

State of the Art Brain tumor imaging

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WHO Blue Books

Radiology Advisory Board - 2020 -23

Acknowledgements.....

- Team at Tata Memorial Hospital -
Dr Tejpal Gupta
- Dr Adithyan and Dr Jalali - Apollo
Chennai

Neuroimaging armamentarium

- Conventional
- Diffusion
- Perfusion - DSC and ASL
- Spectroscopy
- DTI
- Functional - task / resting state
- APT
- PET MRI
- Radiomics
- Quantitative
- Artificial Intelligence

Outline.....

- Radiogenomics - concept
- Medulloblastomas
- Gliomas
- ASL
- Amide proton transfer (APT) imaging

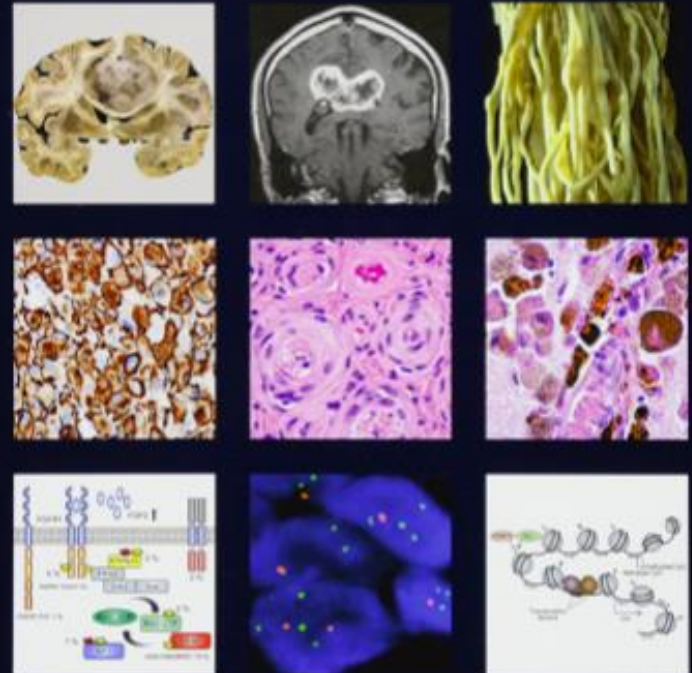


World Health Organization Headquarters

WHO Blue Books Radiology Advisory Board

WHO Classification of Tumours of the Central Nervous System

David N. Louis, Hiroko Ohgaki, Otmar D. Westler, Webster K. Cavenee, David W. Ellison,
Dominique Figarella-Branger, Arie Perry, Guido Reifenberger, Andreas von Deimling



Pathology - Paradigm Shift

Until 2016, gliomas (and all CNS tumors)
classified solely by **HISTOLOGY**

New classification WHO 2021- focus is on

GENETIC ORIGINS AND PATHWAYS

plus

HISTOLOGY

Genetics of cancer

- Each cell contains approx 30,000 different genes
- These control division, proliferation, life
- Genes are on chromosomes. Each gene has correct instructions to make protein. Protein has specific function for the cell. and control cellular working by making proteins - accurate fixed pathways
- Cancer begins when genes mutate / change - abnormal protein is formed - which gives abnormal signal and hence there is uncontrolled cellular proliferation - cancer

Radiogenomics/Radiomics

Study of the *correlation* -

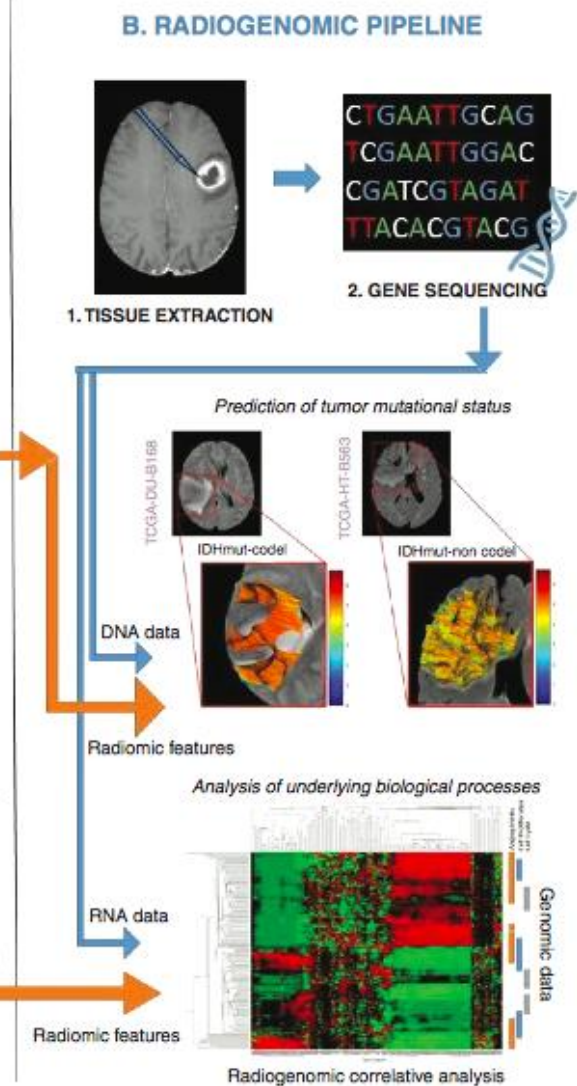
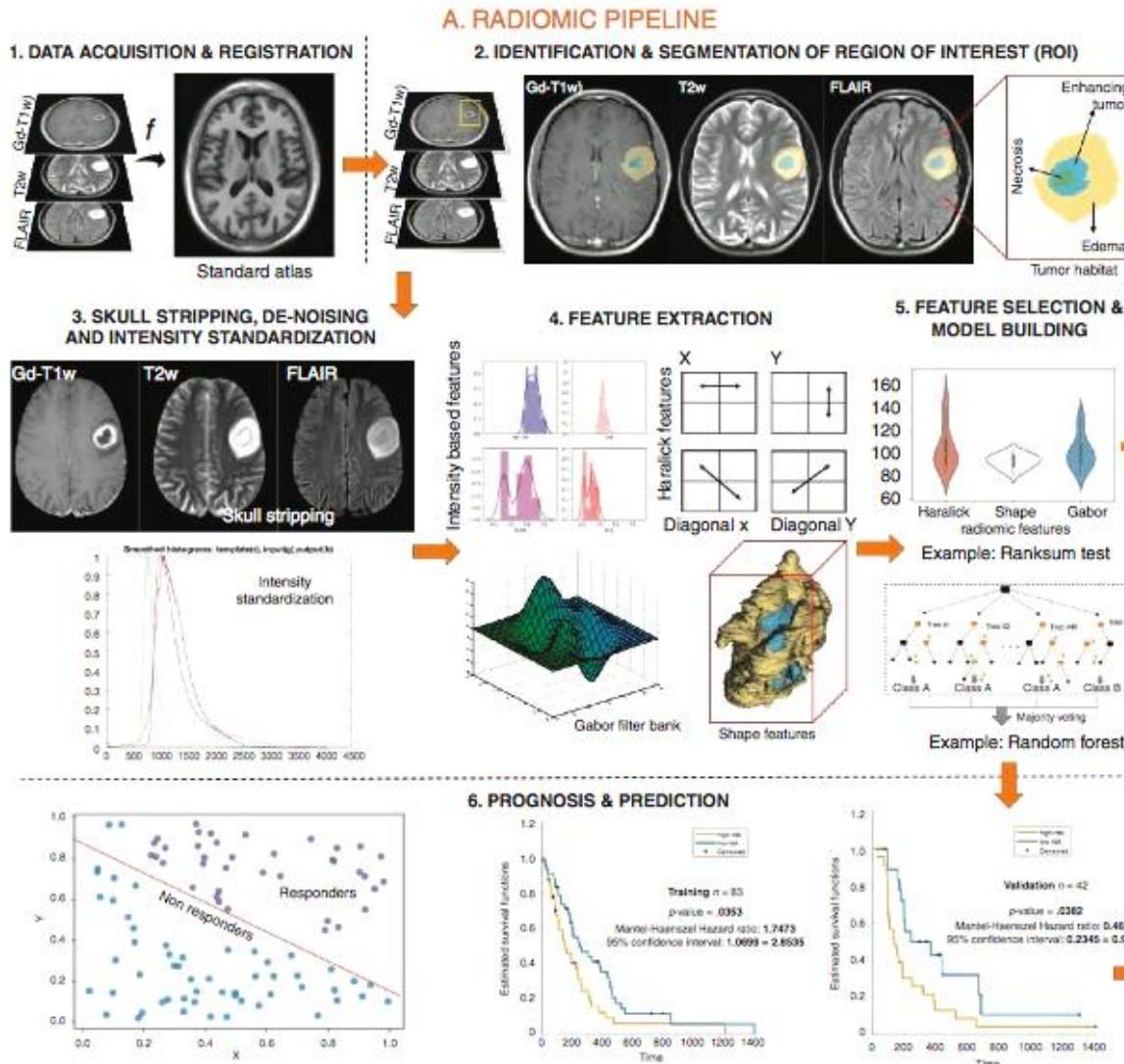
imaging features (eg. contrast enhancement, edema, necrosis, etc) and

genetic profile of the tumor (eg. IDH1/2 mutation, 1p/19q codeletion, MGMT gene promoter methylation, molecular subgrouping, etc)

and/or disease-related outcomes (eg. progression-free survival, overall survival, etc)

A more formal definition

Radiomics refers to the *extraction and analysis* of large amounts of advanced *quantitative imaging features* with high throughput from *medical images* (eg. CT, PET/CT or MRI). Radiomic data are in a *mineable* form that can be used to build *descriptive models* relating *image features* to *phenotypes* or *gene-protein signatures*. The core hypothesis of radiomics is that these models can provide valuable *diagnostic, prognostic or predictive information*



Steps of radiogenomics based approach

conversion of medical images into mineable data

- (1) image acquisition and registration,
- (2) segmentation of region of interest,
- (3) preprocessing,
- (4) feature extraction,
- (5) feature selection and building machine learning models for predictive and prognostic applications
- (6) radiogenomic associations to either predict a genotype or identify the biological processes that drive the tumor biology.

