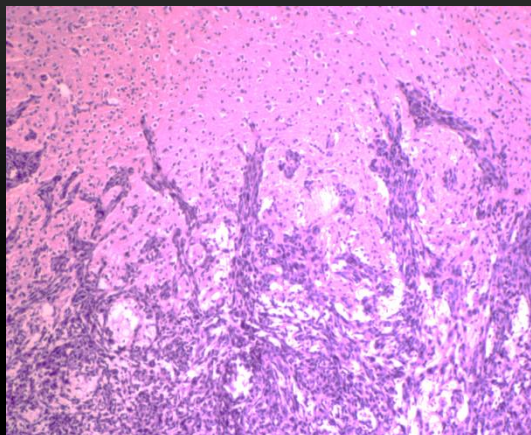
# BRAIN SHIFT (EFFECT ON STEREOTACTIC LOCALIZATION)

Tissue shift occur in surgery due to:

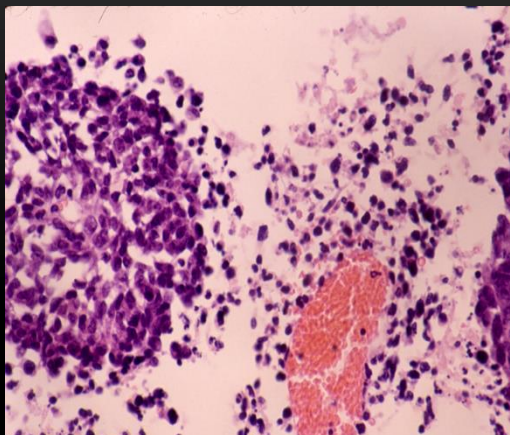
- \* Tumor decompression
- \* Collapse of brain around operative site
- \* Loss of cerebrospinal fluid
- \* Cortical swelling



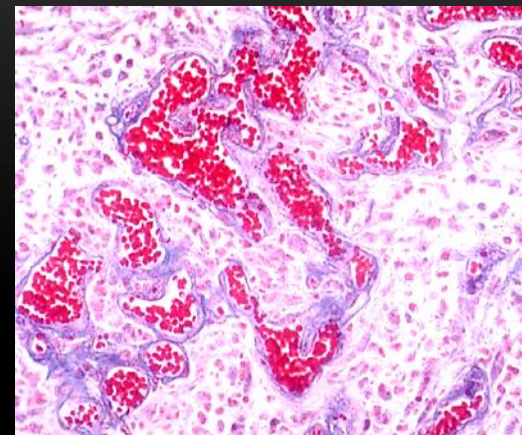
# INFILTRATION



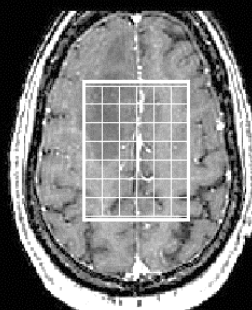
# HYPOXIA



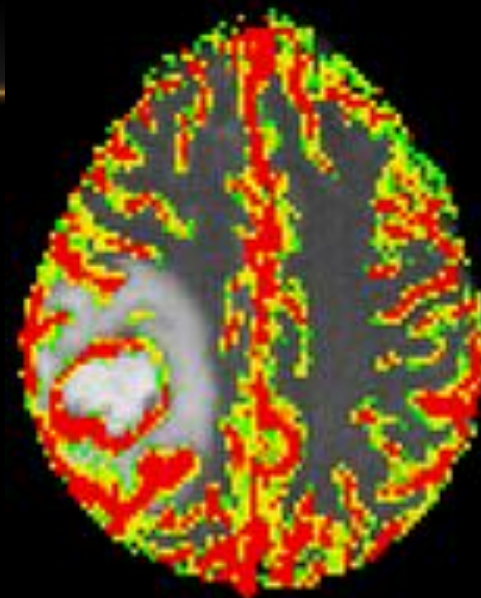
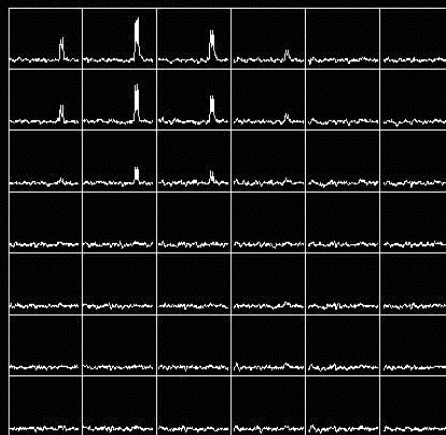
# ANGIOGENESIS



