



Brain Neoplasms

Matthew Breen MD

Clinical Assistant Professor

NYU Grossman School of Medicine

New York, NY

Modified with permission from Rajan Jain MD

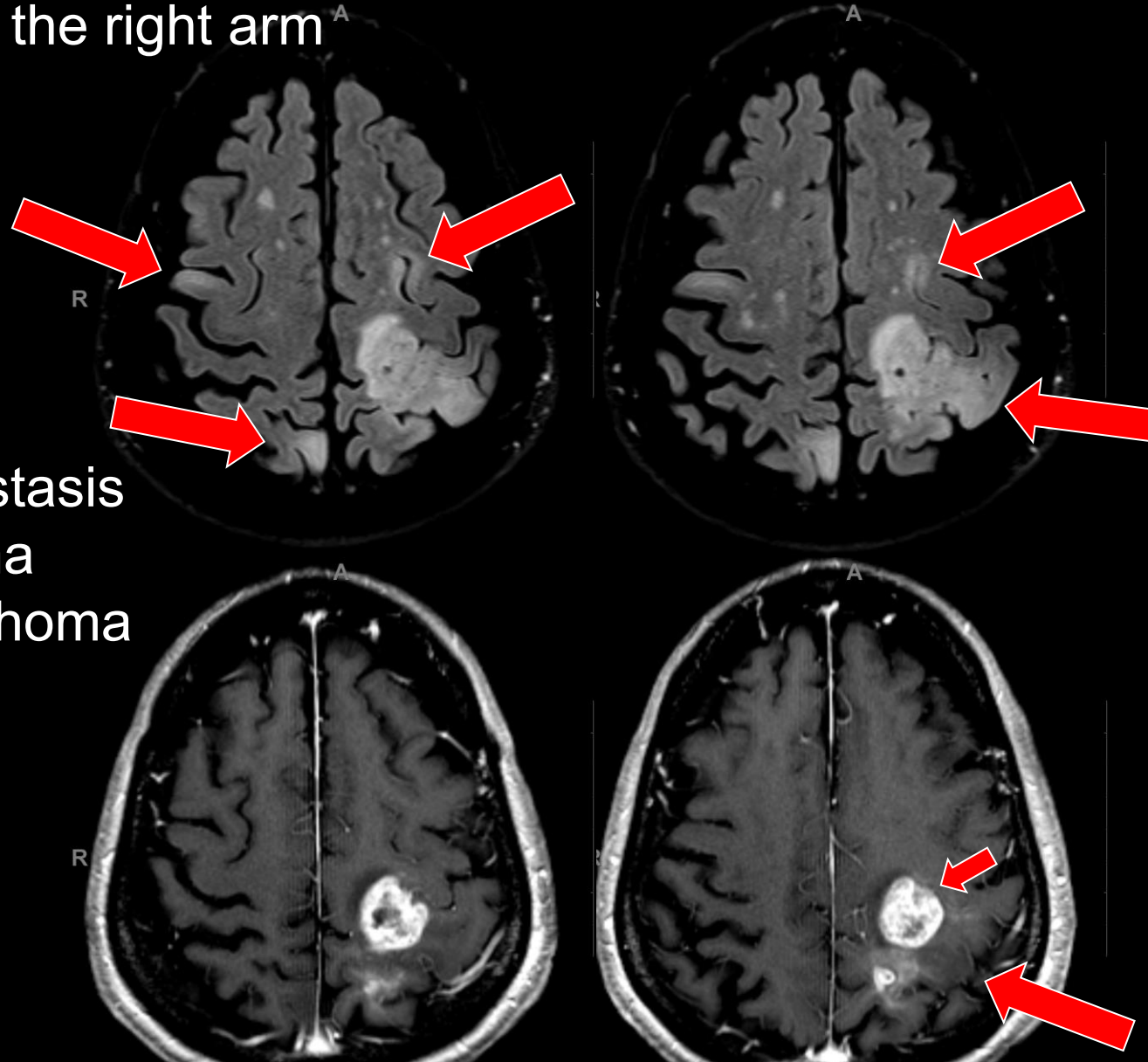


Features of diffuse gliomas that are misdiagnosed on initial neuroimaging: a case control study

M. D. Maldonado¹ · P. Batchala¹ · D. Ornan¹ · C. Fadul² · D. Schiff² · J. N. Itri³ · R. Jain^{4,5} · S. H. Patel¹

- **More likely to undergo acute stroke workup (Framing Bias):** Radiologists are influenced by the way a problem is worded or framed. The diagnostic possibilities are mentally restricted by the referral situation.
- **Less likely to enhance**
- **Less likely to demonstrate necrosis or midline shift**

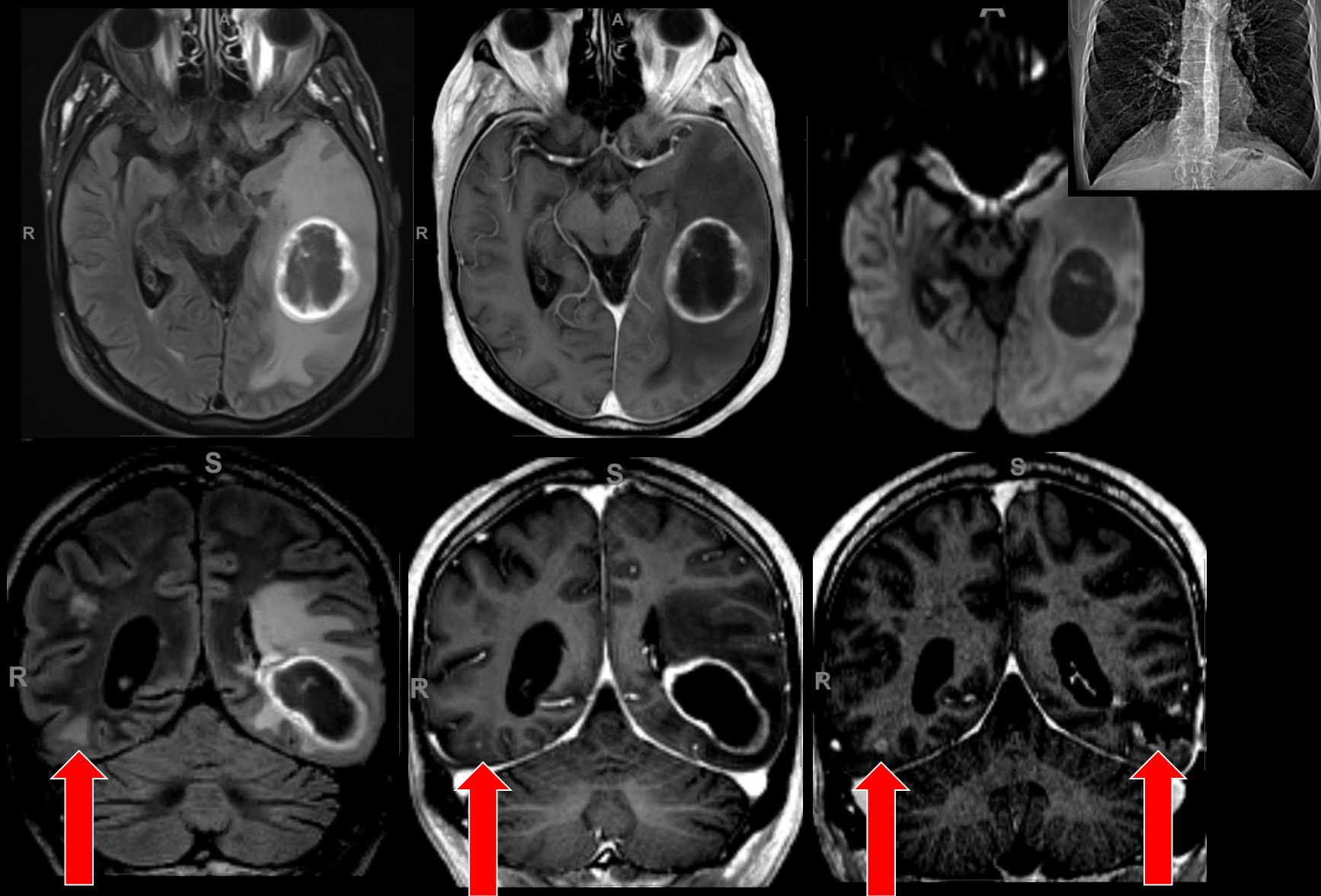
73 F, Jerking movements of right mid to lower abdomen that spread to the right arm



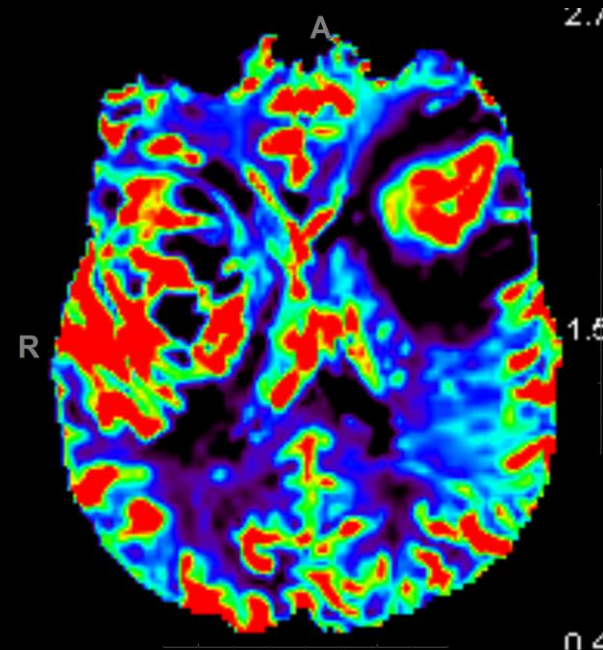
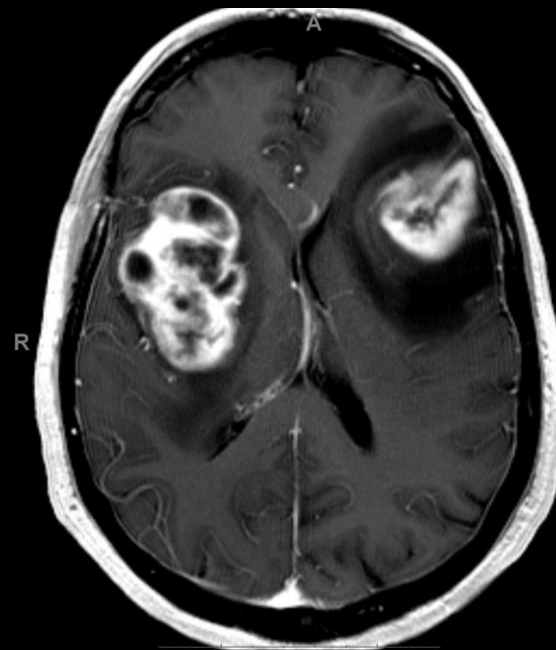
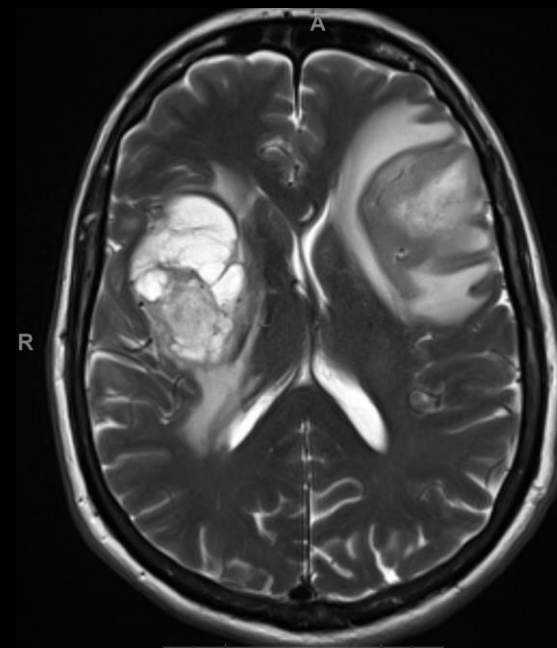
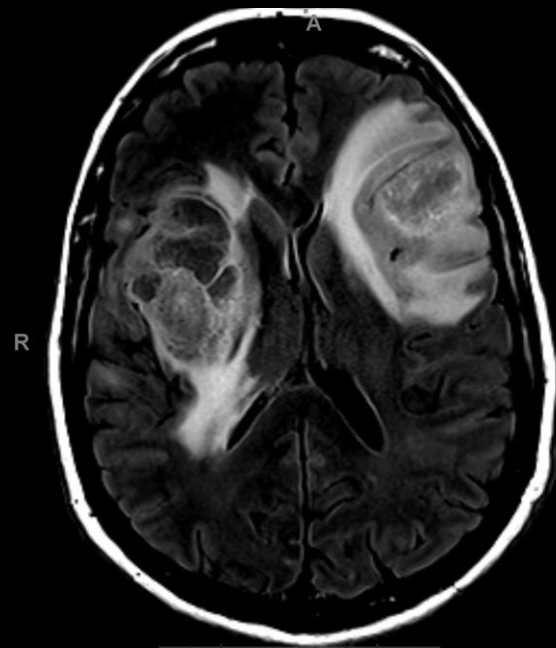
- Metastasis
- Glioma
- Lymphoma

Integrated diagnosis: Grade 4, Glioblastoma, IDH-wt

69 year old man with speech difficulty

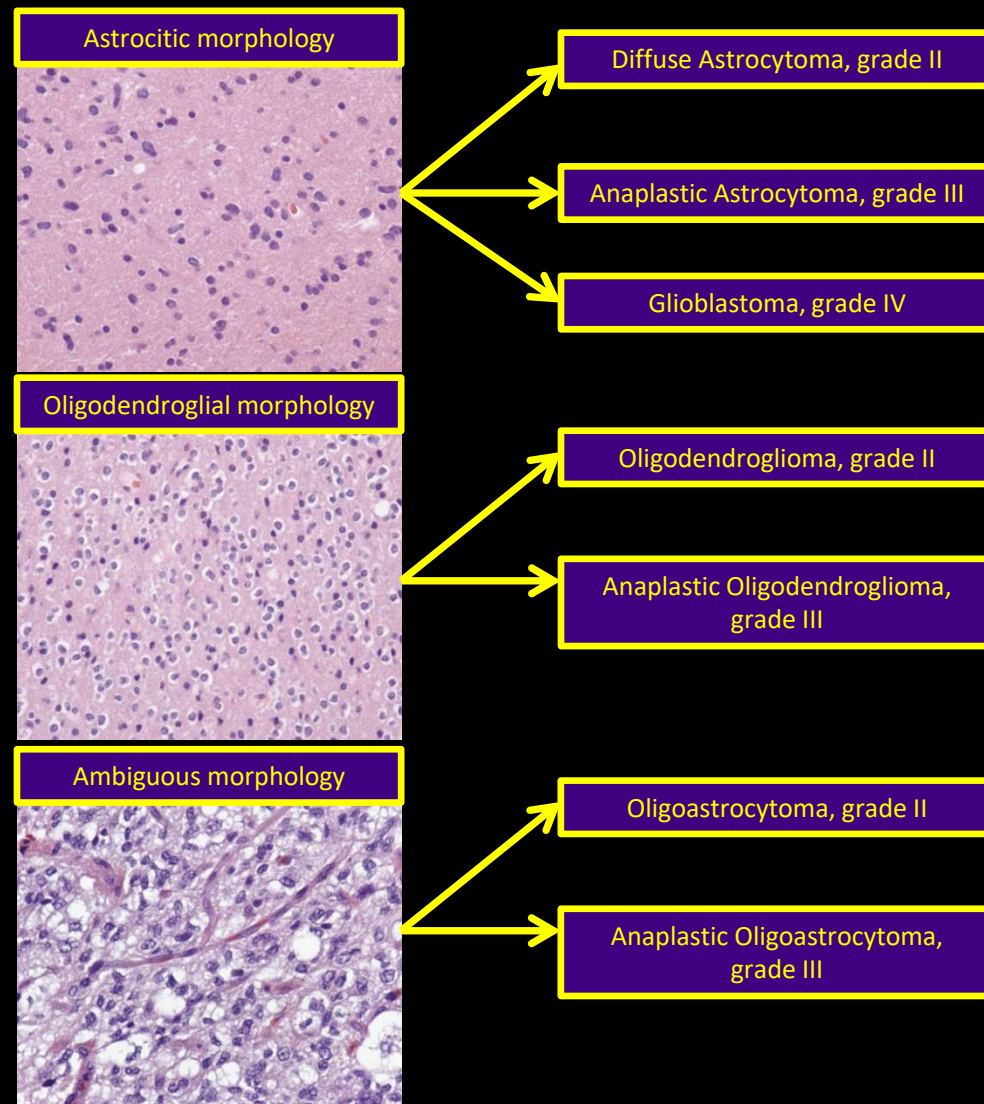


68 M, multi-centric GBM



- The 2007 WHO classification of tumors of the central nervous system divided gliomas as astrocytic, oligodendroglial, oligoastrocytic or ependymal tumors.