Radiogenomics in Neuro-Oncology

- Medulloblastoma
- Adult Diffuse Glioma
- Brain metastases
- Meningioma
- PCNSL

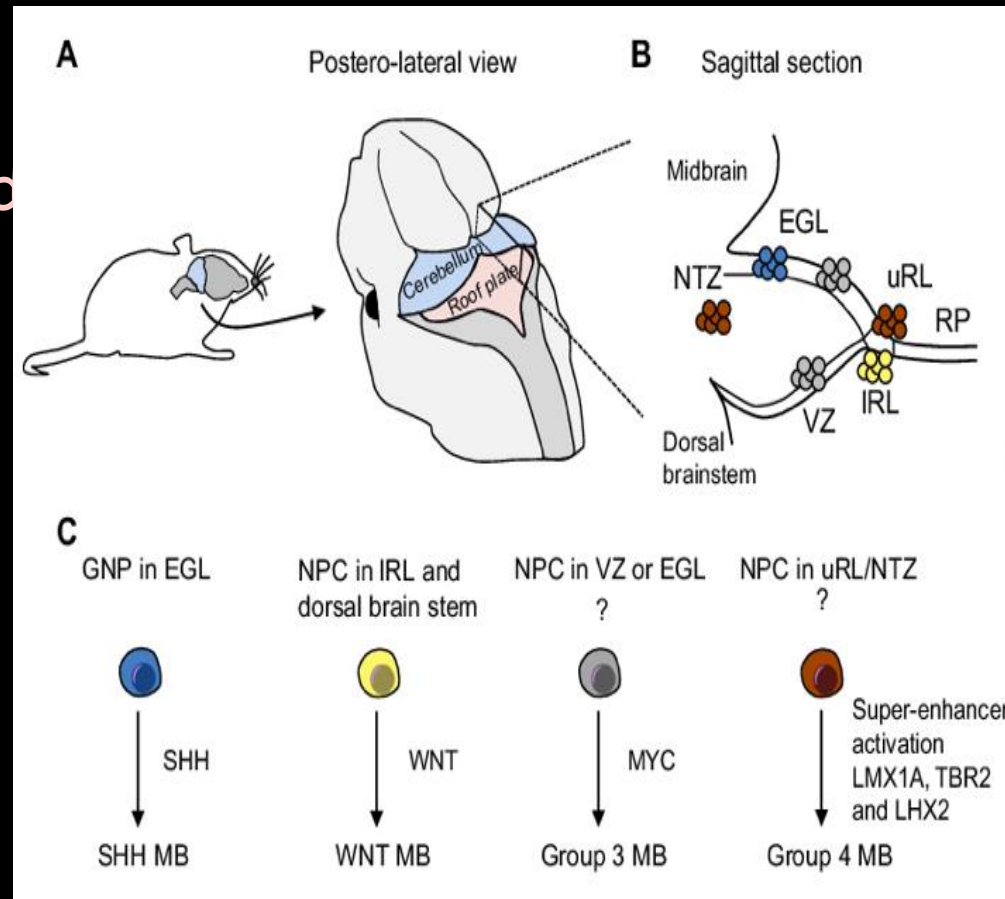
Medulloblastoma - subtypes

WNT - lower rhombic lip and dorsal brain stem

SHH - external granule layer

Group 3 - Ventricular zone or external granule layer

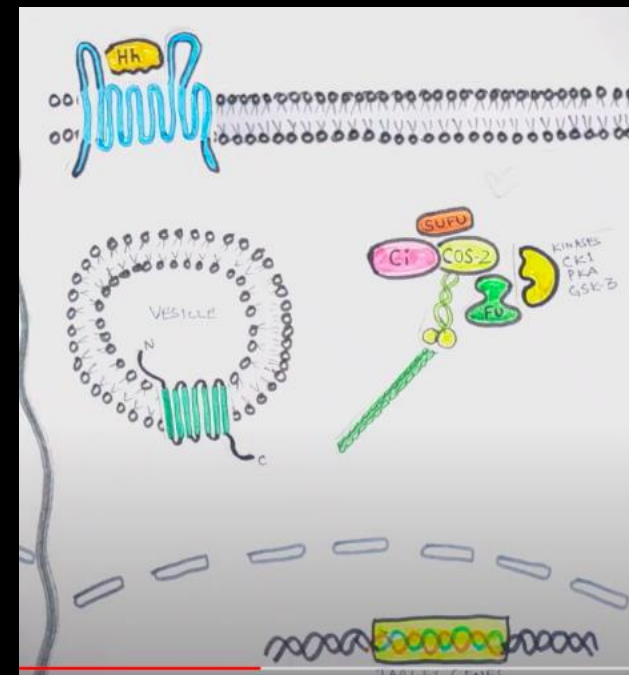
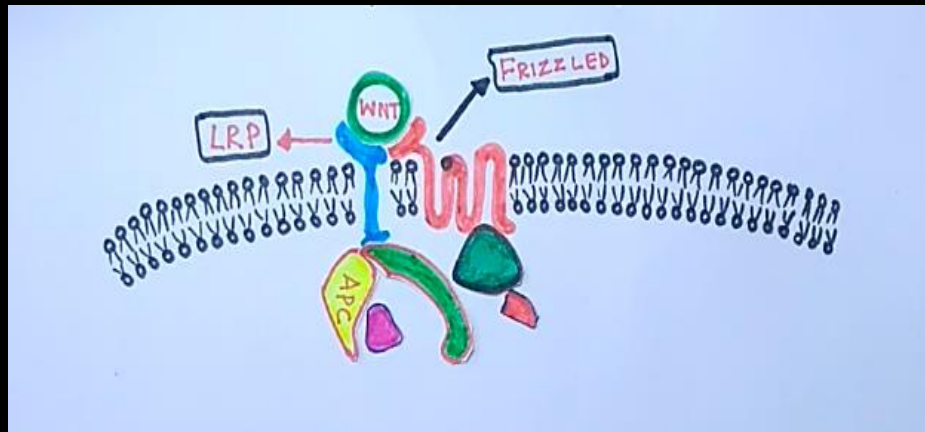
Group 4 - upper rhombic lip / nuclear transitory zone



Medulloblastoma - subtypes

WNT pathway

SHH - Sonig hedgehog pathway

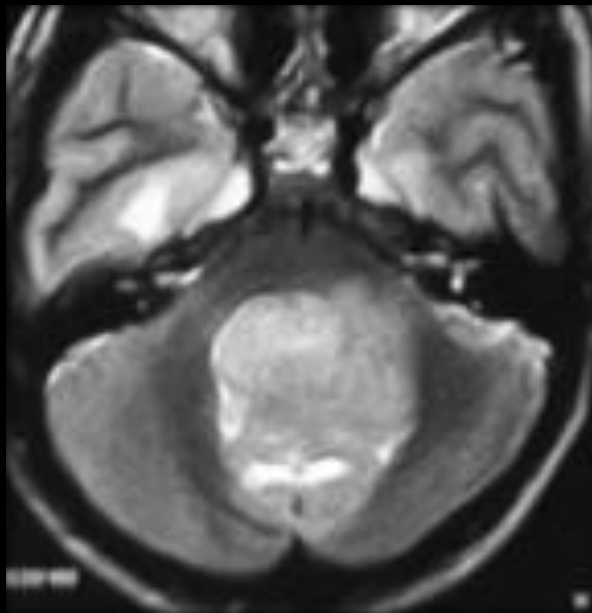


Medulloblastoma - subtypes

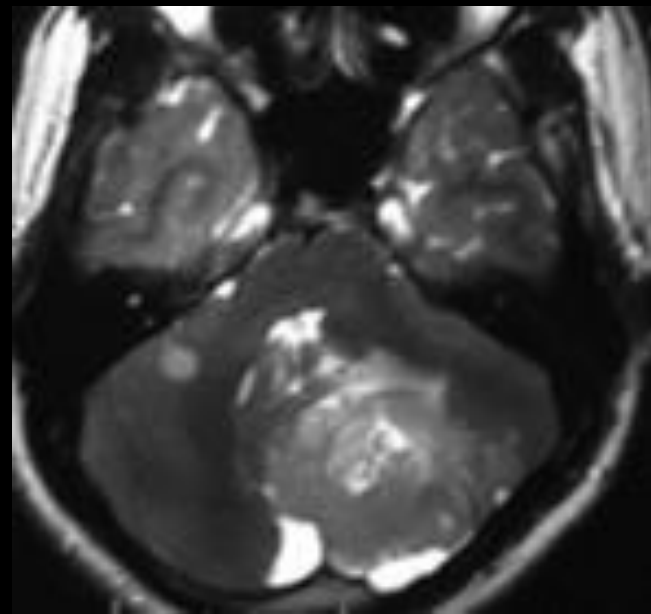
WNT pathway

SHH - Sonig hedgehog pathway

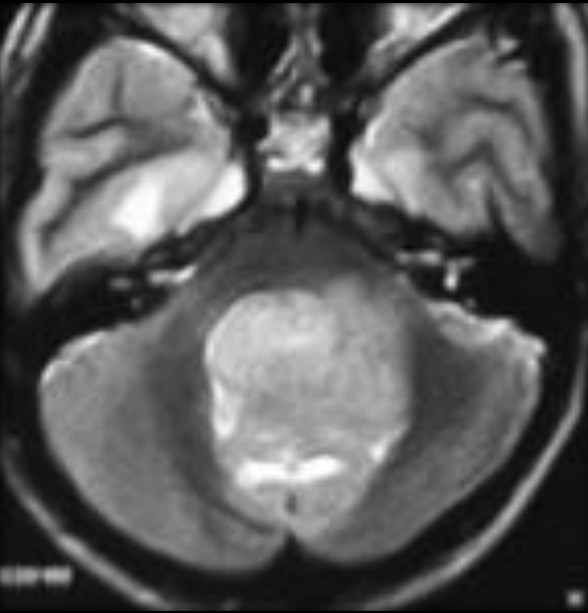
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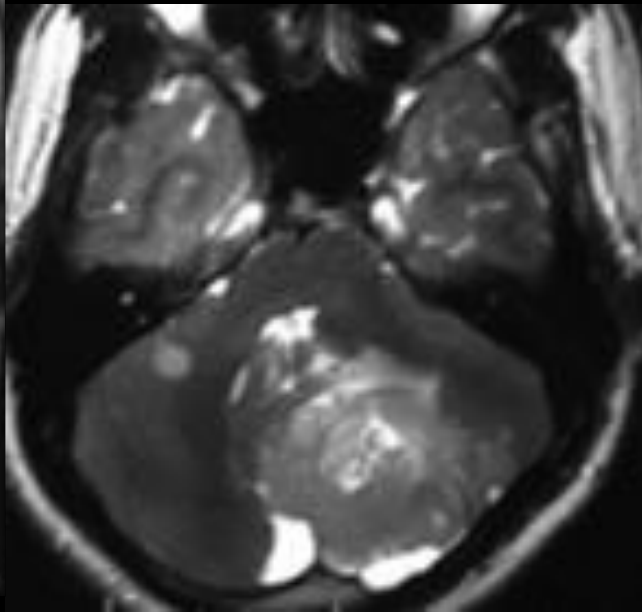
SHH



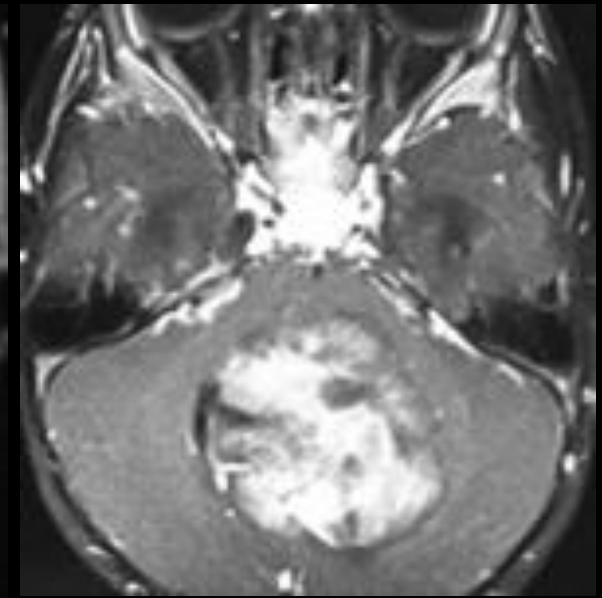
Medulloblastoma - subtypes



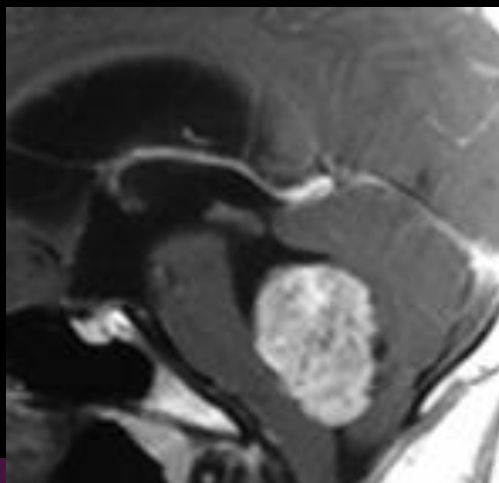
WNT



SHH



Group 3



Group 4

Nomograms based on preoperative multiparametric magnetic resonance imaging for prediction of molecular subgrouping in medulloblastoma: results from a radiogenomics study of 111 patients

Archya Dasgupta, Tejpal Gupta, Sona Pungavkar, et al
Neuro-Oncology, Volume 21, Issue 1, January 2019,
Pages 115–124,

Radiogenomics in medulloblastomas

CP angle - 75 % WNT - 100 % PPV

Hemispheric - 54 % SHH - 100 %

Midline - Ill-defined margins - group 3

Midline - Non-enhancing - group 4

Strahlenther Onkol 2022 Mar;198(3):291-303. Epub 2022 Jan 21.

Prognostic impact of semantic MRI features on survival outcomes in molecularly subtyped

medulloblastoma. Dasgupta, Pungavkar et al

Radiogenomics in medulloblastomas

Low risk - WNT - surgery and Chemo
Omit Radiotherapy - can leave residual

High risk - group 3 and 4 -
Multimodal treatment with targetted
therapy.

Radiogenomics in Diffuse gliomas

IDH1 and IDH2

ATRX

p53

BRAF V600E

H3K27M

H3 G34R/V

TERT mutation

CDKN2A/B homozygous deletion

EGFR amplification

1p/19q codeletion

Diffuse gliomas

IDH mutation

Precancerous cell

Histone mutation

Diffuse midline glioma

IDH wild type

Glioblastoma

1p/19q deletion

Oligodendroglioma

ATRX loss

Astrocytoma

IDH as a prognostic marker

IDH mutant GBMs have an improved survival (~30 mos) over wild-type (~15 mos)

Additionally, presence of IDH mutation (~10% of GBM), implies tumor arose from degeneration of initial lower grade glioma

Wild-type GBM (~90%) implies a de novo tumor which did not develop from a low grade precursor

IDH mutation

- Frontotemporal
- Well-defined margins
- Large
- Non-enhancing
- Solid / cystic

ATRX mutation

Alpha-thalassemia/mental retardation syndrome x-linked gene

Loss of function almost always occurs in the setting of IDH mutation - thus making it a powerful marker for astrocytoma

Presence of ATRX function loss correlates with a favorable prognosis in astrocytoma

Mutation/loss of function almost never occurs in the setting 1p/19q codeletion

1p/19q oligodendroglioma marker

Deletions involving the 1p and 19q chromosomal arms - detected by FISH analysis

Considered to be an objective marker of oligodendroglioma cellular lineage



1p/19q co-deletion

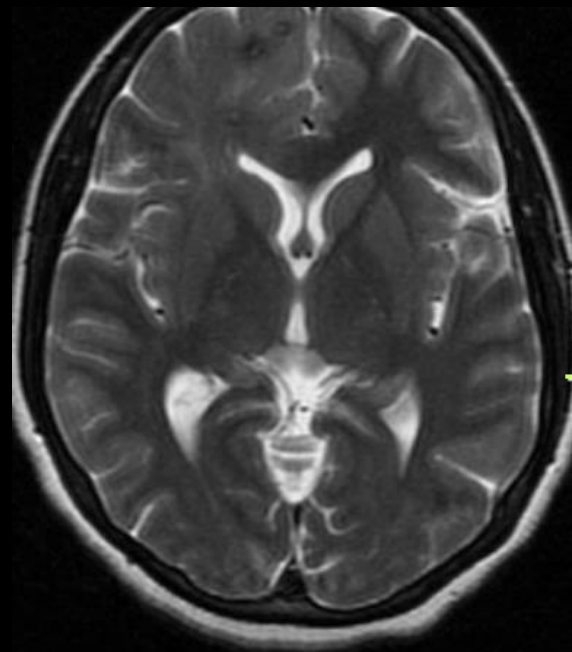
- Ill-defined
- Frontal lobes
- Calcification
- < 50 % T2/ FLAIR mismatch
- Cortical location