# DIFFUSION



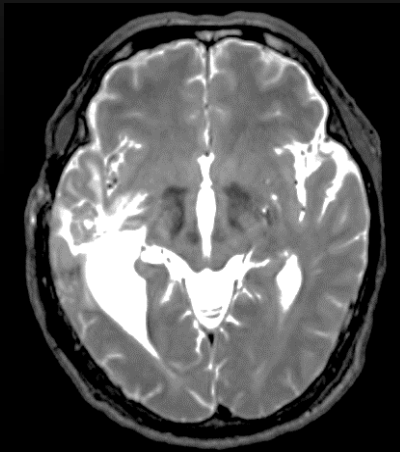
# Lactate MRS



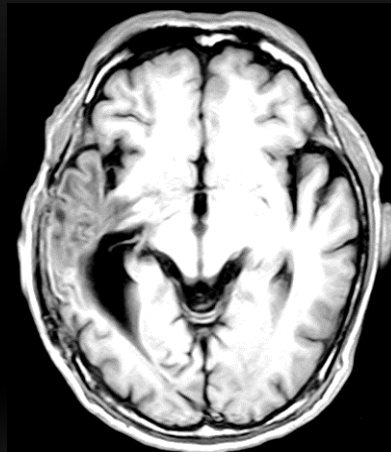
# PERFUSION

# COMPREHENSIVE BRAIN IMAGING – TUMOR

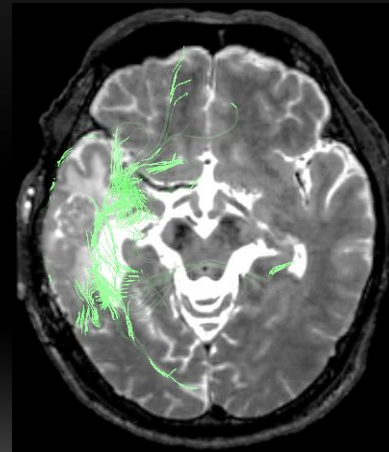
T2W



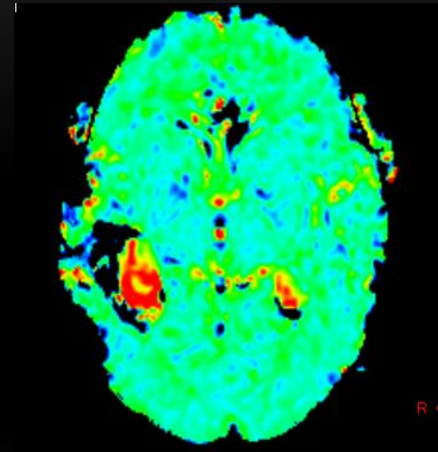
T1W IR



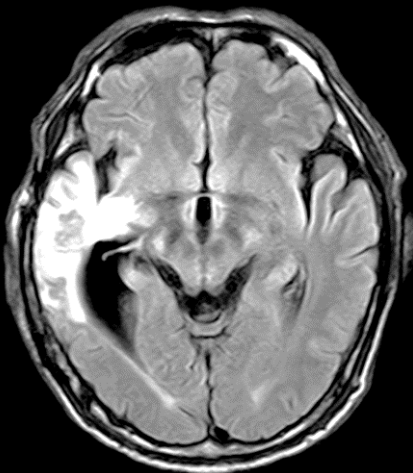
FiberTrak



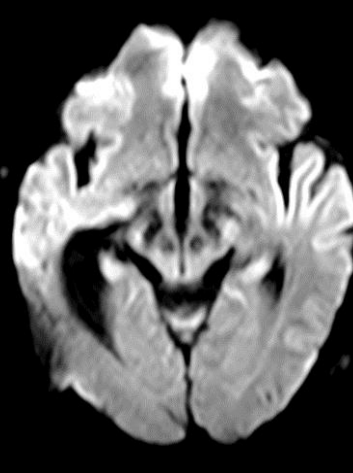
Perfusion



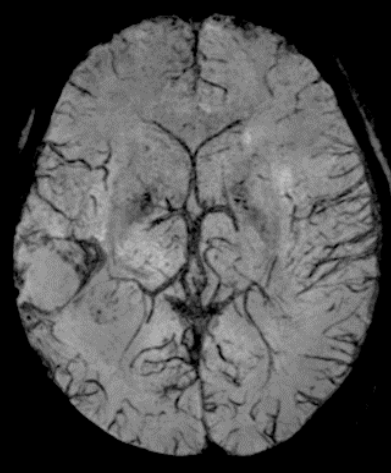
FLAIR



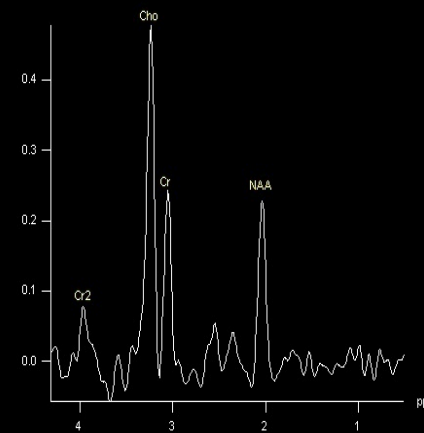
DWI



Venous Bold



MRS



# Latest Rush to Higher Fields?

TESLA ENVY??????????

Thank you for your  
patience !



