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Neurosurgery Breakout Session

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CNS Malignancy

Blake Phillips MD FAANS

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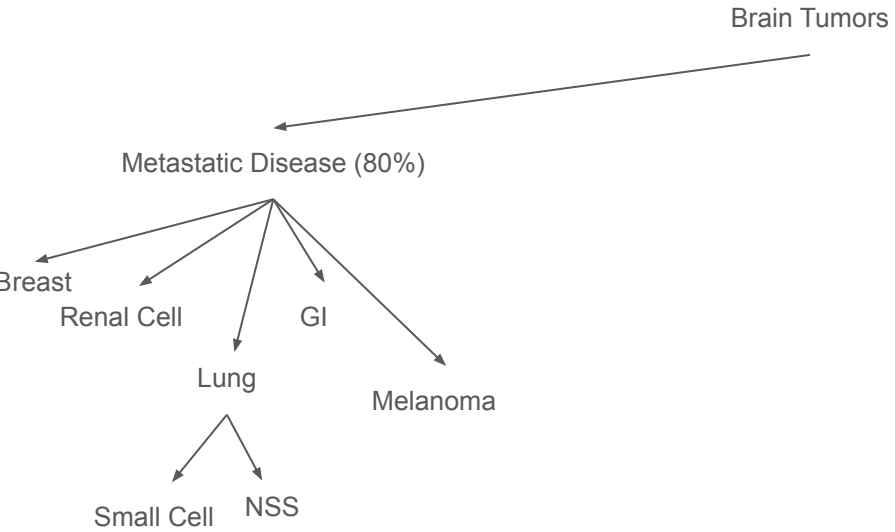
Objectives

1. Understand the different categories of brain tumors

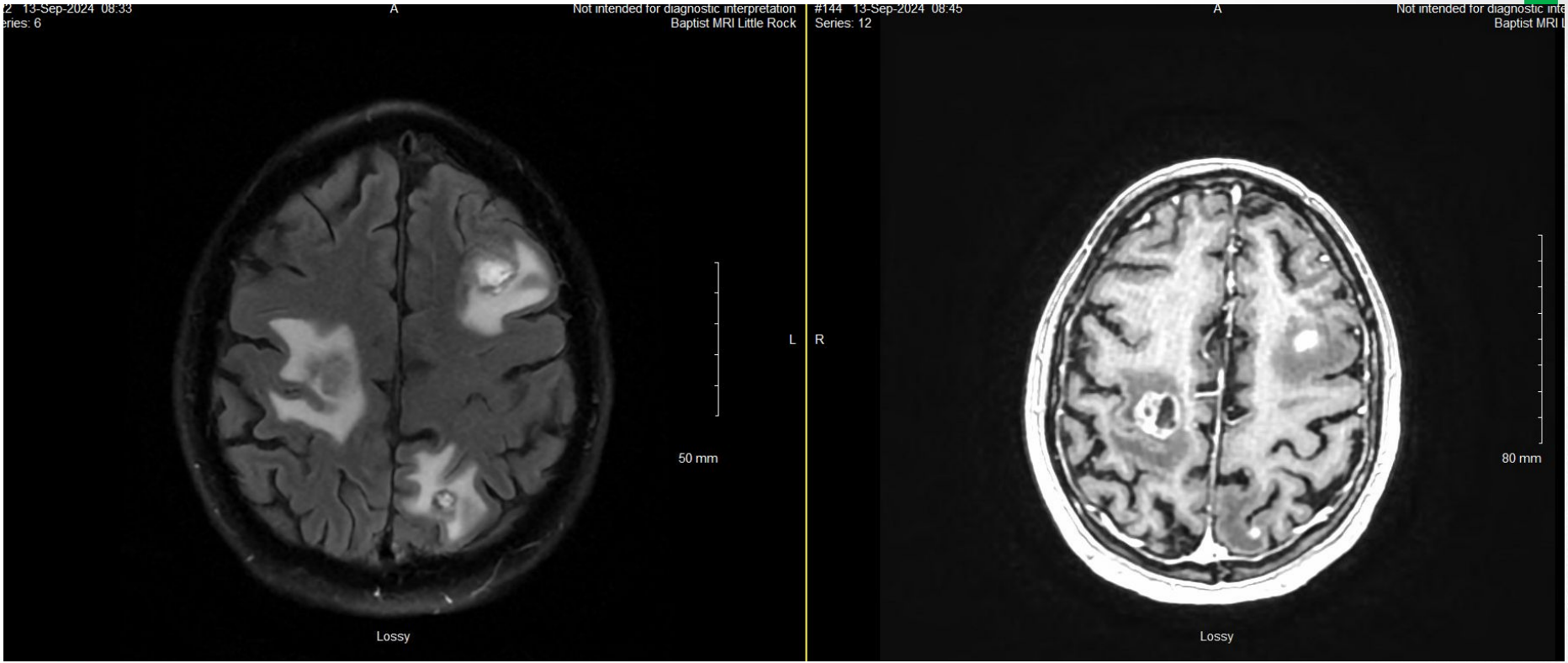
2. Understand the different treatment options

3. Provide a brief overview on new treatment developments

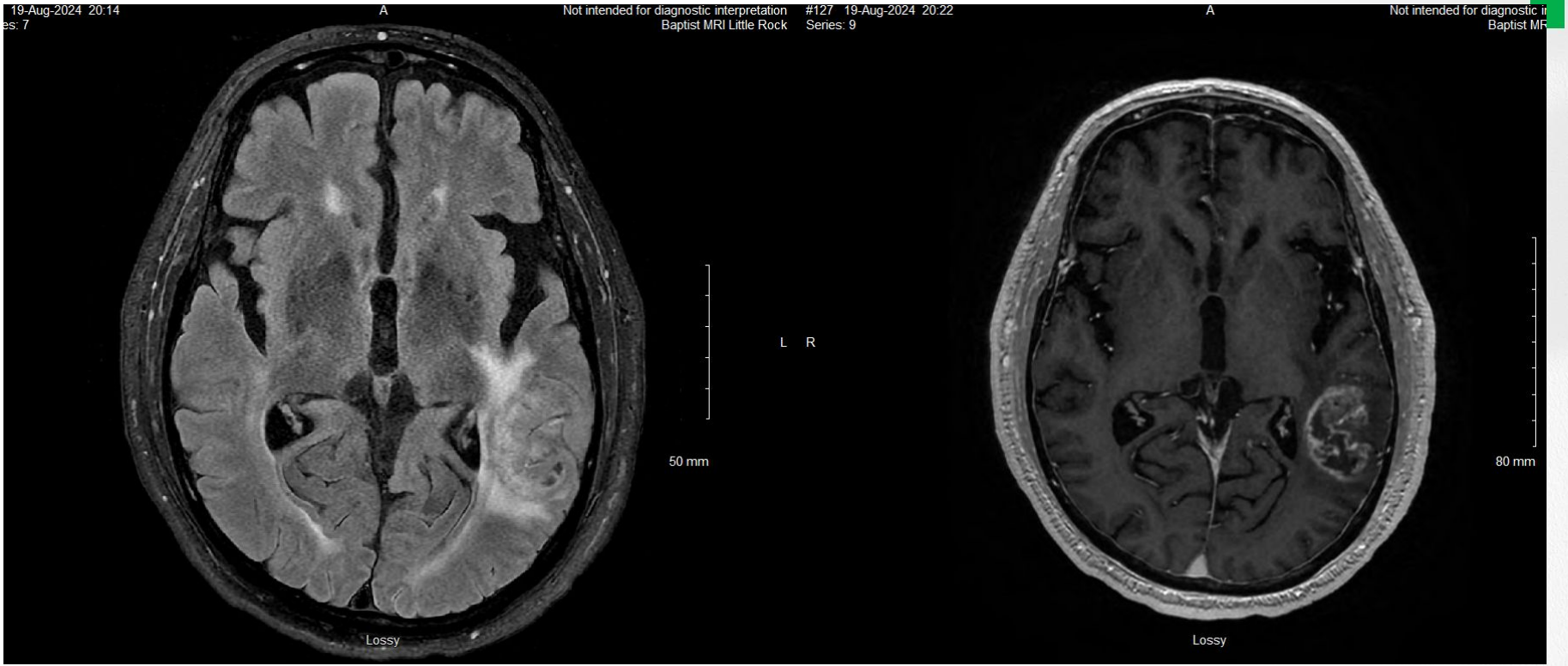
30,000ft view



Brain Metastasis



Brain Metastasis



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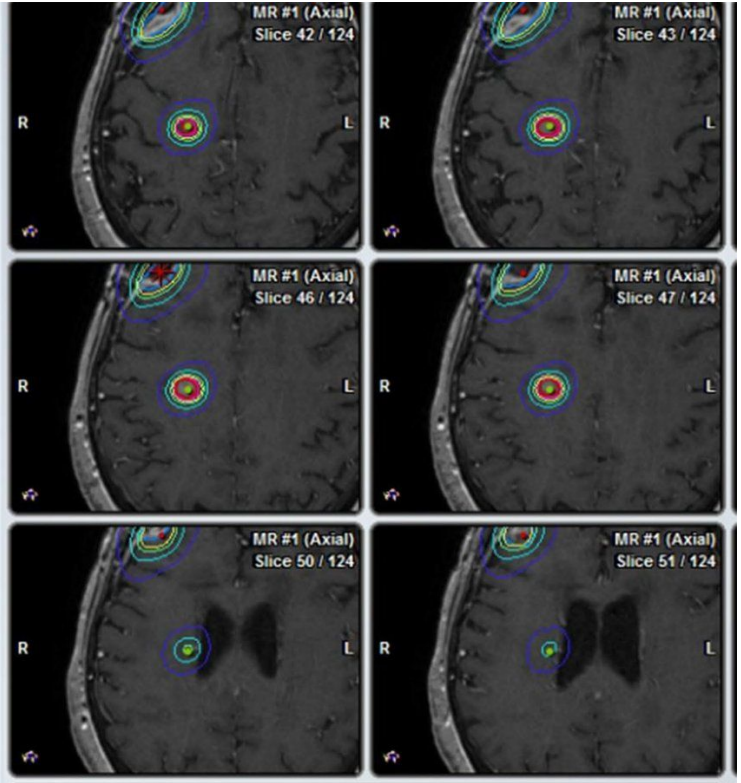
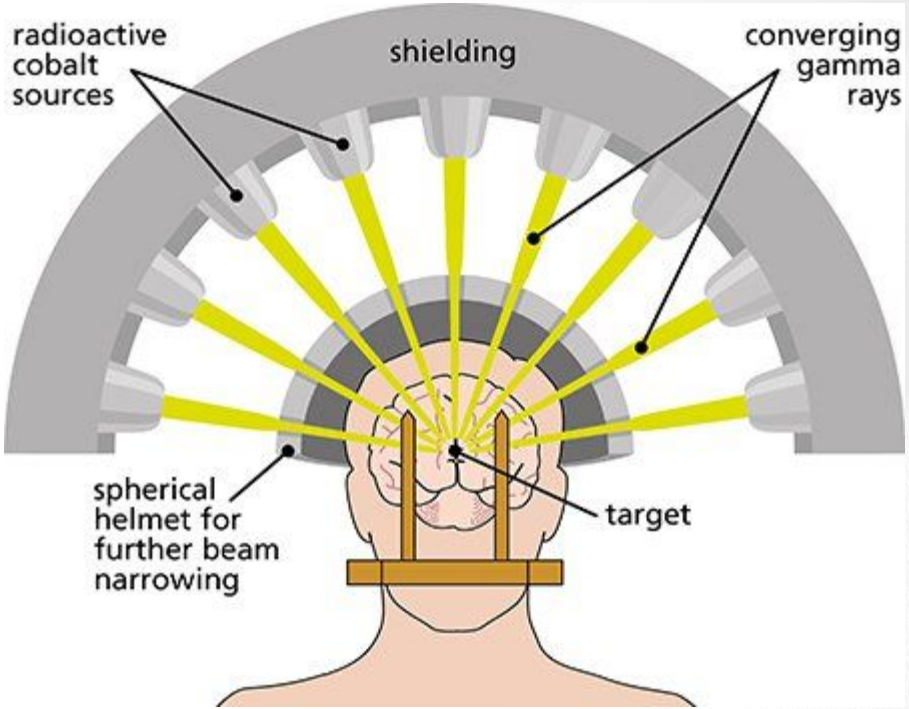
Advances in Brain Metastasis Management

- Chemotherapy combos
- Targeted Therapies
- Immunotherapies

- Stereotactic Radiosurgery
- WBRT
  - Hippocampal preserving
- Proton Beam Therapy 

Stereotactic Radiosurgery





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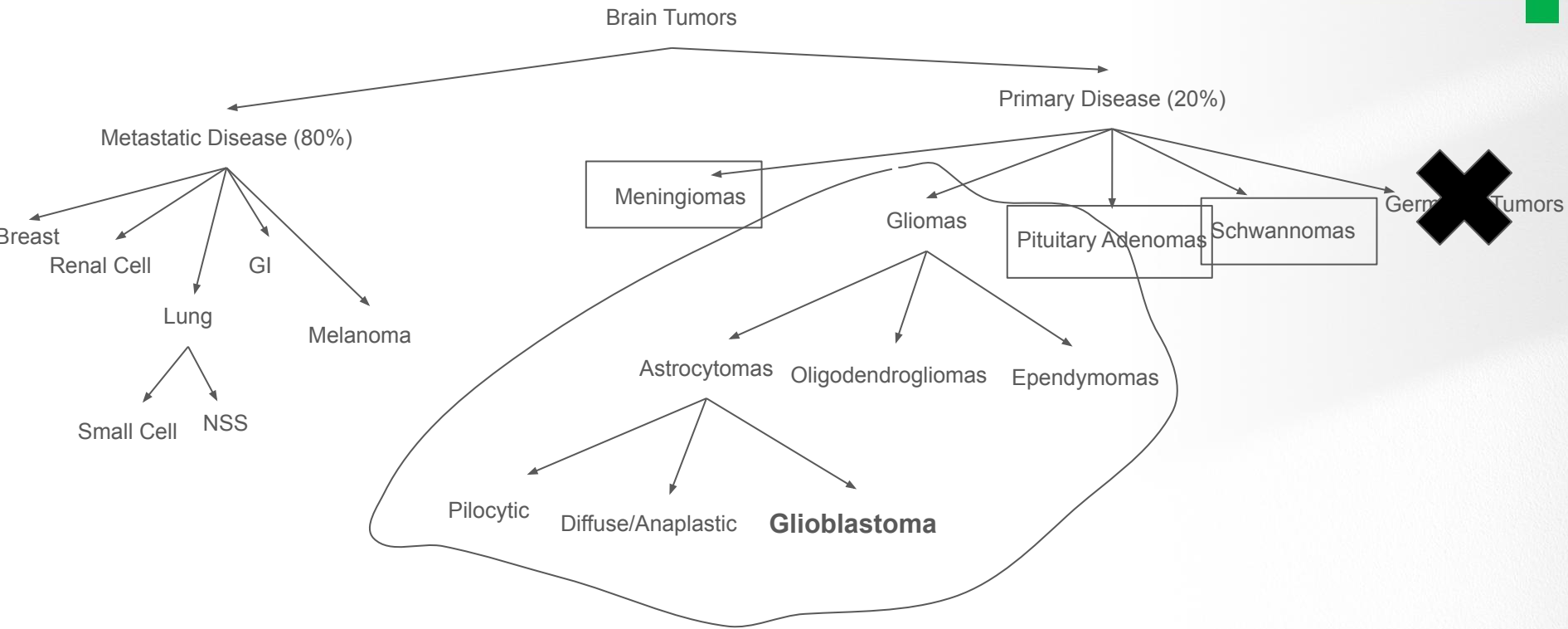
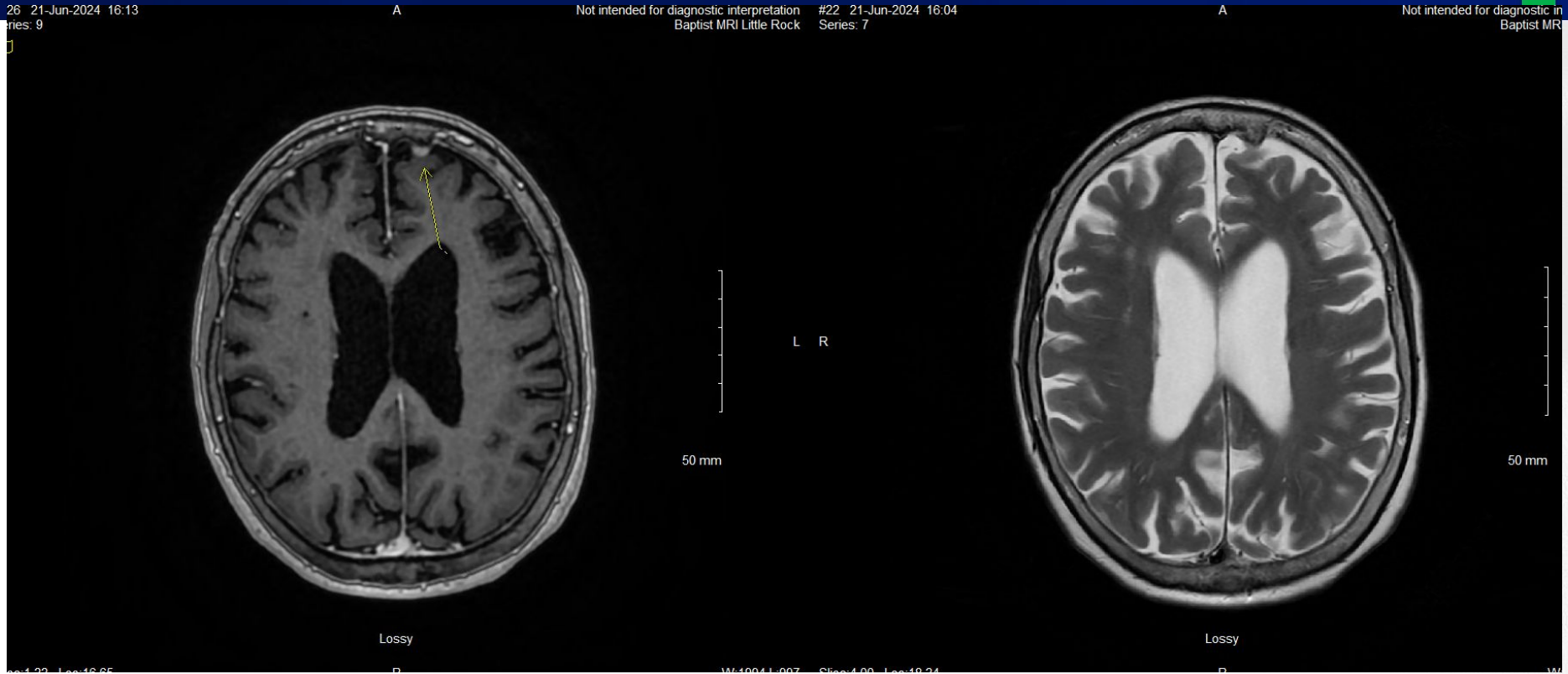