Indistinct margins Calcium seen

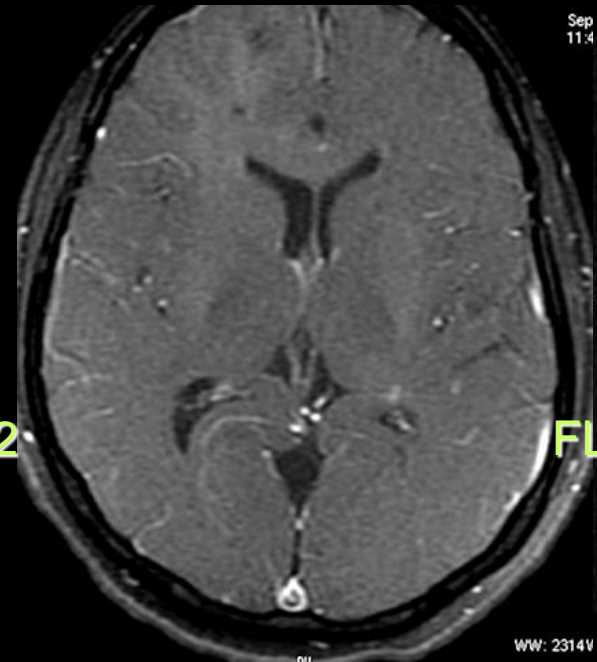
T2

T1

GRE



T2

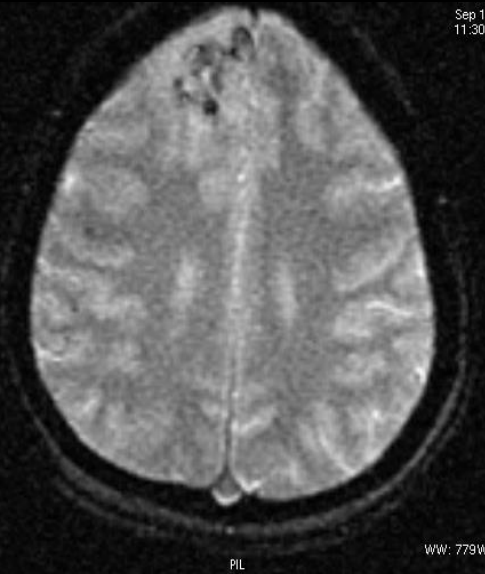


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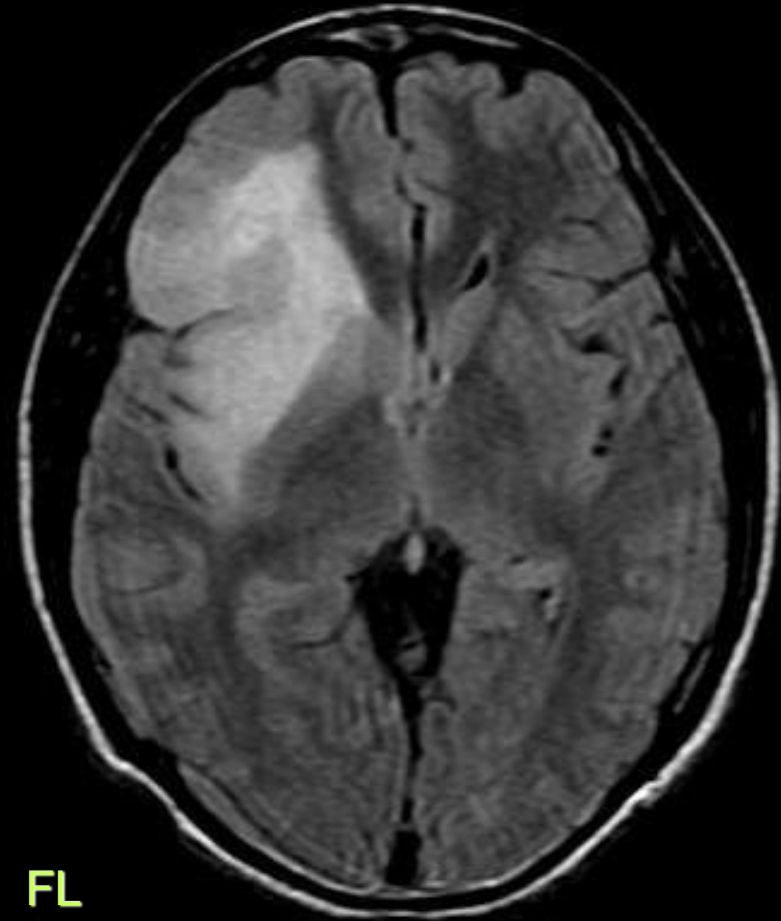
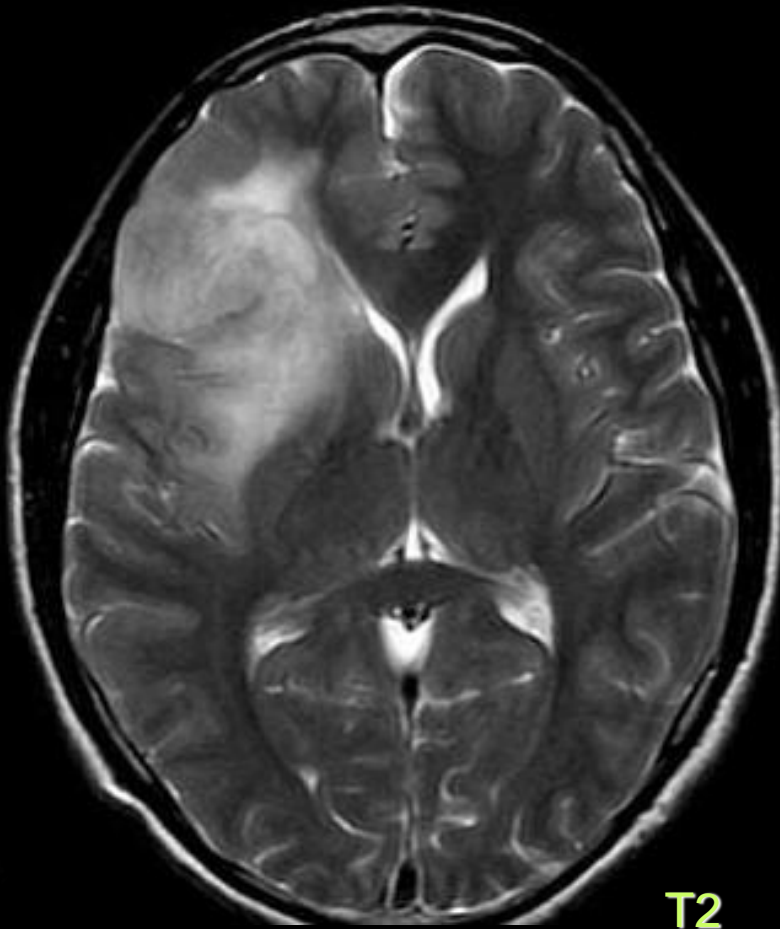
Sep 11
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PIL

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Adult type diffuse glioma
1p/19q codeleted tumor

Indistinct margins with no mismatch



Adult type diffuse glioma
1p/19q codeleted tumor

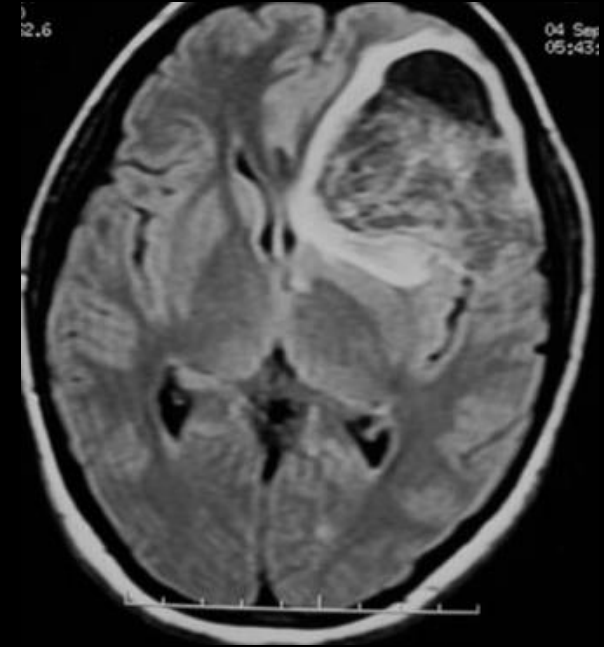
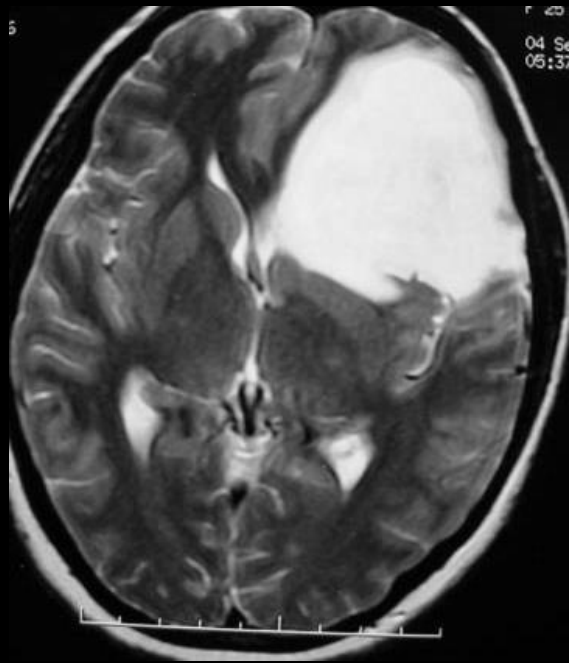
T2 / FLAIR MISMATCH