- High inter-observer variability
- Inability to predict clinical outcome



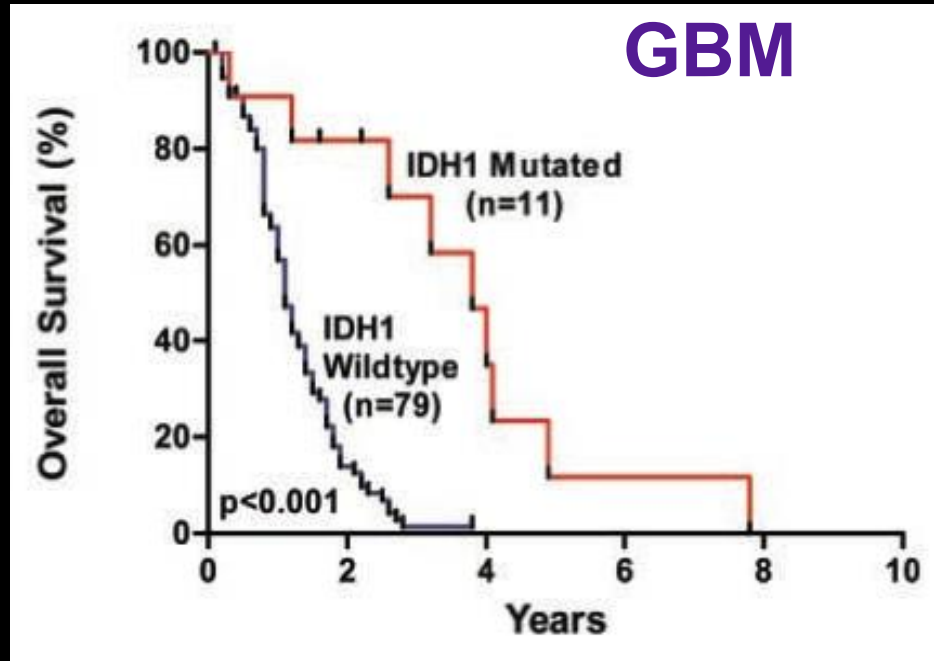
Louis DN, Ohgaki H, Wiestler OD et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol* 2007; 114: 97-109

van den Bent MJ. Interobserver variation of the histopathological diagnosis in clinical trials on glioma: a clinician's perspective. *Acta Neuropathol* 2010; 120: 297-304

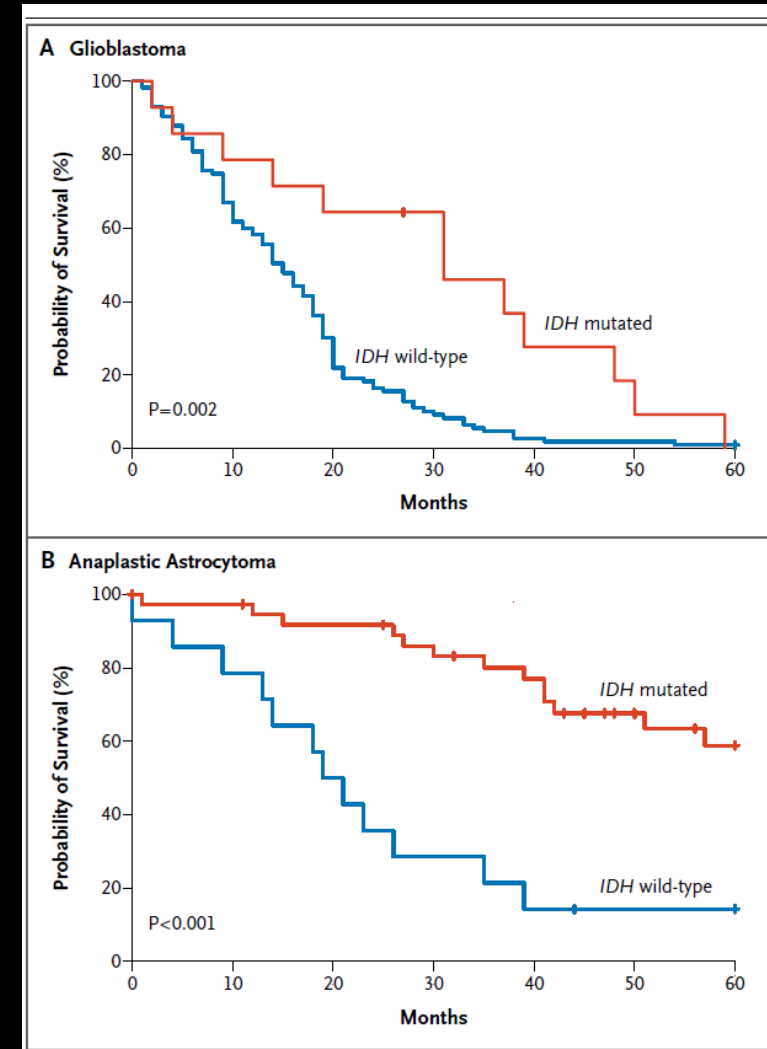
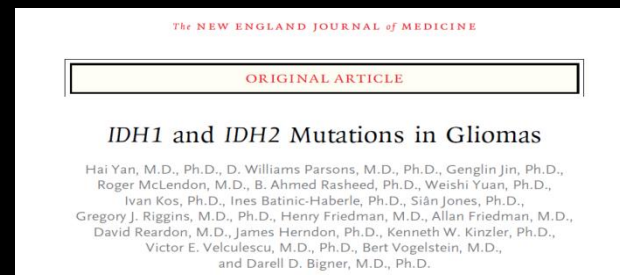
Brat DJ, Veraak RG, Aldape KD, et al. Comprehensive, integrative genomic analysis of lower-grade gliomas. *N Engl J Med* 2015; 372(26): 2481-2498

Appin CL, Brat DJ. Molecular Pathways in Gliomagenesis and Their Relevance to Neuropathologic Diagnosis. *Adv Anat Pathol* 2015;22:50-58

IDH Mutation Status: paradigm shift in classification and management of Gliomas



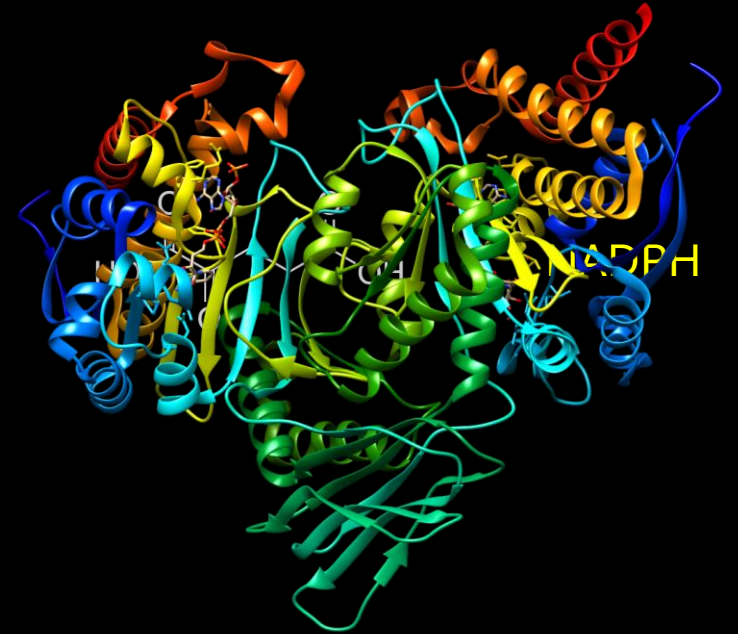
Parsons et al. Science 2008



Yan et al NEJM 2009

IDH (Isocitrate dehydrogenase)

- Five genes encode for three human IDH catalytic isozymes:
 - IDH1, IDH2 (NADP⁺ dependent)
 - and IDH3 (NAD⁺ dependent)
- Converts isocitrate to alpha-ketoglutarate, produces NADPH (or NADH)
- Immunohistochemistry – detects approx. 90% of IDH mutations
- Pyrosequencing or Next Gen Sequencing



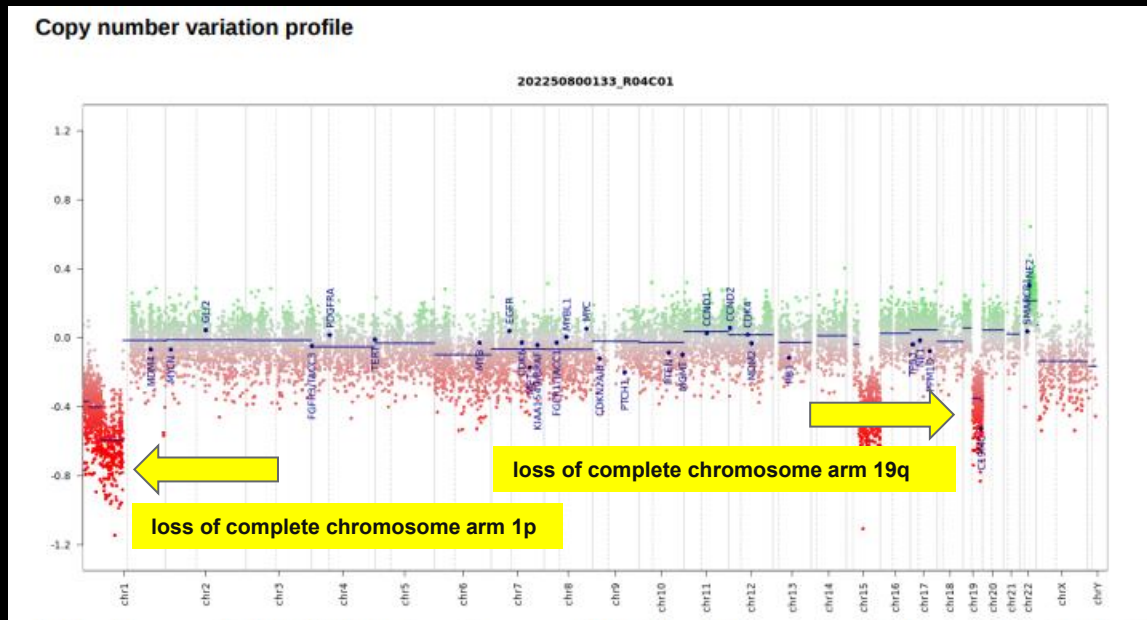
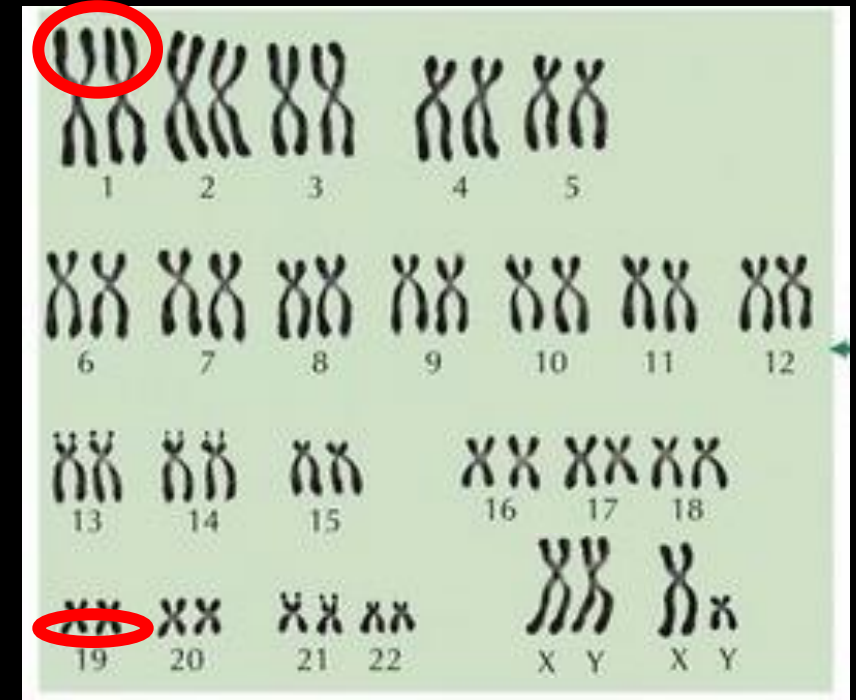
IDH (Isocitrate dehydrogenase)

- IDH mutations occur early in gliomagenesis
- change the function of the enzymes and causing them to produce **2-hydroxyglutarate**, a possible onco-metabolite, and to **not produce NADPH**
- Exactly how IDH mutation contributes to oncogenic transformation remains controversial

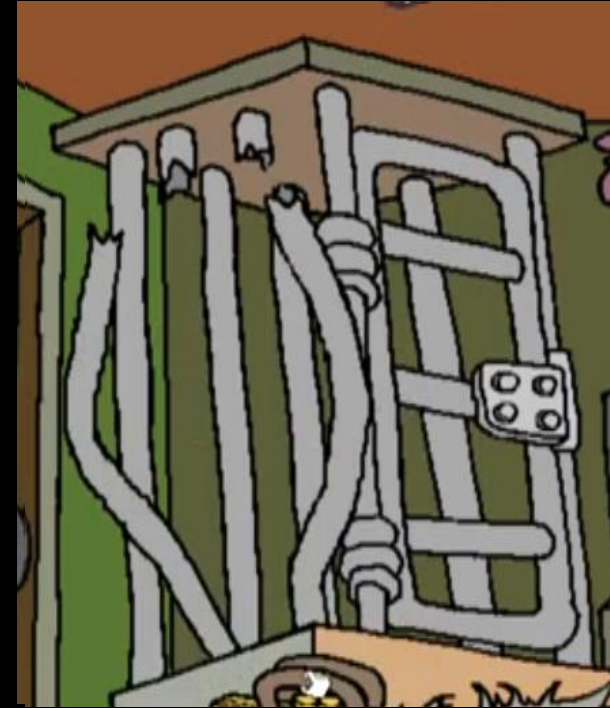
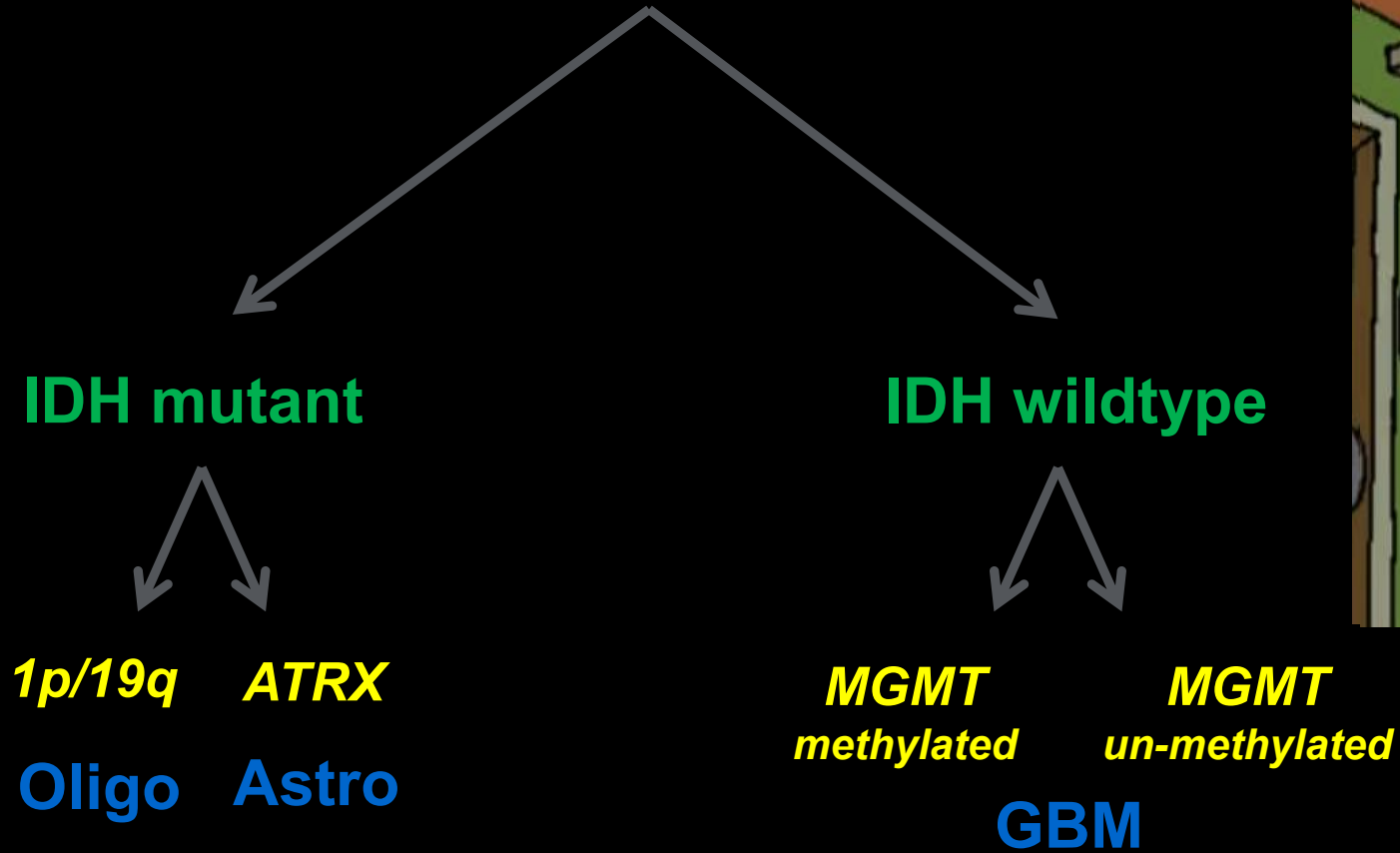


1p19q

- Co-deletion of short arm of chromosome 1 (1p) and long arm of chromosome 19 (19q)
- Co-deletion of 1p19q is a prognostic marker and predicts response to PCV chemotherapy and radiation



Adults Diffuse Gliomas



15 years 8 years

2-3 years

1 year

Younger
patients

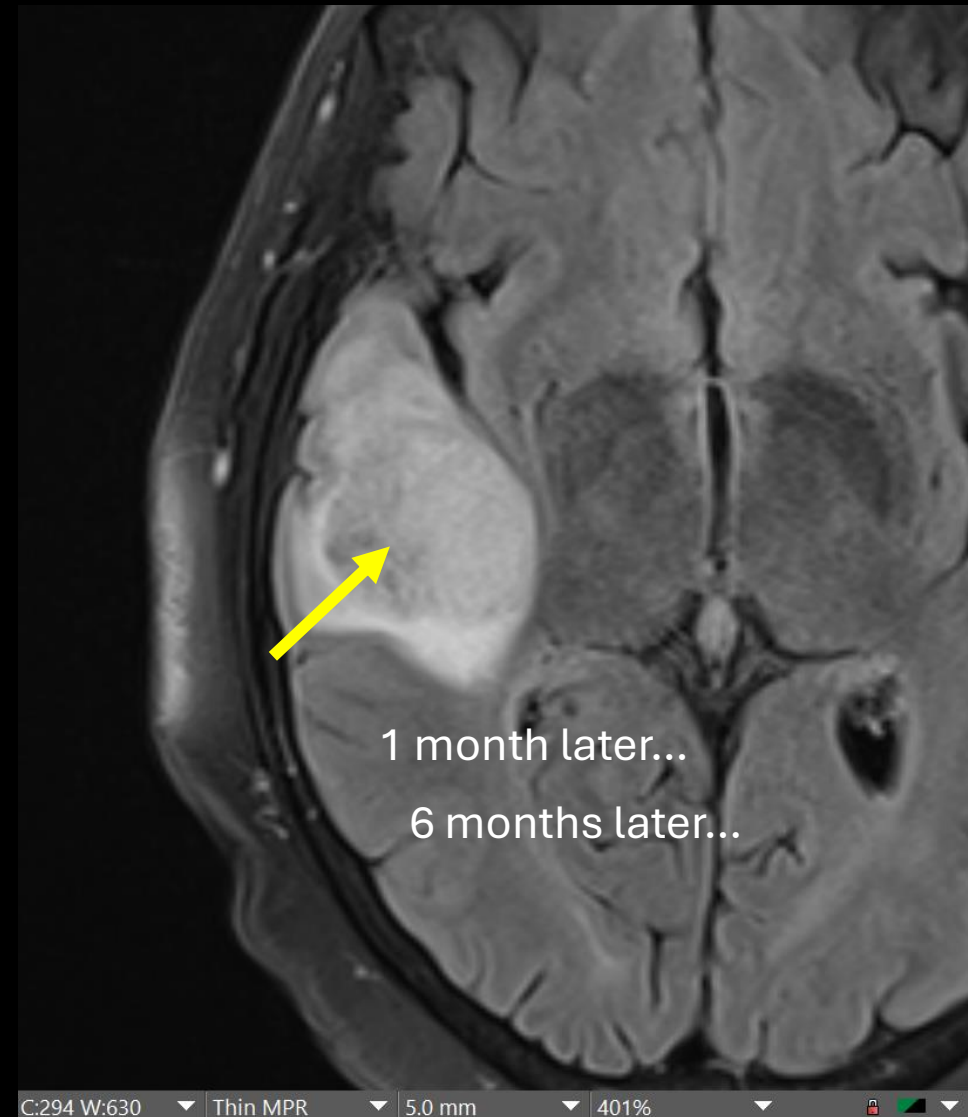
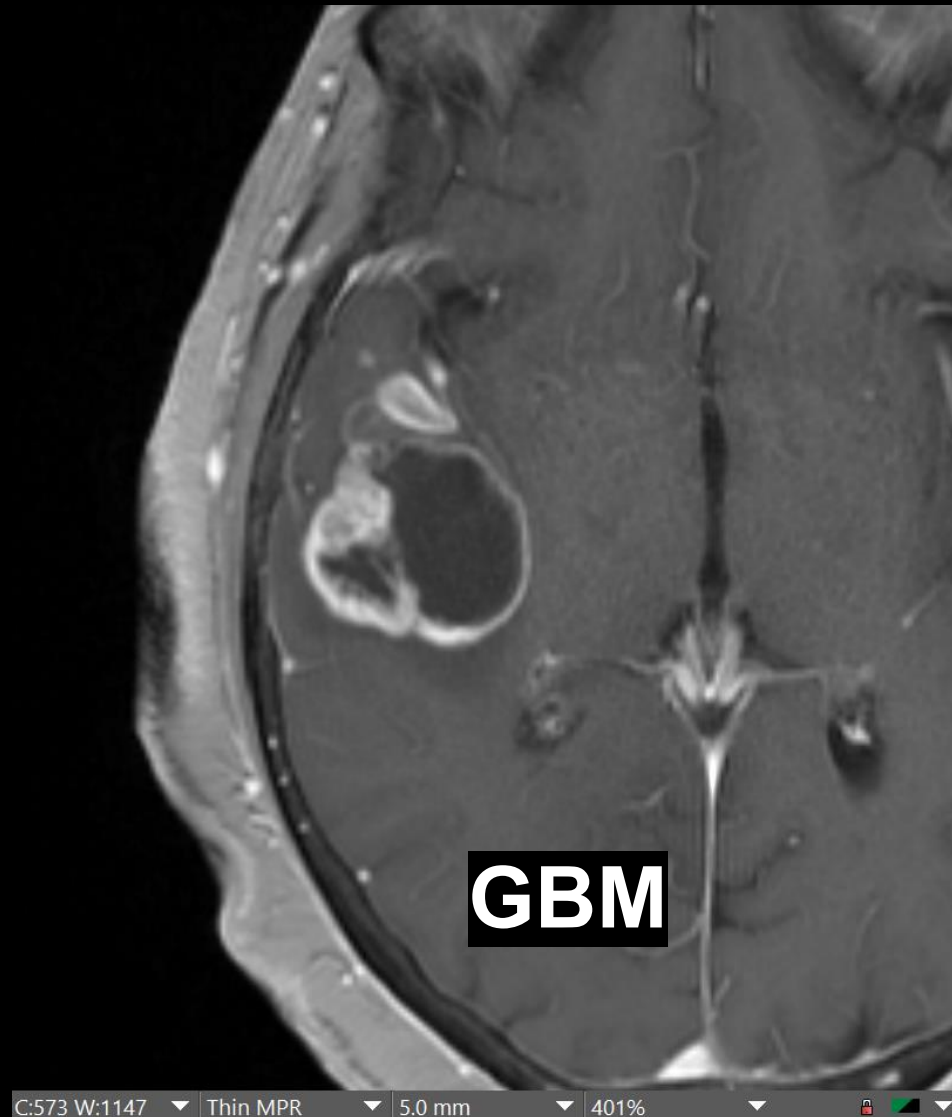
Older
patients