Meningiomas

- Mostly (90%) benign tumors of the meninges
- Location
  - Typically convexity
  - Can be anywhere
- Types
  - **Meningothelial**
  - Fibroblastic
  - Transitional
  - Psammomatous
  - Lymphocytic
- Treatment based on size and growth rate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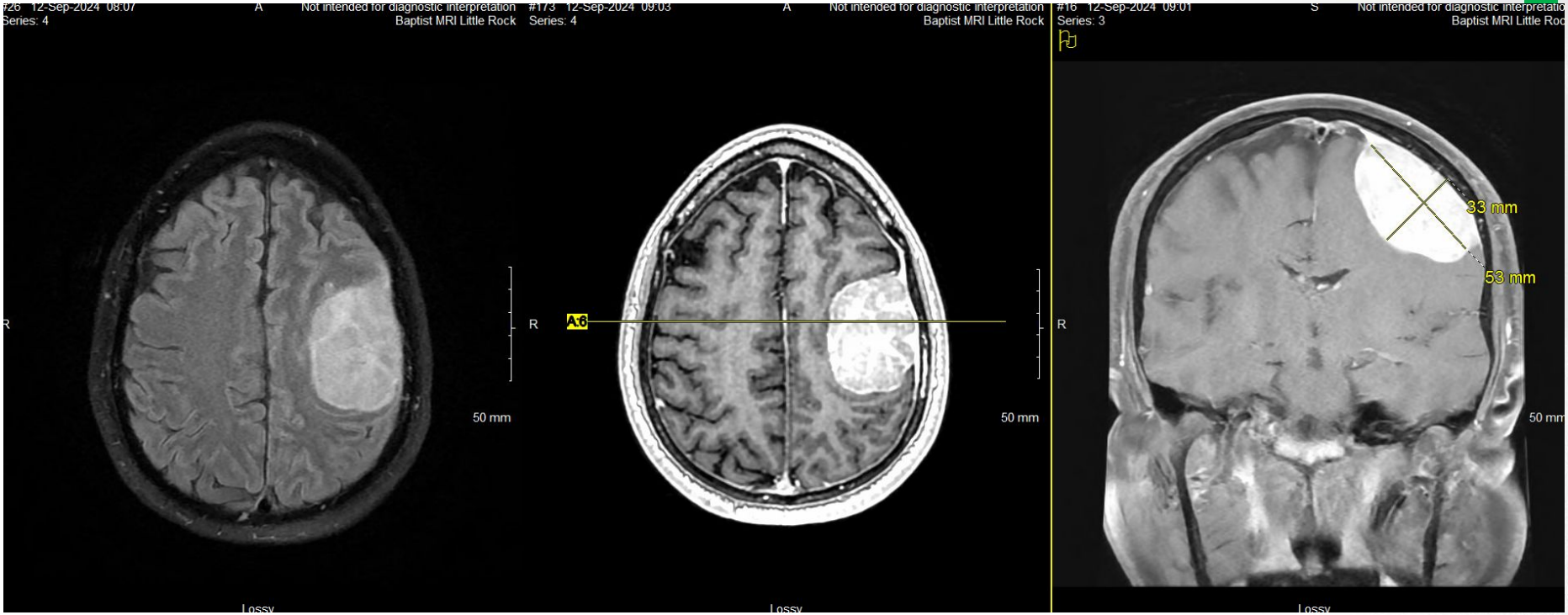

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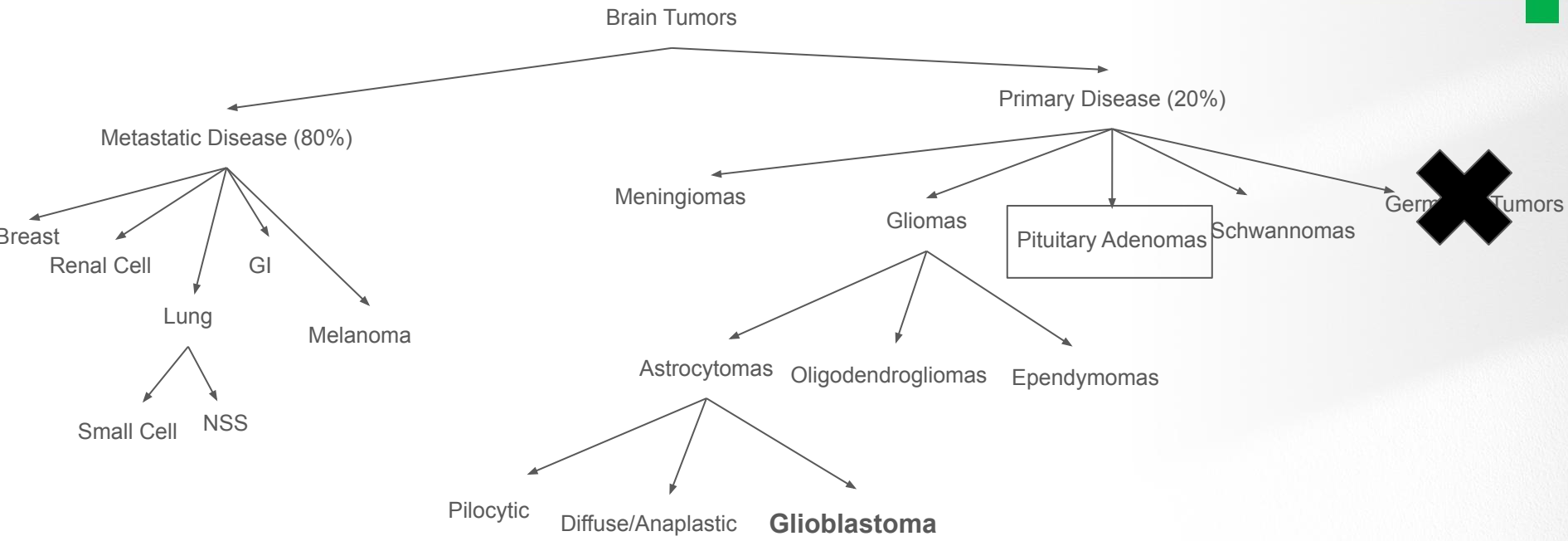
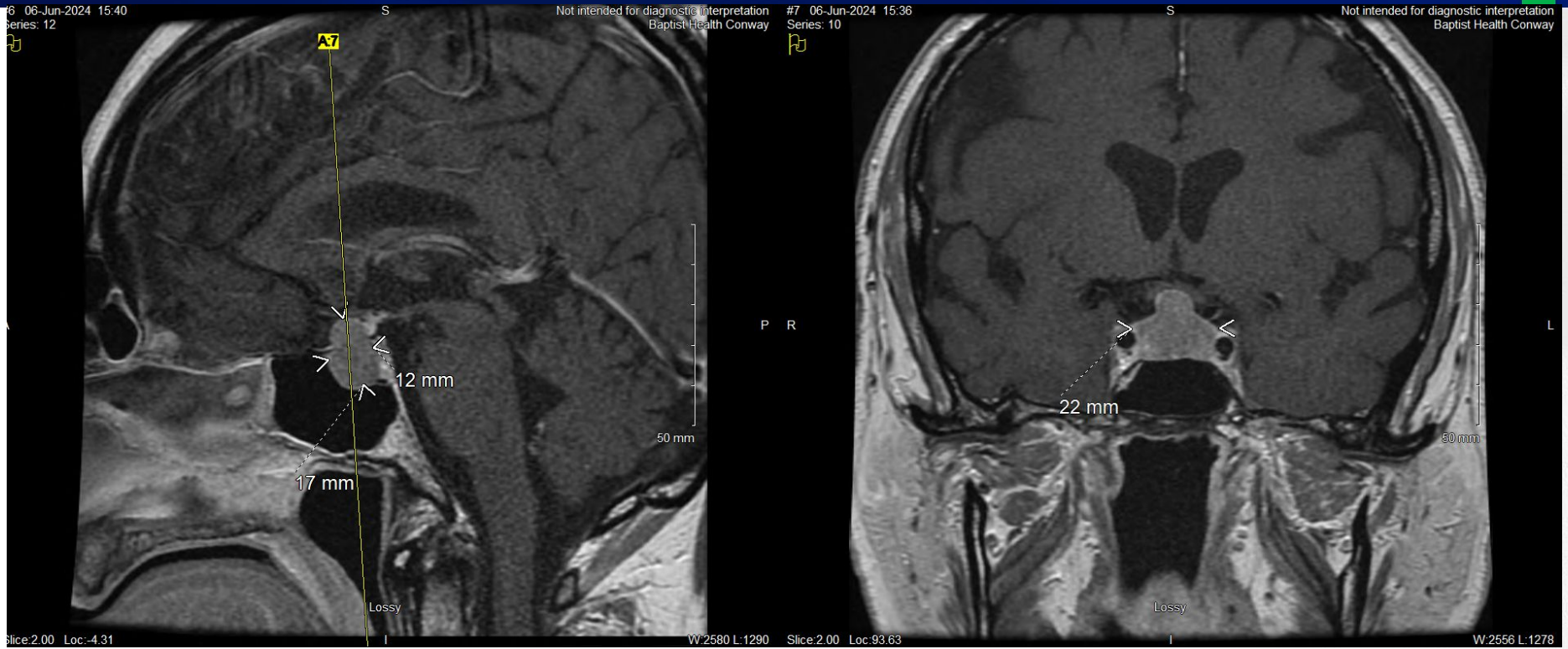
30,000ft View



Pituitary Adenomas

- Benign tumors of the pituitary gland
- Location
  - Sella turcica
  - Suprasellar extension
- Secreting vs Non-secreting
  - GH producing
  - TSH producing
  - ACTH producing
  - Prolactin Producing
- Treatment based on secretory status
  - Non-secreting → surgery
  - Secreting → surgery vs medical management



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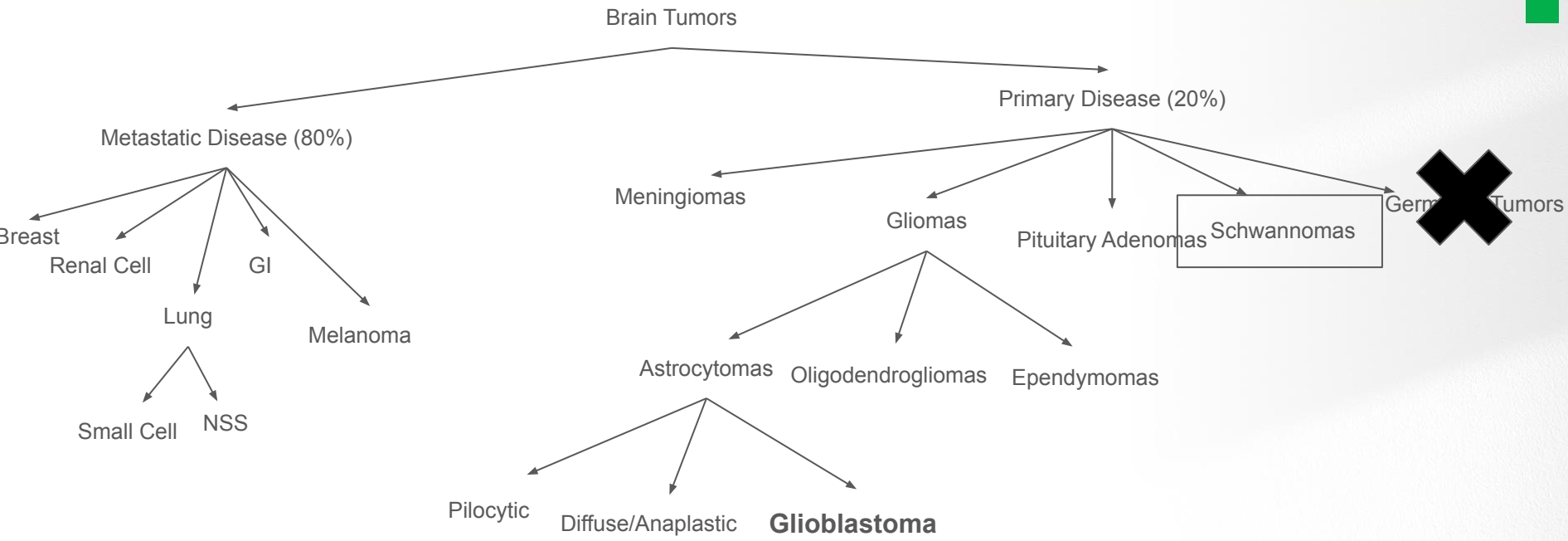
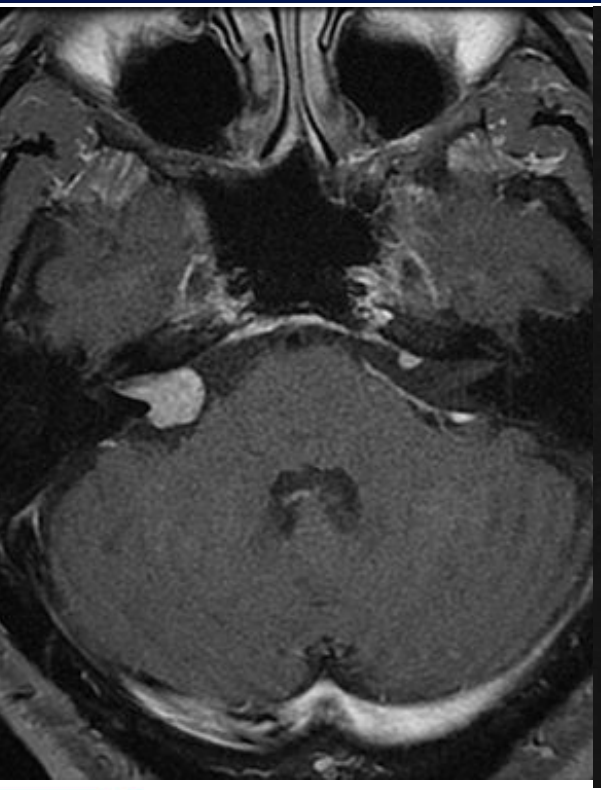
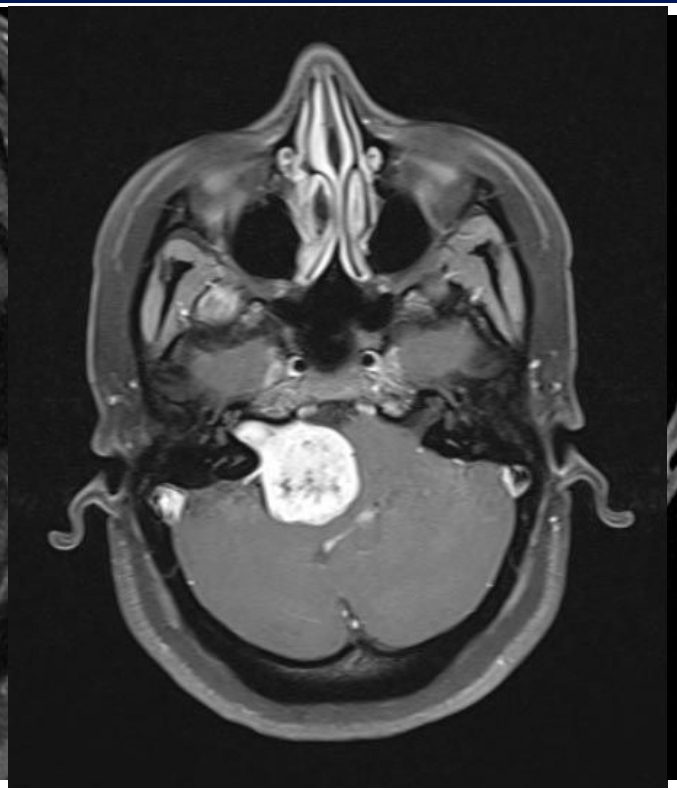
30,000ft View

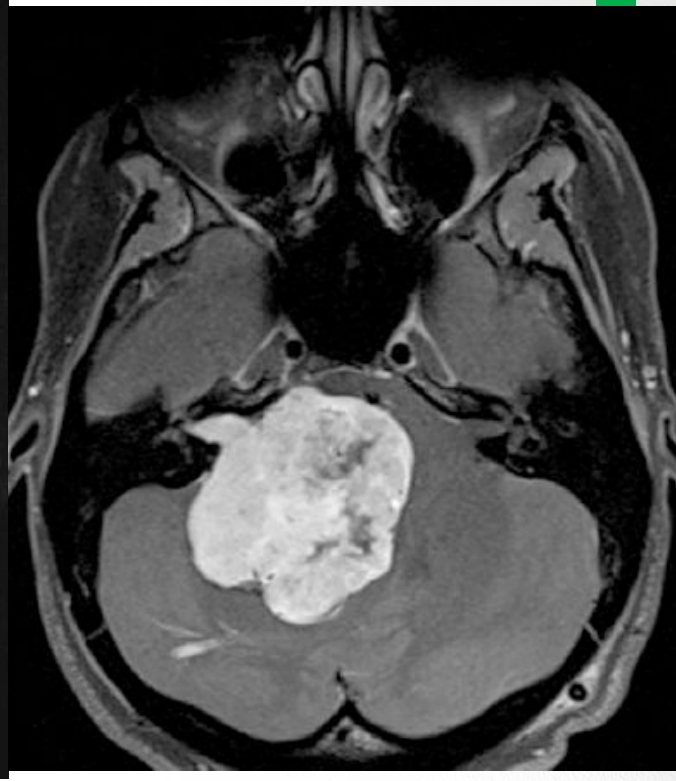


Schwannomas

- Benign tumors of the Schwann Cell
- Location
  - **Acoustic (vestibulocochlear n.)**
  - Facial n.
  - Trigeminal n.
- Treatment based on size
    - Small (<3cm) vs large
    - Rapidly growing
  - Observation vs surgery vs radiosurgery