Biomarker for IDH-1 mutated

T2

T1

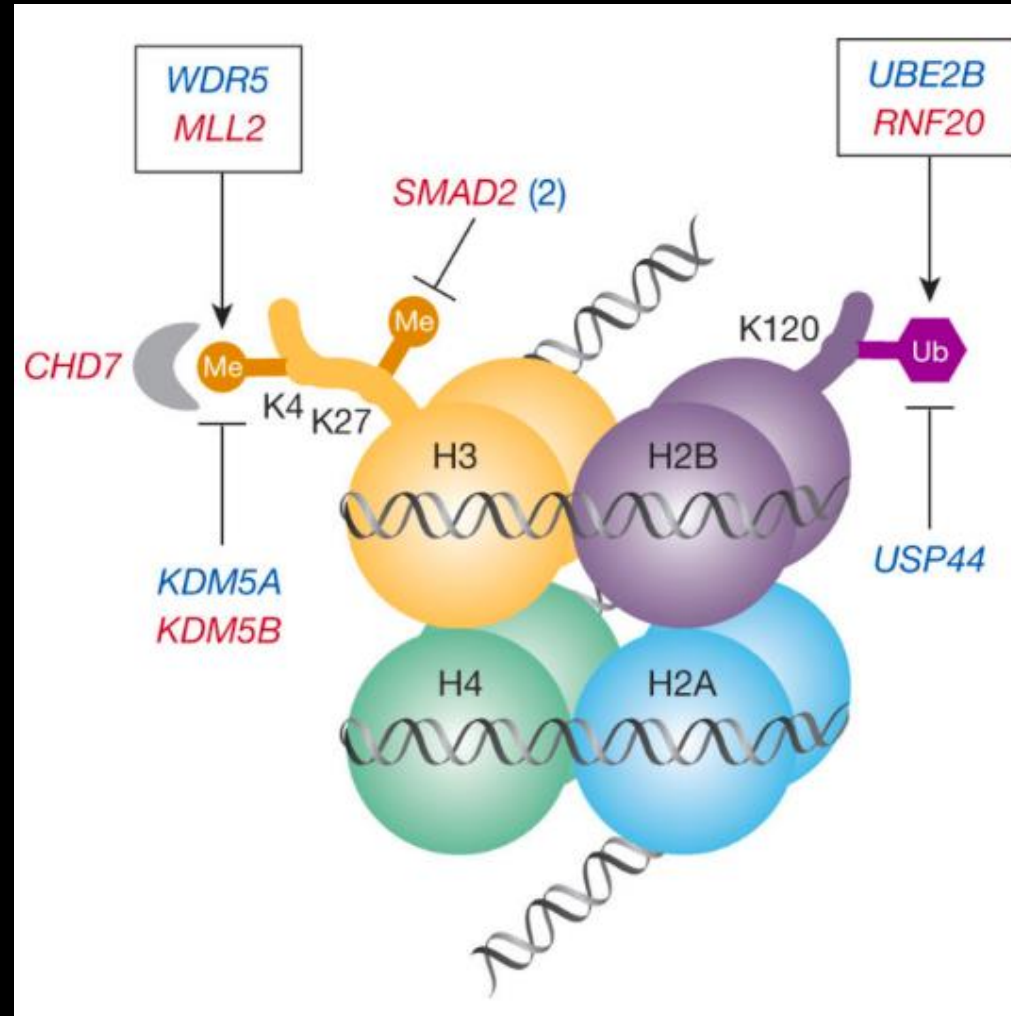
FLAIR



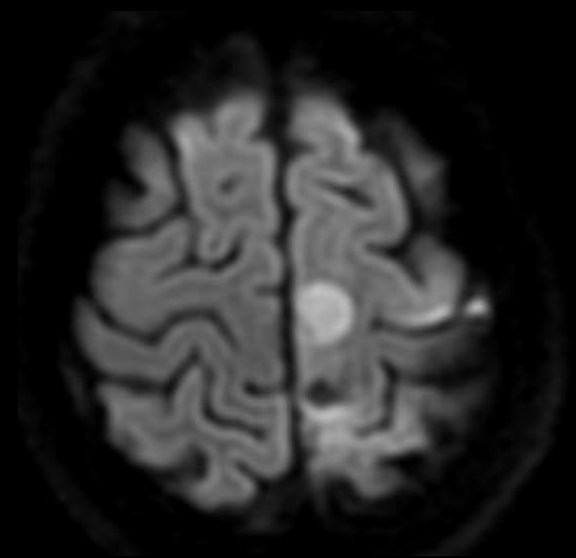
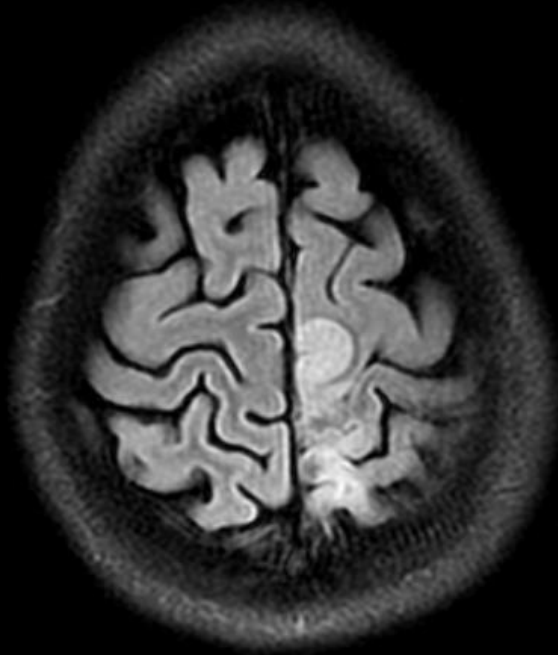
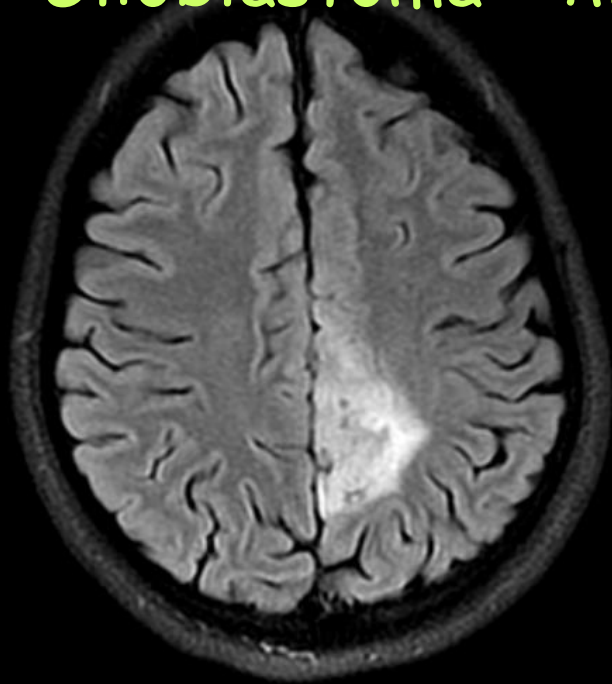
Adult type diffuse glioma
1p/19q non codeleted

Histone mutation

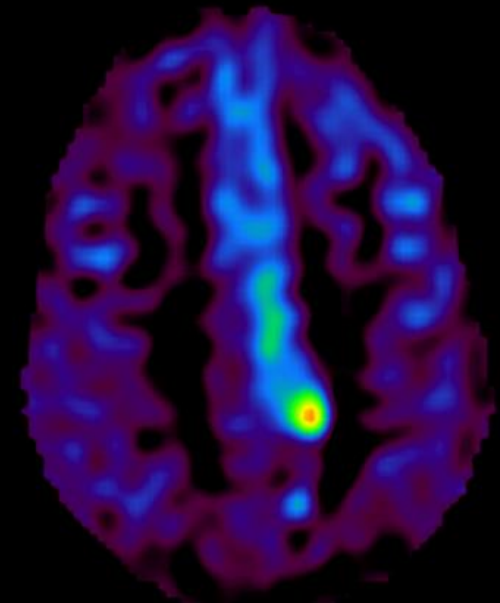
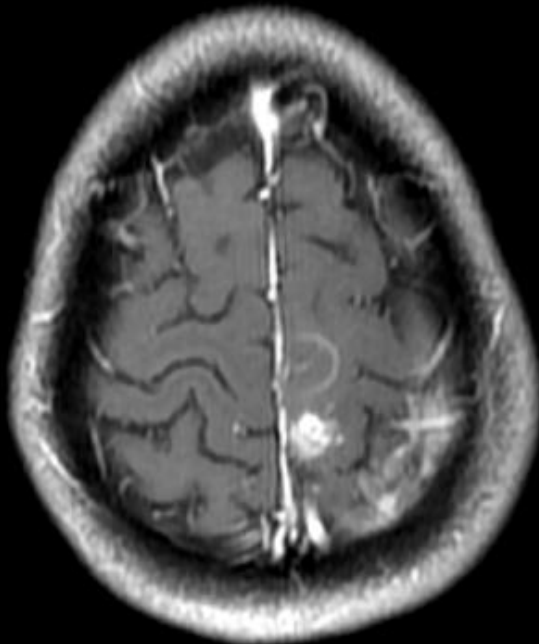
- Midline
- Diffuse
- Heterogeneous
- Multifocal
- Poor prognosis