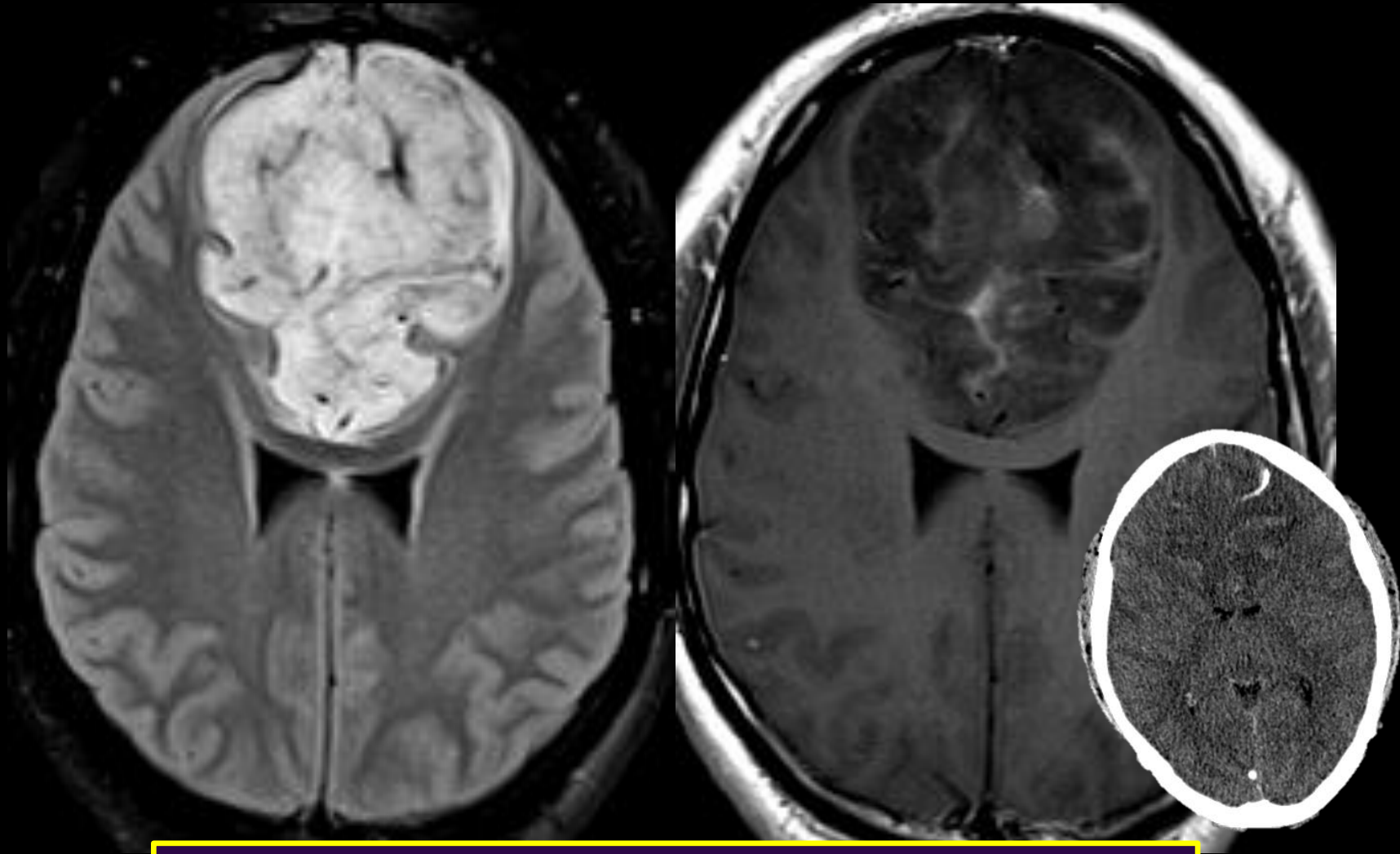
2 things you want to know “*Preimage*”?’

- Age
 - Young kids: BRAF/MAPK, H3K27
 - Young adults: IDHmut, H3K27
 - >40 years: IDHwt
- Clinical presentation
 - Asymptomatic, headaches, seizures: IDHmut
 - Seizures: BRAF/MAPK
 - Subacute neurological deficits: IDHwt

68 year old woman, surveillance for vestibular schwannoma



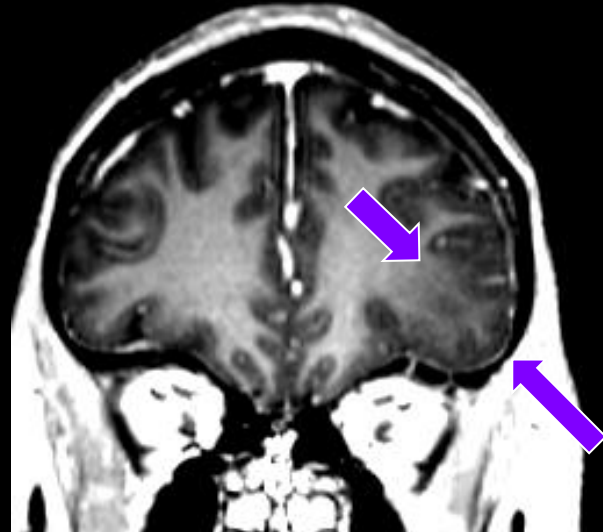
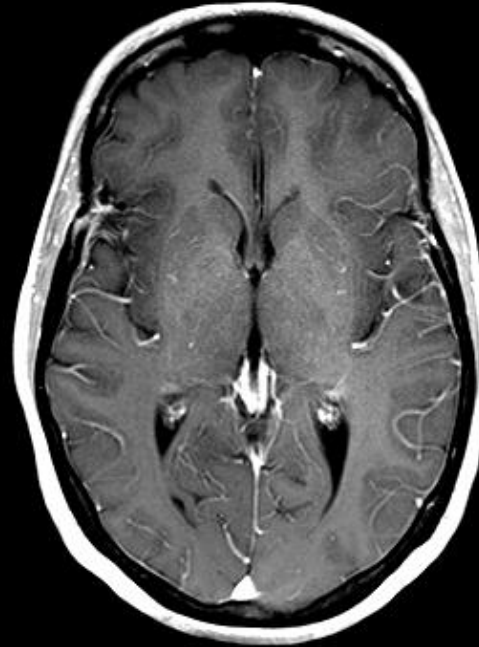
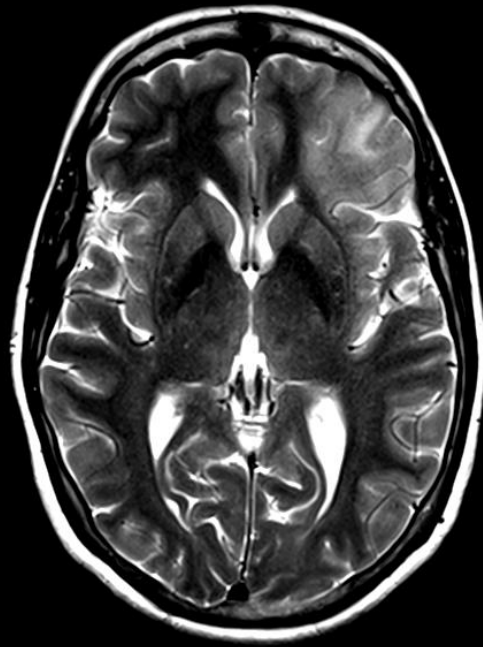
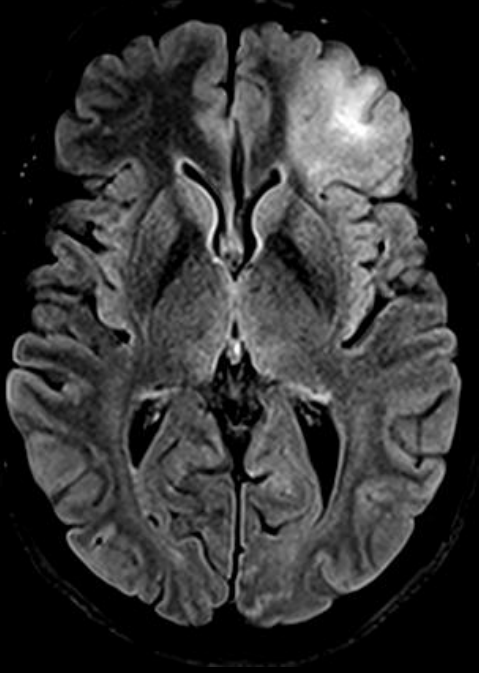
28 M, clinically intact, headaches



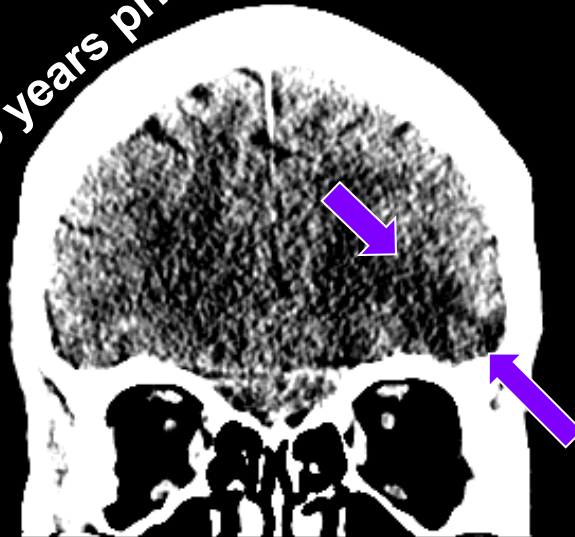
Integrated diagnosis: Oligodendroglioma,
grade II, IDH-mutant and 1p/19q codeleted

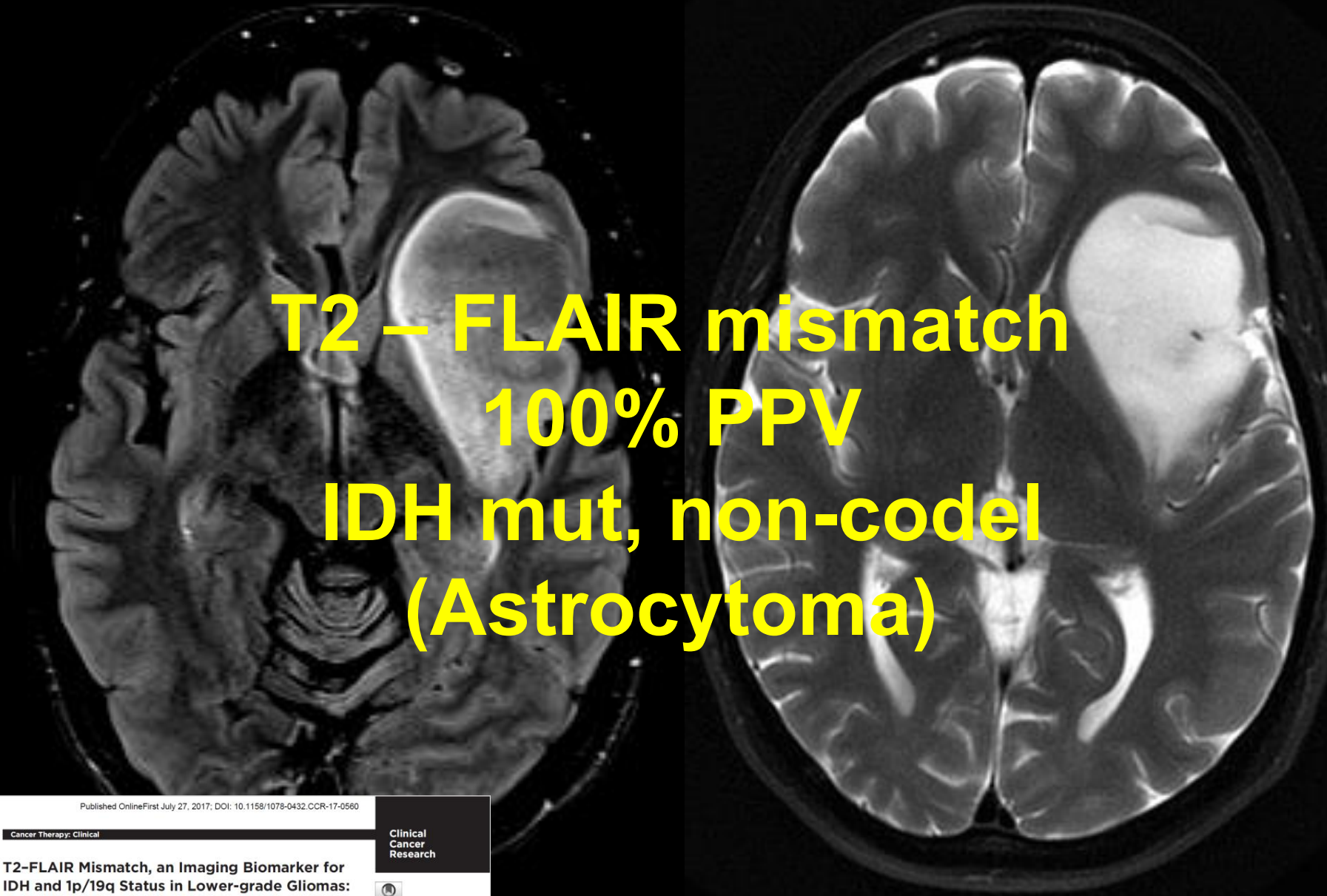
57 F, anxiety and headaches

IDH-mutant Glioma



8 years prior





**T2 – FLAIR mismatch
100% PPV
IDH mut, non-codel
(Astrocytoma)**

Published OnlineFirst July 27, 2017; DOI: 10.1158/1078-0432.CCR-17-0560

Cancer Therapy: Clinical

Clinical
Cancer
Research

**T2-FLAIR Mismatch, an Imaging Biomarker for
IDH and 1p/19q Status in Lower-grade Gliomas:
A TCGA/TCIA Project**

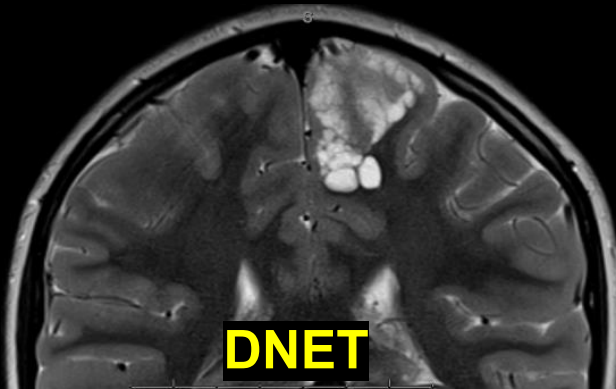
Sohil H. Patel¹, Laila M. Poisson², Daniel J. Brat³, Yueren Zhou², Lee Cooper^{4,5},
Matija Snuderl⁶, Cheddhi Thomas⁵, Ana M. Franceschi⁷, Brent Griffith⁸,
Adam E. Flanders⁹, John G. Golfinos¹⁰, Andrew S. Chi^{10,11}, and Rajan Jain^{7,10}



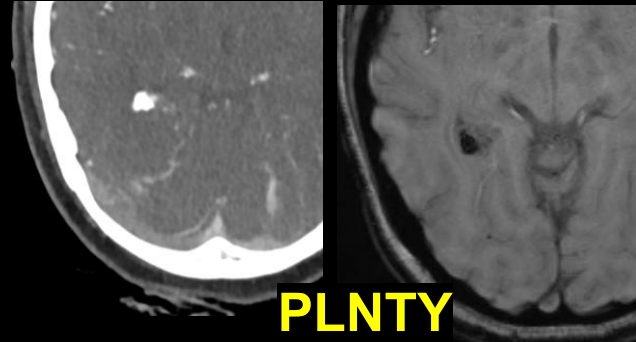
Clin Cancer Res. 2017 Jul 27.