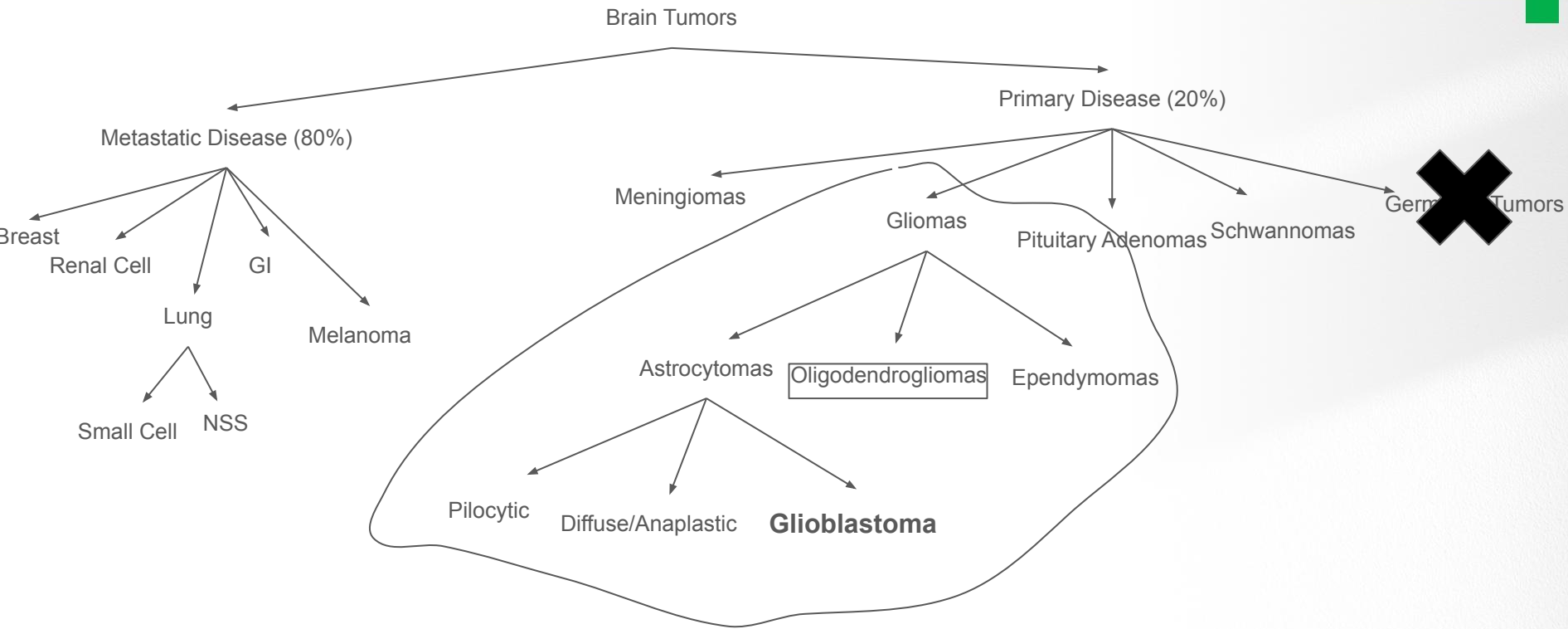






Gliomas

30,000ft View

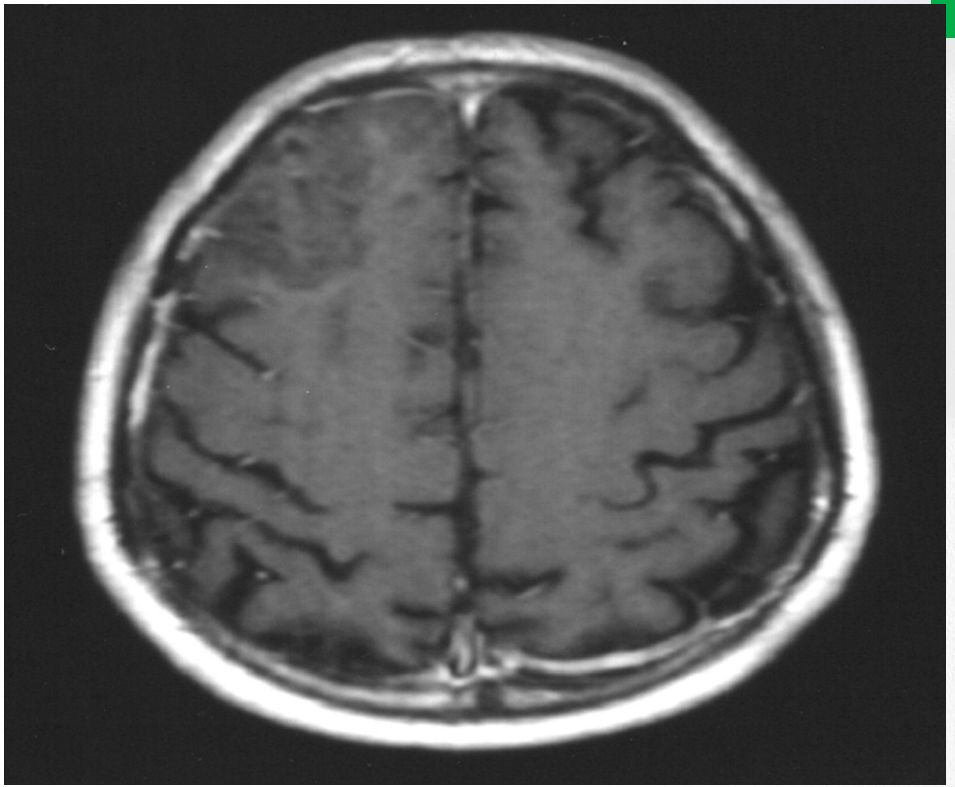


Oligodendrogliomas

- Diffusely infiltrative
- Location:
  - Cerebral hemisphere
  - >50% frontal lobe
- Peak incidence: 40-45 years
- Prognosis:
  - Average survival of 10-15 yrs for grade 2, and 3-5 yrs for grade 3
  - Presence of codeletion of 1p19q improves survival
    - present in 50-80% of cases

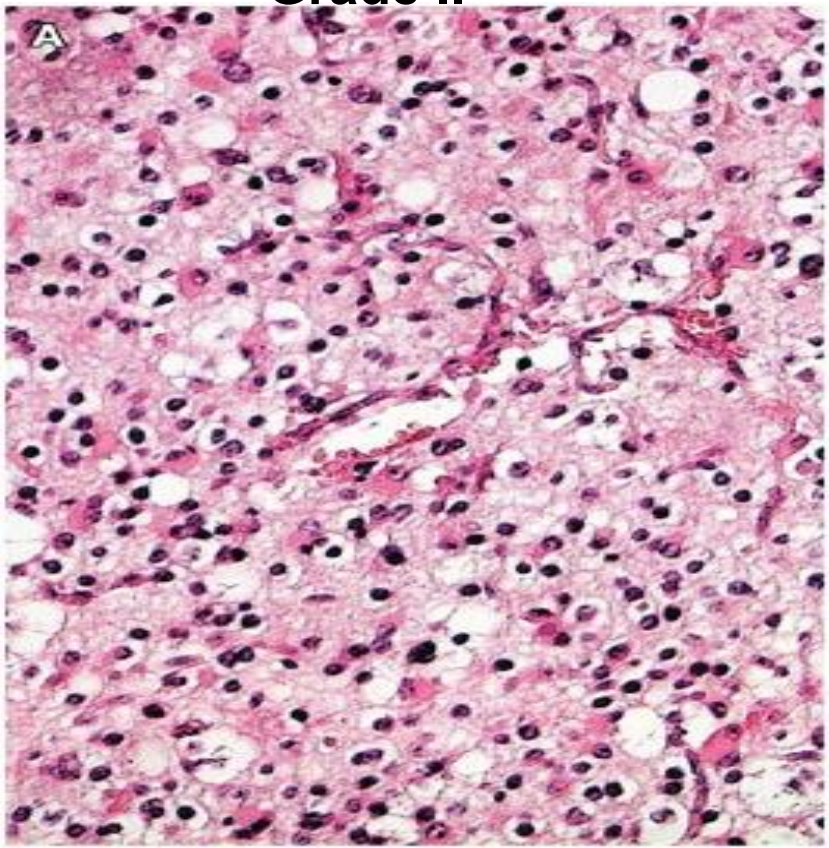
Oligodendroglioma

- Radiologic features
  - Grade II - nonenhancing masses (T2 weighted and FLAIR MRI)
  - Grade III tumors are typically enhancing
  - Intratumoral **calcifications** are common

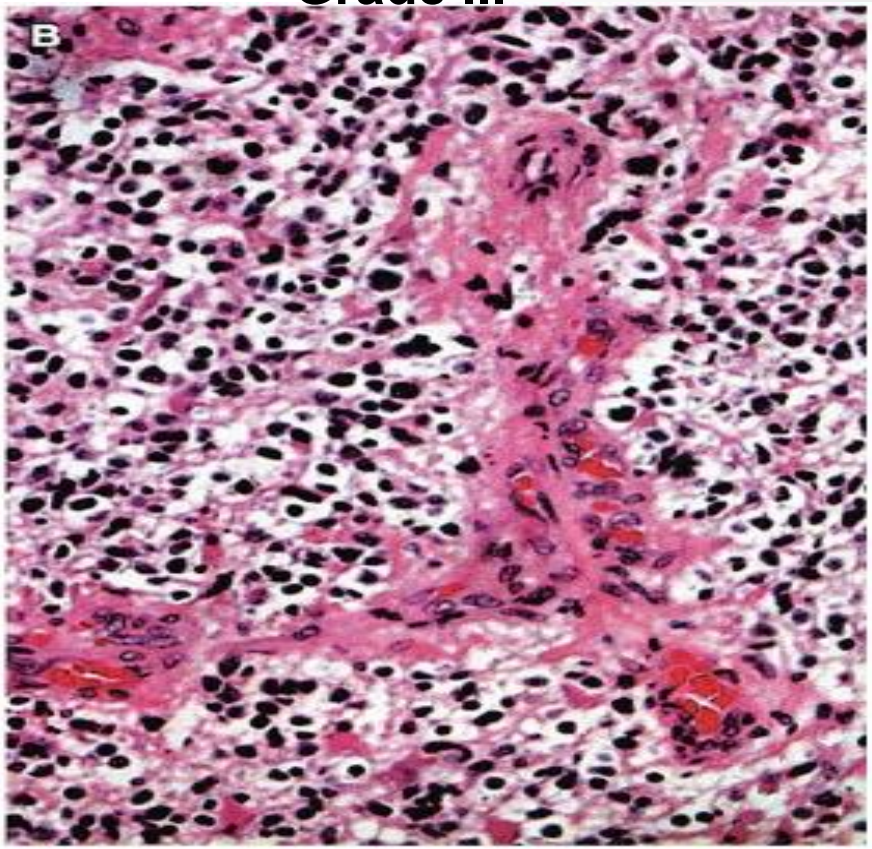


Oligodendroglioma

Grade II



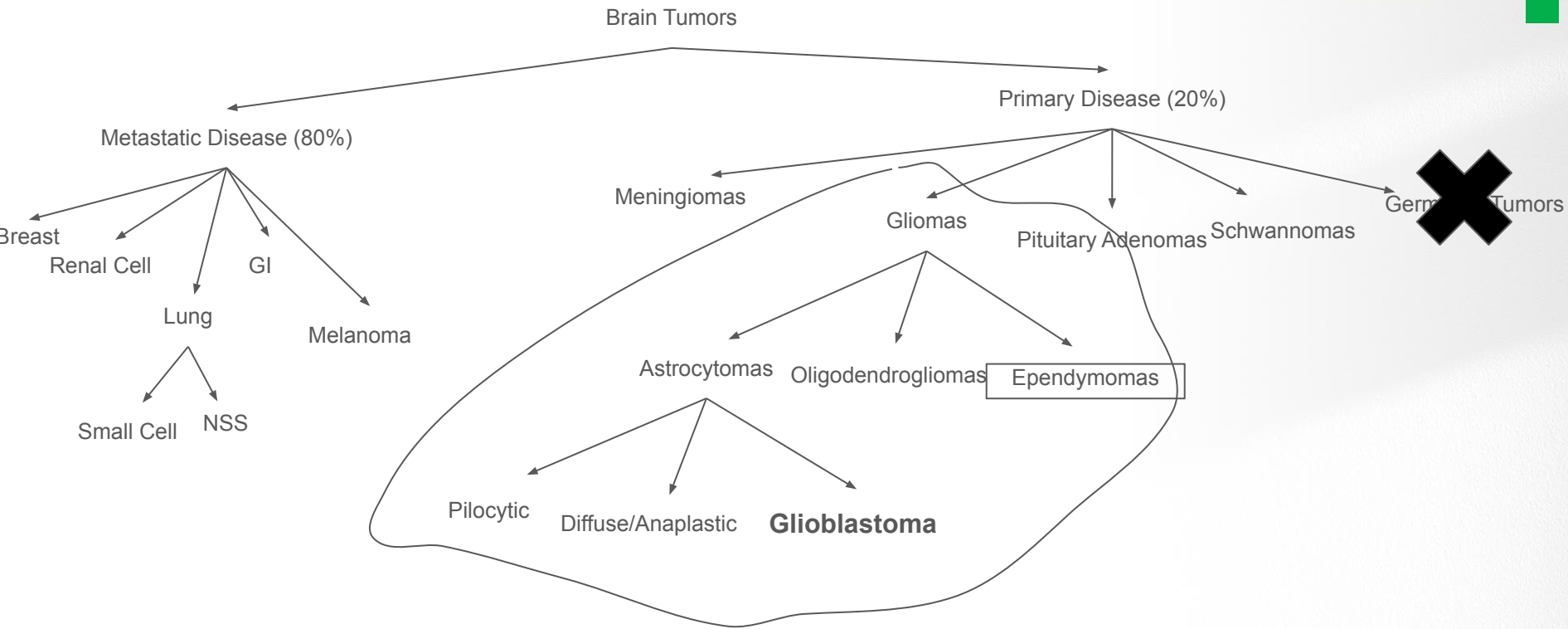
Grade III



Oligodendroglioma Management

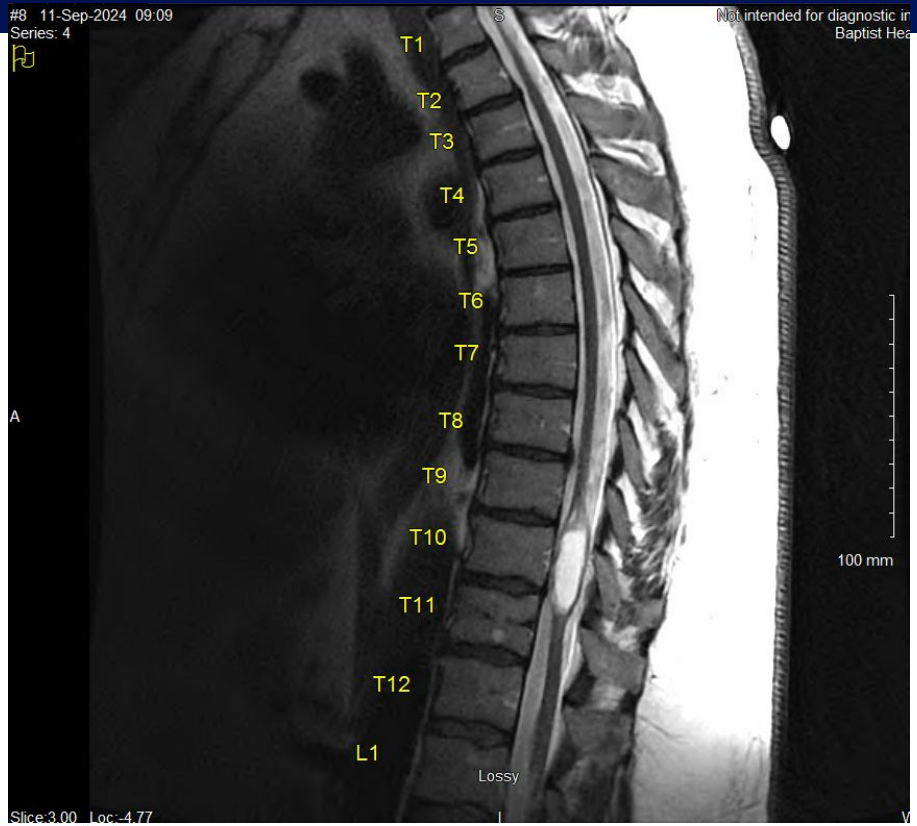
- Grade II
  - Observation
  - Surgery alone
  - Surgery + radiation therapy
- Grade III
  - Surgery
  - Radiation
  - Chemotherapy
- Grade IV?

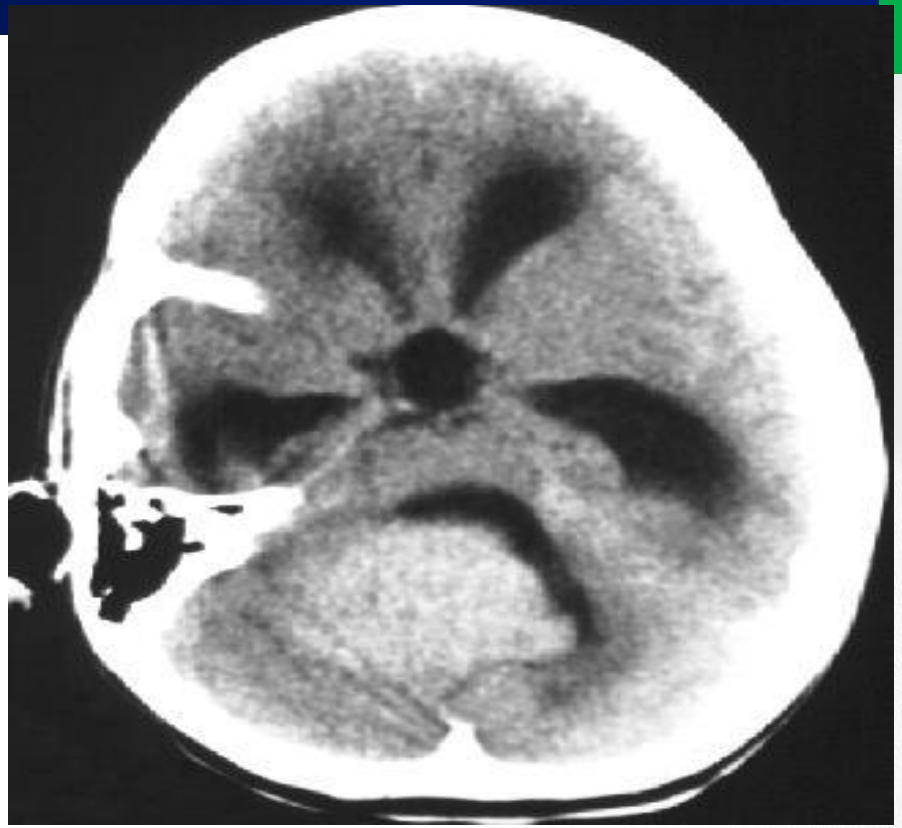
30,000ft View



Ependymomas

- Well circumscribed lesion arising from the ependymal surface.
- Location:
  - Pediatrics - 4th ventricle
  - Adults - spinal cord
- Peak incidence (bimodal):
  - 0-16yrs - intracranial tumors
  - 30-50yrs - spinal tumors
- Prognosis is better in spinal than intracranial tumors
  - Grade is less predictive of prognosis than in other gliomas