# Diffuse Astrocytic and Oligodendroglial Tumors

## (1) Preliminary Typing and Grading (Histomorphology)

**Growth pattern**  
diffusely infiltrative  
circumscribed/solid

**Lineage**  
astrocytic, oligodendroglial  
ependymal, other

**Grade**  
nuclear atypia, cellular pleomorphism,  
mitoses, microvascular proliferation,  
(pseudopalisading) necrosis

WHO grade II - III

WHO grade IV

WHO grade IV  
Diffuse midline glioma

## (2) Molecular Testing

IDH mutant

IDH mutant or WT

IDH mutant

IDH wild type

IDH wild type

IDH mutant

IDH wild type

Nuclear ATRX  
retained

Nuclear ATRX  
retained or lost

Nuclear ATRX  
lost

Nuclear ATRX  
retained

Nuclear ATRX  
retained

Nuclear ATRX  
lost

Nuclear ATRX  
retained or lost

1p19q codeleted

1p19q codeleted  
or intact

1p19q intact

1p19q intact

1p19q intact

1p19q intact

1p19q intact

H3-K27M mutant

## (3) Final Integrated Diagnosis

**Oligodendroglioma**  
WHO grade II or III  
IDH mutant  
1p19q codeleted

**Mixed Oligo-astrocytoma**  
NOS

**Astrocytoma**  
WHO grade II or III  
IDH mutant

**Astrocytoma**  
WHO grade II or III  