MAPK pathway gliomas:

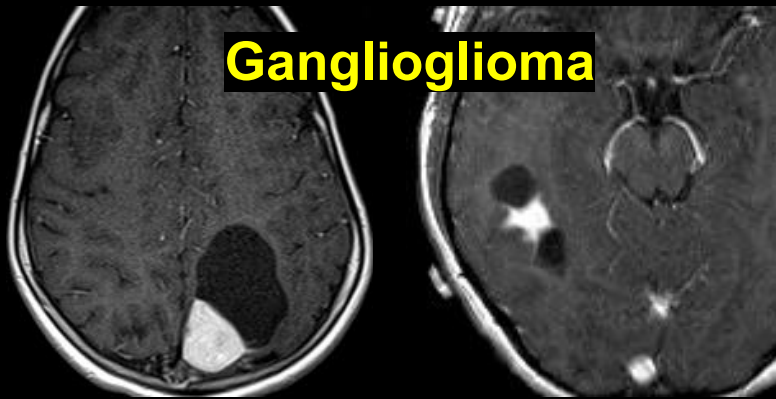
young, *seizures*, cortical, cyst with mural nodule



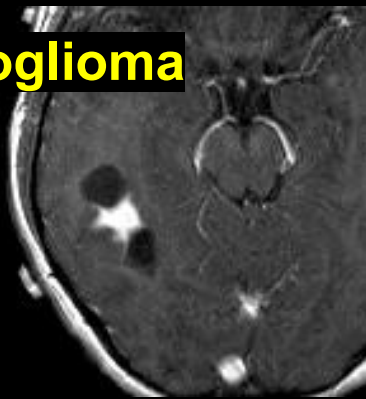
13 M, fell at school



16F, seizure



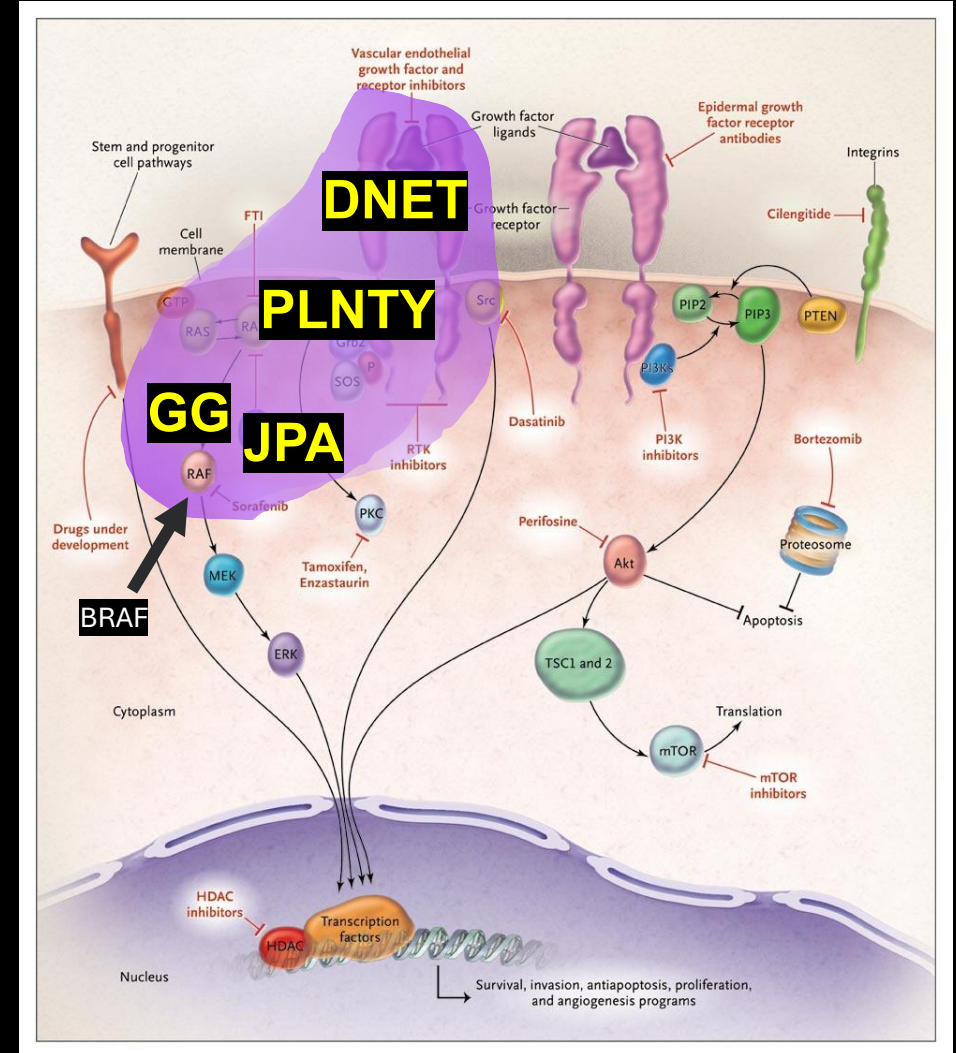
7 F, seizures



14 M, seizures



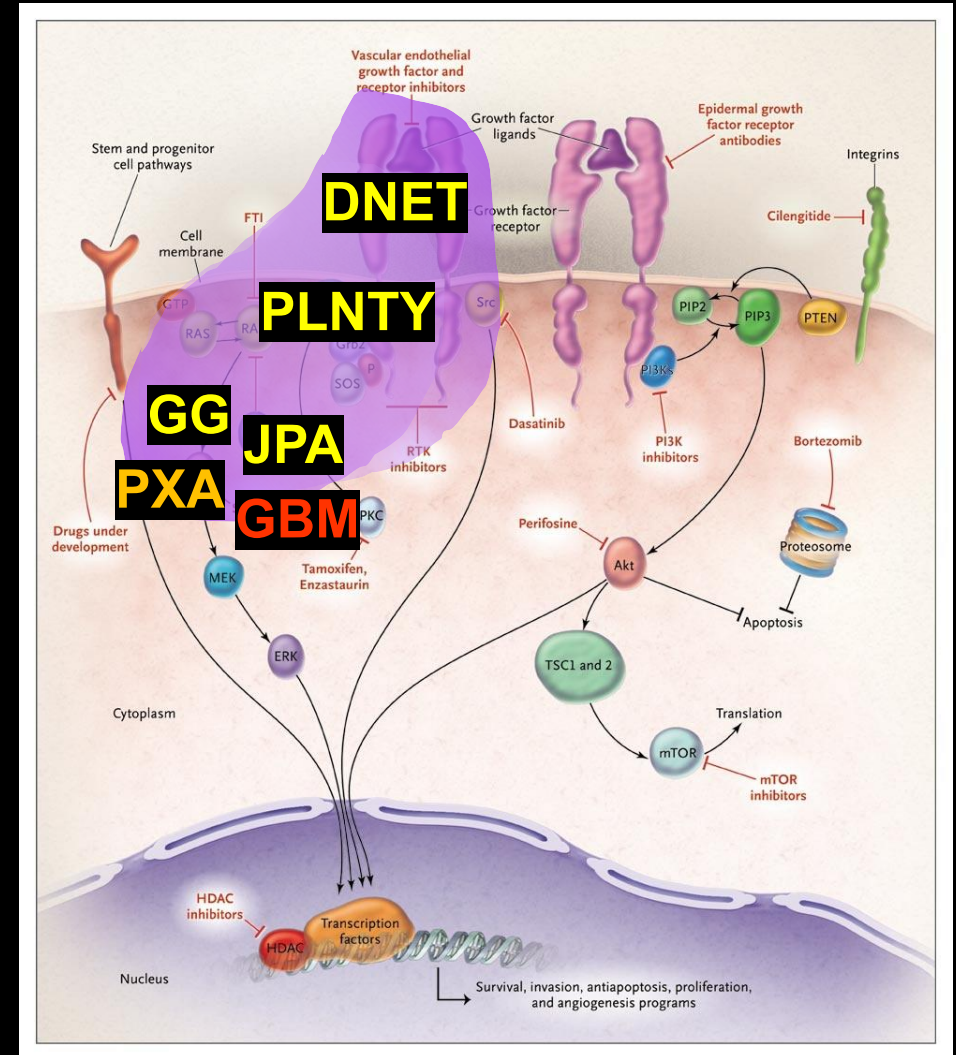
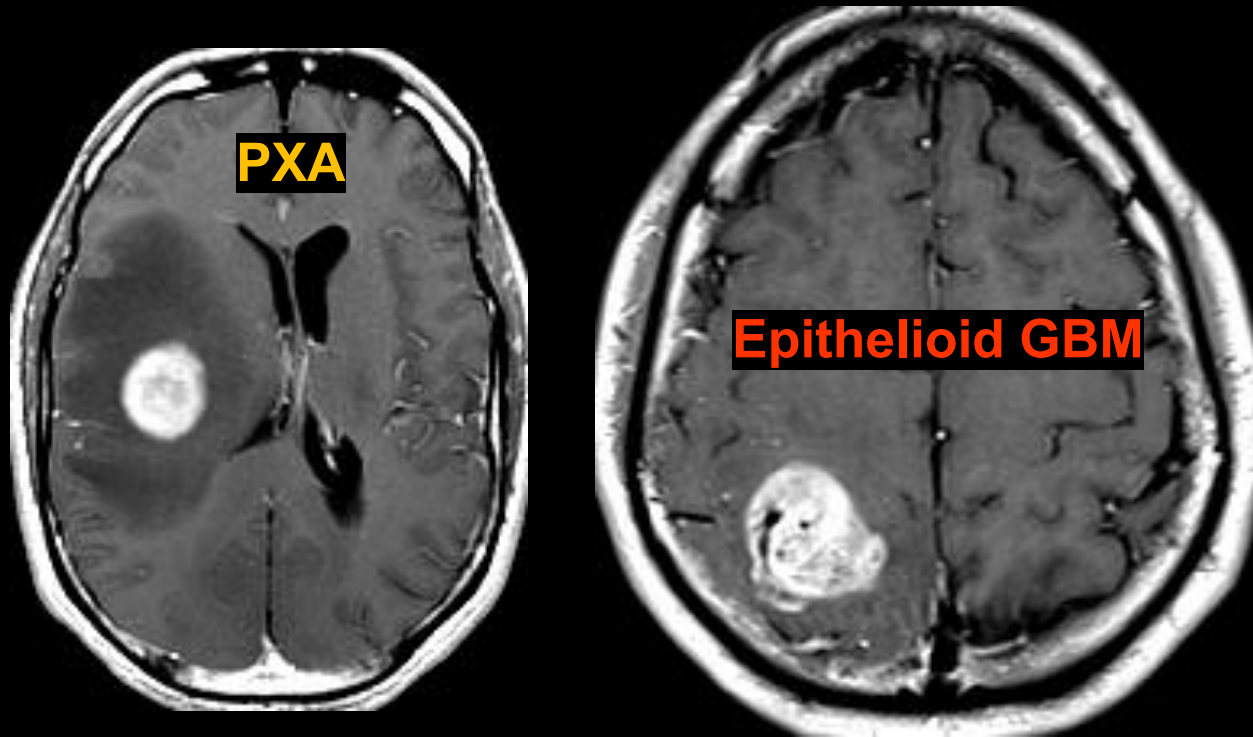
10 M, headaches



Wen PY, Kesari S. Malignant gliomas in adults. N Engl J Med. 2008 Jul 31;359(5):492-507. doi: 10.1056/NEJMra0708126. Erratum in: N Engl J Med. 2008 Aug 21;359(8):877. PMID: 18669428.

MAPK pathway gliomas:

young, *seizures*, cortical, cyst with mural nodule



Wen PY, Kesari S. Malignant gliomas in adults. N Engl J Med. 2008 Jul 31;359(5):492-507. doi: 10.1056/NEJMra0708126. Erratum in: N Engl J Med. 2008 Aug 21;359(8):877. PMID: 18669428.

Glioneuronal / Neuronal Tumors

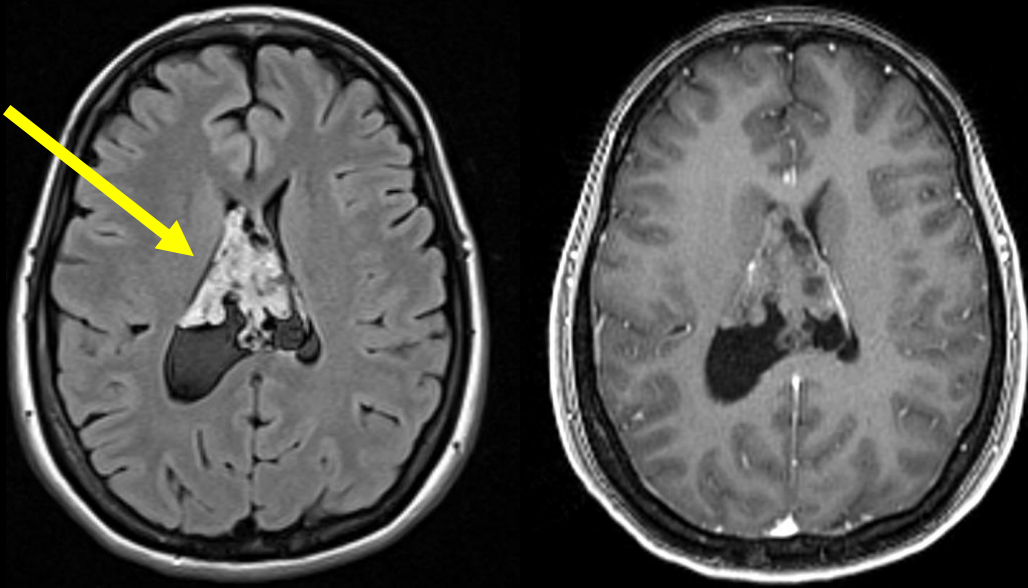
“Long term epilepsy associated tumors” – LEATS

- DNET
 - bubbly, cortical
- Ganglioglioma
 - cyst/mural nodule, temporal > frontal
- PLNTY
 - calcified, temporal > frontal

Circumscribed Astrocytic Gliomas

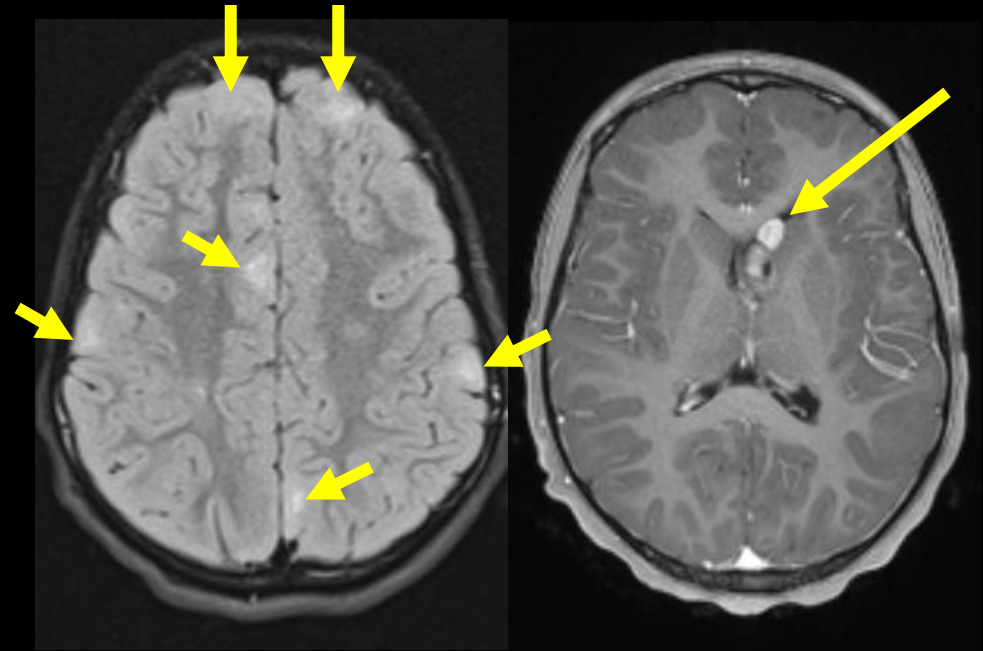
- Pilocytic astrocytoma
 - cyst/mural nodule in cerebellum
- Pleomorphic Xanthoastrocytoma (PXA)
 - enhancing mural nodule with dural tail

Glioneuronal / Neuronal Tumors



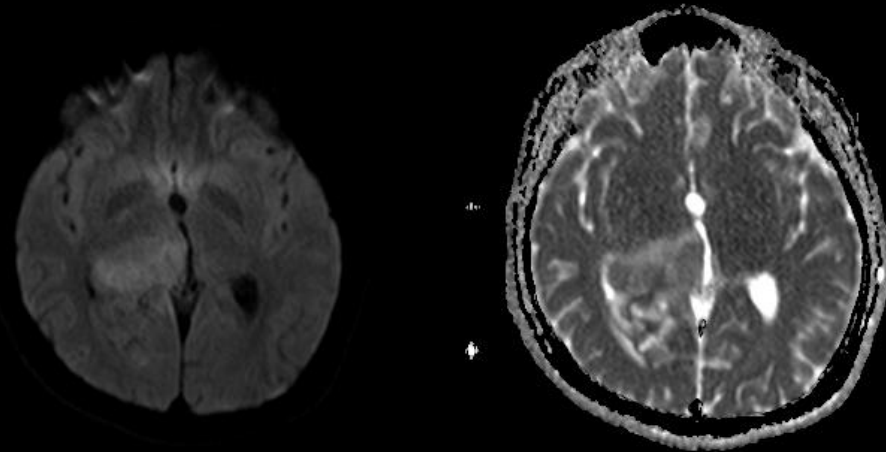
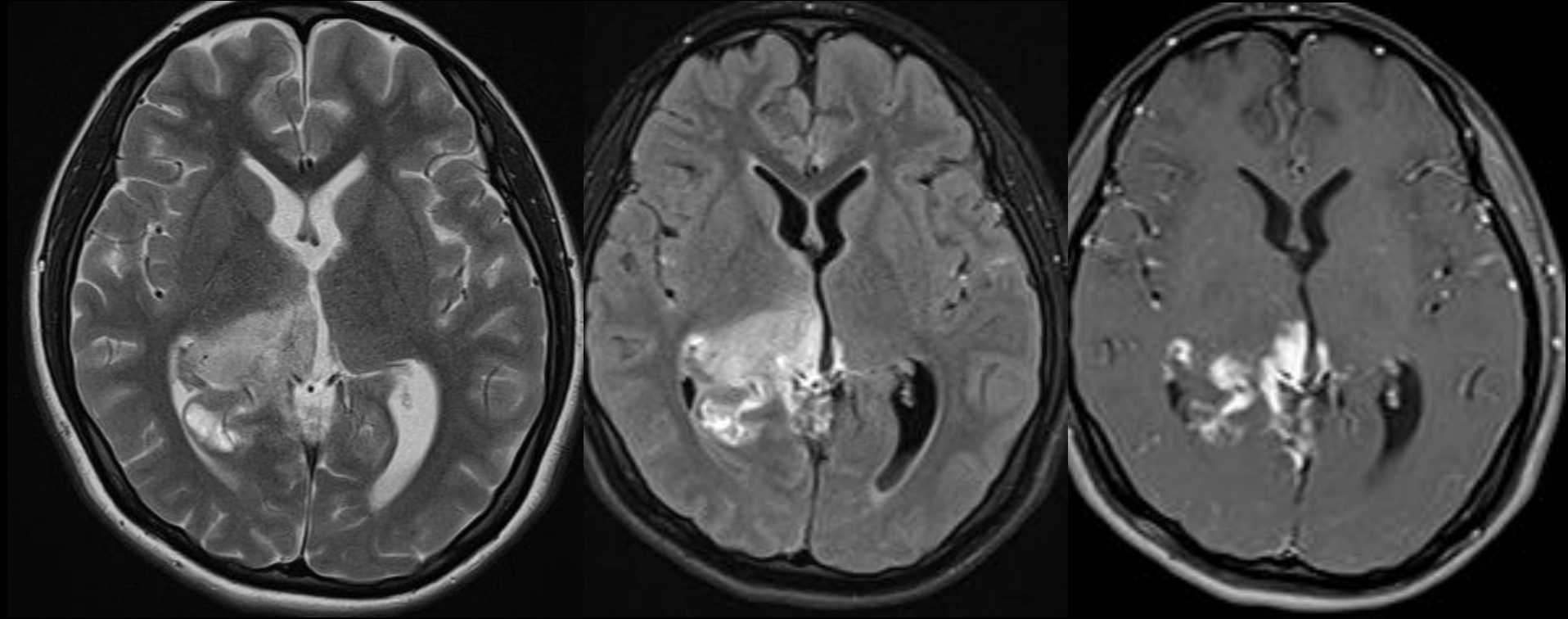
- Central neurocytoma — septum pellucidum