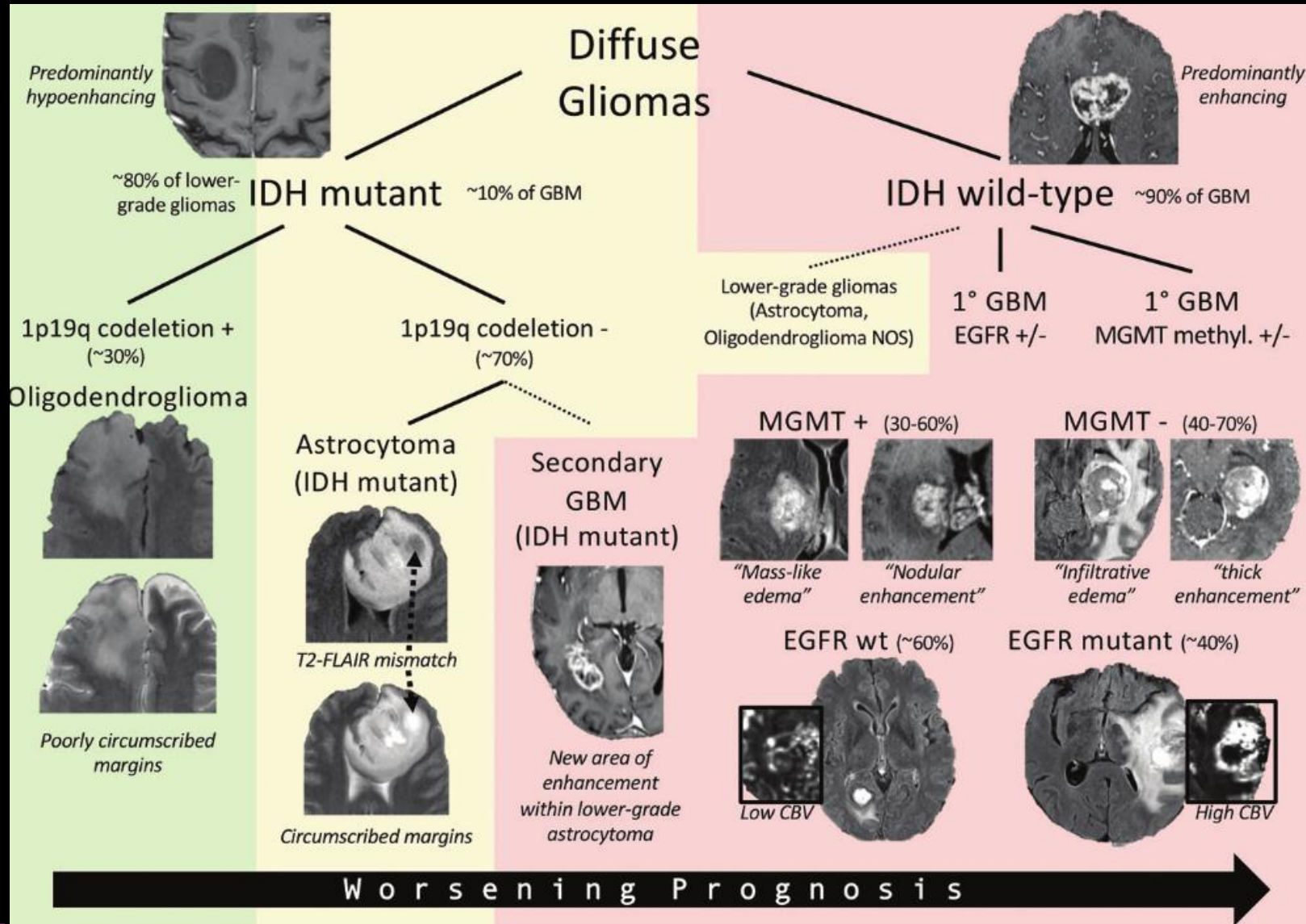
Glioblastoma - histone mutated



- Midline
- Diffuse
- Heterogeneous
- Multifocal

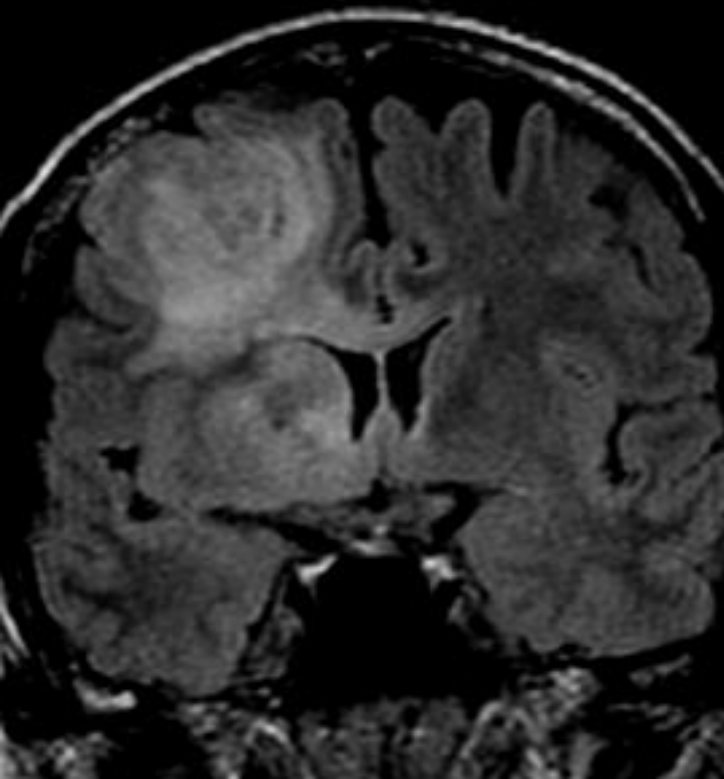


Genomic and radiogenomic landscape of adult diffuse glioma

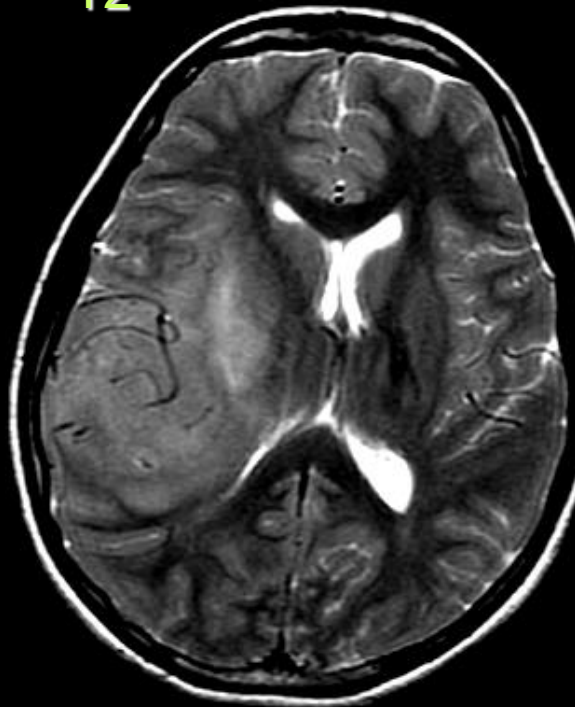


Middle aged lady with seizures
since 1 month

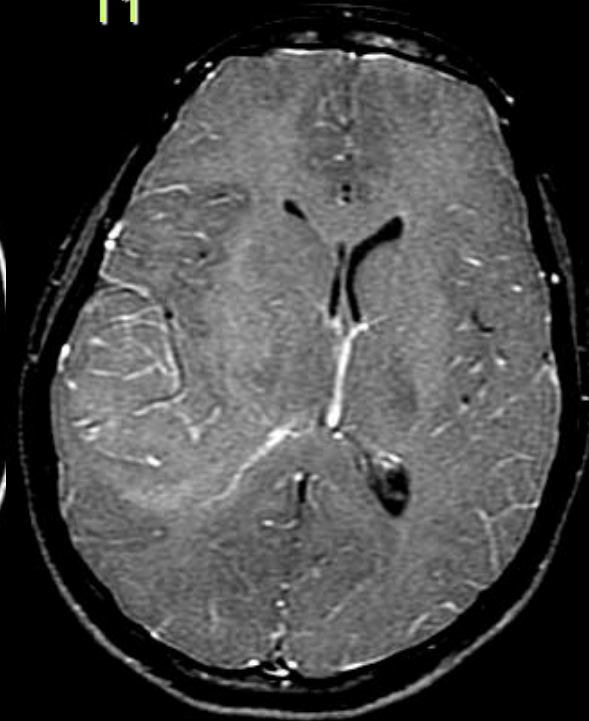
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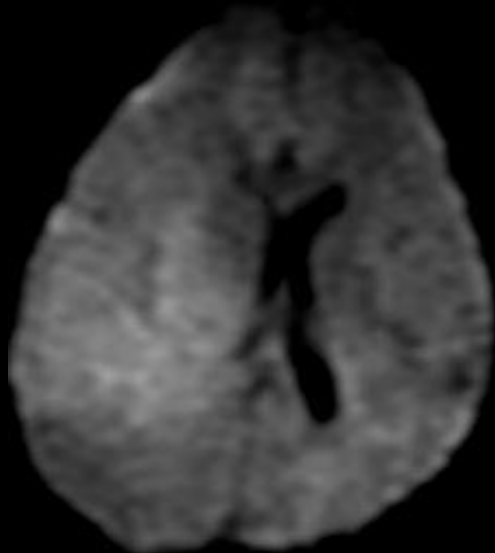
T2



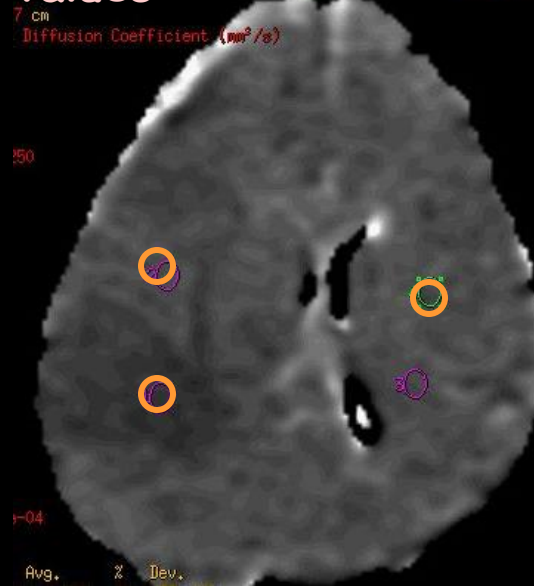
T1



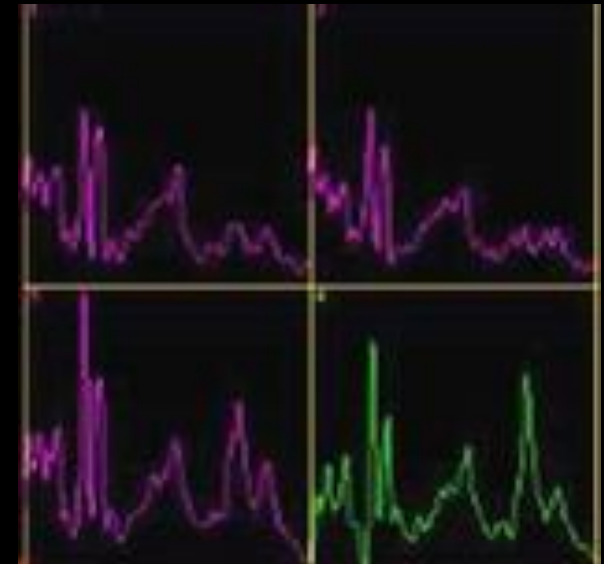
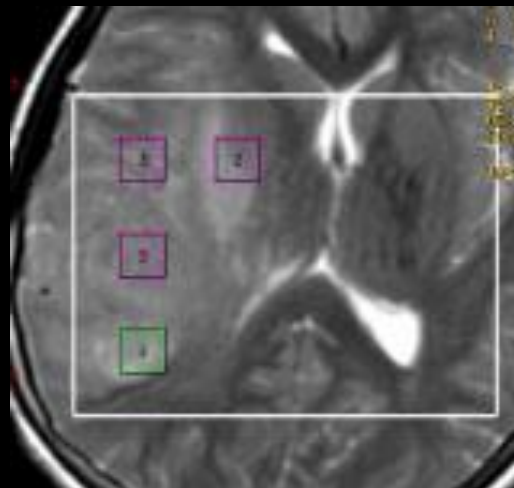
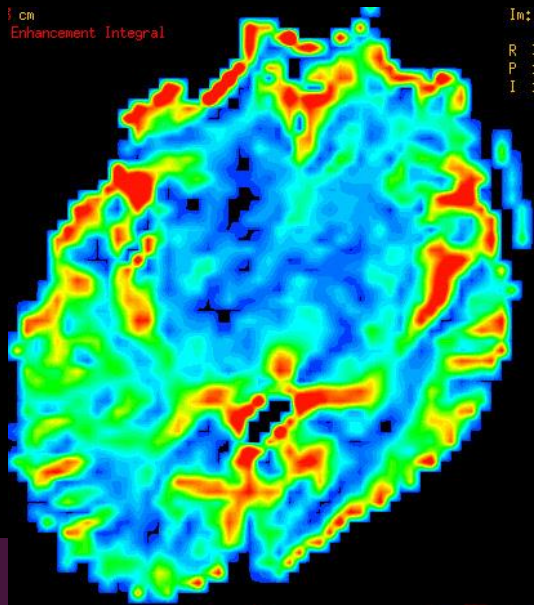
Restricted diffusion



Reduced ADC values



MR perfusion - Increased

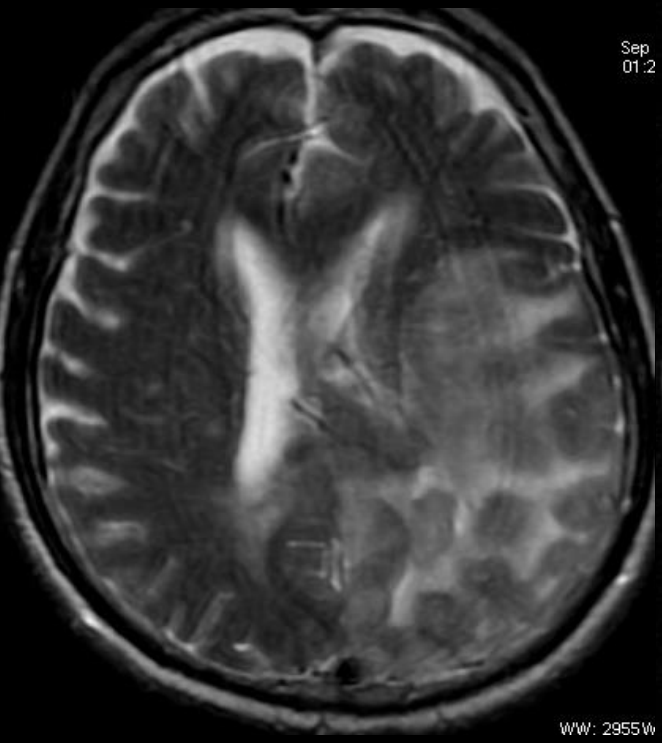


PREDICT HISTOGENETICS

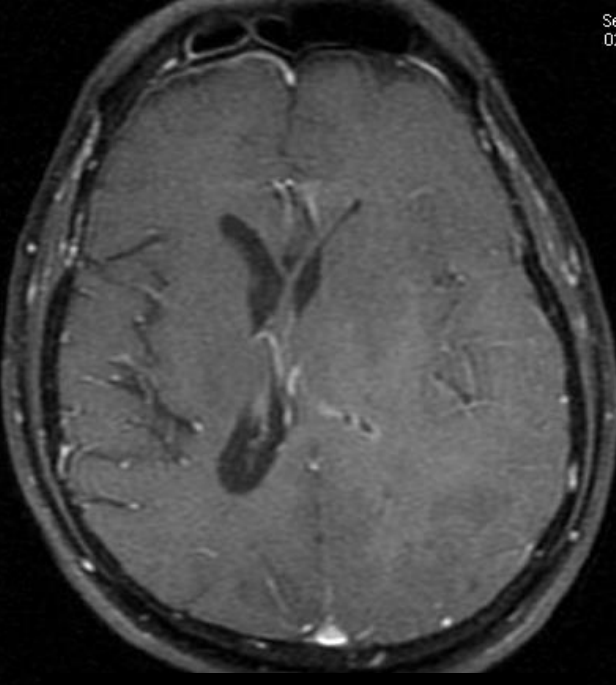
- Adult type diffuse glioma
- Diffuse ill-defined margins
- IDH 1 mutated, ATRX lost
- Grade 3