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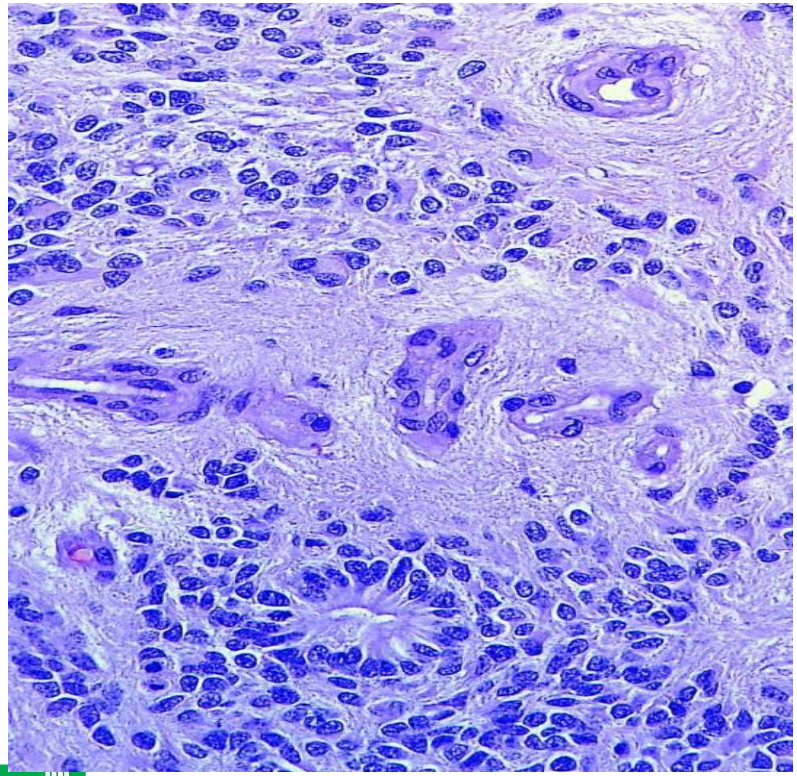
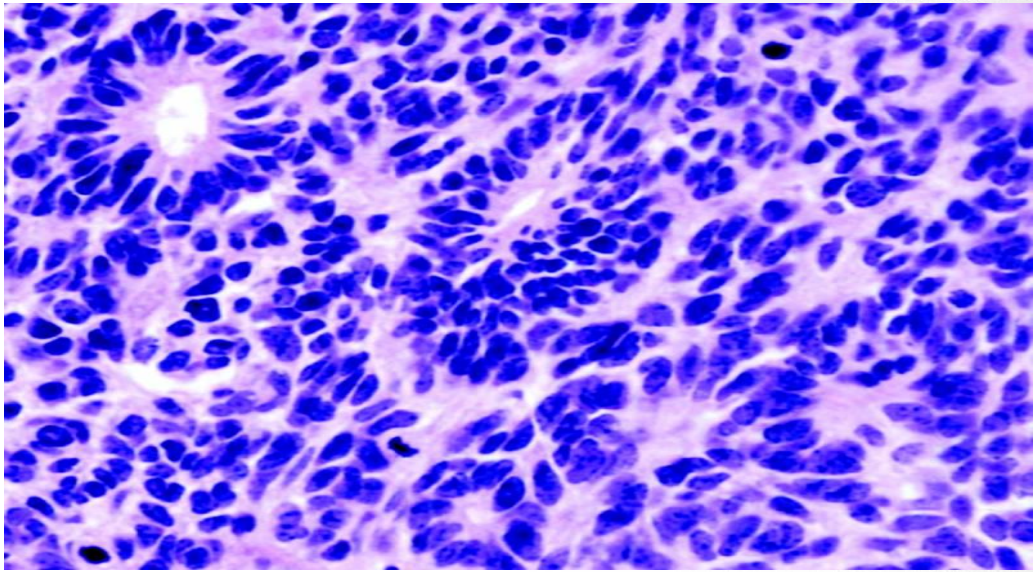


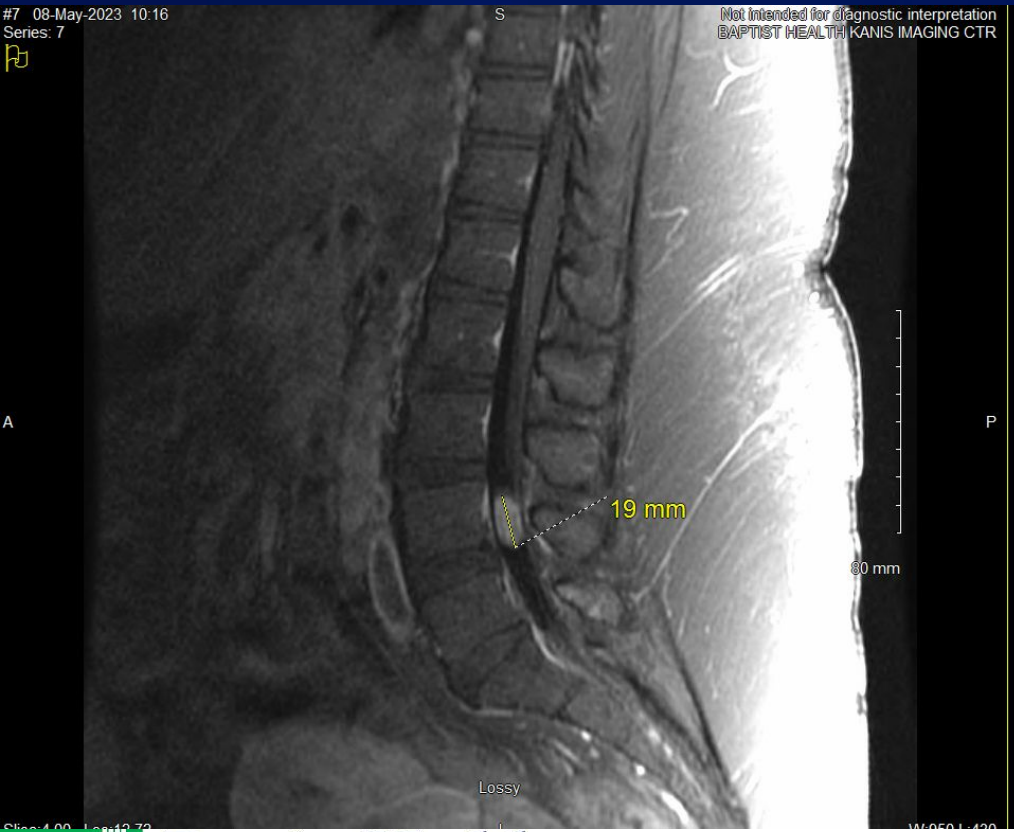


Ependymoma Treatment

- Gross total resection is tantamount
- Radiation therapy:
  - Close to critical structures
  - Age/comorbidities preclude surgery
  - Grade III?
  - Possible residual
- Chemotherapy?
  - Nah…

Myxopapillary Ependymoma

- Subtype of ependymomas.
- Location - almost exclusively at the conus or filum terminale
- Peak incidence between 30-50yrs
- Prognosis
  - WHO grade I
  - Resection is curative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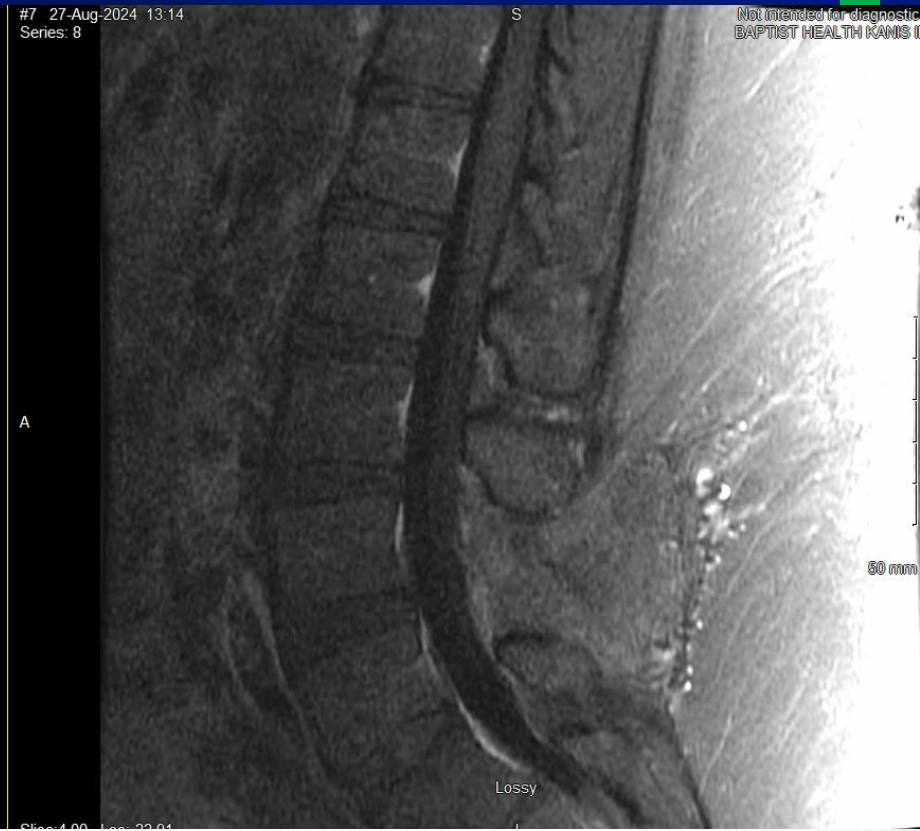
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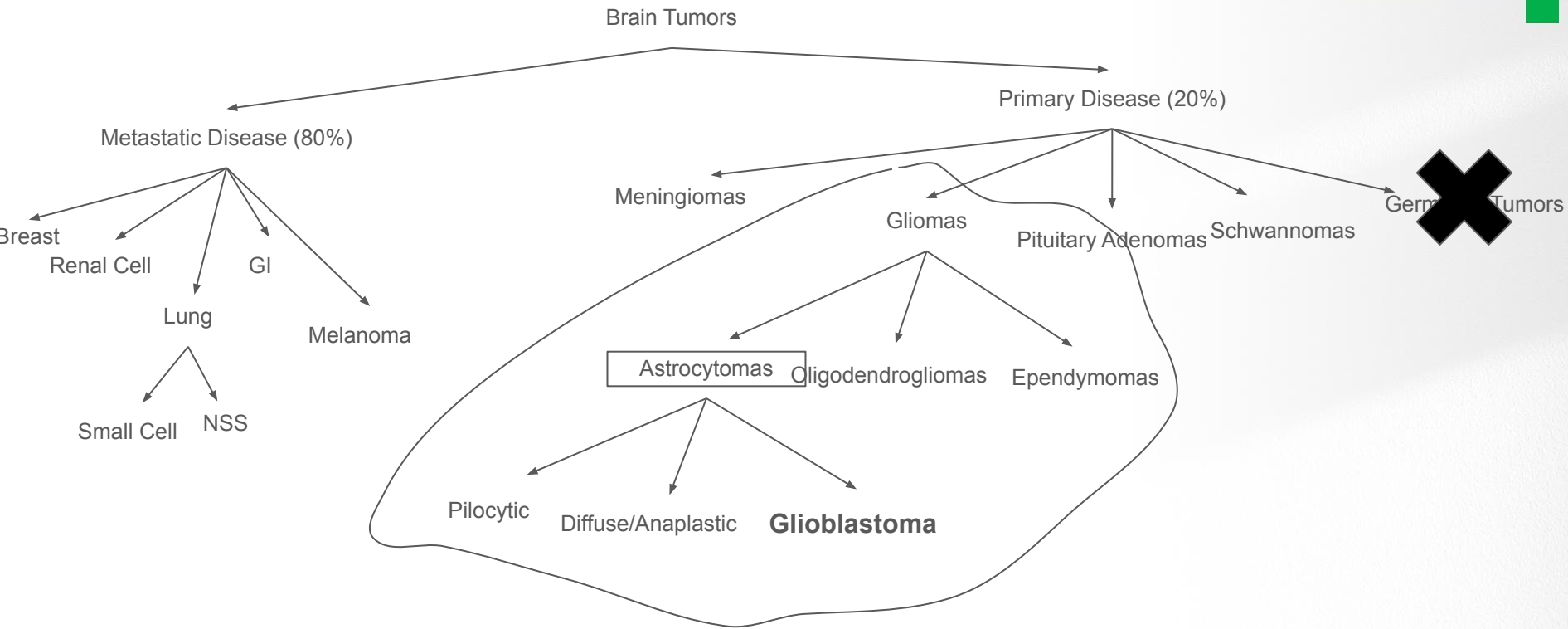

Astrocyto

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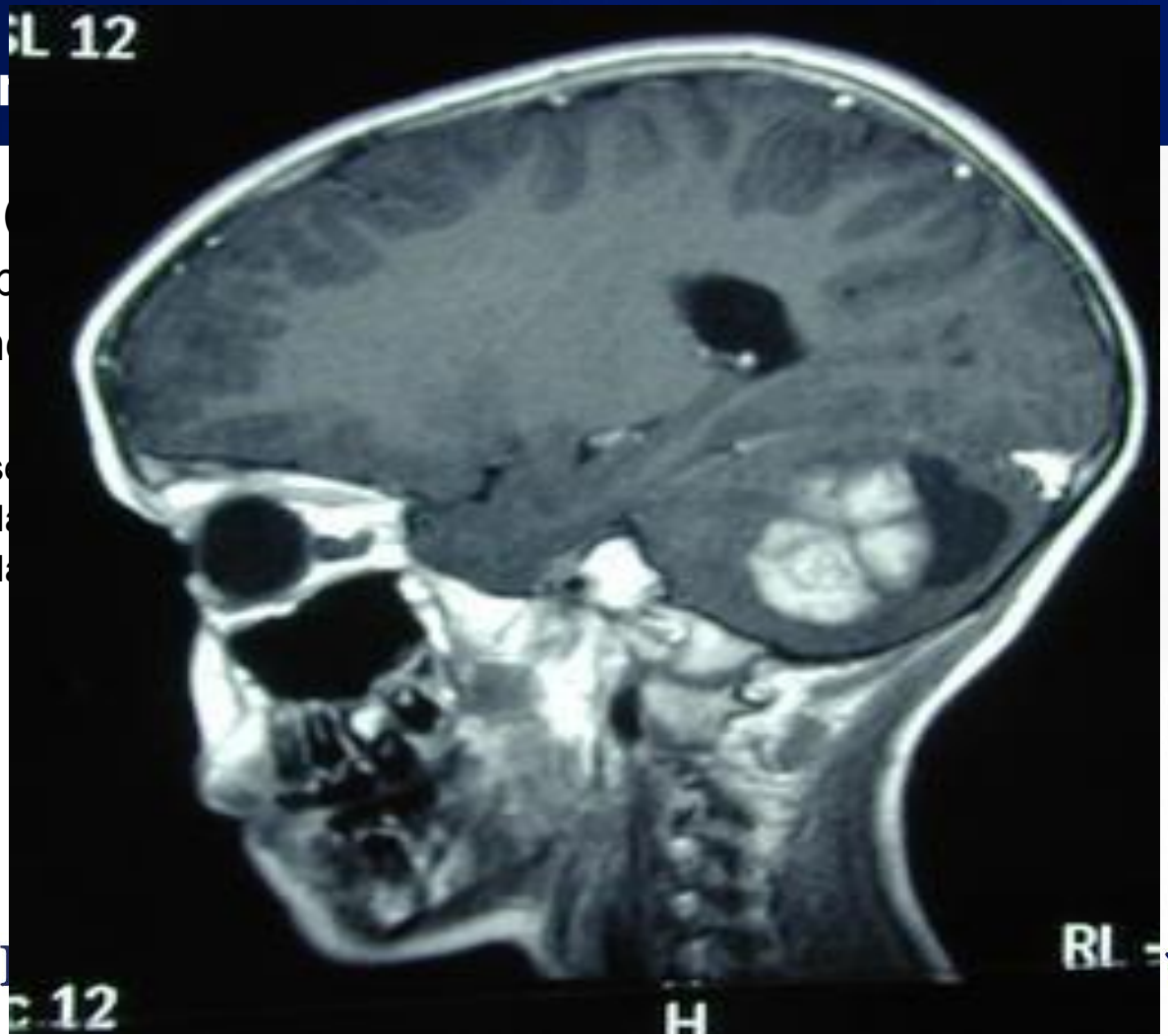
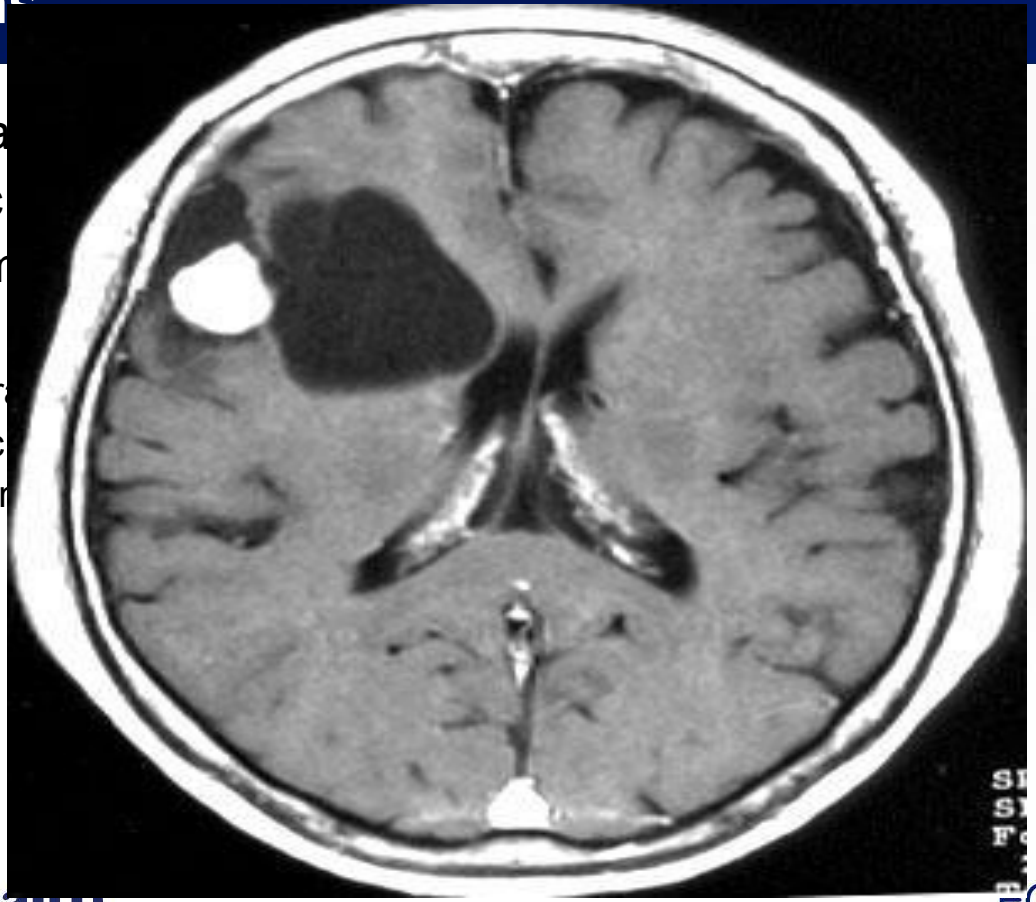
- Pleomorp
- Subepen
- Diffuse
  - Diffus
  - Anapl
  - Gliobl