Circumscribed Astrocytic Gliomas

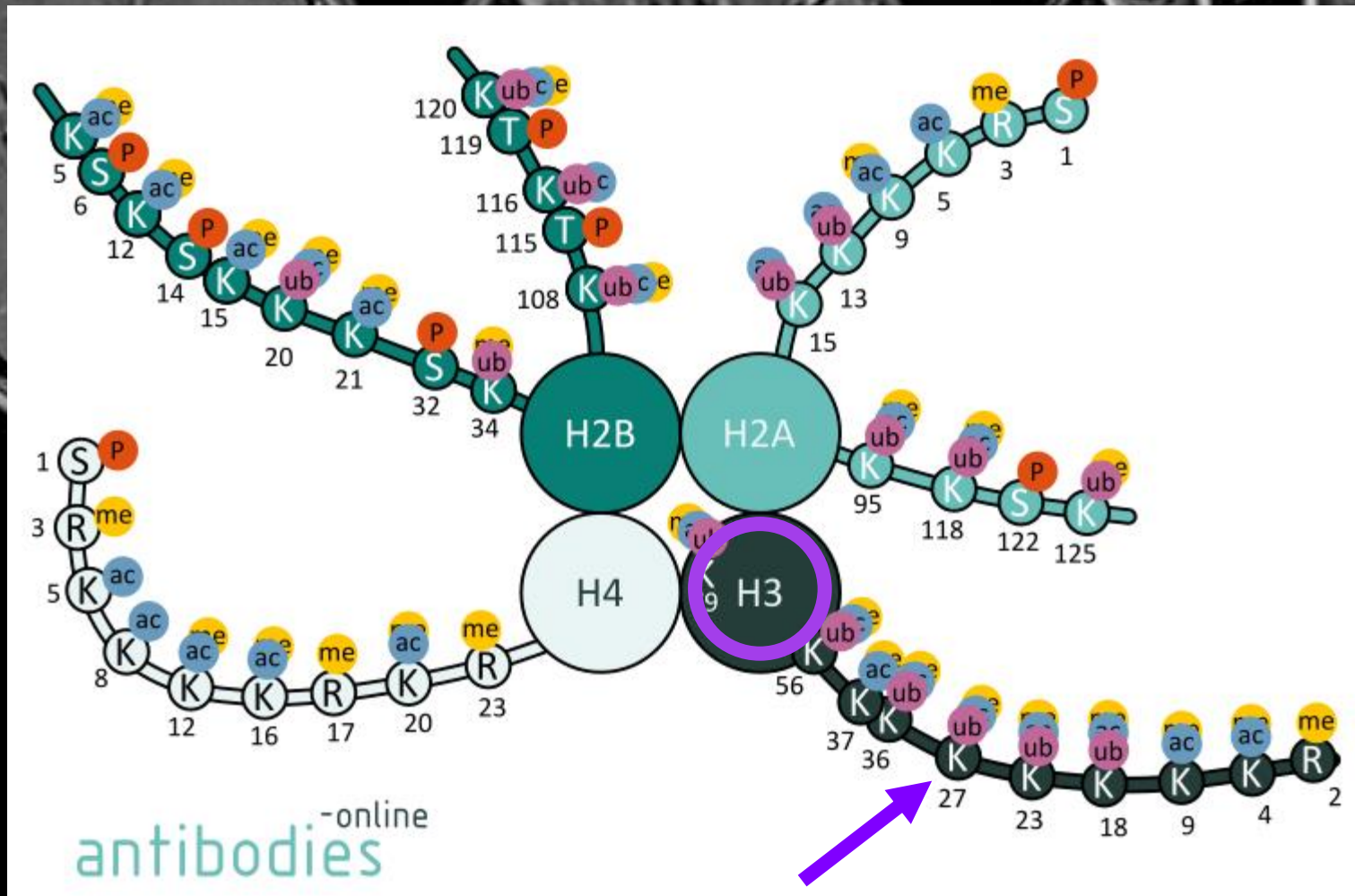


- Subependymal giant cell astrocytoma (SEGA)
 - foramen of Monro, tuberous sclerosis

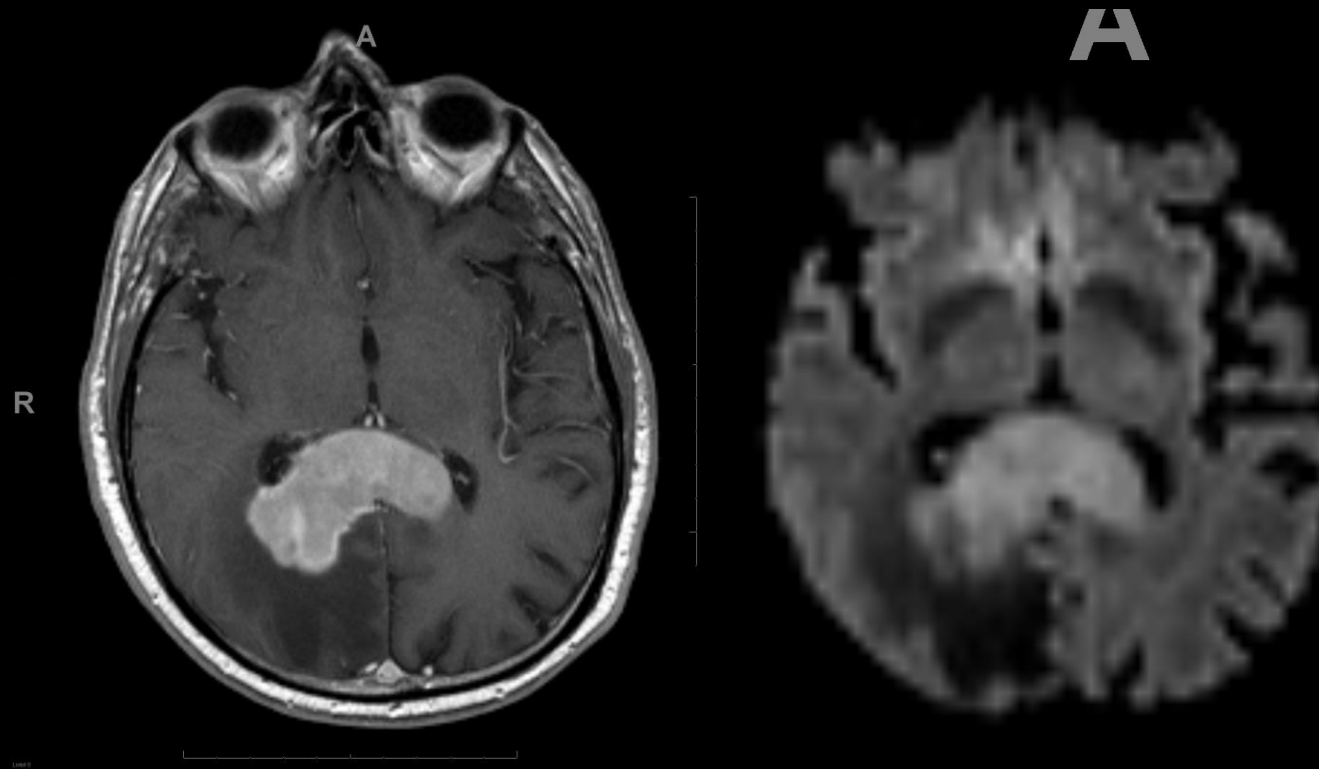
15M, headache, vomiting



15M, headache, vomiting

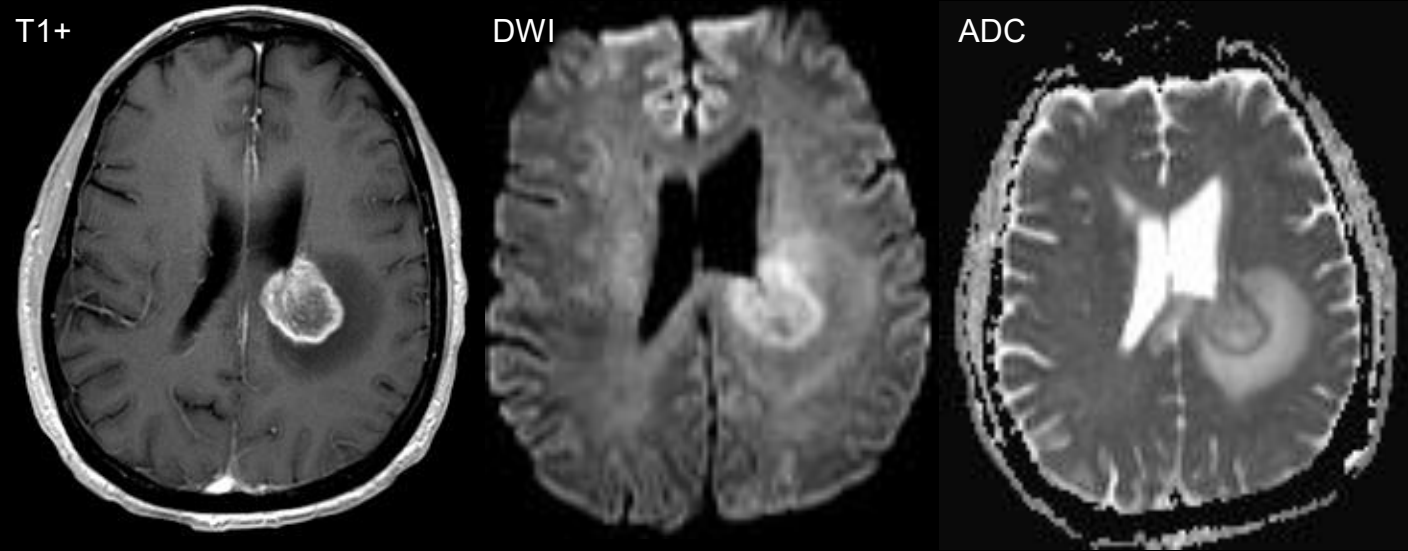


Primary CNS Lymphoma

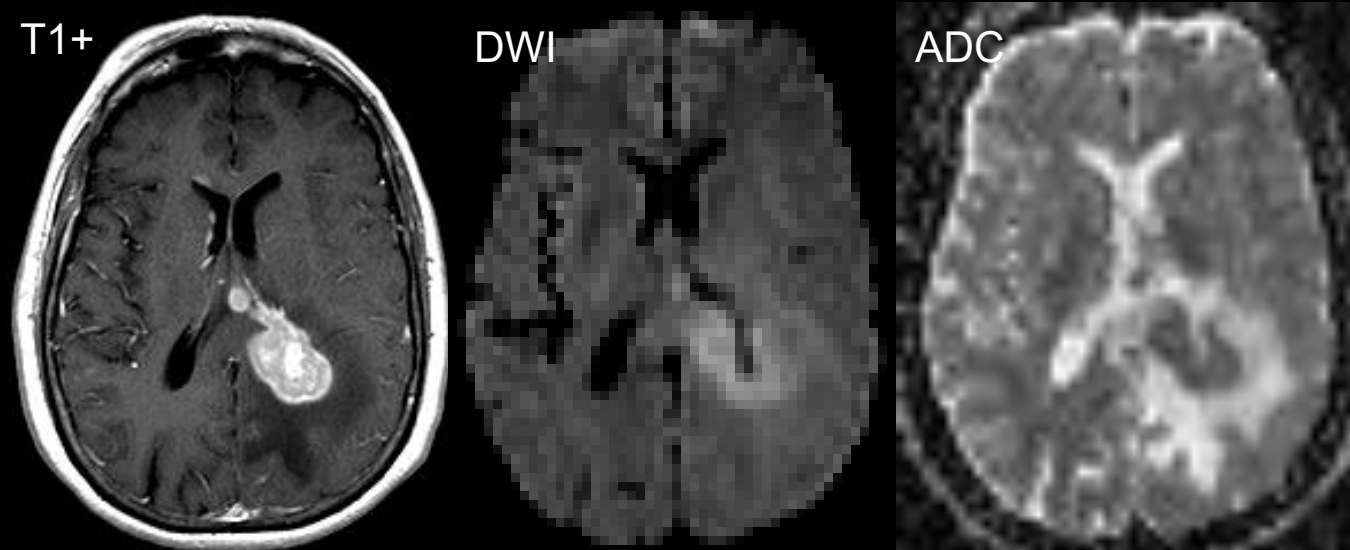


GBM or lymphoma?

Patient 1

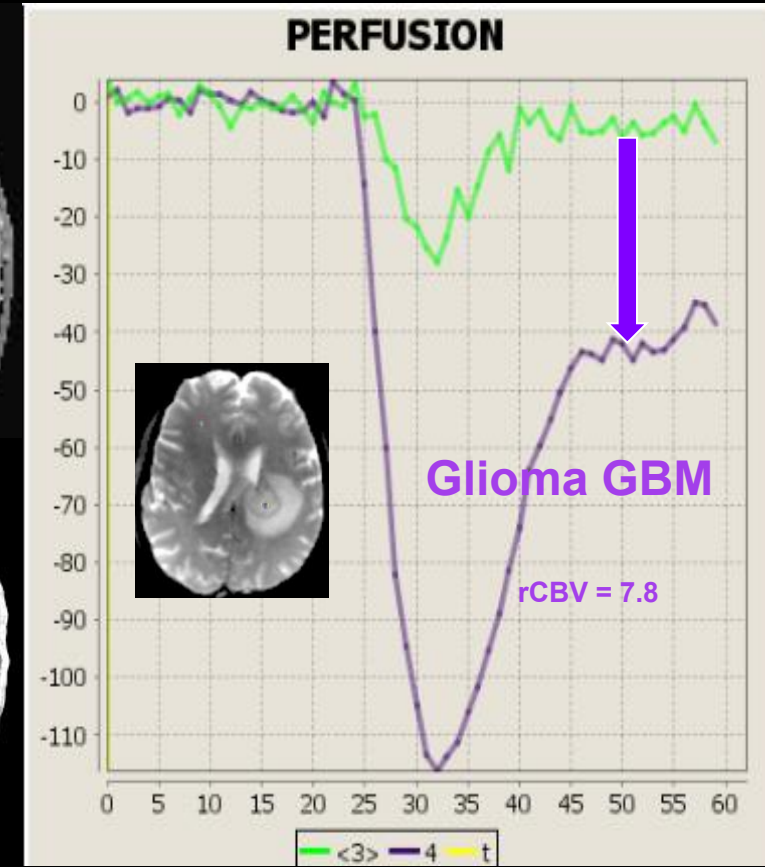
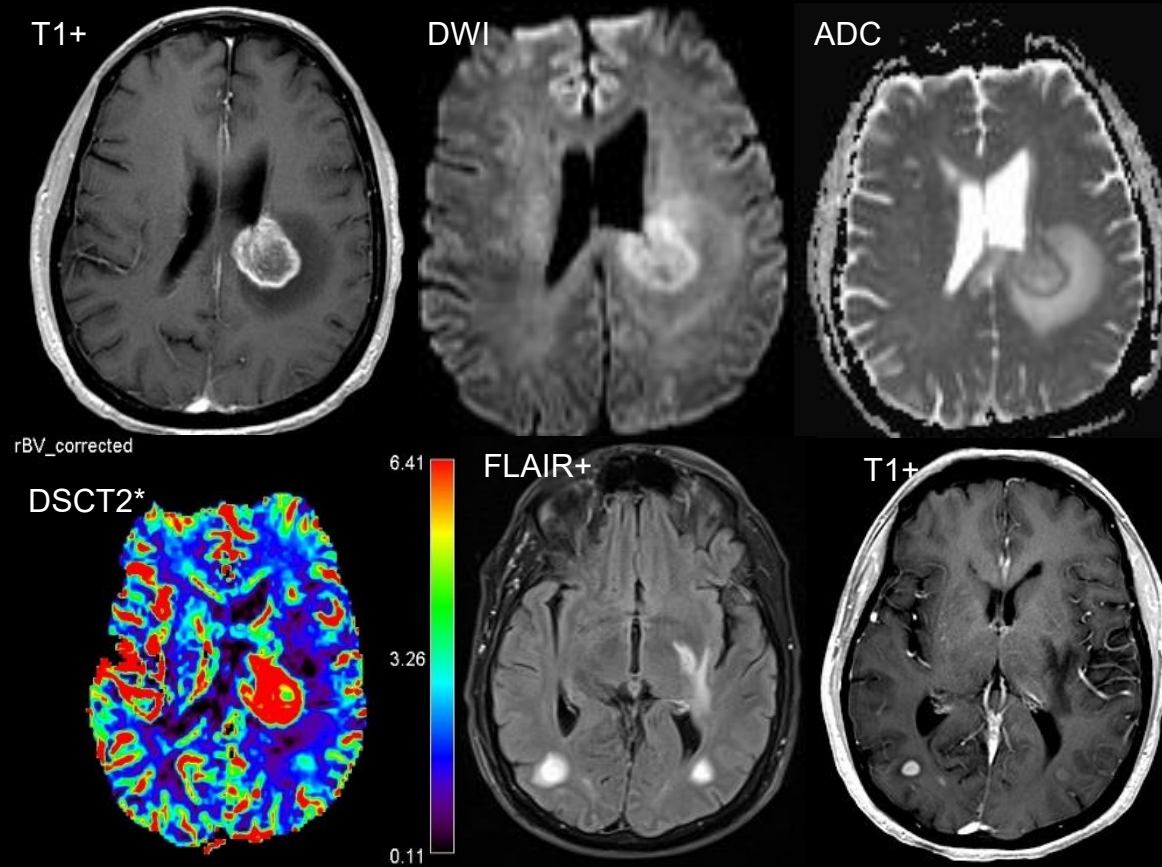