Anaplastic astrocytoma

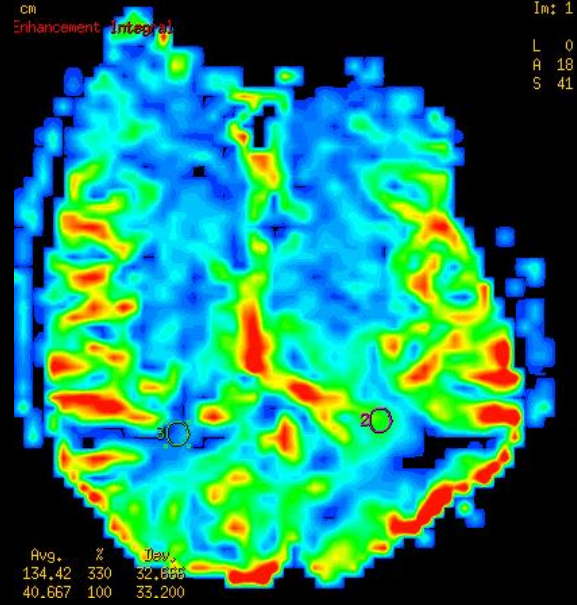
T2



T1



Perf

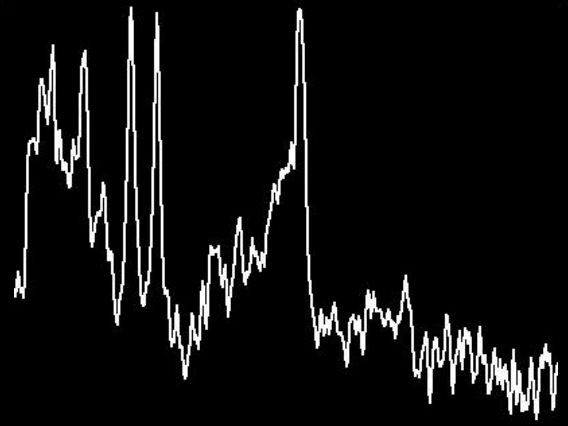


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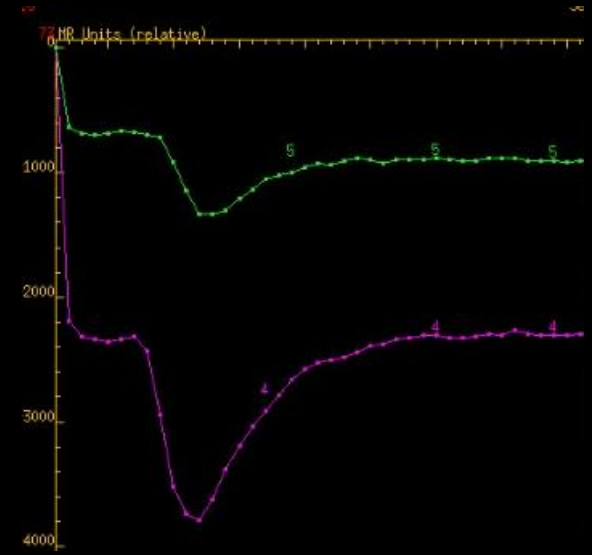
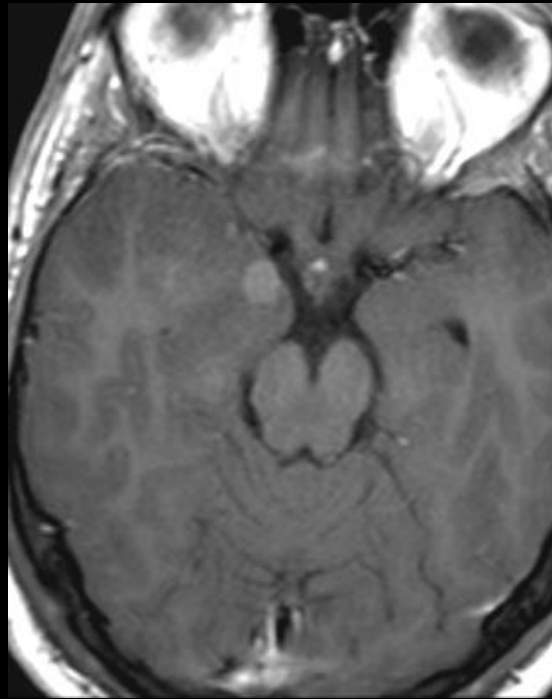
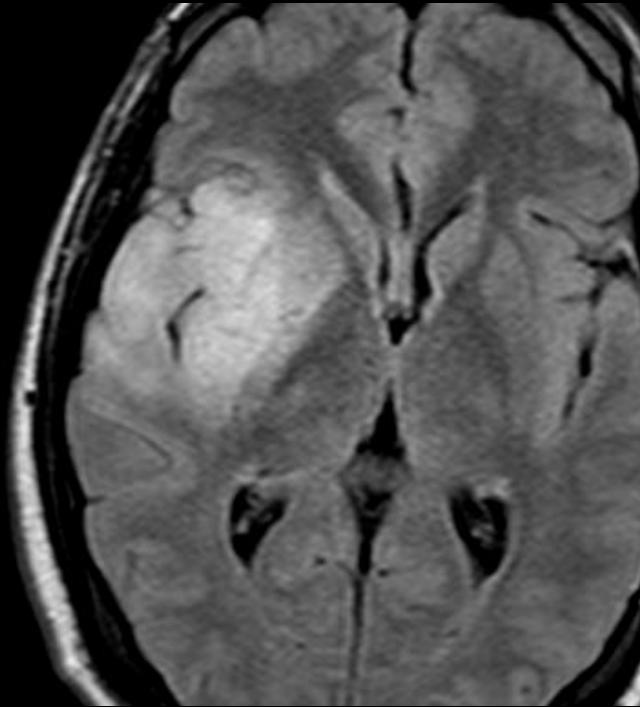
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PREDICT HISTOGENETICS

- Adult type diffuse glioma
- Cortex thick - Oligo component
- IDH1 mutated, 1p-19q codeleted
ATRAX retained
- Grade 3

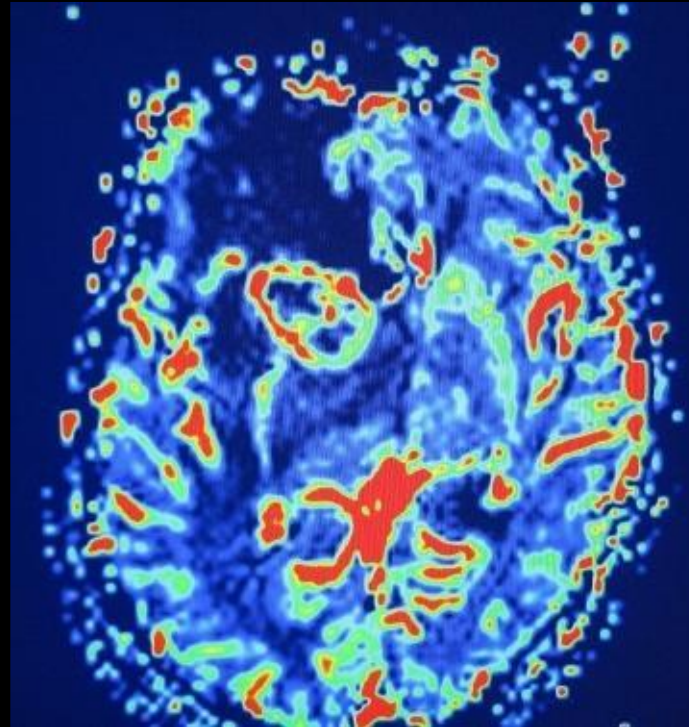
Anaplastic oligodendroglioma



PREDICT HISTOGENETICS

- Adult type diffuse glioma
- Astrocytoma as no cortical thickening
- IDH mutated / ATRX lost
- 1p/19q non deleted
- Grade 4

Secondary glioblastoma



PREDICT HISTOGENETICS

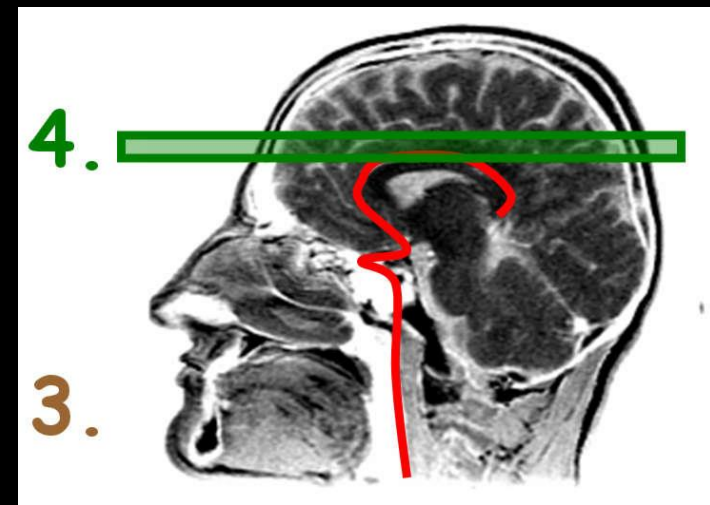
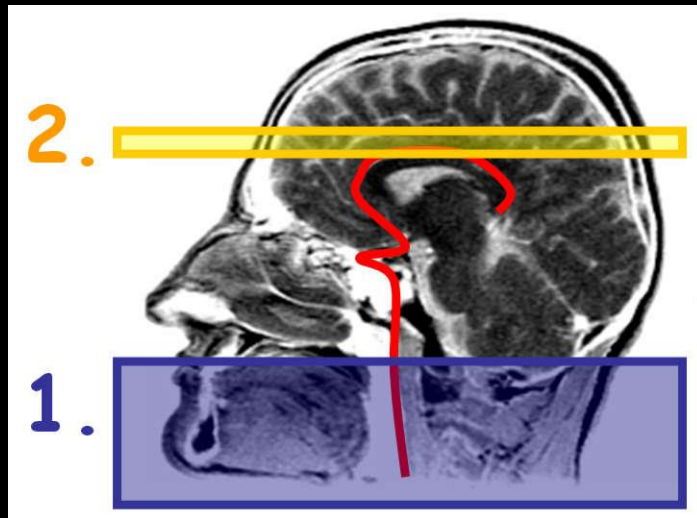
- Adult type diffuse glioma
- Astrocytoma
- IDH wild type
- Grade 4

Primary glioblastoma

Introduction to ASL

- Taking advantage of arterial water in flowing blood as a freely diffusible tracer
- Can measure absolute CBF
- Low sensitivity (blood is ~3% by volume in brain parenchyma)