IDH wild type

**Glioblastoma**  
WHO grade IV  
IDH wild type

**Glioblastoma**  
WHO grade IV  
IDH mutant

**Diffuse midline glioma**  
WHO grade IV  
H3-K27M mutant

## (4) Additional Molecular Alterations

TERTp mutant  
CIC mutant  
FUBP1 mutant

TP53 mutant

EGFR amplification  
EGFRvIII

TP53 mutant  
- 10q

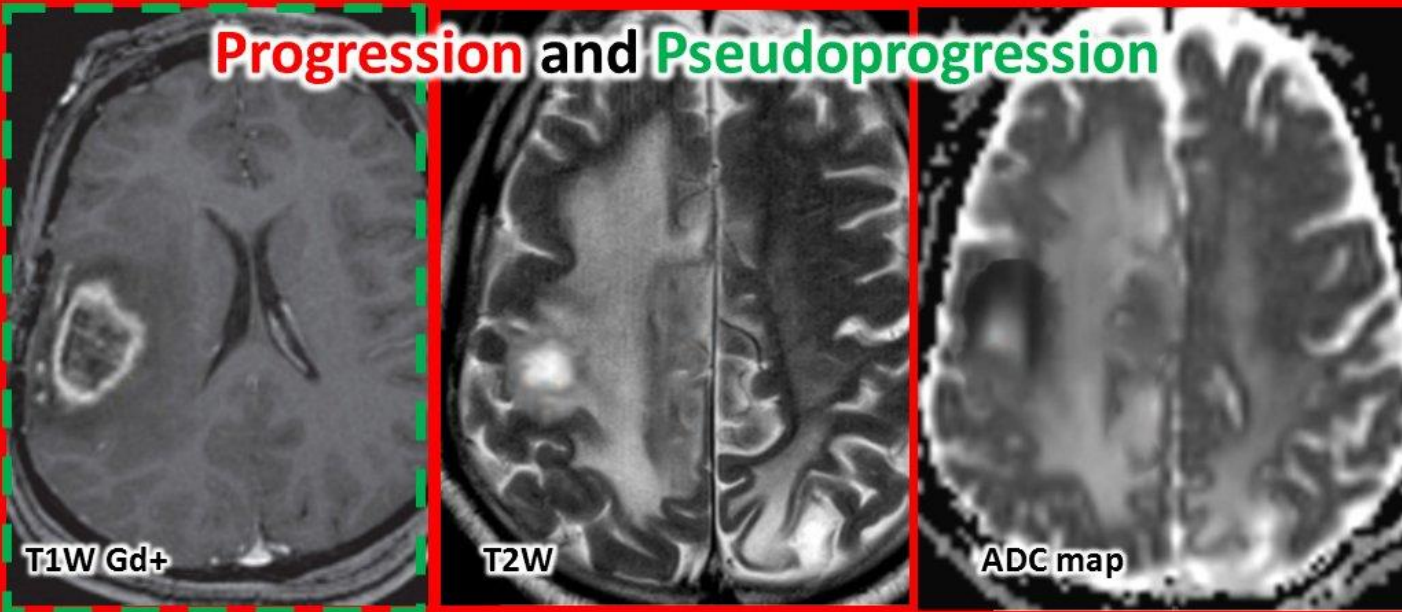
HIST 1H3B/C  
H3F3A

TERTp mutant  
+7/-10

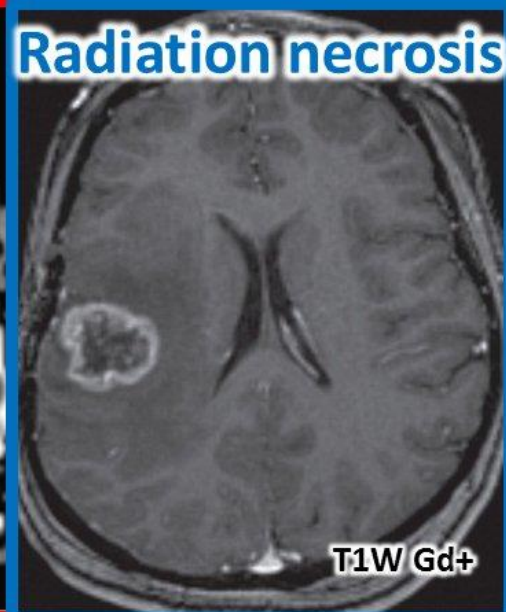
MGMT promoter methylation



# Progression and Pseudoprogression



# Radiation necrosis



- Months – years after RT
- RANO: T1W is >25% ↑, T2/FLAIR is ↑, new lesion, ↓ clinical status
- Imaging:
  - T1 Gd+ MRI: Ring-like enhancement
  - T2W: hyperintense core, surrounding edema
  - ADC map from DWI: hypointense signal surrounding hyperintense core
  - DWI: ↓ diffusion around ring
  - MR perfusion: ↑ blood volume

- ~2-6 months after RT
- Damage to oligodendrocytes, transient interruption of myelin synthesis
- More common in MGMTm
- Imaging:
  - T1W Gd+ MRI: Ring-like enhancement
  - T2W MRI: hyperintense around ring
  - DWI: ↑ diffusion around ring