Patient 2



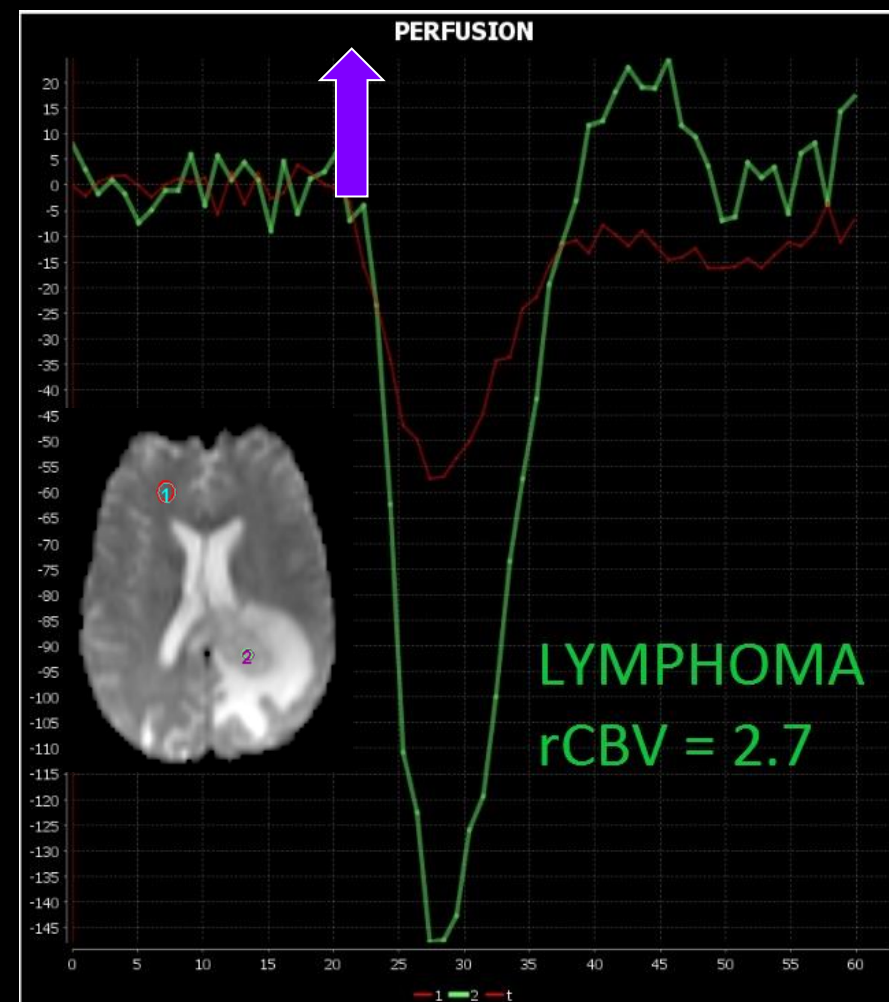
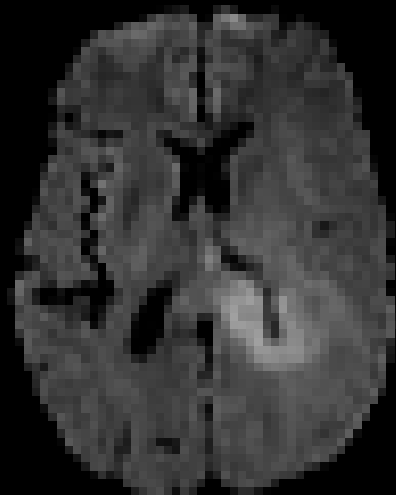
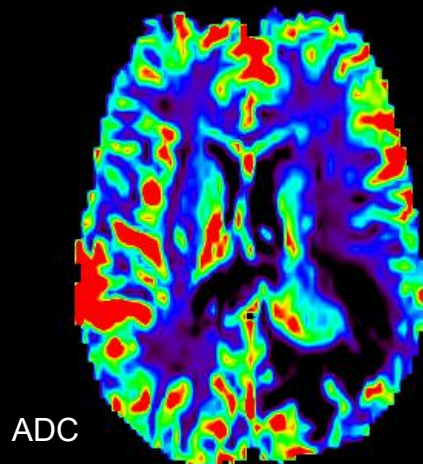
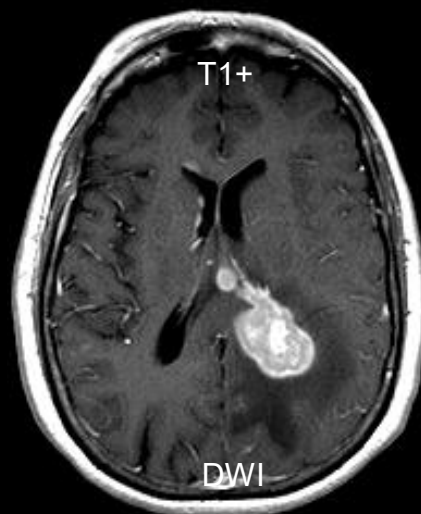
67 M

Patient 1

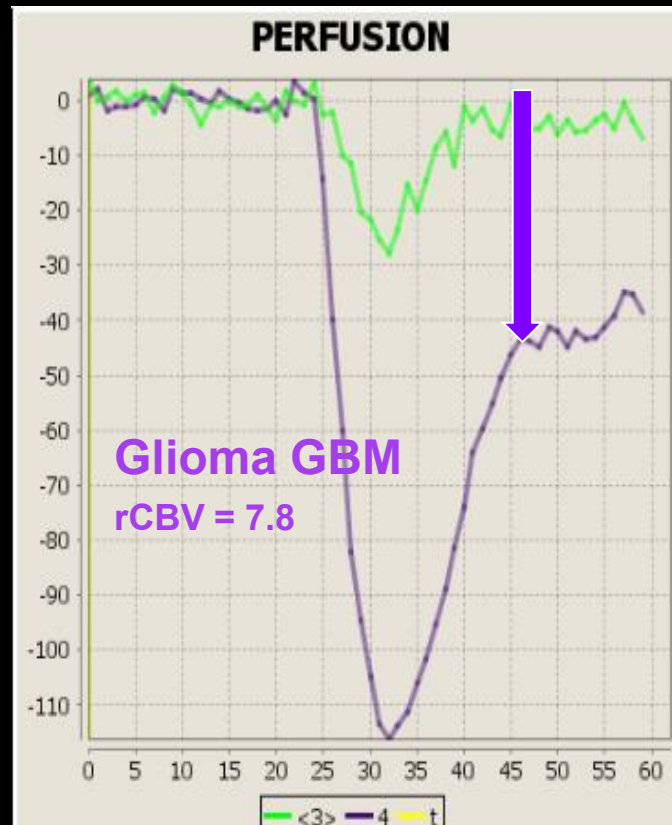


69 F

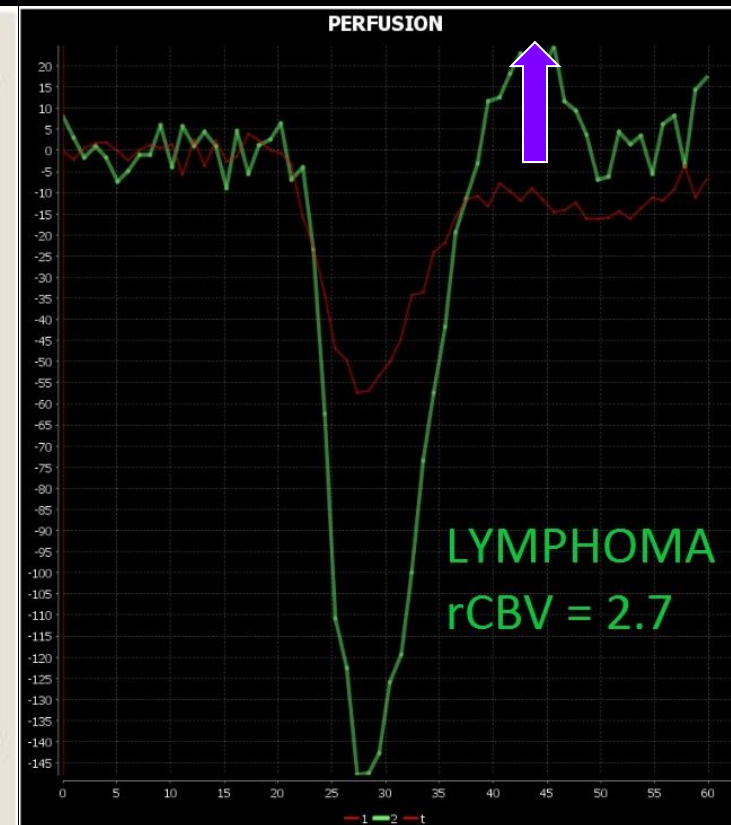
Patient 2



Lymphoma vs High-grade Glioma

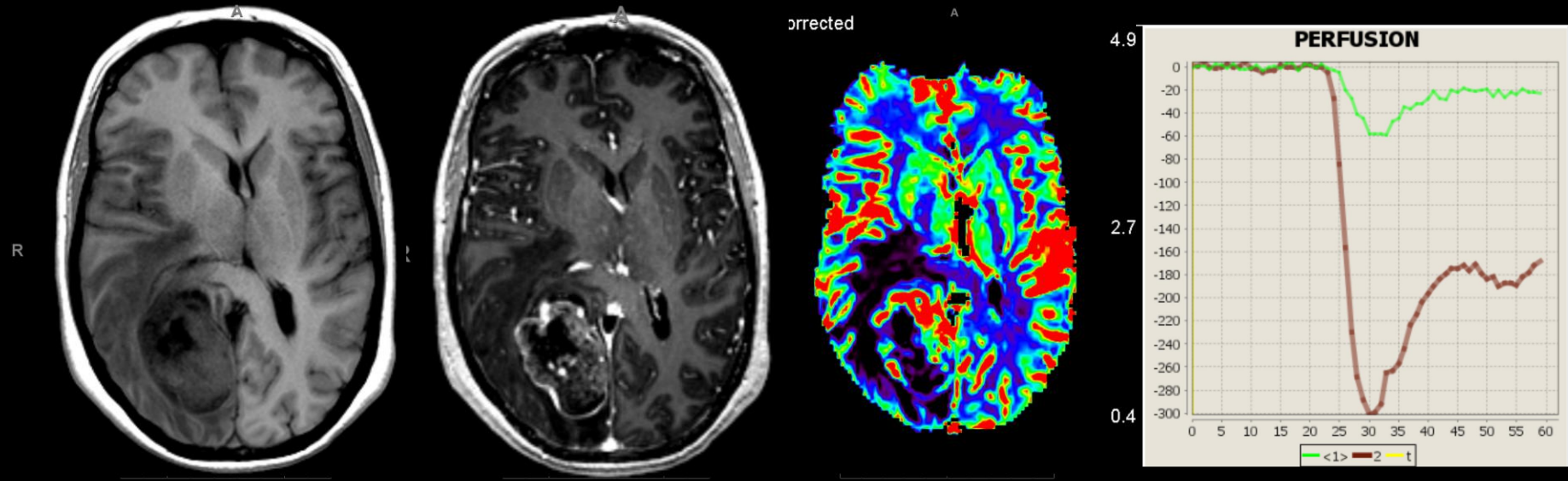


T2* leakage effects

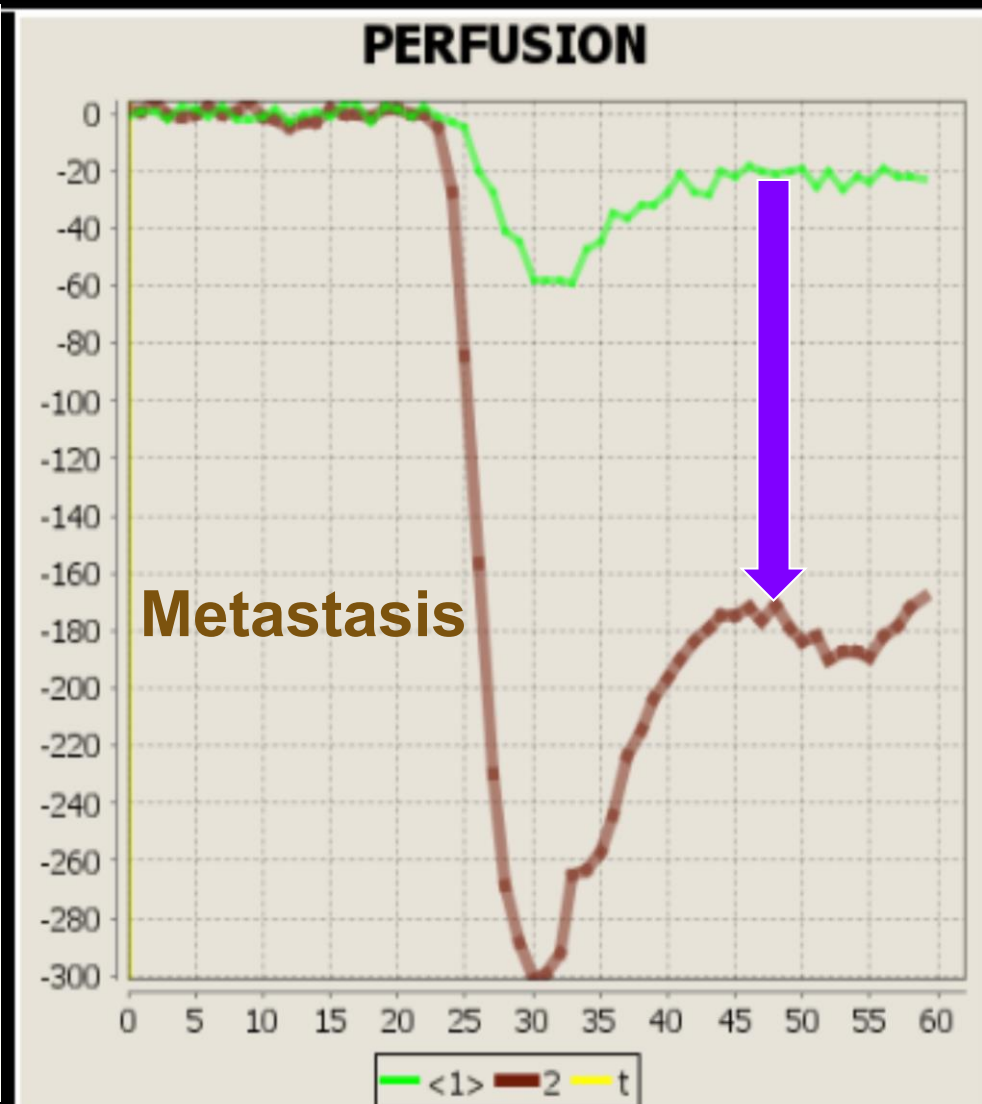
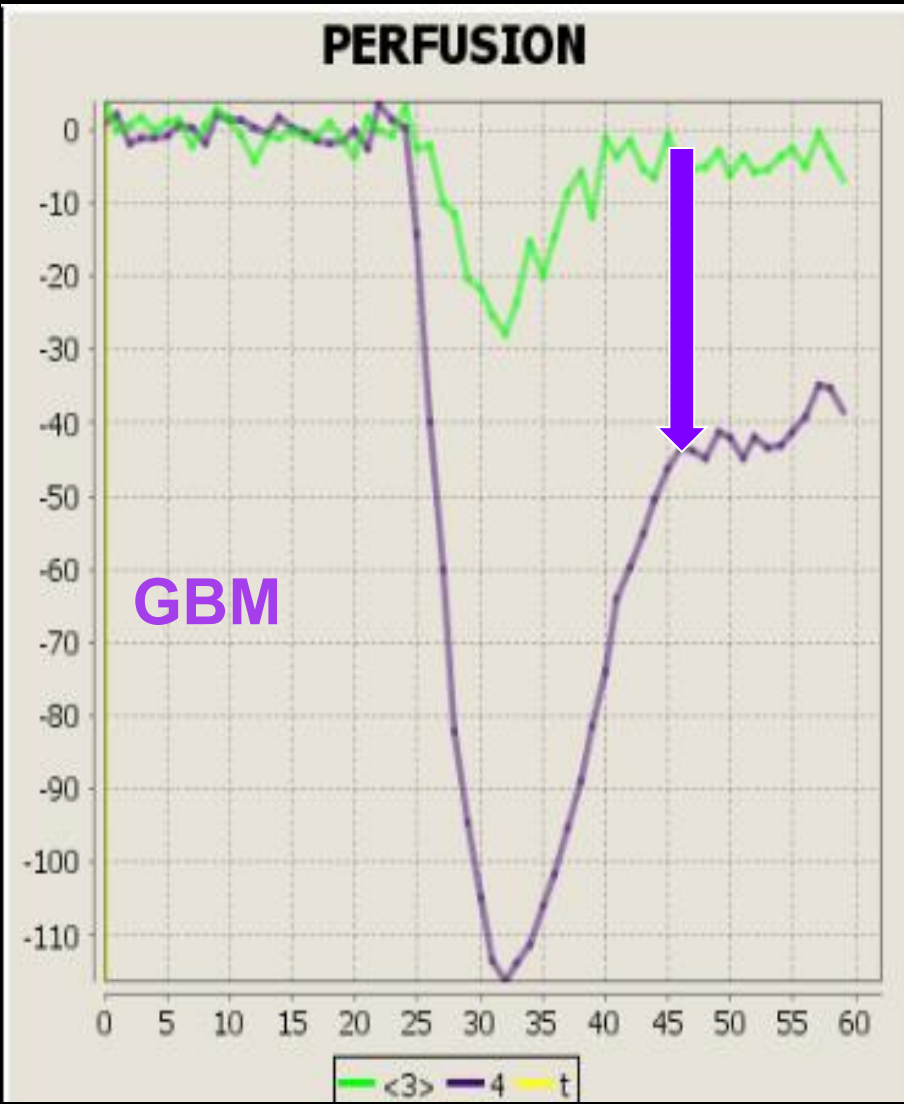