Principle of ASL



1. **Tag** inflowing arterial blood by magnetic inversion

Allow delay time

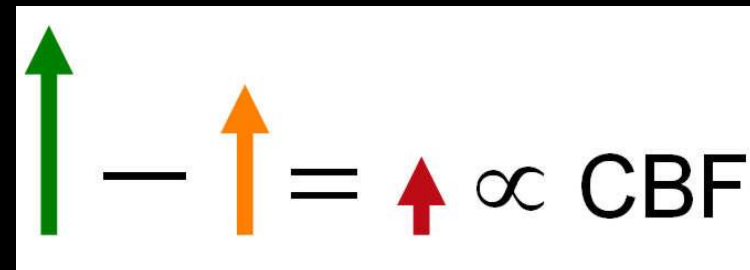
2. Acquire the **TAG IMAGE**

ASL: Hybrid

Pseudo Continuous labeling - pCASL

3. Repeat without **tag**

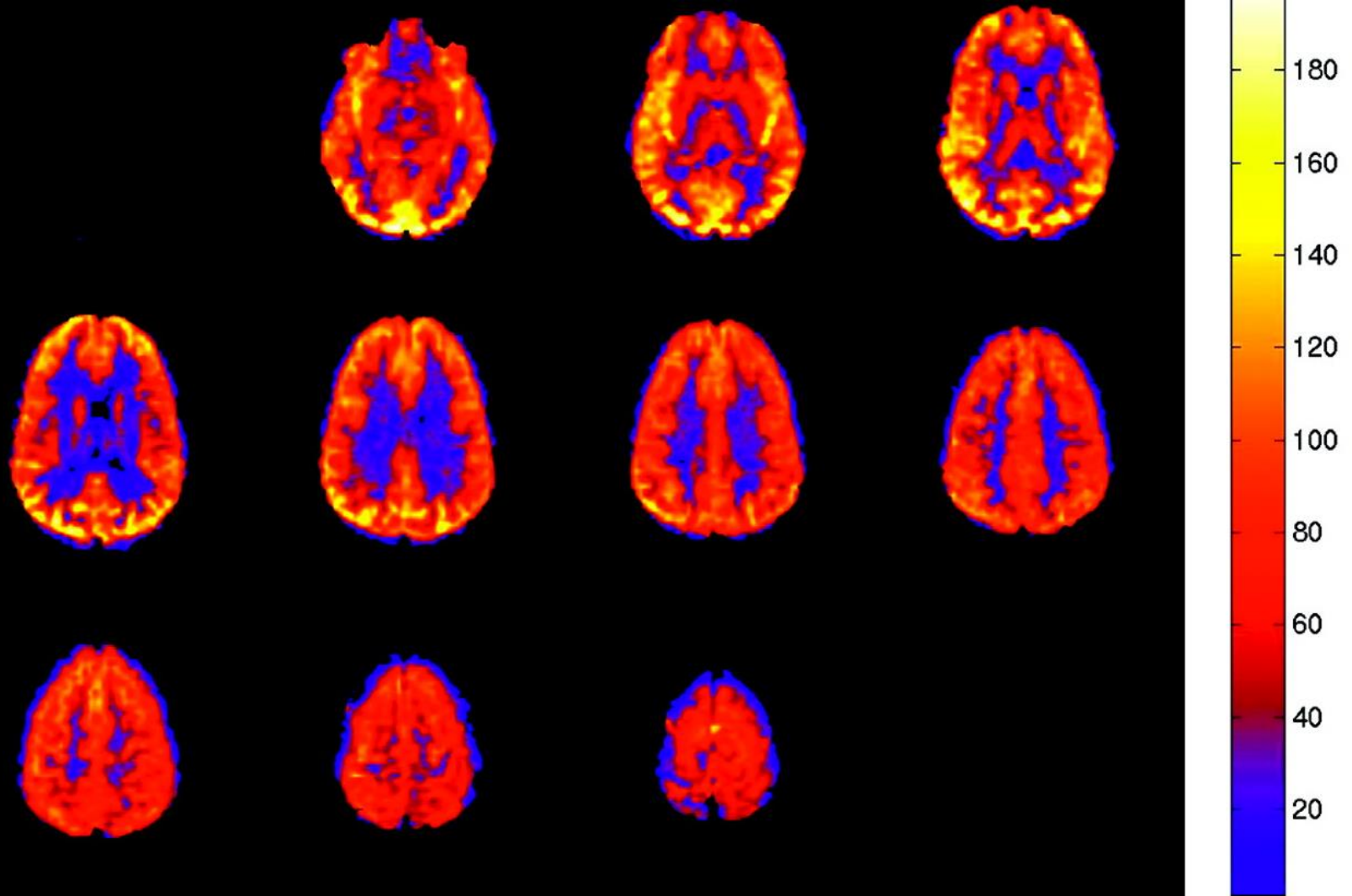
4. Acquire the **CONTROL IMAGE**



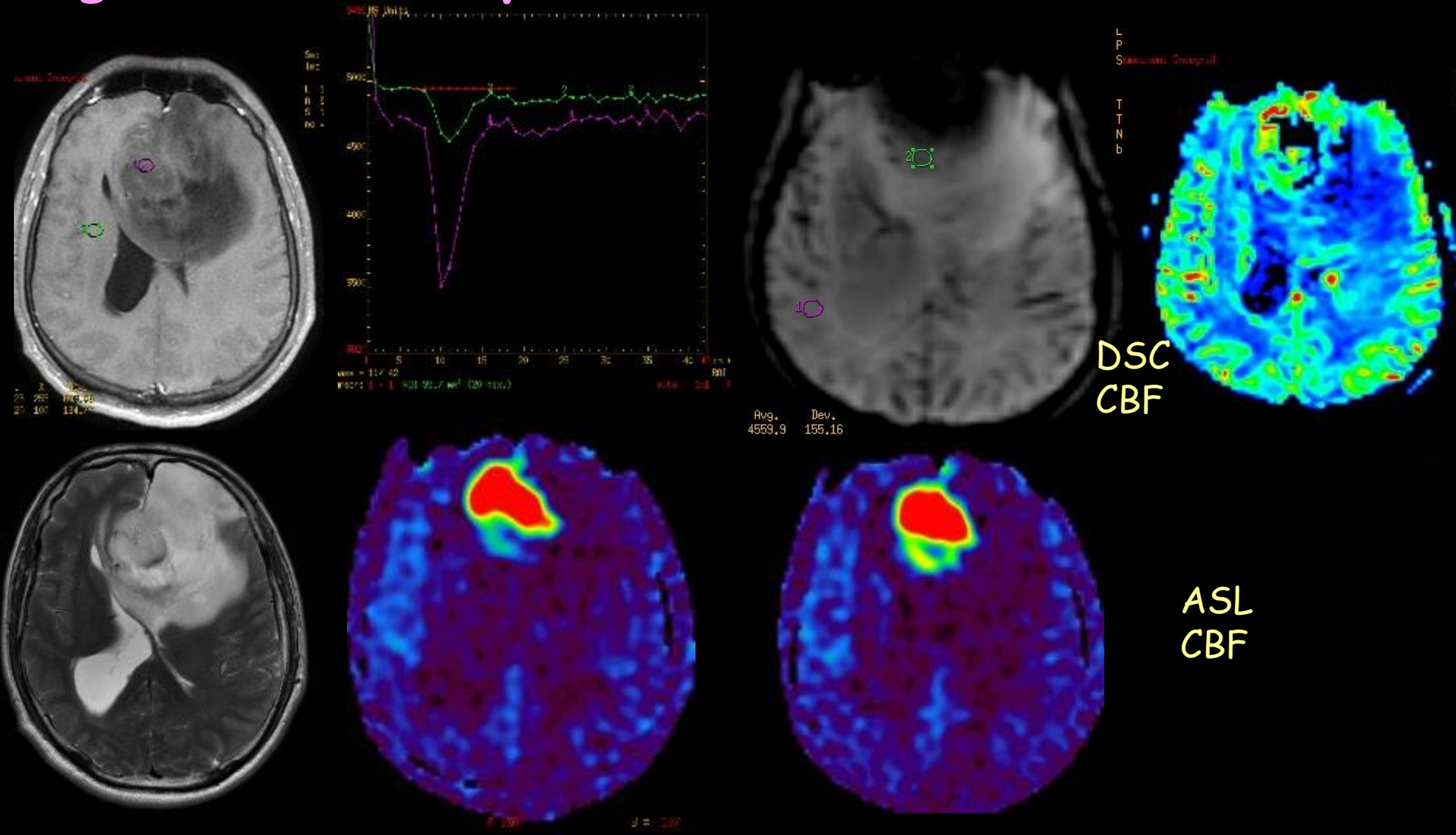
$$\uparrow - \uparrow = \uparrow \propto \text{CBF}$$

$$M_{\text{control}} - M_{\text{tag}} = \Delta M$$

Normal ASL CBF map



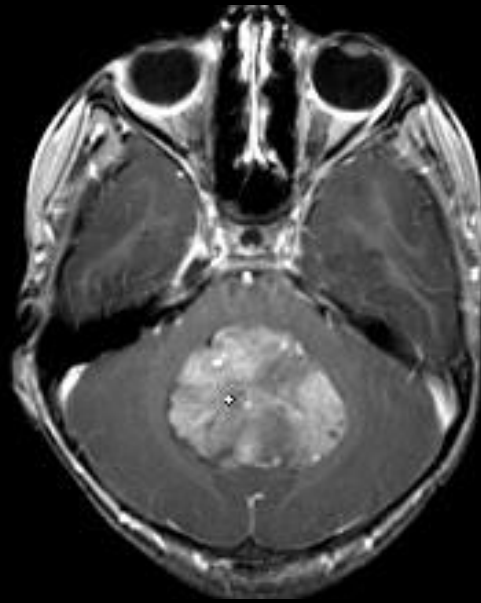
Infiltrative tumor - grade 3 astrocytoma



0.0cm

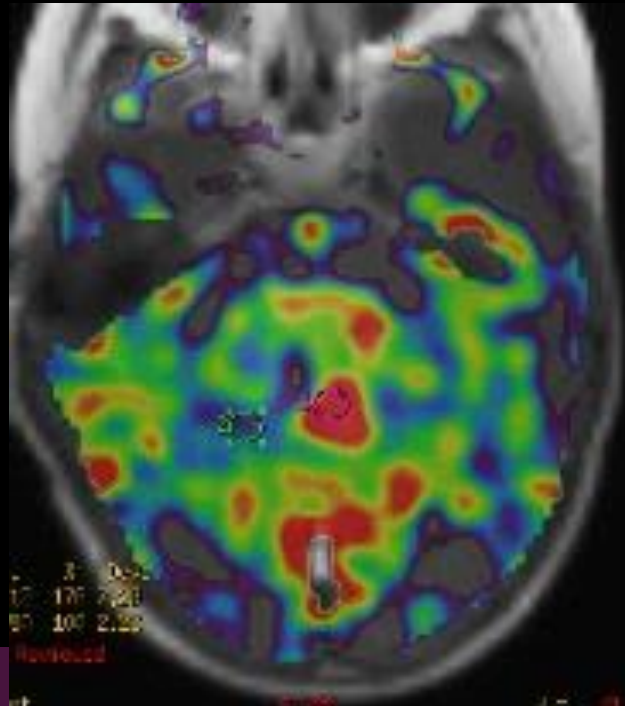
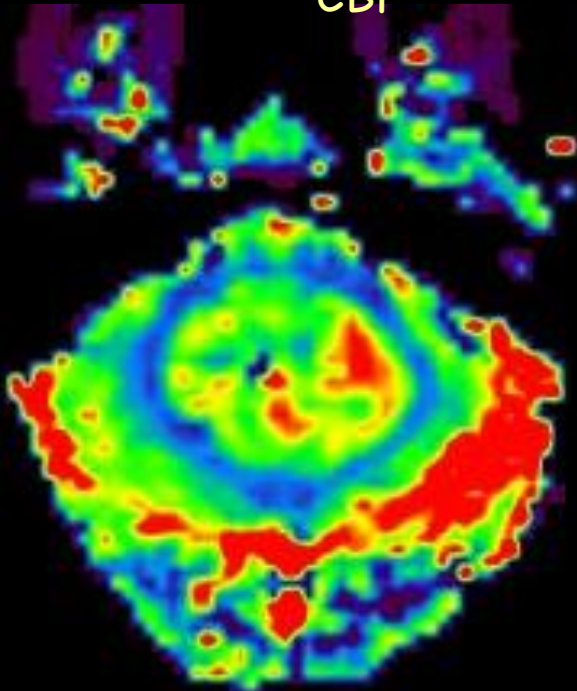


DSC
CBF



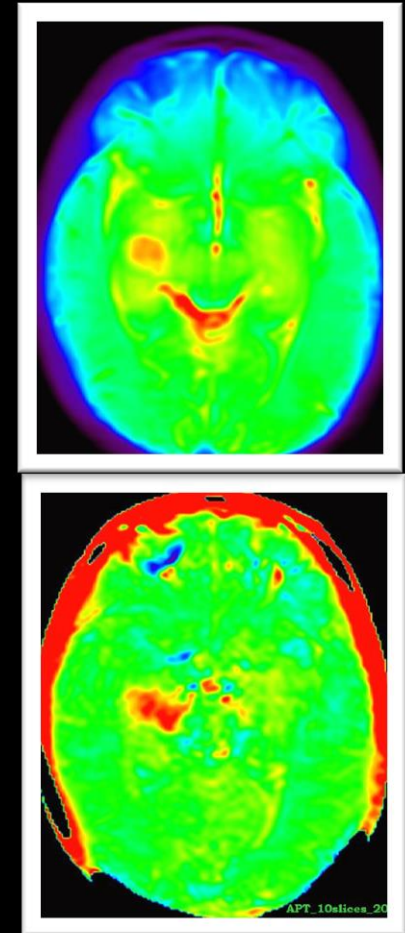
ASL
CBF

Medulloblastoma

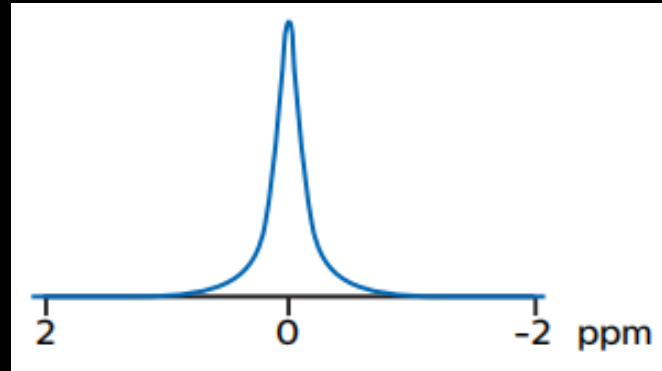
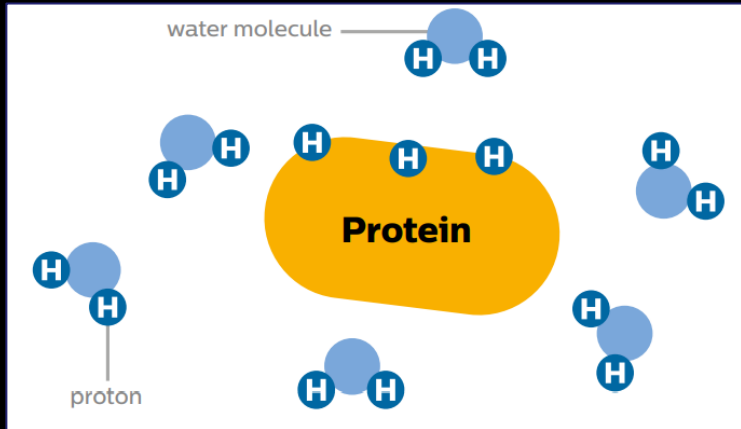


APT - Amide proton transfer CEST imaging

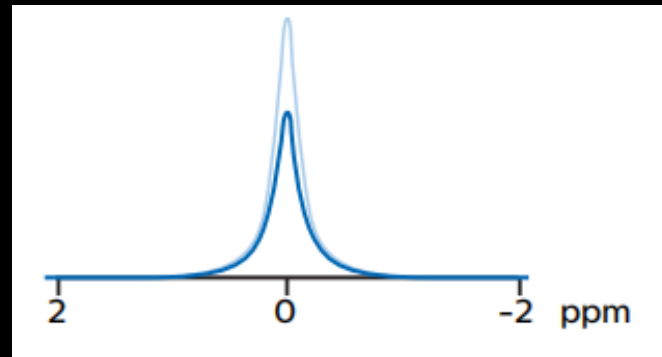
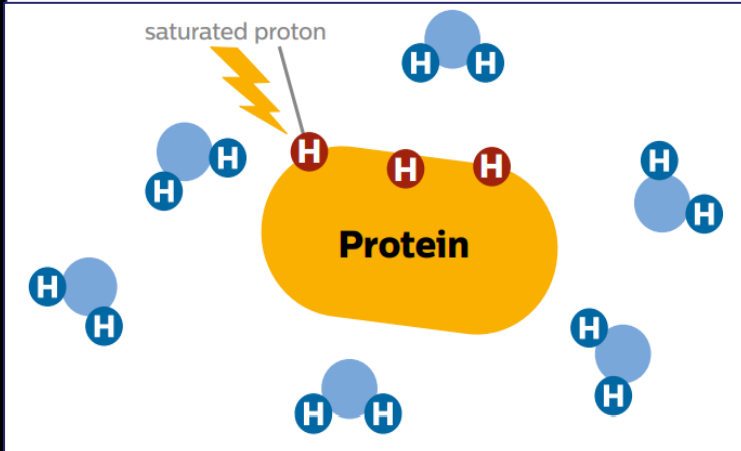
- Amide Proton Transfer (APT) imaging - uses endogenous proteins and peptides to produce a contrast media free molecular MR image
- MR signal is correlated with cell proliferation - a marker of tumour activity