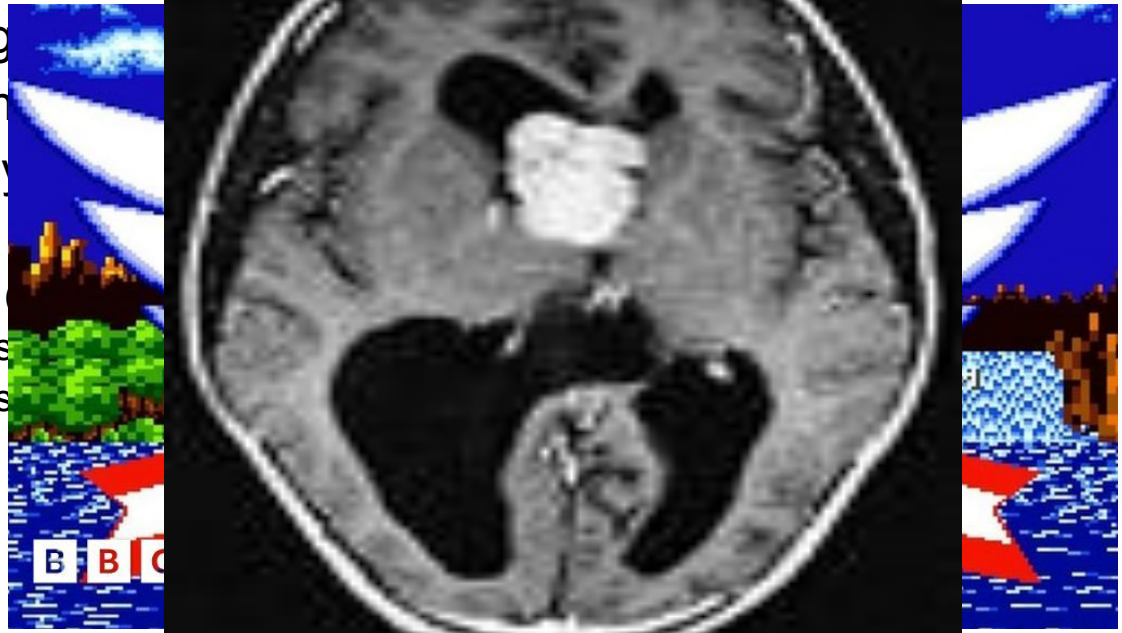
Astrocytomas

- Pilocytic (gra
- Pleomorphic
- Subependym
- Diffuse
  - Diffuse (gr
  - Anaplastic
  - Glioblastor



Astrocytomas

- Pilocytic (g
- Pleomorph
- Subependy
- Diffuse
  - Diffuse (
  - Anaplas
  - Glioblas



Astrocytomas

- Pilocytic (grade I)
- Pleomorphic Xanthoastrocytoma
- Subependymal Giant Cell Astrocytoma
- Diffuse
  - Diffuse (grade II)
  - Anaplastic (grade III)
  - Glioblastoma (grade IV)

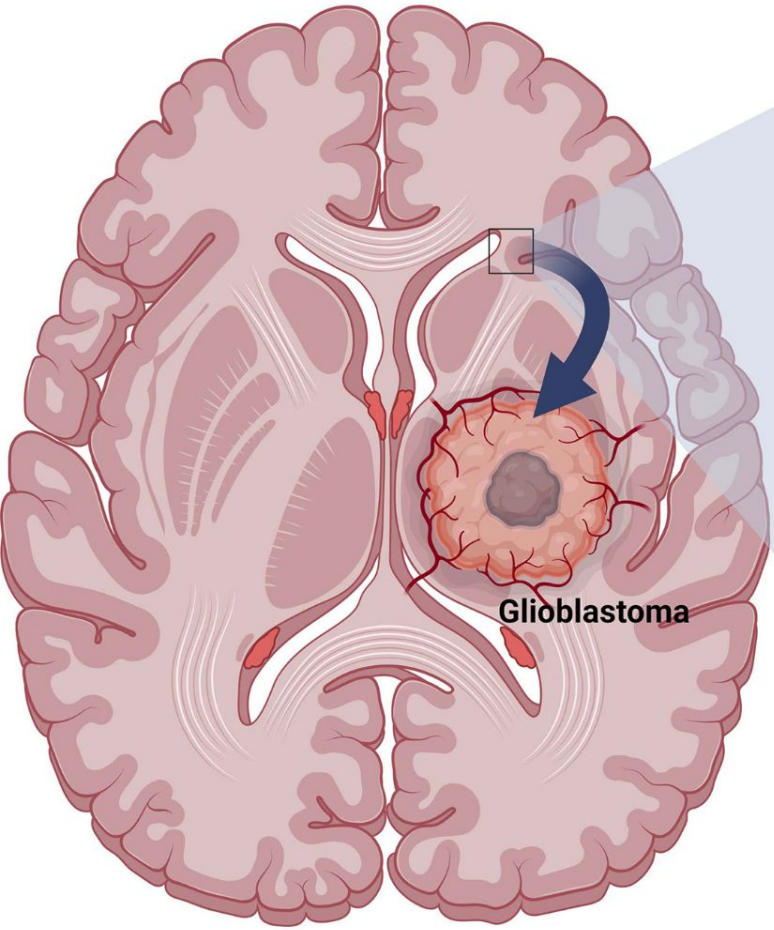
Diffuse Astrocytoma

- 40% of primary intracranial tumors
- Occur at all ages
  - Median age 30-40 for grade II, 40-50 for grade III, and 50-60 for grade IV
- Most arise in the cerebral hemispheres with a **subcortical** epicenter, but may be seen anywhere along the neural axis
- Radiologic features
  - Grade II are typically nonenhancing masses with increased signal on T2 weighted and FLAIR MRI
  - Grade III (anaplastic) are typically nonenhancing or focally enhancing
  - Grade IV (glioblastoma multiforme) are usually ring enhancing or may be a “butterfly lesion across the corpus callosum
  - In treated gliomas, radiation necrosis can appear identical to tumor recurrence

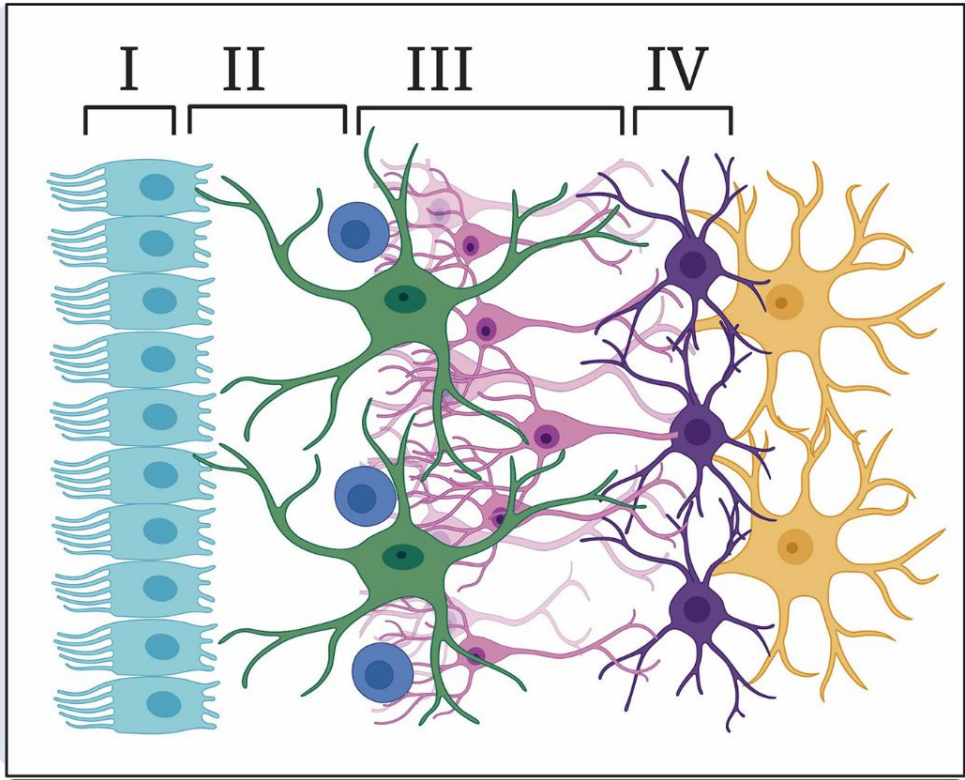
Diffuse Astrocytomas

Cellular and extracellular elements with the putative molecular mechanisms that could determine the biological signature of GBM, according to a specific anatomical localization. ECM: extracellular matrix; GSC: glioma stem cell; NSC: neural stem cell; SGZ: subgranular zone; SVZ: subventricular zone.

Cellular and Extracellular Elements	Anatomical Localization	Putative Mechanism	Ref.	GBM Biological Signature
NSC	SVG, SGZ	Age-related decline of the tumor-suppressor BMP7	[24,28,29,30]	GBM growth
NSC or progenitor cells	Subcortical white matter	Reactivation of migratory genes (EGF, Lck)	[35,92]	GBM invasiveness
Human ectodermic progenitors	Cortex	Differentially expressed genes (i.e., NEUROD6, ID2, LMO4)	[89,90]	GBM lateralization
Developing Astrocytes (B1 cells)	SVZ, Cortex	EGF overexpression	[42,43]	GBM invasiveness
Astrocytic subpopulations	Thalamus, Cortex, Brainstem	Mesenchymal signature (cluster B); Epilepsy-associated genes enrichment (cluster C)	[49]	GBM invasiveness
Astrocytes	Cerebellum, primary visual and dorsal prefrontal cortices	GLAST/GLT-1 overexpression	[16,63,64,93]	GBM growth (spared regions)
Neurons	Cerebellum	PD-L1 overexpression. Neurostatin release.	[59,60]	GBM growth (spared regions)
Oligodendrocytes	White matter	Nogo, semaphorin, ephrins downregulation	[3,52]	GBM invasiveness
Extracellular matrix	Hippocampal inlet, amygdala, and hypothalamus	Particular asset of aggrecan expression in contrast to Tenascin-R.	[69,79]	GBM growth (spared regions)
GSC	Left temporal lobe	MGMT methylated promoter; EGFR amplification	[16,86]	Bulky phenotype (short overall survivor)
GSC	Right temporal lobe	MGMT unmethylated promoter; IDH1 WT; Mesenchymal signature	[16]	Diffusive phenotype (short overall survival)
GSC	Frontal lobe	Focal PTEN loss; $IDH1^{R132mut}$;$p53^{mut}$; Focal EGFR amplification; Proneural signature	[16,87]	Diffusive phenotype

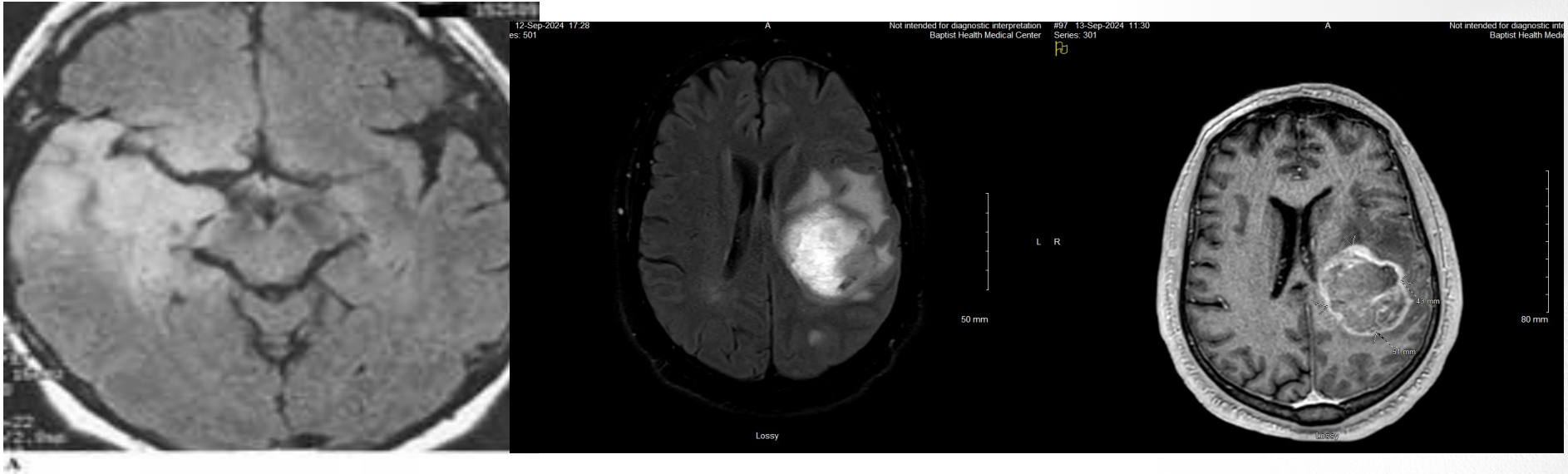


Subventricular zone layers



Ependymal cells Astrocytes **Neuroblasts** Neural stem cells **Oligodendrocytes** Neurons

Diffuse Astrocytoma



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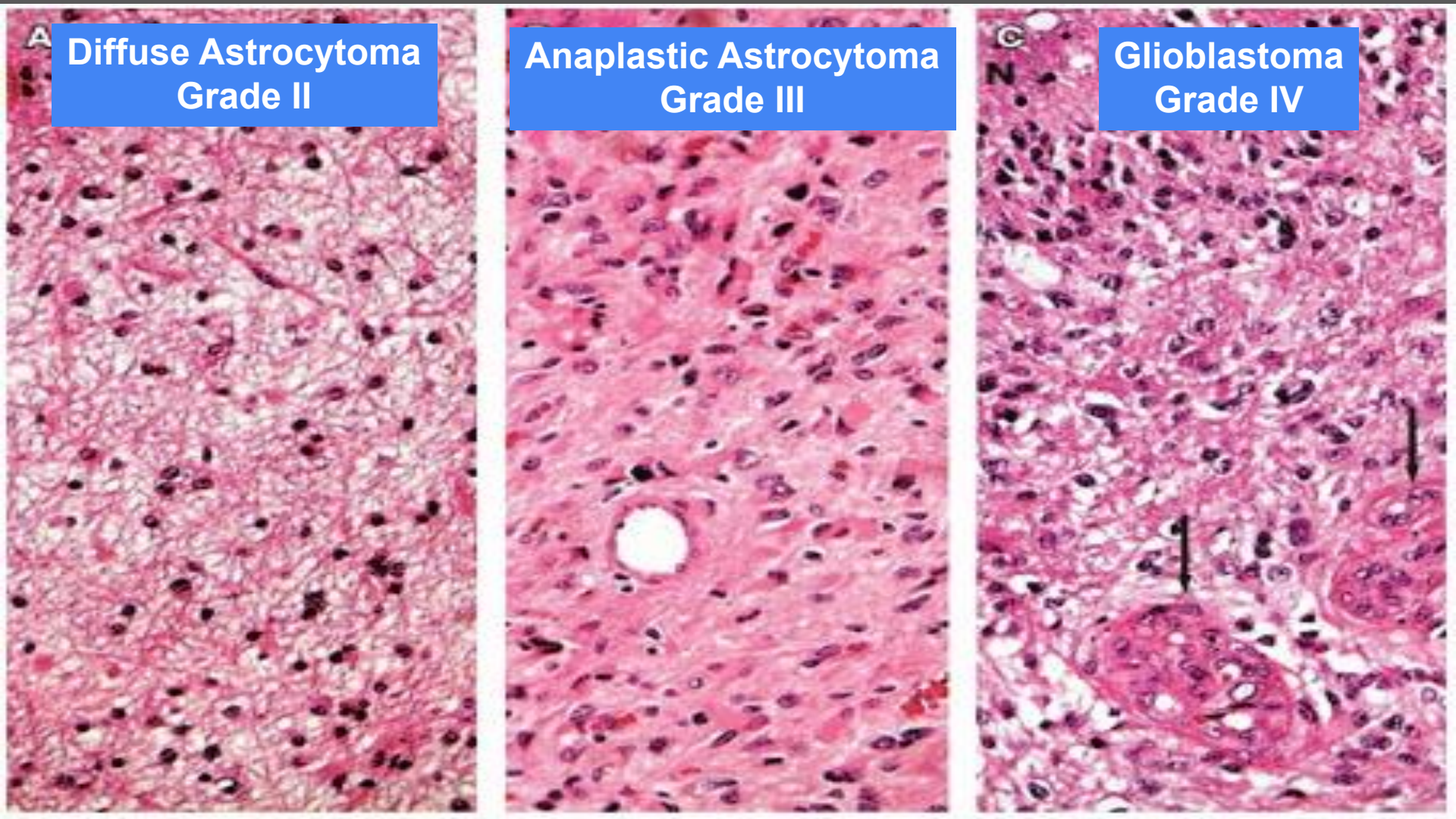
Diffuse Astrocytoma Management

- Surgical resection first line treatment
  - Poorly defined borders
  - Often vascular (more so in higher grades)
    - May encounter necrosis and hemorrhage
  - Not surgically curable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Diffuse Astrocytoma
Grade II
Anaplastic Astrocytoma
Grade III
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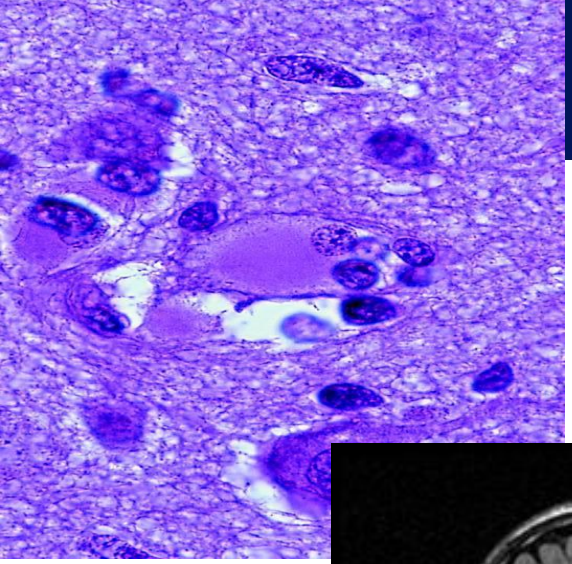
Glioblastoma
Grade IV

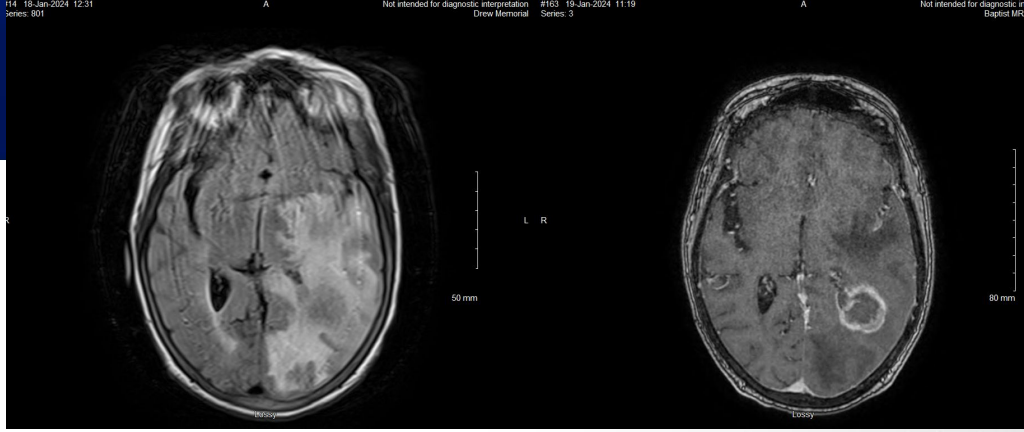
Diffuse Astrocytoma Management (cont)