T1 leakage effects

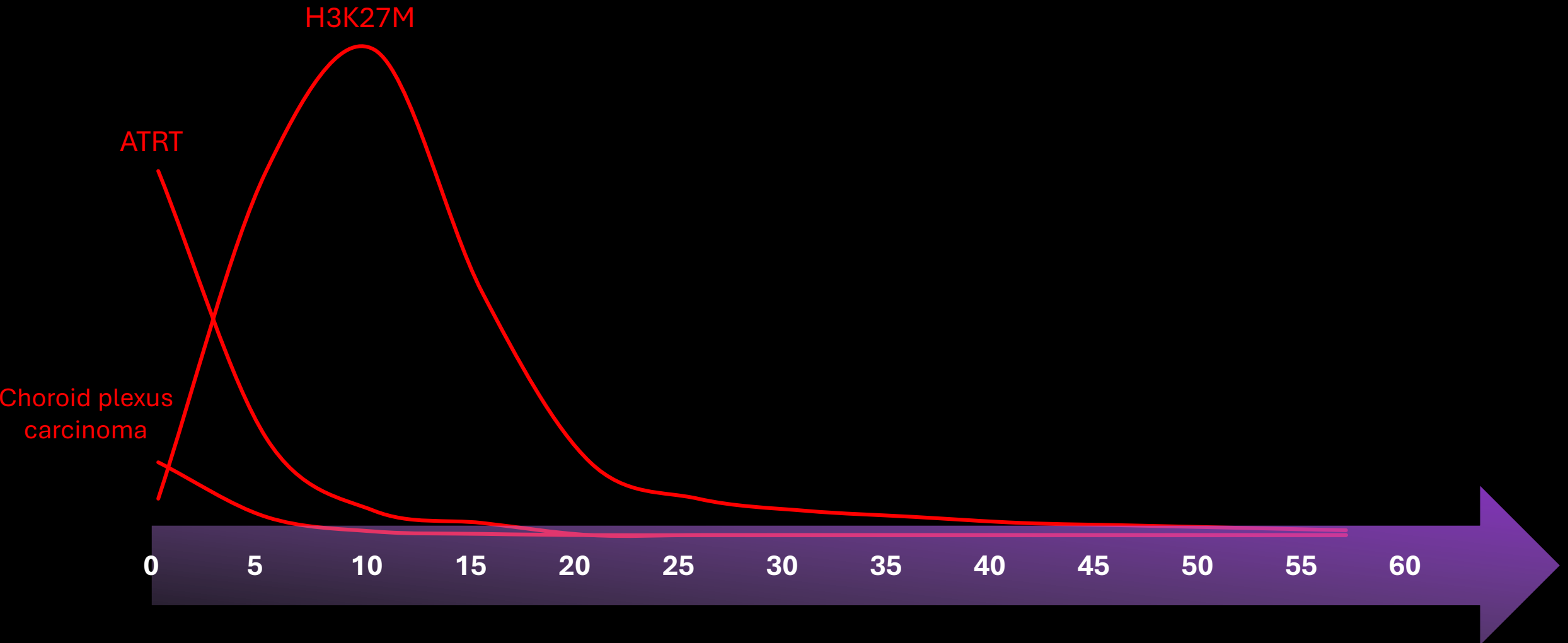
57 M



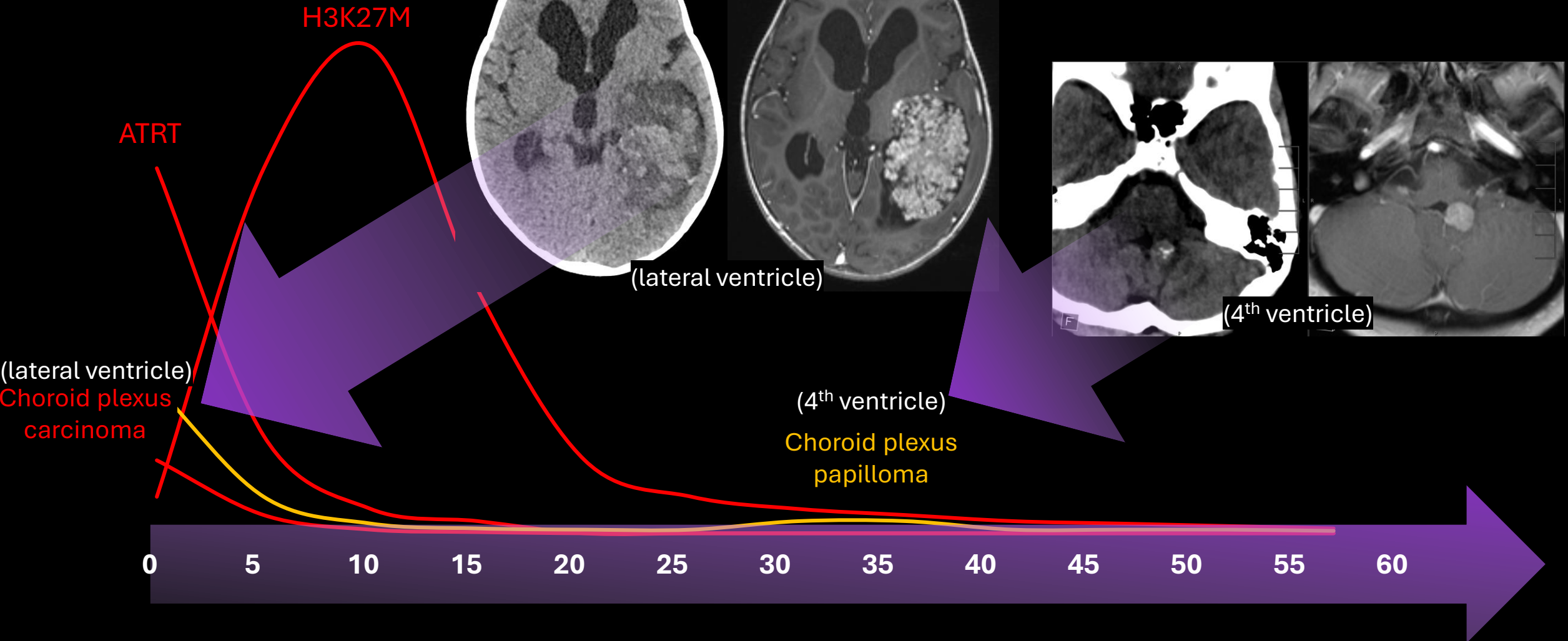
Thyroid cancer metastasis



Posterior fossa masses

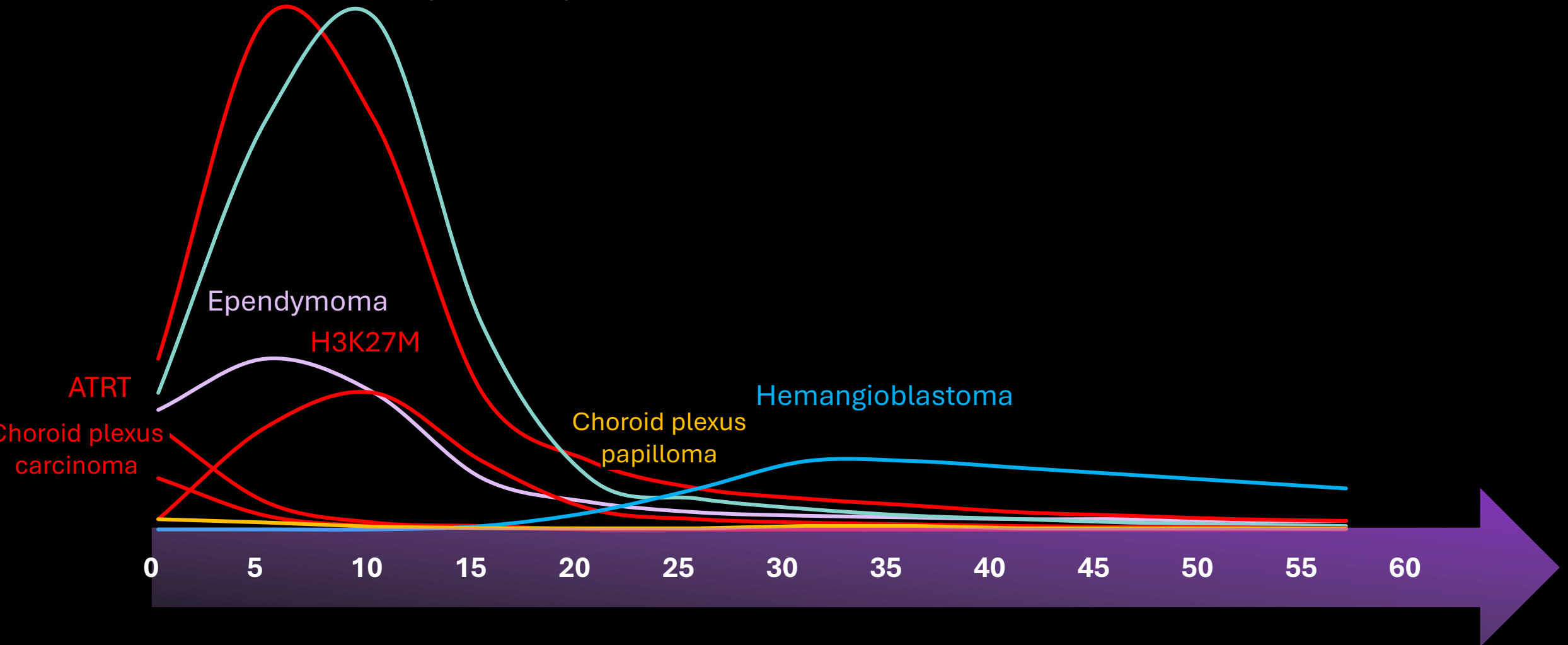


Posterior fossa masses

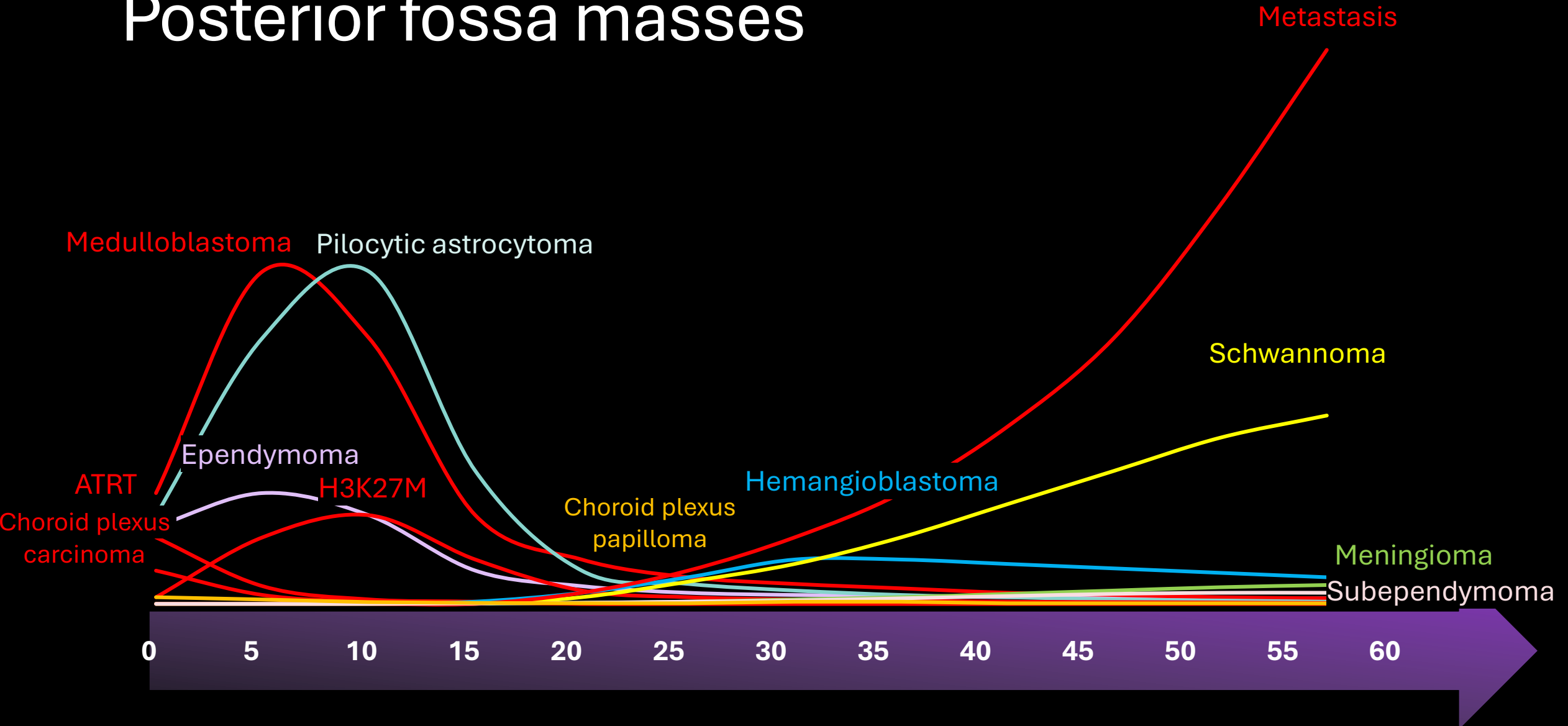


Posterior fossa masses

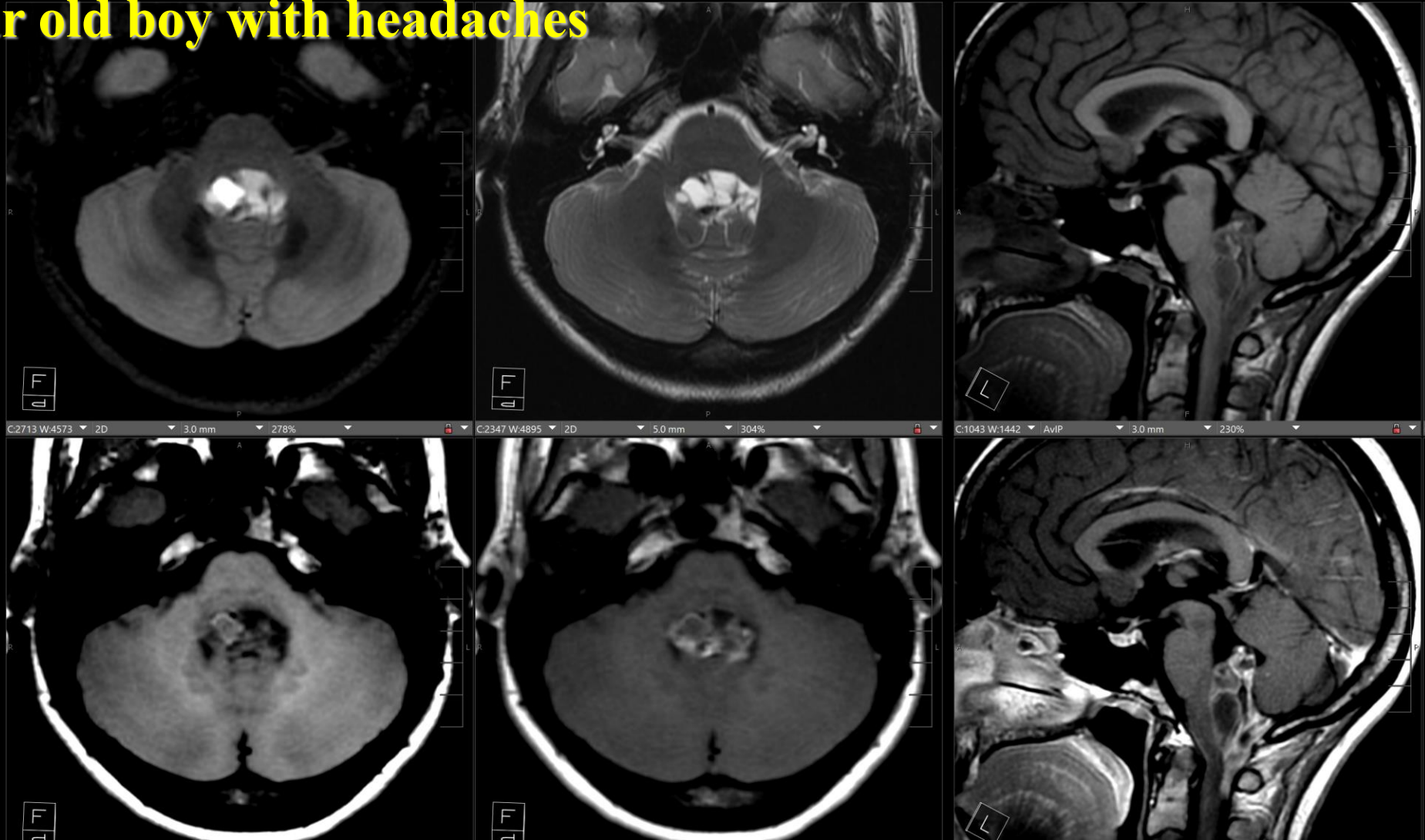
Medulloblastoma Pilocytic astrocytoma



Posterior fossa masses



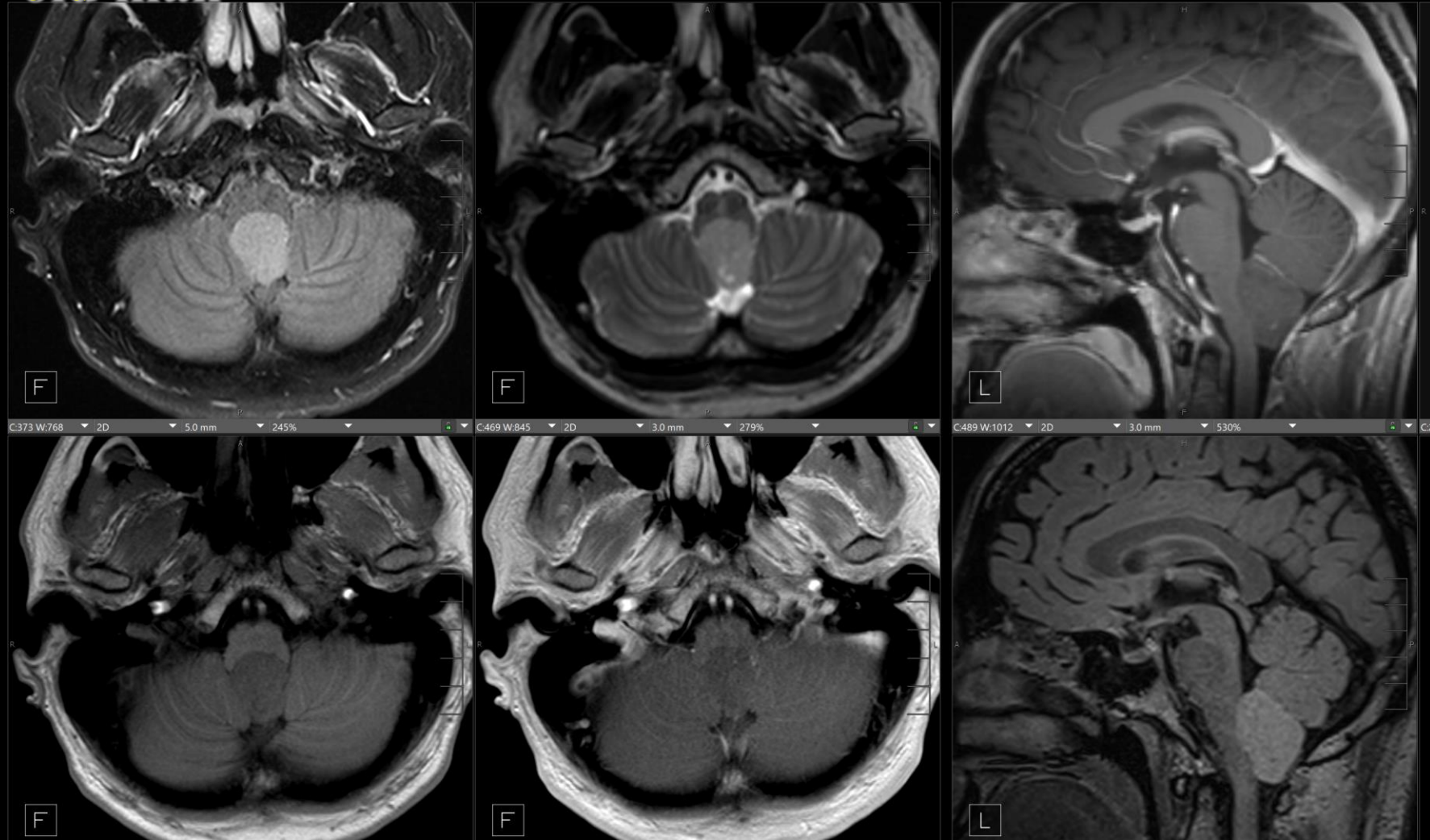
4 year old boy with headaches



Ependymoma



50 year old man



Subependymoma

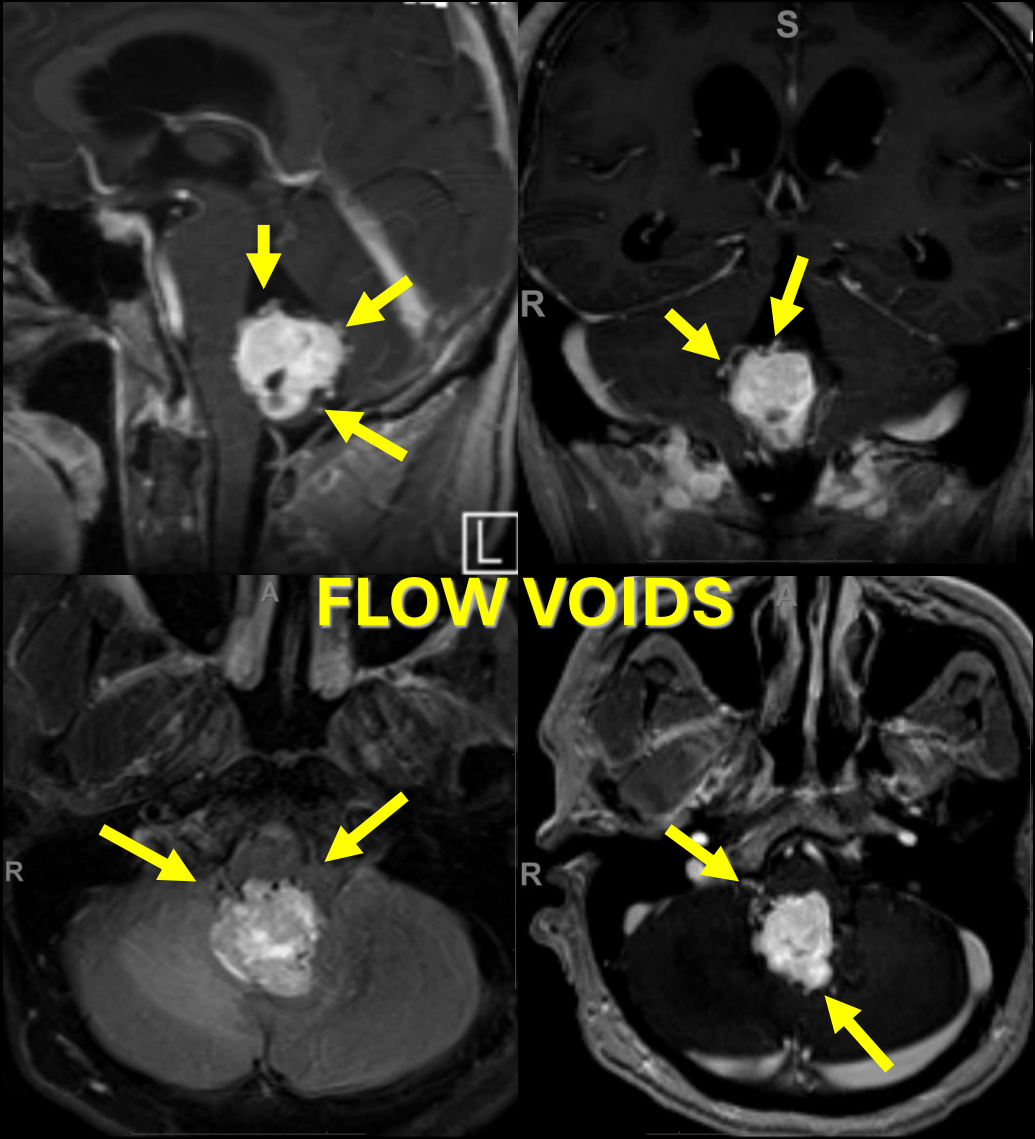
Ependymoma

- Mostly children (~5-7 years)
(Adults get spinal ependymomas)
- More enhancement
- More calcification

Subependymoma

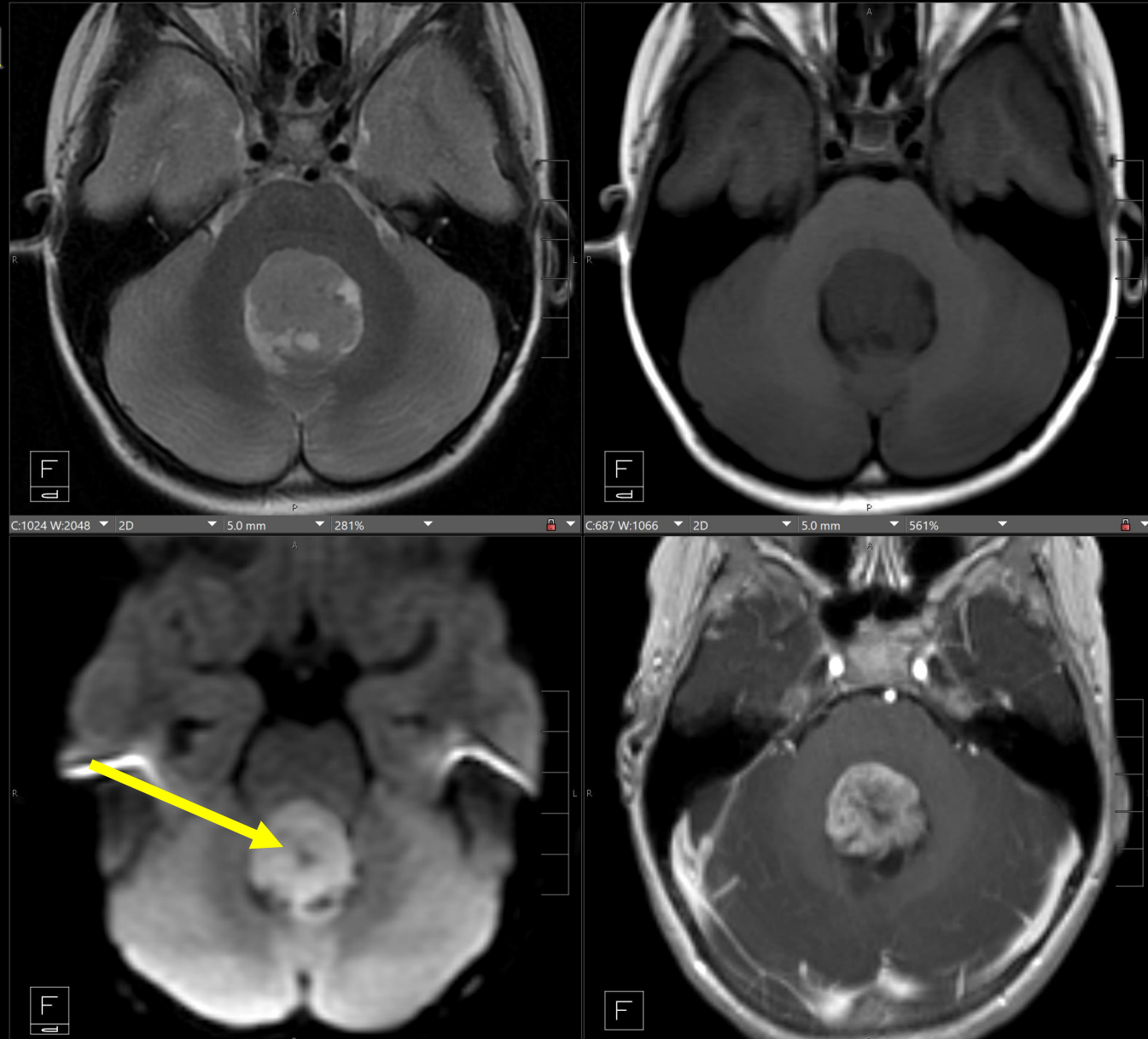
- Adults (~50 years)
- Less enhancement