- Months – years after RT
- T2W MRI: “cut pepper” appearance

## MRS

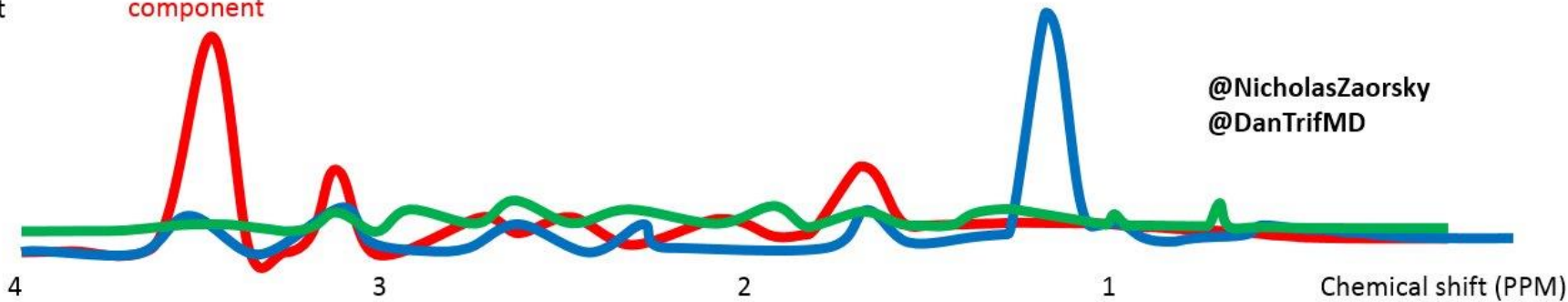
Amount

**Choline (Cho)**  
Cell membrane component

**Creatine (Cr)**  
ATP recycler

**N-acetylasparatate (NAA)**  
Neuron metabolite

**Lactate, lipids (Lac / Lip)**  
Trauma metabolite



@NicholasZaorsky  
@DanTrifMD

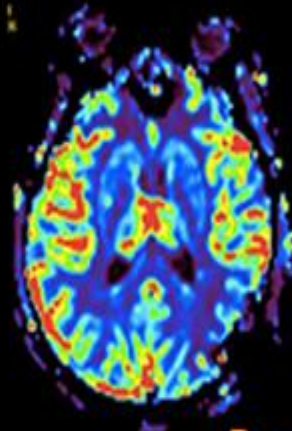
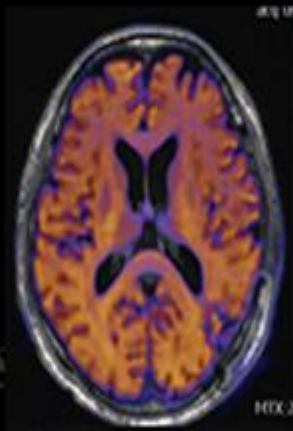
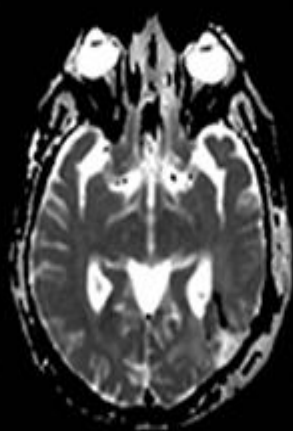
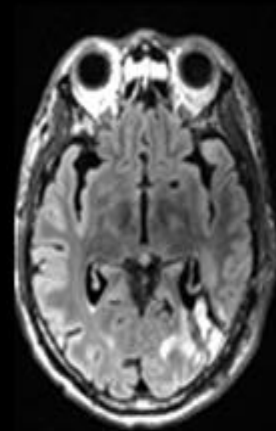
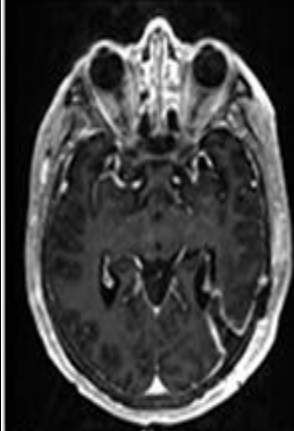
T1-POST