- Grade II
  - Observation
  - Surgery + Radiation
  - Prognosis 5-8yrs
    - Better with IDH 1 mutation
    - May eventually transform to Anaplastic or GBM
- Grade III (Anaplastic)
  - Surgery + Radiation + Chemotherapy
  - Prognosis 2-5yrs
    - Will eventually transform to GBM
- Grade IV (Glioblastoma)
  - Surgery + Radiation + Chemotherapy
  - Prognosis 12-18mo
    - 25% 1yr survival
    - 5% 5yr survival
    - Recurrence is guaranteed

Glioblastoma Variants

- Gemistocytic
  - Gemistocytes should comprise >20% of tumor
  - May indicate less aggressive form of GBM
- Gliomatosis cerebri
  - May radiographically resemble WHO 2-4
  - Involves 3 or more lobes of the brain
  - Highly aggressive
- Gliosarcoma
  - Marbled areas of GBM and sarcoma
  - Highly aggressive

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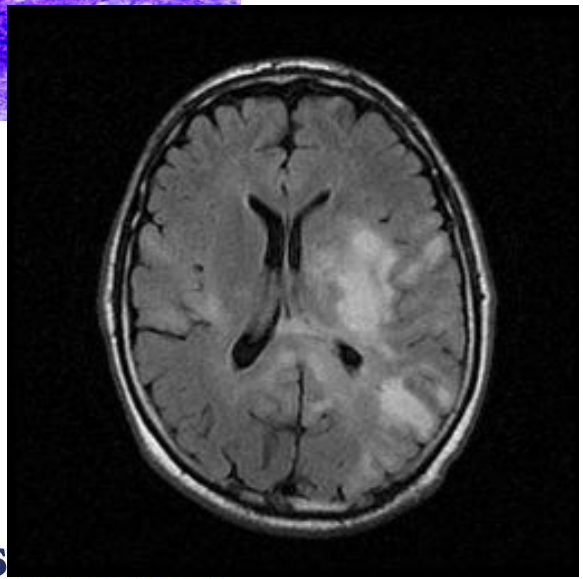

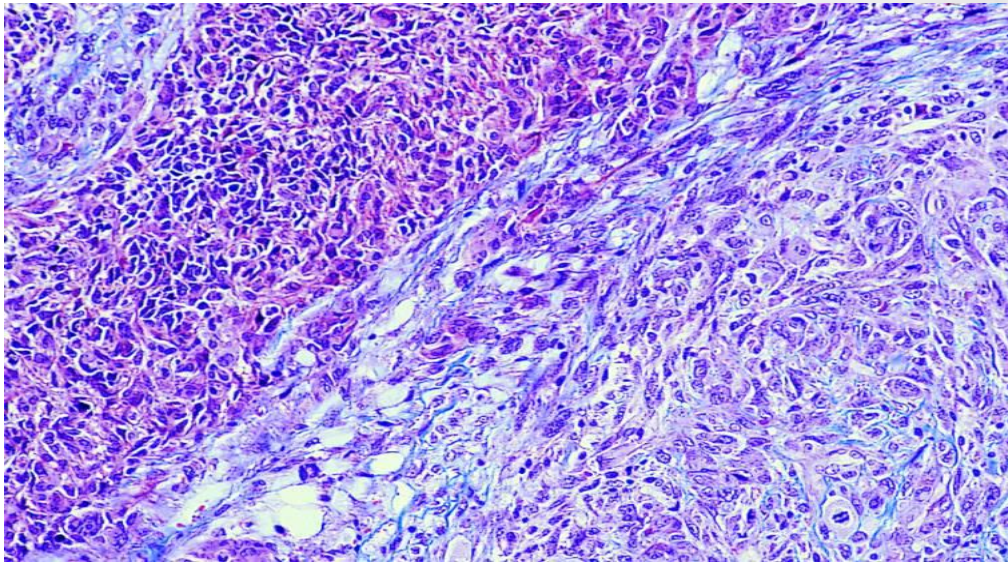

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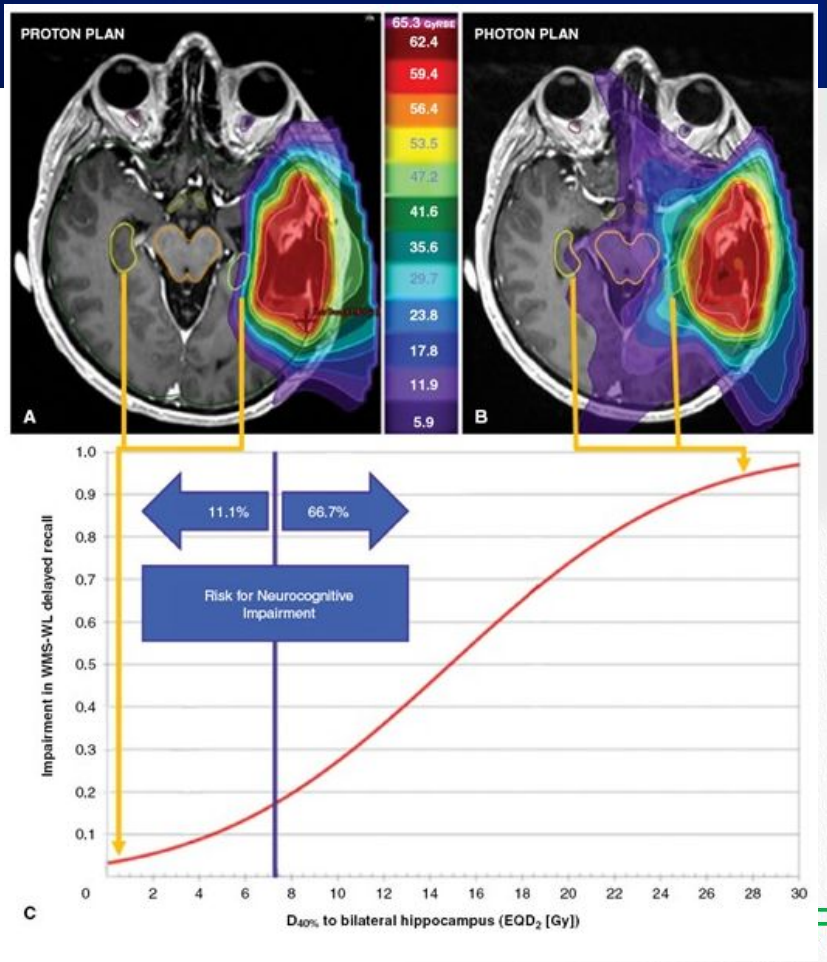
Advances in GBM management

- Chemotherapy
  - Immunotherapy
    - CAR T cell therapy - modifying a patient's immune cells to target GBM cells
    - Promising in clinical trials
      - MD Anderson and Mayo Clinic
  - Immune checkpoint inhibitors
    - Promotes immune cells to recognize and attack GBM cells
    - Not been shown to be as effective as immunotherapy
  - Molecular targeting
    - Identifying and targeting molecular signatures within GBM cells
- Radiation
  - Hippocampal Preserving WBRTX
  - Stereotactic Radiosurgery
    - Available for recurrent lesions

Proton Beam Radiation Therapy

- Improved Precision
- Lower local radiation doses
- Improved long term cognitive results
  - Maybe more useful in LGG
- Particularly useful in tumors near critical structures



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Questions?

Thank You!

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In the Cards:
Agitation in Neuroscience Patients

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BHRI Stroke Medical Director
M3 Clerkship Director
UAMS Department of Physical Medicine & Rehabilitation

UAMS
University of Arkansas for Medical Sciences

Disclosures

No financial disclosures

UAMS
University of Arkansas for Medical Sciences

Goals and Objectives

1. Define agitation as it relates to brain injury

2. Discuss risk factors for developing agitation

3. Review potential medical issues that can cause agitation and the relevant work up for diagnosis

4. Review treatment options for agitation management in the neuroscience patient including:
   - Environmental modification
   - Behavioral modification
   - Pharmacological treatment options.

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What is agitation? It depends on the card that's drawn!

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What is agitation?

"episodic motor or verbal behavior which interfered with patient care or clearly required physical or chemical restraints to prevent damage to persons or property"

"state of aggression during posttraumatic amnesia"

"combination of behaviors including aggression, akathisia, disinhibition, emotional lability, motor restlessness, impulsivity, disorganized thinking, perceptual disturbances, impaired ability to sustain attention, and reduced

"presence of 24 hours (six 4-h increments) of ABS scores >21 within a 48-hour period at some point during the inpatient rehabilitation stay"

"episodic motor or verbal behavior that interfered with patient care, therapy, or safety"

"Uncoordinated motor agitation is typical of the awakening period: …projection against bed rails, the patient gets up from the bed and sits back down continuously. At a more advanced stage, more evolved behaviors may be observed: …taking the bed or chairs apart, trying to remove constraints, destroying or dismantling the equipment in the room like the toilet, bathroom, electrical system), these behaviors can be associated with running away, non-stop calls, screams... Sexual disinhibition is also typical of this stage. Sometimes observed as verbal, even physical, violent uncontrolled aggressive behaviors"

"thrashing of extremities, truncal rocking, dislodging intravenous tubes and catheters, yelling, combativeness, and attempts to get out of bed"

To simplify:

- Agitation can be defined as an EXCESS of behavior that interferes with care and causes risk to patient, property and/or staff.
  - Includes some combination of aggression (verbal or physical), explosive anger, restlessness, disinhibition, akathisia, inappropriate vocalizing, and/or emotional liability
  - Behaviors must be present in the absence of other physical, medical or psychiatric causes

Agitation is in the cards…expect it!

- Agitation is often part of the brain injury recovery process
  - *Incidence varies from 11-70%*
- Agitation occurs most often during the post-traumatic amnesia (PTA) time period.
- Cognition improves before agitation improves

Therefore agitation is usually SELF-LIMITING

  - *Duration of several days to several weeks*
  - *Typically resolves within 4 weeks*

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Etiology

unknown	• Multifactorial pathology
Anatomy	• injury to the frontal lobes, temporal lobes, prefrontal cortex, thalamus, and limbic system
Physiology	• impaired regulation of serotonin, norepinephrine, and dopamine.
Premorbid	• psychiatric/mood disorders, personality disorders, substance abuse
Medical	• infection, pain, electrolyte imbalance, worsening brain injury, seizures

Predictors: impaired cognition, PTA, & lower functional status

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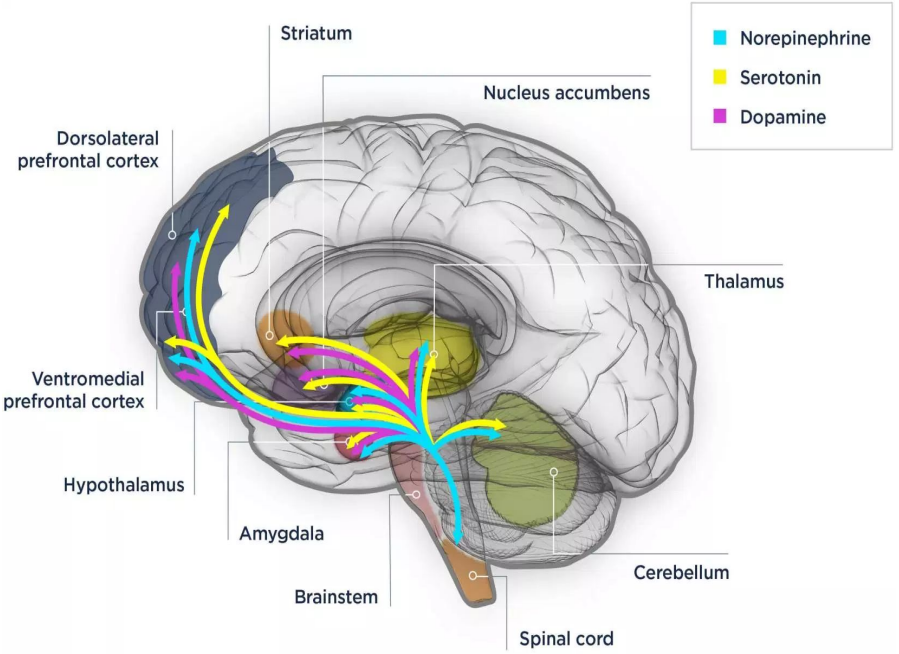
Anatomy of Agitation

NEUROTRANSMITTERS

- Serotonin
  - Regulates mood, memory processing, anxiety, sleep, cognition
  - Loss of Serotonergic regulation results in disinhibition, aggression, and agitation

- Norepinephrine
  - Regulates mood, arousal, cognition (role in attention/concentration, memory, processing speed)

- Dopamine
  - Regulates arousal, movement, pleasure/reward, cognition, psychosis, perseverations/compulsions



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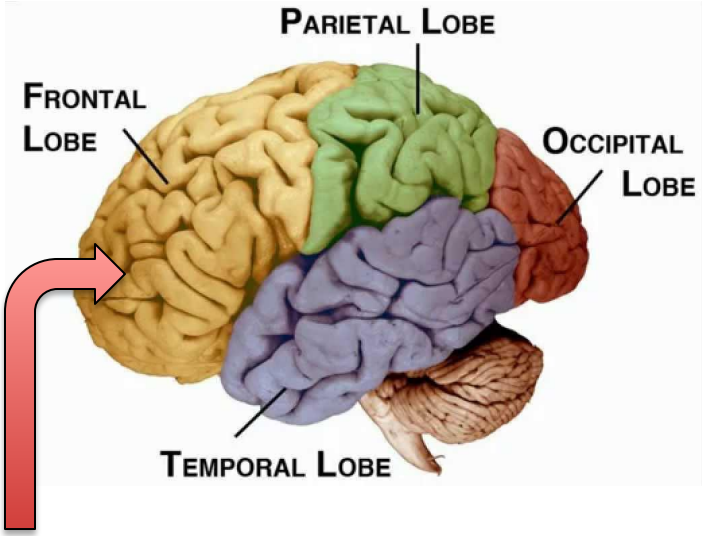
Anatomy of Agitation

Frontal Lobe	Problem Solving, Emotion, Complex Thought, Decision-making, Inhibition, Pleasure
Temporal Lobe	Retention of visual memories, comprehending language, storing new memories, emotion, deriving meaning



Prefrontal cortex

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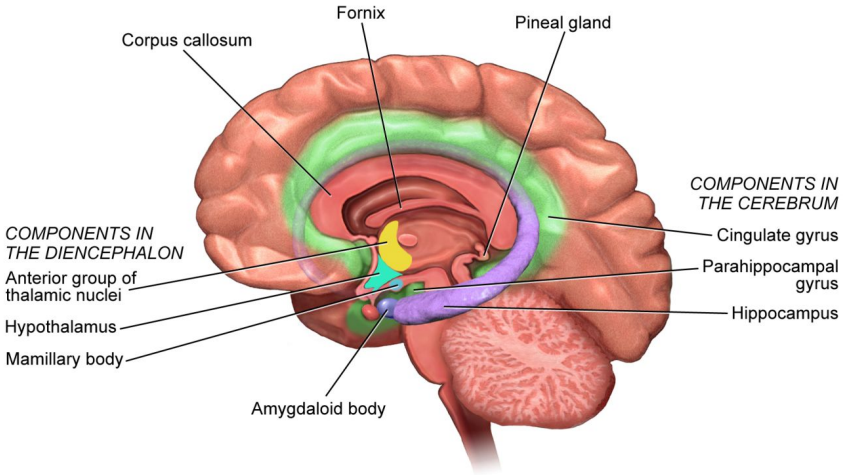
Anatomy of Agitation

Limbic system

Hippocampus	Consolidation of new memories
Nucleus accumbens	Reward, pleasure, and addiction
Hypothalamus	Endocrine system, defensive behaviors, aggression
Mammillary bodies	Recall memory
Thalamus	Arousal/consciousness, memory
Septal nuclei	Pleasure
Entorhinal cortex	Memory
Amygdala	Emotion - fear, anxiety, aggression, rage



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Beyond the Poker Face: Assessing Agitation

PTA	Agitation
Galveston Orientation and Amnesia Test (GOAT)	Agitated Behavior Scale (ABS)
Orientation Log (O-Log)	Overt Aggression Scale (OAS)

GALVESTON ORIENTATION AND AMNESIA (GOAT)

- Reliable and valid indicator of PTA in TBI patients
  - Does not measure agitation
- Score of 75 or more on 2 consecutive occasions is considered to indicate that patient is out of PTA
- Can be administered daily until patient is out of PTA

The Galveston Orientation and Amnesia Test (GOAT)

Question	Error score	Notes
What is your name?	/ 2	Must give both first name and surname.
When were you born?	/ 4	Must give day, month, and year.
Where do you live?	/ 4	Town is sufficient.
Where are you now?		
(a) City	/ 5	Must give actual town.
(b) Building	/ 5	Usually in hospital or rehab center. Actual name necessary.
When were you admitted to this hospital?	/ 5	Date.
How did you get here?	/ 5	Mode of transport.
What is the first event you can remember after the injury?	/ 5	Any plausible event is sufficient (record answer)
Can you give some detail?	/ 5	Must give relevant detail.
Can you describe the last event you can recall before the accident?	/ 5	Any plausible event is sufficient (record answer)
What time is it now?	/ 5	1 for each half-hour error, etc.
What day of the week is it?	/ 3	1 for each day error, etc.
What day of the month is it? (i.e. the date)	/ 5	1 for each day error, etc.
What is the month?	/ 15	5 for each month error, etc.
What is the year?	/ 30	10 for each year error.
Total Error:		
100 - total error		Can be a negative number.