- Less calcification
 - *Mnemonic SUB-ependymoma

60 year old man



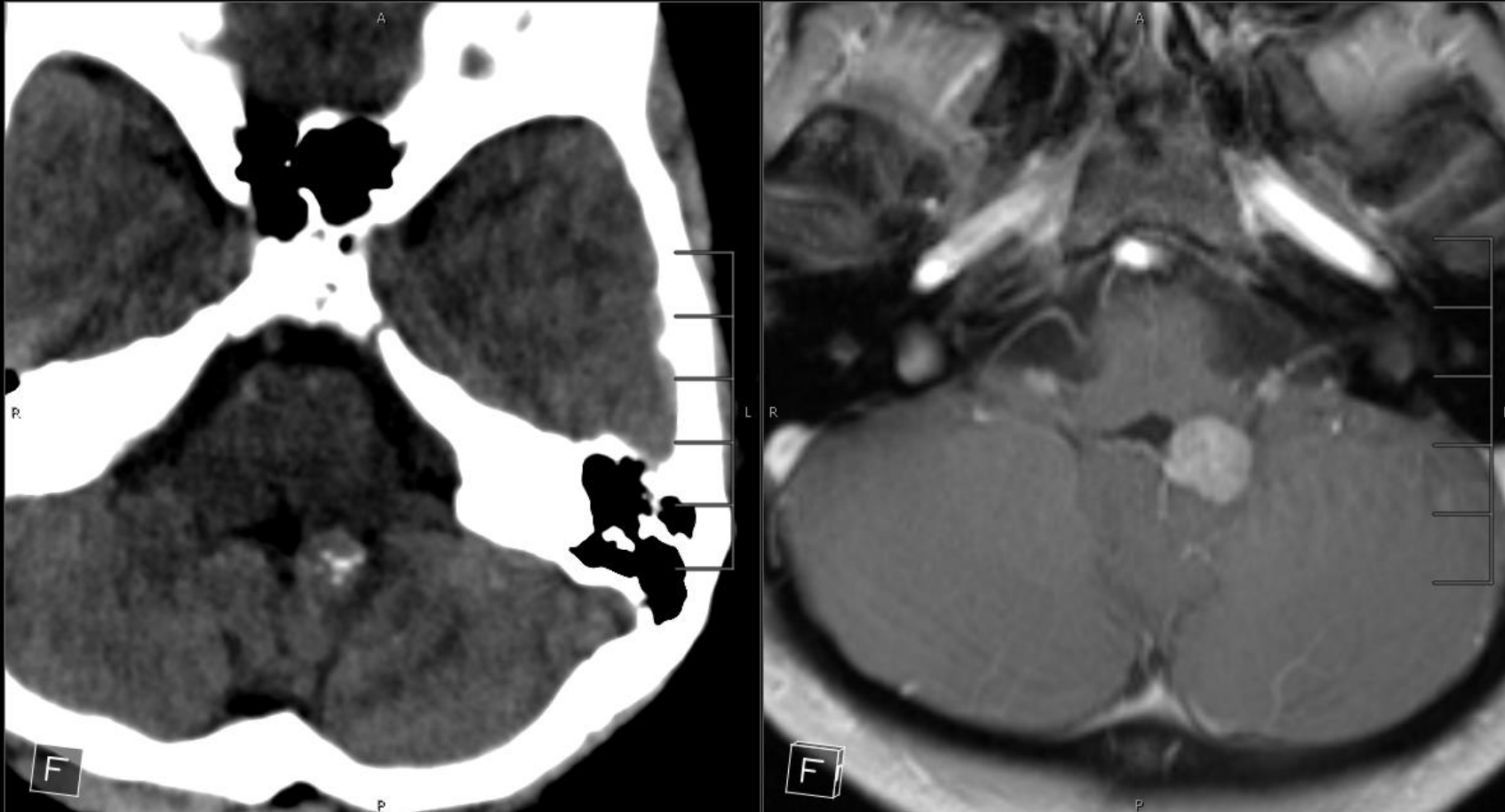
Hemangioblastoma

6 year old girl



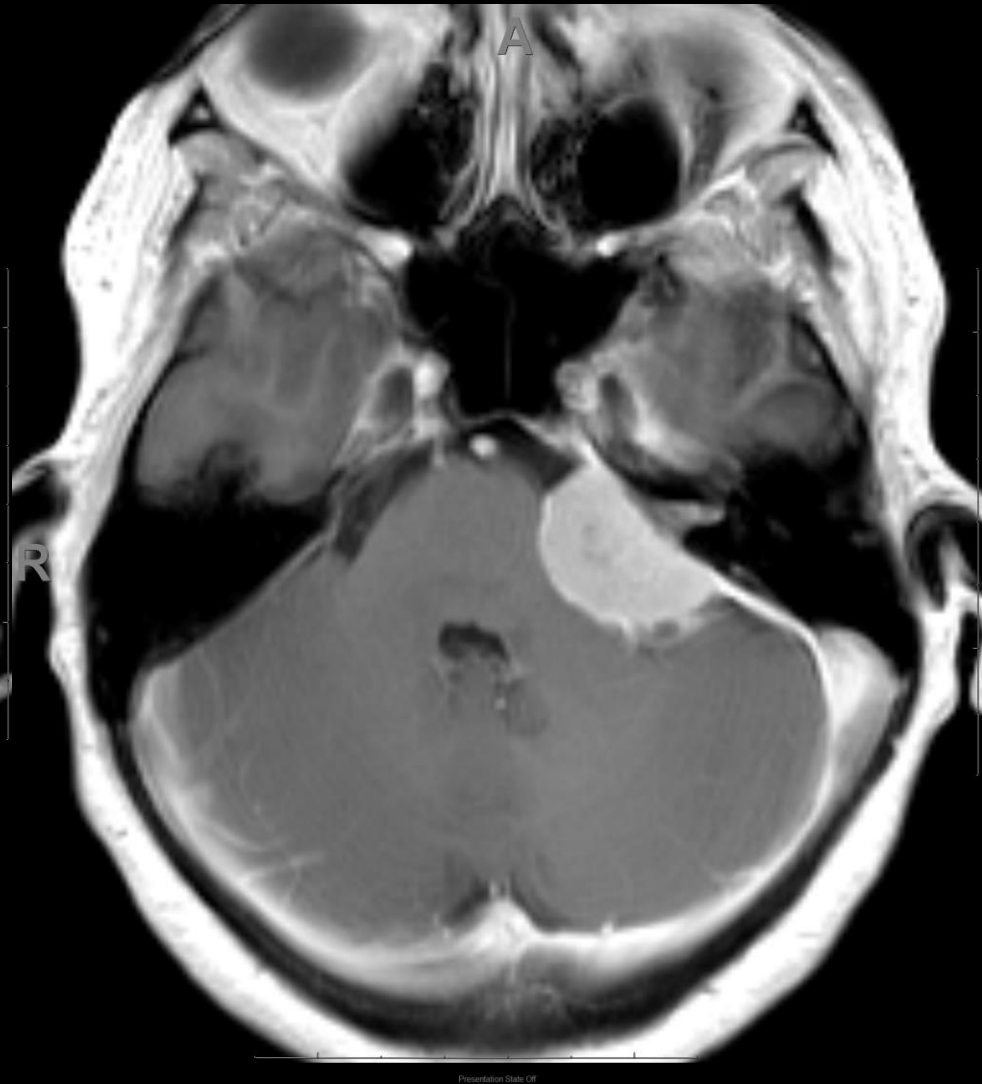
Medulloblastoma

32 year old woman



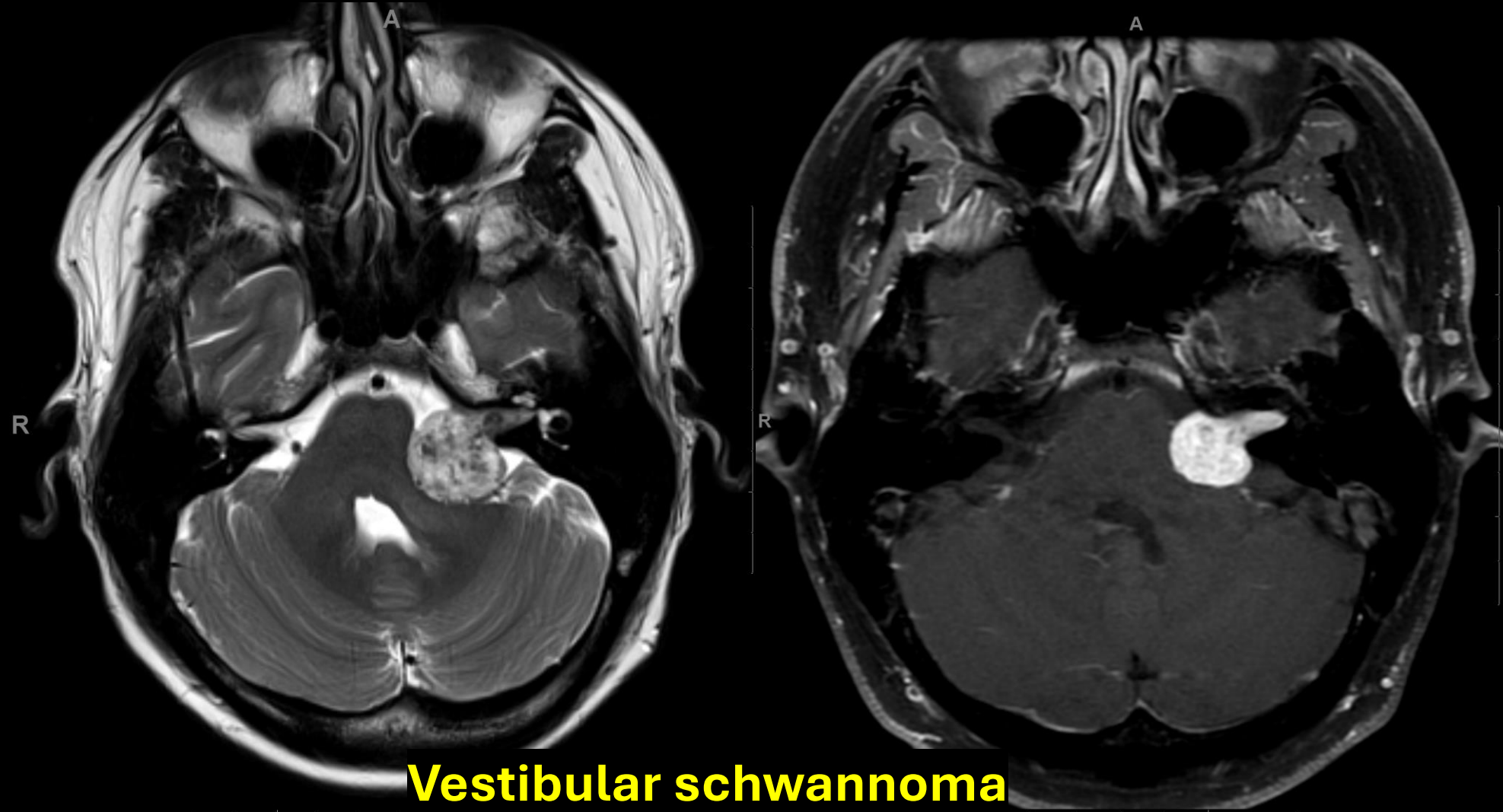
Choroid plexus papilloma

62 year old woman



CPA meningioma

39 year old woman



Vestibular schwannoma
“Acoustic neuroma”

Take home points

- **AGE** and **HISTORY** are critical considerations for an appropriate differential diagnosis.
- Tumors are increasingly defined by their **molecular characteristics**, which provide better prognostic and treatment information.
- Over **age 40**, assume a glioma is high grade.
- Never assume a glioma is low grade without evidence of stability or indolent behavior.