FLAIR

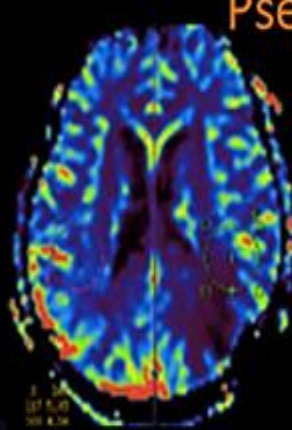
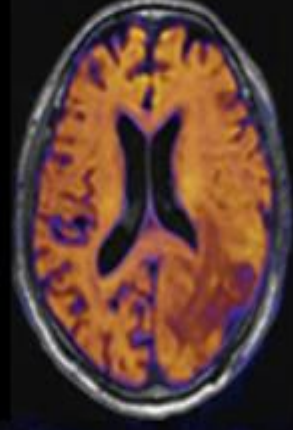
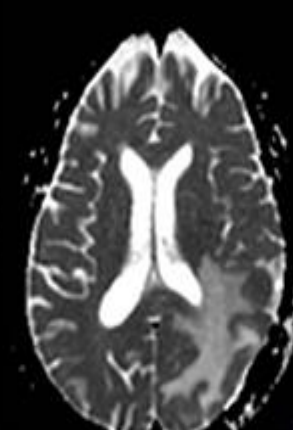
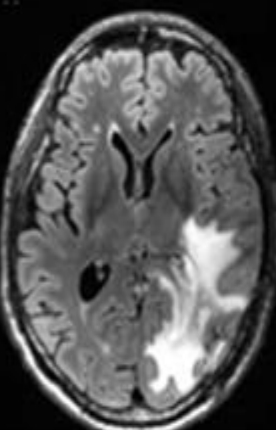
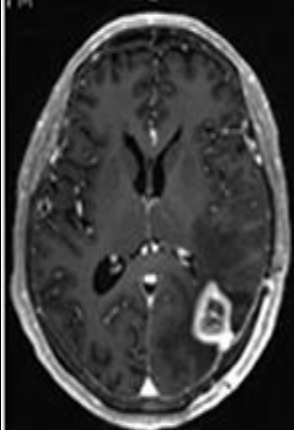
ADC

RSI-CM

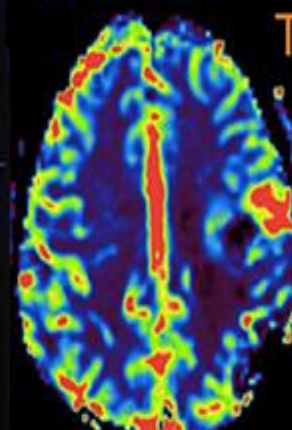
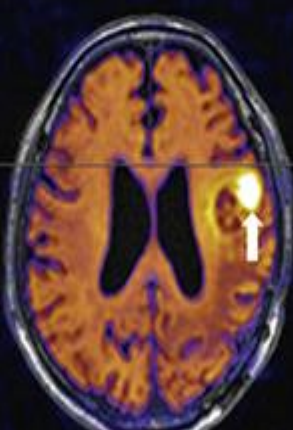
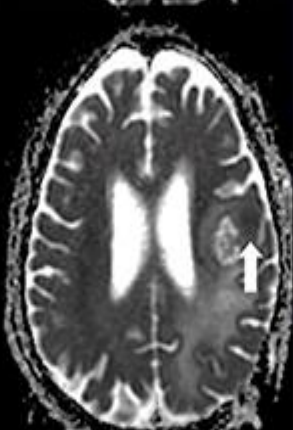
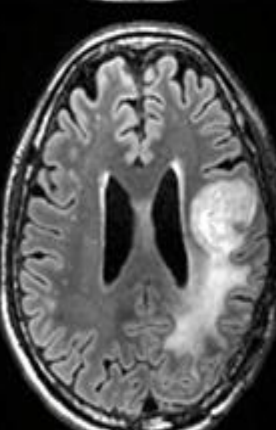
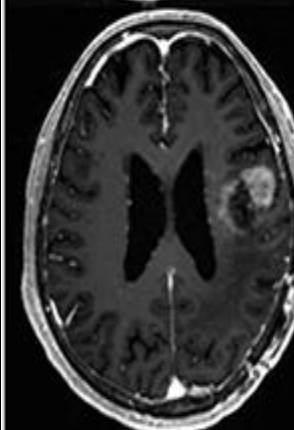
DSC-MRI



Baseline  
after 6 weeks of  
chemoradiation



Pseudoprogression  
3 months after  
initiation of  
immunotherapy



True progression  
6 months after  
baseline