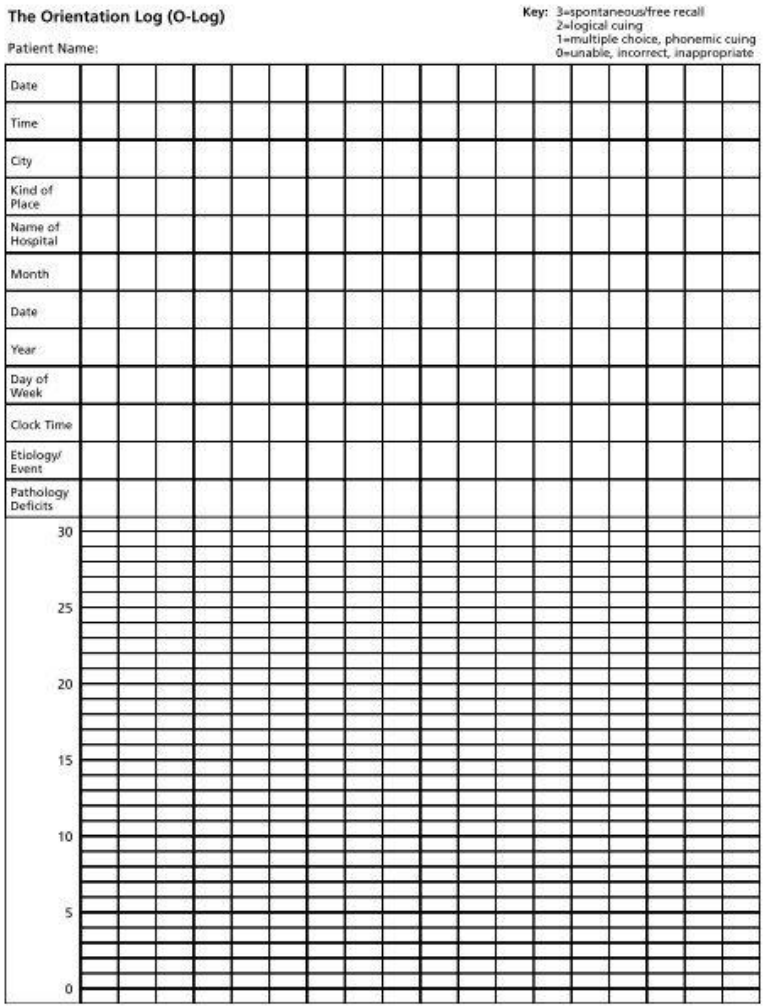
76-100 = Normal
66-75 = Borderline
< 66 = Impaired

Patient last name: .....
Patient first name: .....

Date of birth: ..../..../.....
Date: ..../..../.....

ORIENTATION LOG (O-LOG)

- Does not specifically measure agitation
- Score of 25 or more on 2 consecutive occasion that patient is out of PTA
- Can be administered daily until patient is out



AGITATED BEHAVIOR SCALE (ABS)

- Only measure of agitation developed specifically for and validated in the TBI population
- High intra- and inter-rater reliability
- Used for for monitoring patient's recovery progression and assessing effectiveness of interventions

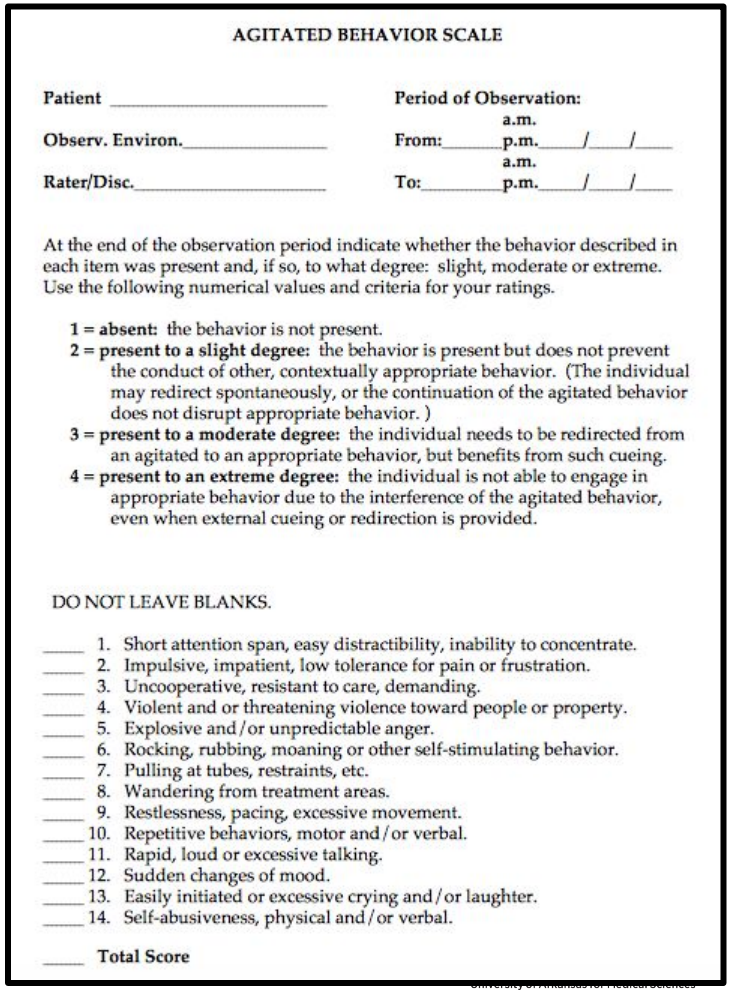
Total Score

<21 Normal

22-28 Low agitation

29-35 Moderate agitation

>35 Severe agitation



AGITATED BEHAVIOR SCALE

Patient _____ Period of Observation:

Observ. Environ._____ From:_____a.m./p.m.____/____/____

Rater/Disc._____ To:_____a.m./p.m.____/____/____

At the end of the observation period indicate whether the behavior described in each item was present and, if so, to what degree: slight, moderate or extreme. Use the following numerical values and criteria for your ratings.

1 = **absent:** the behavior is not present.
2 = **present to a slight degree:** the behavior is present but does not prevent the conduct of other, contextually appropriate behavior. (The individual may redirect spontaneously, or the continuation of the agitated behavior does not disrupt appropriate behavior.)
3 = **present to a moderate degree:** the individual needs to be redirected from an agitated to an appropriate behavior, but benefits from such cueing.
4 = **present to an extreme degree:** the individual is not able to engage in appropriate behavior due to the interference of the agitated behavior, even when external cueing or redirection is provided.

DO NOT LEAVE BLANKS.

____ 1. Short attention span, easy distractibility, inability to concentrate.
____ 2. Impulsive, impatient, low tolerance for pain or frustration.
____ 3. Uncooperative, resistant to care, demanding.
____ 4. Violent and or threatening violence toward people or property.
____ 5. Explosive and/or unpredictable anger.
____ 6. Rocking, rubbing, moaning or other self-stimulating behavior.
____ 7. Pulling at tubes, restraints, etc.
____ 8. Wandering from treatment areas.
____ 9. Restlessness, pacing, excessive movement.
____ 10. Repetitive behaviors, motor and/or verbal.
____ 11. Rapid, loud or excessive talking.
____ 12. Sudden changes of mood.
____ 13. Easily initiated or excessive crying and/or laughter.
____ 14. Self-abusiveness, physical and/or verbal.

____ **Total Score**

OVERT AGGRESSION SCALE (OAS)

- Observational scale that requires training to administer
- Can be completed in 3-5 minutes
- Developed for mental health population
- Allows recording of type, severity and frequency of different aggressive behaviors such as verbal, physical against objects, physical against self and physical against others
- There are additional items that register the intervention applied by the staff

The Modified Overt Aggression Scale (MOAS)*

Patient_____ **Date**_____

INSTRUCTIONS
Rate the patient's aggressive behavior ***over the past week***. Select as many items as are appropriate.

SCORING
1. Add items within each category.
2. In the scoring summary, multiply sum by weight and add all the weighted sums for total weighted score. Use this score to track changes in level of aggression over time.

***Verbal Aggression*: Verbal hostility, statements or invectives that seek to inflict psychological harm on another through devaluation/degradation, and threats of physical attack.**
___ 0. No verbal aggression
___ 1. Shouts angrily, curses mildly, or makes personal insults
___ 2. Curses viciously, is severely insulting, has temper outbursts
___ 3. Impulsively threatens violence toward others or self
___ 4. Threatens violence toward others or self repeatedly or deliberately (e.g., to gain money or sex)
___ **SUM VERBAL AGGRESSION SCORE**

***Aggression Against Property:* Wanton and reckless destruction of ward paraphernalia or other's possessions.**
___ 0. No aggression against property
___ 1. Slams door angrily, rips clothing, urinates on floor
___ 2. Throws objects down, kicks furniture, defaces walls
___ 3. Breaks objects, smashes windows
___ 4. Sets fires, throws objects dangerously
___ **SUM PROPERTY AGGRESSION SCORE**

***Autoaggression:* Physical injury toward oneself, self-mutilation, or suicide attempt.**
___ 0. No autoaggression
___ 1. Picks or scratches skin, pulls hair out, hits self (without injury)
___ 2. Bangs head, hits fists into walls, throws self on floor
___ 3. Inflicts minor cuts, bruises, burns or welts on self
___ 4. Inflicts major injury on self or makes a suicide attempt
___ **SUM AUTOAGGRESSION SCORE**

***Physical Aggression*: Violent action intended to inflict pain, bodily harm, or death upon another.**
___ 0. No physical aggression
___ 1. Makes menacing gestures, swings at people, grabs at clothing
___ 2. Strikes, pushes, scratches, pulls hair of others (without injury)
___ 3. Attacks others, causing mild injury (bruises, sprains, welts, etc.)
___ 4. Attacks others, causing serious injury (fracture, loss of teeth, deep cuts, loss of consciousness, etc.)
___ **SUM PHYSICAL AGGRESSION SCORE**

SCORING SUMMARY

Category	Sum Score	Weights	Weighted Sum
Verbal Aggression		X1	
Aggression Against Property		X2	
Autoaggression		X3	
Physical Aggression		X4	
Total Weighted Score			

RANCHO LOS AMIGOS (RLA) SCALE

- Represents typical progression of recovery in TBI
- These patients have deficits in attention, memory, initiation, problem solving, sequencing, information processing speed, and safety awareness
- Dynamic scale- patients can fluctuate between levels

Ranchos Los Amigos Scale for Cognitive Function			
Level	Response	Assistance	Description
I	Non-responsive	Total	No response to stimuli
II	General response	Total	Generalized response to pain
III	Localized response	Total	Responds directly to stimuli; inconsistent response to commands
IV	Confused-agitated	Maximal	Brief and non-purposeful attention; unable to cooperate
V	Confused-inappropriate	Maximal	Inconsistent response to commands; may become easily agitated
VI	Confused-appropriate	Moderate	Consistently follows simple directions
VII	Automatic-appropriate	Minimal	Unaware of own limitations; oppositional/uncooperative
VIII	Purposeful-approriate	Stand-by	Consistently oriented; attends to familiar tasks; aware of limitations; may be depressed and irritable

Stacking the Deck:
Identifying risk factors and causes of agitation early

- Obtain detailed HPI, medical comorbidities, and an in-depth social history
  - Location of brain lesions
  - Medical issues that can result in complications/infections/pain/psychiatric complications
  - Social habits that could result in withdrawal
- Perform a comprehensive physical exam
  - vital signs
  - neurologic examination,
  - cardiopulmonary evaluation,
  - musculoskeletal examination.

Evaluation should include assessment for secondary conditions common in TBI which may contribute to agitation (e.g., aphasia, vision impairments, attention and alertness)

Differential diagnosis

MEDICAL

- Medication Side effects
  - opioids, benzodiazepines, dopamine agonists (Metoclopramide), H_2-receptor antagonists (Famotidine), Levatiracetam, and anticholinergic medications (Oxybutynin)
- Pain: Headache, lacerations, wounds, post-op, heterotopic ossification, spasticity, shoulder subluxation, occult fracture, etc.
- Infection
- Metabolic disturbance (electrolytes, thyroid, hypoglycemia)
- Hypoxemia (Pulmonary Embolism)
- Urinary retention/incontinence
- Bowel incontinence, nausea, constipation

Differential diagnosis

NEUROLOGIC

- Hydrocephalus
- Seizures
- Intracranial mass lesions
- Rebleed, intracranial hemorrhage

PSYCHIATRIC

- Personality disorders/Psychosis/Anxiety/Mood disorders
- Sundowning in patients with dementia
- Substance use/Acute intoxication

Diagnostic work up for the agitated patient

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KNOW WHEN TO HOLD'EM, KNOW WHEN TO FOLD'EM…

So the work up is unremarkable…now what?

Agitation is a diagnosis of exclusion after other conditions have been ruled out

Once all other issues are ruled out THEN symptoms can exclusively be attributed to AGITATION.

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Why do we care about Agitation after TBI?

- Frustrating for providers/staff/families
- Diverts attention away from other activities
  - Can result in medical complications
- Discharge planning for agitated patients can be problematic
  - *Associated with longer lengths of stay in both hospital and acute rehabilitation settings, increased cost of care, and increased amount of support needed after hospitalization.*
  - *Can impede community reintegration including alienation from family, loss of employment, and potential legal issues.*

Management is essential to ensure everyone's safety, ease caregiver burden, and maximize cooperation in treatment.

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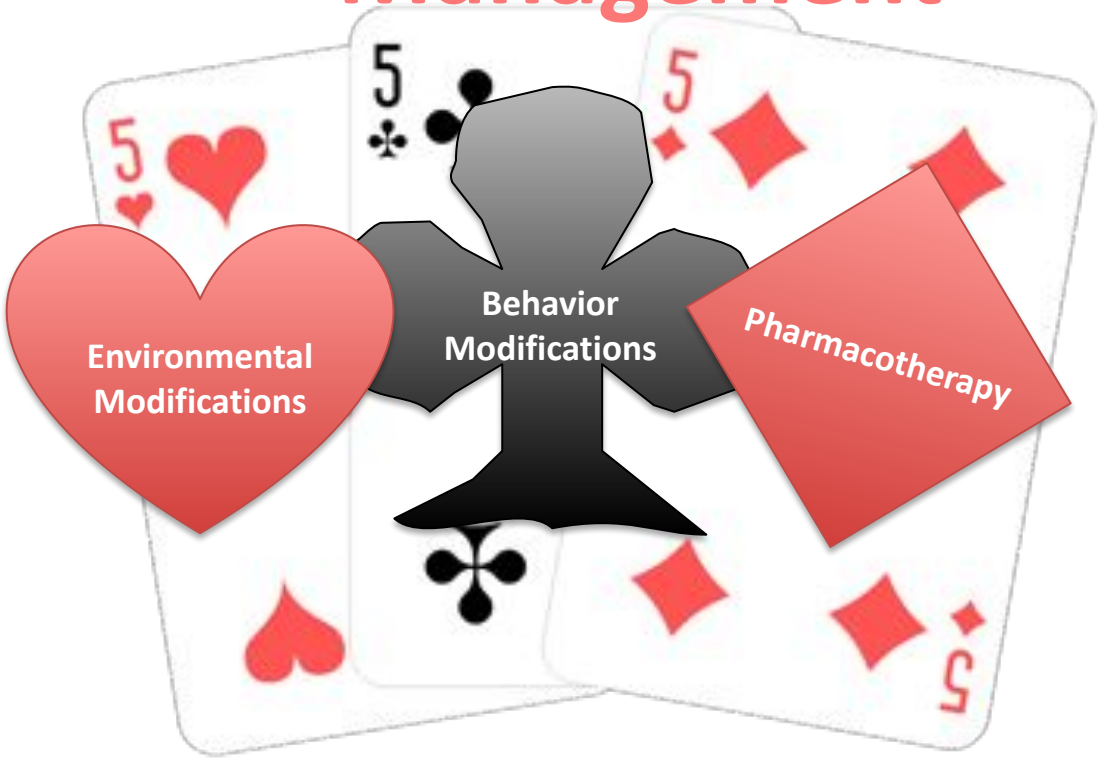
Agitation Management



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Environmental Modifications

FIRST LINE INTERVENTION

Reduce stimuli

- Private Room
- Minimize light, noise, and distractions - Low level lighting, draw curtains, turn off television, etc.
- Limit number of visitors at one time
- Staff and family should speak in low volume, slowly, one at a time
- Implement rest periods throughout the day to minimize impact of fatigue
- Meals in isolated area (rather than in communal dining room)
- Quiet, isolated treatment areas

Environmental Modifications

- **Avoid/minimize restraints**: Use non-contact restraints if able (i.e. safety net beds), padded hand mittens, one-to-one staff supervision
- **Minimize tubes and lines**
  - Discontinue as soon as medically safe to do so
  - Disguise them if essential for patient care (i.e. Place abdominal binder, wrap IV lines with gauze, Kerlix)
- **Frequent re-orientation** by staff and family
- **Consistent schedule and staff**
- **Timed toileting**
- **Create a familiar environment**: Allow family to bring in personal possessions
- **Ensure good sleep cycle regulation and sleep quality**
  - Encourage good sleep hygiene
  - Consider use of Trazodone, Melatonin

Harmful to self

Disruptive to other patients

Does not follow weight bearing, helmet precautions

High elopement risk

Not manageable with cubicle bed / net bed

Sitter: When to Order

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Behavioral Modifications

- Indulge the restlessness
  - Allow patient to pace (if safe) or be walked/wheeled around by family/staff
  - Mobile patients may require a closed unit or sensors for safety
- De-escalation techniques
- Structured behavioral programs
  - Written behavioral plan: staff/ family agreement
  - Identify antecedent behaviors
  - Quantify acceptable/problematic behaviors
  - Environment: special beds, time out, control stimuli
  - Redirect behavior: physical activity with coach
  - Co-Treat for safety

Approach agitated patients thoughtfully and cautiously!