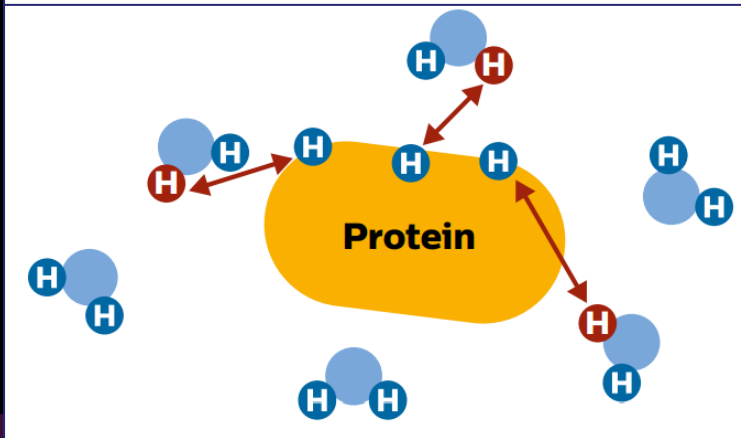
PRINCIPLE



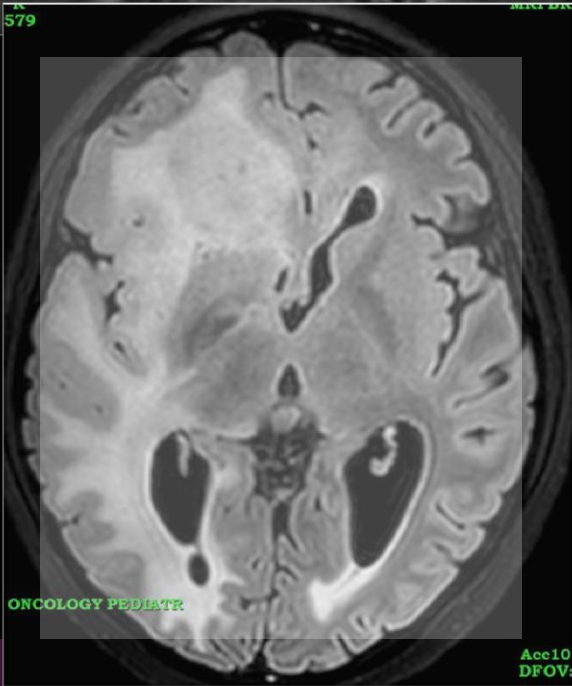
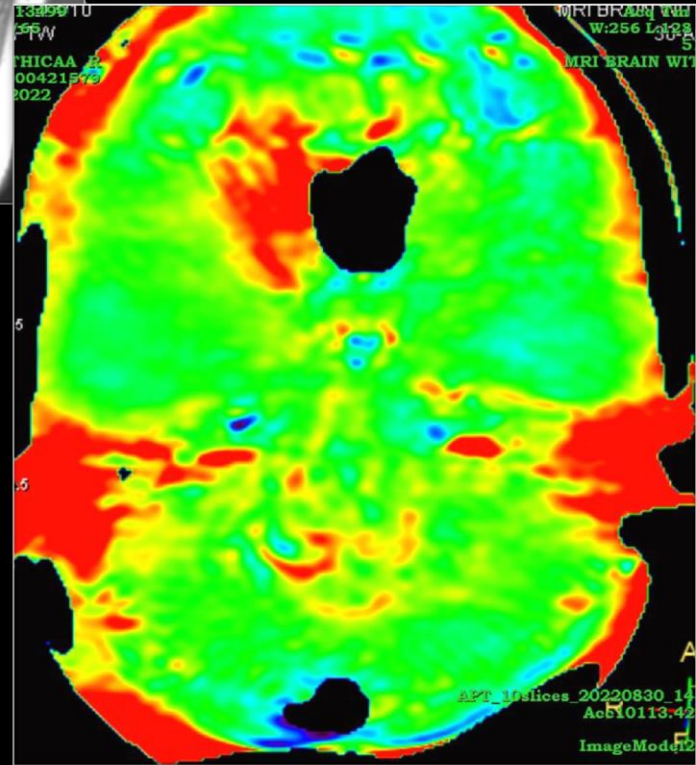
MR signal of water is high

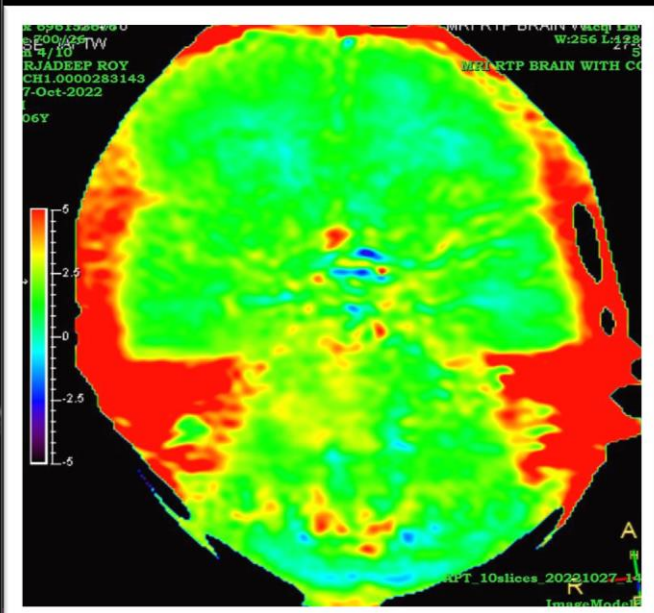
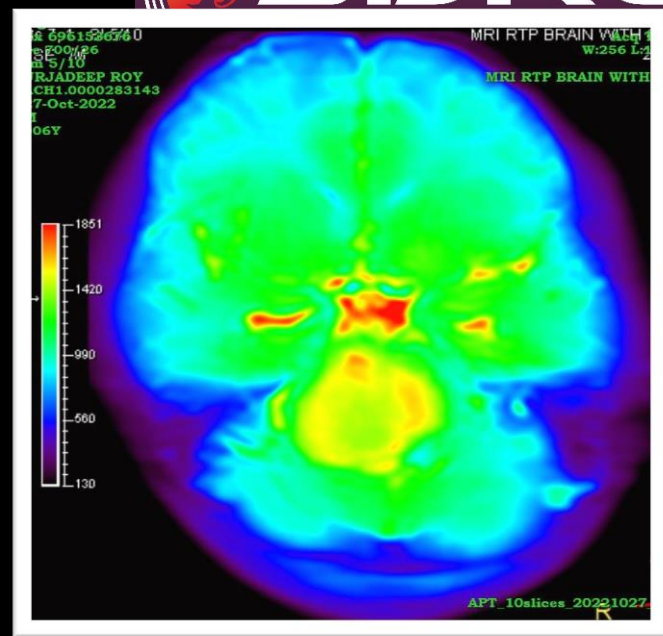
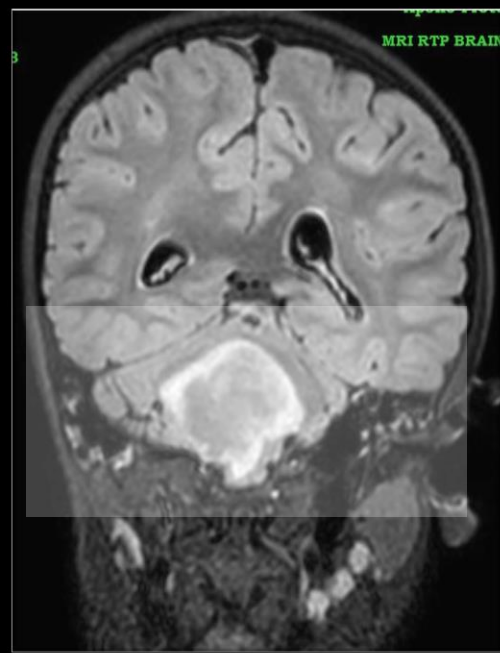
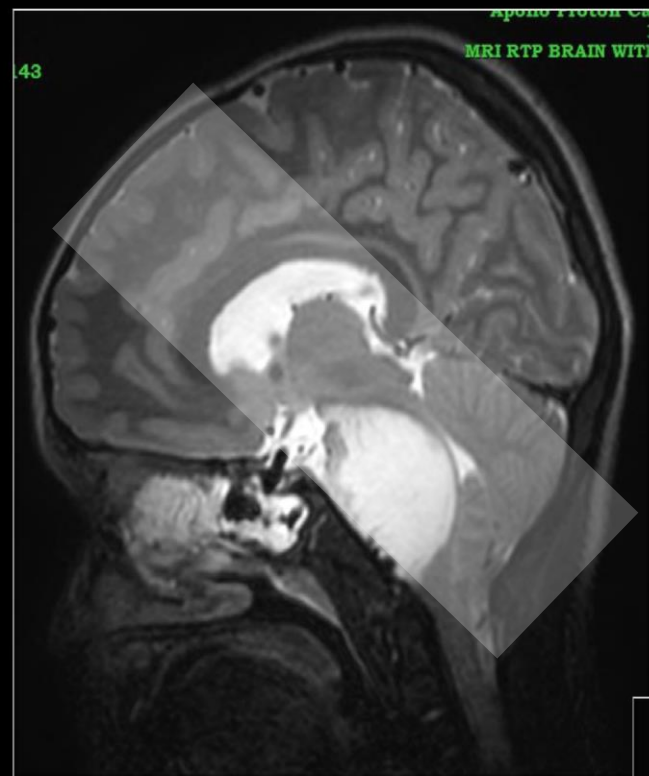


**MR signal of water is reduced
Due to the proton exchange**



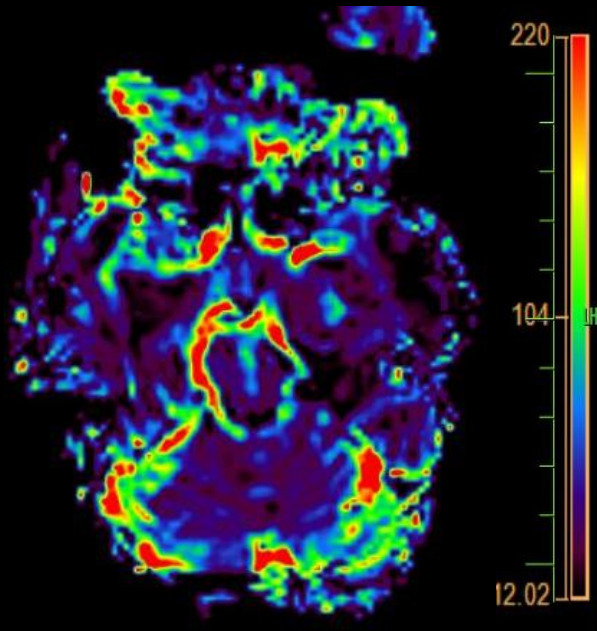
The APT effect -reduction in bulk water intensity due to chemical exchange of water protons with labeled backbone amide protons at 3.5 ppm.



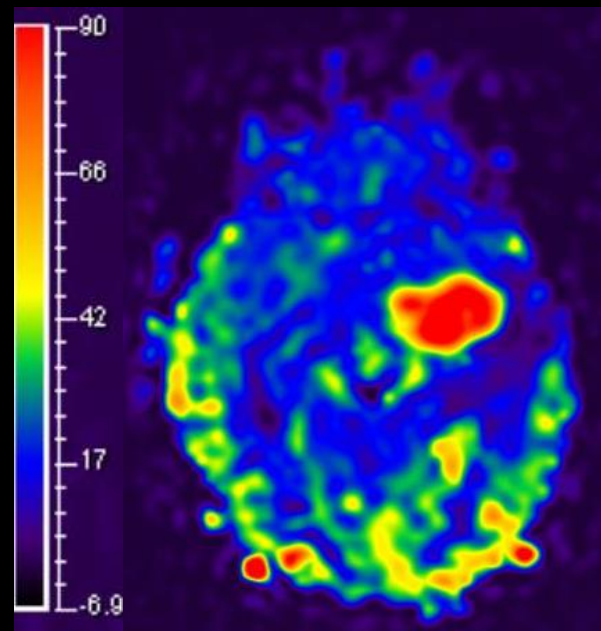


TYPES OF MR PERFUSION

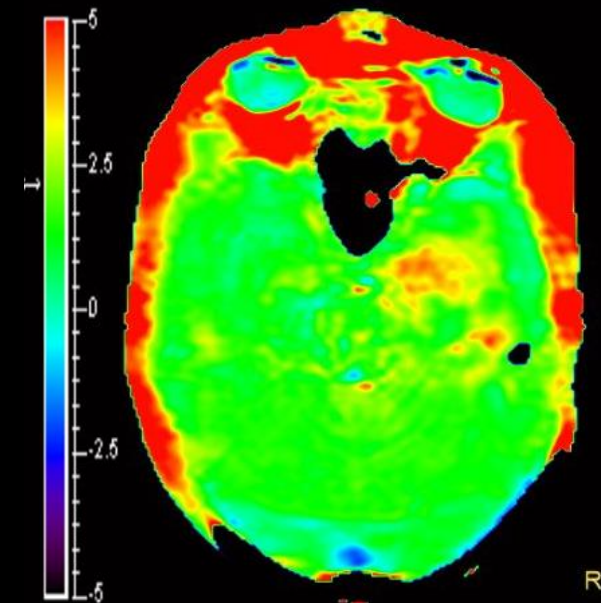
DSC PERFUSION



ASL PERFUSION



APT IMAGING



IMAGING - A paradigm shift.....

- Tumor burden
- Genetic Pathway
- Targetted treatment plan / choice
- Prognosis
- Change management

Tumor protocol - State of the Art

- T1, T2, Flair, T2* / SWI / SWAN
- Coronal T2
- Post contrast T1 fat sat, SOS spine imaging
- Diffusion & ADC
- MR Spectroscopy
- Perfusion
- ASL - Arterial spin labelling
- APT - Amide proton transfer
- DTI (in selected cases)
- fMRI (in selected cases)

Radio - proposed multilayered reporting format

- Layer 1 - Integrated diagnosis, in consideration with location and age
- Layer 2 - Descriptive
 - a. Signal characteristics incl diffusion and gradient echo
 - b. Extent - relationship to imp structures
 - c. Size - 3 othogonal planes when poss
 - d. Mass effect
- Layer 3 -
 - a. Perfusion incl ASL
 - b. Spectro

Summary

Multidisciplinary approach

Ready for the future



Team - Surgeon, oncologist, radiologist,
pathologist, geneticist and data scientists



THANK YOU!!!!!!!!!!