Education:

- Approach from the front, respect personal space
- Use social greetings: these are cues to relax
- Avoid sudden grabbing or touching of the patient
- Provide patient with choice instead of command
- Do not correct confused statements.
  - Instead of disagreeing, make a neutral statement or re-direct attention to another topic
- Positive reinforcement
- Formally end the interaction as patient may not be aware of normal social cues
- Care team and family should have knowledge of potential situations that trigger agitated or aggressive behaviors so these can be avoided

In general…

Pharmacological Management

- Reserved for:
  - patients who exhibit agitated behaviors despite environmental and behavioral modification

- As with most medications:
  - "start low, go slow"
  - begin with the lowest dose available and slowly increase for effectiveness

- Frequent reassessment is essential to determine need for continuation of the pharmacologic agent(s)

Before showing your hand:

things to consider before medicating an "agitated" TBI patient

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The Winning Hand: Drugs Classes for Agitation Management

Beta-blockers

Antidepressants

Antipsychotics

Neurostimulants

Mood stabilizers

Antiepileptics

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Beta-Blockers

Medication	Dosage	Benefits	Important Side Effects	Comments
Propranolol	Starting dose: 20-60mg/day, divided BID–QID Maximum dose up to 420mg/day has been used	*Best evidence for efficacy* Also treats dysautonomia, anxiety, tremor, and migraines Improves restlessness and disinhibition	Hypotension Bradycardia Depression Lethargy Decreased Libido	No adverse effect on motor or cognitive recovery

Antiepileptic drugs (AEDs)

Medication	Dosage	Benefits	Important Side Effects	Comments
Carbamazepine	Aggression limiting effects seen with dosing 300-900mg/day, divided BID-TID		Hyponatremia Sedation Nausea Rare but serious: • Aplastic anemia • Agranulocytosis • Stevens-Johnson • syndrome	Improvement in behavior within 4 days Monitor serum levels for toxicity Potential to negatively impact psychomotor speed
Valproic Acid	Starting dose: 250mg BID May be titrated 250mg every 2-3 days to max of 2500mg/day	Less likely than carbamazepine to have negative impact on cognition and has safer side effect profile	Sedation Nausea/vomiting Weight gain Hepatotoxicity	Potential for rapid efficacy

Antidepressants

Medication	Dosage	Benefits	Important Side Effects	Comments
Selective Serotonin Reuptake Inhibitors (SSRIs) ex. Sertraline, Citalopram	Starting dose: dependent on agent selected, start at lowest available dose Dosing titrated every 3-7 days	Helpful for agitation with depressive or behavioral component Can improve symptoms of Kluver-Bucy syndrome and pseudobulbar affect	Hyponatremia Decreased libido Serotonin syndrome QTc prolongation	Antidepressant effect noted in 2 or more weeks, quicker time to effect for behavioral disorders
Trazodone	Starting dose: 50-100mg Increased sleep usually seen by 150mg	Shown to decrease agitation and aggressive behaviors Can also be used for sleep cycle regulation	Anticholinergic effects Priapism Sedation QTc prolongation	Can precipitate serotonin syndrome if used with an SSRI

Antidepressants continued…

Medication	Dosage	Benefits	Important Side Effects	Comments
Tricyclic Antidepressants (TCAs) ex. Amitriptyline	Starting dose: dependent on agent selected, start at lowest available dose Dosing titrated every 3-7 days	May be recommended as a 2nd line agent	• Sedation • QTc prolongation • Lowers seizure threshold • Anticholinergic effects	May increase confusion
Lithium	Starting dose: 300mg BID Titrate by serum drug levels and side effects: 0.5-1.2mEq/L is therapeutic and >1.4mEq/L is toxic	Can help in patients with mania and cyclic mood disorders	• Increased thirst • Polyuria • Sedation • Movement disorders • Seizures • QTc prolongation • Renal impairment	May cause decreased cognition and lethargy

Antipsychotics

Medication	Dosage	Benefits	Important Side Effects	Comments
Typical Antipsychotics ex. Haloperidol		Typically reserved for **SEVERE** agitation or aggressive **CRISIS**	Extrapyramidal effects Neuroleptic malignant syndrome QTc prolongation Sedation	• Can be given IM, IV • Deleterious effects on cognition and motor recovery • Prolongs time in PTA • **Not recommended for long term use**
<u>Atypical Antipsychotics</u> ex. Olanzapine, Quetiapine, Ziprasidone, Risperidone	Starting dose: dependent on agent selected, start at lowest available dose	Better side effect profile compared to typical agents Consider if agitation associated with paranoia or delusions	Sedation Extrapyramidal symptoms Dizziness QTc prolongation	Some can be given IM (Olanzapine and Ziprasidone) Not recommended for long term use unless concomitant psychiatric disease

Neurostimulants

Medication	Dosage	Benefits	Important Side Effects	Comments
Amantadine	Starting dose: 50mg per day in divided doses, typically morning and noon 200-400mg/day used for improving wakefulness and cognition	Also improves wakefulness, apathy	Irritability/Agitation Tachycardia Elevated BP Lowered seizure threshold	Effects seen within several days Must be weaned when discontinuing due to risk for neuroleptic malignant syndrome with abrupt withdrawal
Methylphenidate	Starting dose 5mg in divided doses, usually at 8AM and noon Doses up to 60mg/day utilized	Can additionally improve attention and concentration	Insomnia Decreased appetite Elevated BP	Quick onset of action

Anxiolytics

Medication	Dosage	Benefits	Important Side Effects	Comments
Buspirone	Usual dose of 5-20mg TID Maximum dosing recommended 60mg/day, but as high as 180/day seen	Can be considered *2nd line* for agitation in the presence of anxiety	Light headedness Headache Risk of serotonin syndrome with concomitant use of antidepressants	2-3 week delay in therapeutic action No respiratory depression, sedation, addictive properties, or adverse cognitive effects
Benzodiazepines ex. Lorazepam, Diazepam	Starting dose: dependent on agent selected, start lowest available dose	Useful for rapid resolution of agitation CRISIS	• ***Paradoxical agitation*** • Anterograde amnesia • **Disinhibition** • Sedation • Impaired coordination • Respiratory depression	Recommend starting long-acting agents concurrently **Delays cognitive recovery** Risk of dependence and addiction

Going all in:

Knowing which medication to choose?

- Each Brain Injury is different
- Choice of therapy should be based on clinical presentation and medical comorbidities
- The ideal agent is non-sedating, would not affect cognitive recovery, and has a low side effect profile

Agents that slow cognition may prolong/exacerbate agitation

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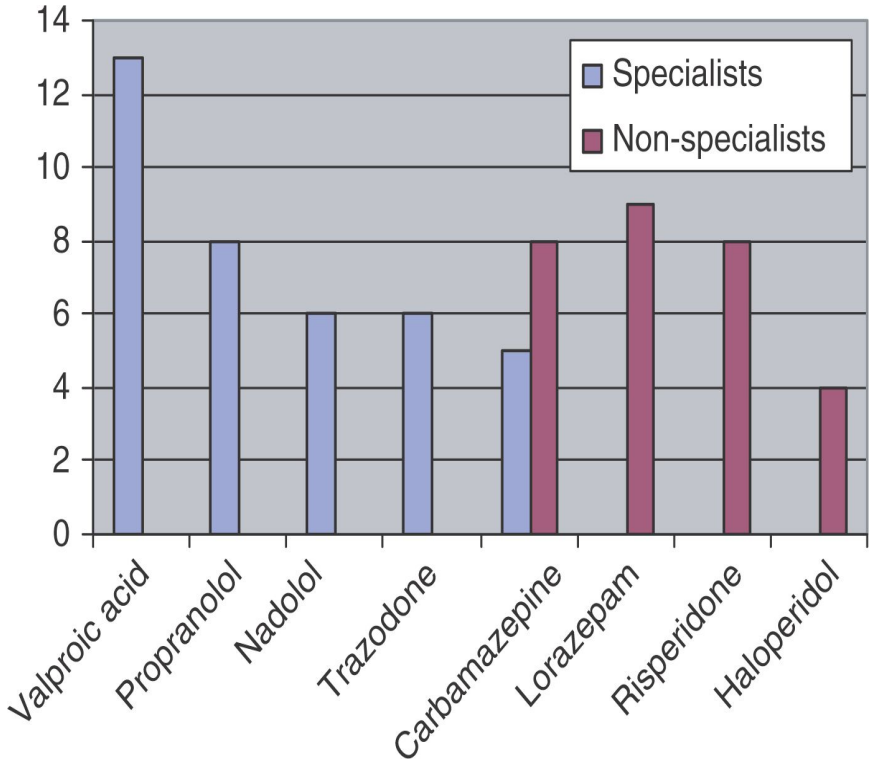
What do the Experts choose?



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Things to Consider with Medical Management of Agitation

Spontaneous recovery vs. medication effect

No good markers of neurotransmitter levels

Deficits overlap clinically, chemically

Variability of response & symptom fluctuations

Poor compliance

Stacking the deck in your favor:

A summary for managing agitation in the neuroscience patient

- Agitation is a self-limiting condition with largely unknown etiology

- Know the injury!!!
  - The more severe the injury and the more confused the patient, the greater the likelihood of agitated behaviors

- Environmental modifications are first line.
  - ***Educate! Educate! Educate!***

- When choosing medications, consider potential secondary benefits, side effects

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QUESTIONS?

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BREAK TIME!

BREAK TIME!

Baptist Health

FOR YOU. FOR LIFE.

Down to the Wire

Neurosurgery Case Reviews

Tim Burson, M.D.
Chief of Neurosurgery
Baptist Health

Baptist Health

Objectives:

1. Identify neuroscience cases of interest to neuroscience providers
2. Discuss case specifics in context of symptoms, imaging, and plan of care
3. Identify at least one important take-away from each case

Disclosures:

None

Case 1

24 yo female with history of COVID a week prior to admission with new onset headache. Was seen at urgent care and headache improved x 48 hours.

Woke up on day of admit with severe headache and presented to the ED.

On exam, she was awake/oriented, face symmetric, and moving all extremities equally. She had difficulty with word finding and occasionally had repetitive speech.

What is the SUSPECTED diagnosis?

A. Primary ICH
B. Underlying mass/tumor
C. Ruptured aneurysm
D. Arterio-venous anomaly
E. Sinus occlusion/thrombosis

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Cerebral angiogram

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C. Ruptured aneurysm
D. Arterio-venous anomaly
E. **Sinus occlusion/thrombosis**

Hospital Course

Concern for worsening brain compression > left hemicraniectomy

Hospital Course

Neurocritical Care Management

- Avoid dehydration
- Hypertonic saline for goal Na+ 140-145
- Seizure prophylaxis
- Close neuro checks
  - episode of right hemiparesis 2-3 / 5 with stable head CT
- Anticoagulation
  - Started heparin drip 48 hours post hemicrani
  - Started apixaban 7 days post hemicrani

- Consulted hematology - Lupus anticoagulant, JAK2 V617F, Beta-2 Glycoprotein, PNH panel, Cardiolipin Ab; negative Factor V Leiden and prothrombin gene mutation

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About Sinus Thrombosis

Incidence

- 3-4 cases per million
- 12 cases per 100,000 peri- and post-partum women
- 3 x more frequently in women of child bearing age - related to estrogen based contraceptives
- most risk in infants during first month of life

Risk Factors

- Any condition leading to a prothrombotic state
  - Oral contraceptives - estrogen based
  - Peripartum
  - Chronic inflammatory diseases
  - Inherited or acquired thrombophilias

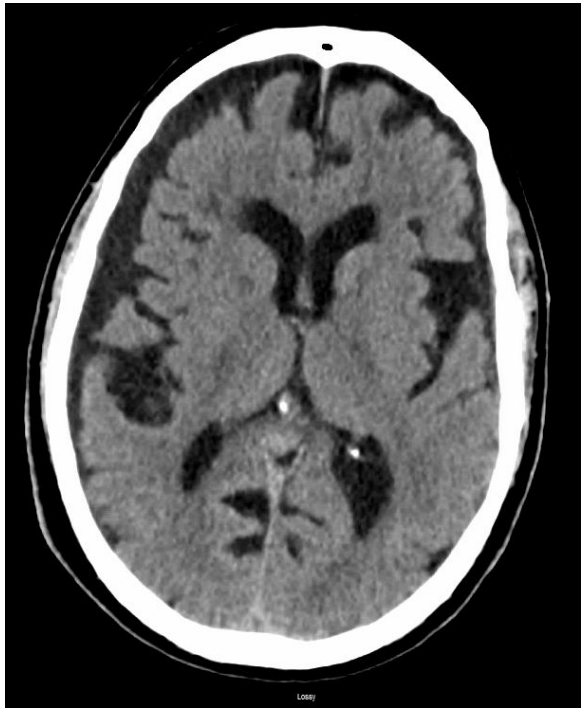
Discharge and Recovery

- Admit to rehab
- Right hemiparesis improved
- Speech improved
- Continued on apixaban
- Cranioplasty after 2 months
- Recovered well

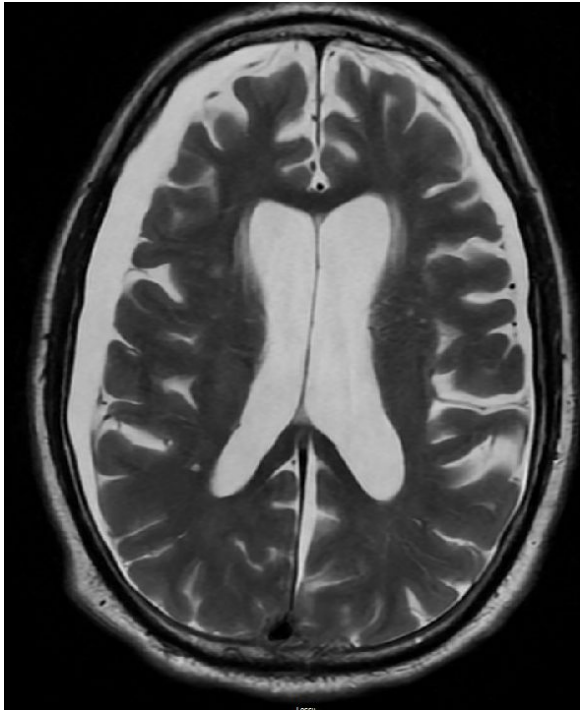
Case 2

76 yo WM with recent history of lumbar laminectomy 1 month prior who was discharged to rehab. In rehab, began having syncopal episodes but denied head trauma or headaches. CT head was obtained at the outside hospital and he was transferred here for further NSGY evaluation.

Case 2 - Head CT/MRI



Diagnosis?



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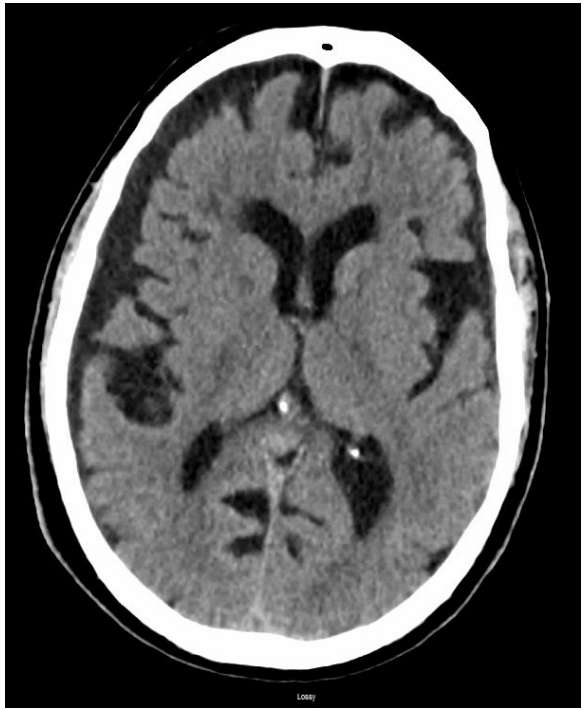
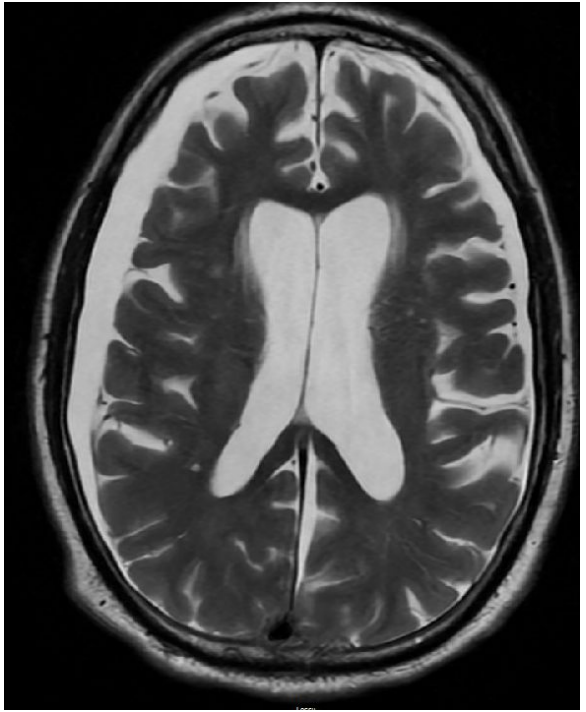


Subdural Hygromas



We had questions….

Why would this patient develop bilateral subdural hygromas after a lumbar spine surgery? Is it relevant?

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On further questioning, we discovered he had a lumbar drain for CSF leak that was removed several days after surgery

We had questions….

Now, what is the relevance of the bilateral subdural hygromas?

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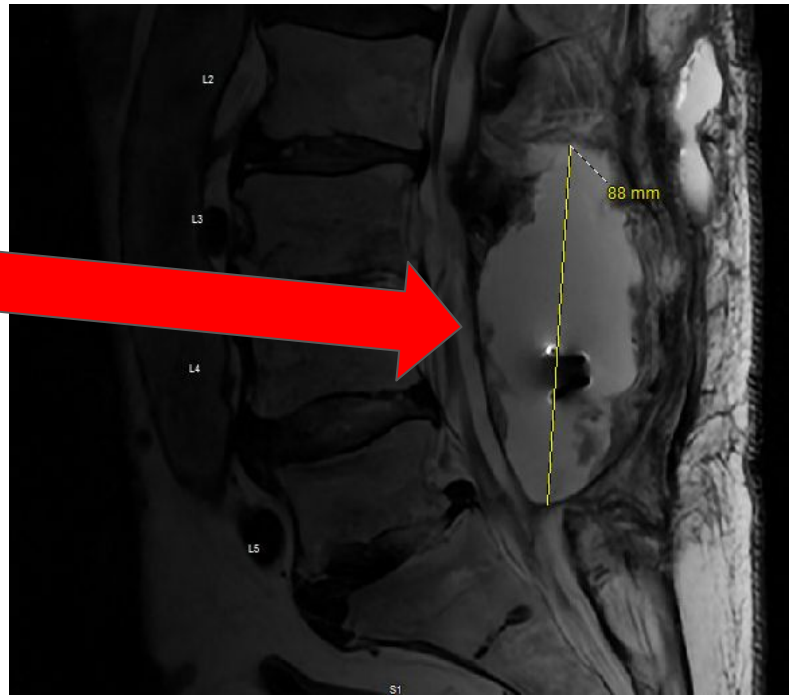
Now, what is the relevance of the bilateral subdural hygromas?

?Intracranial HYPOtension

So…we ordered an MRI lumbar spine

What is the diagnosis here?



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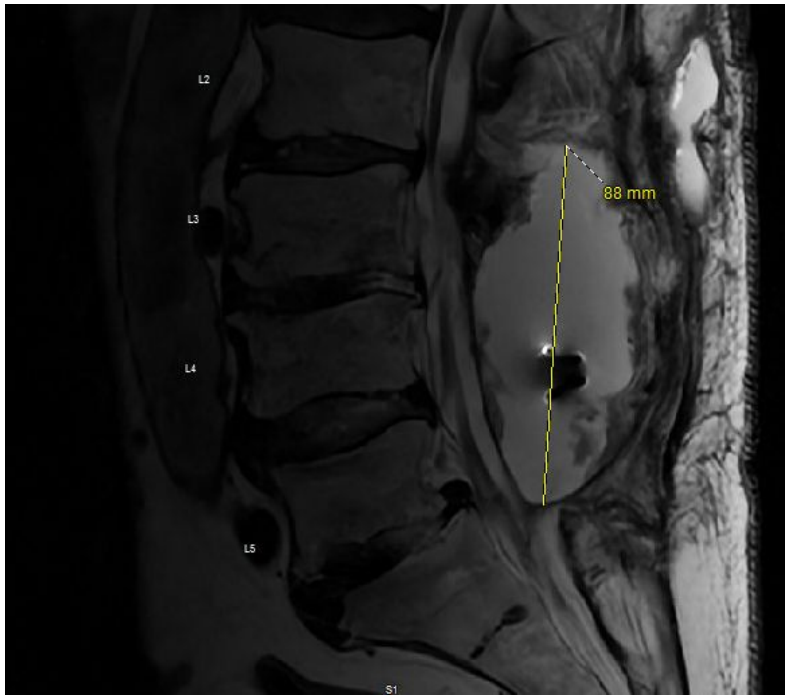

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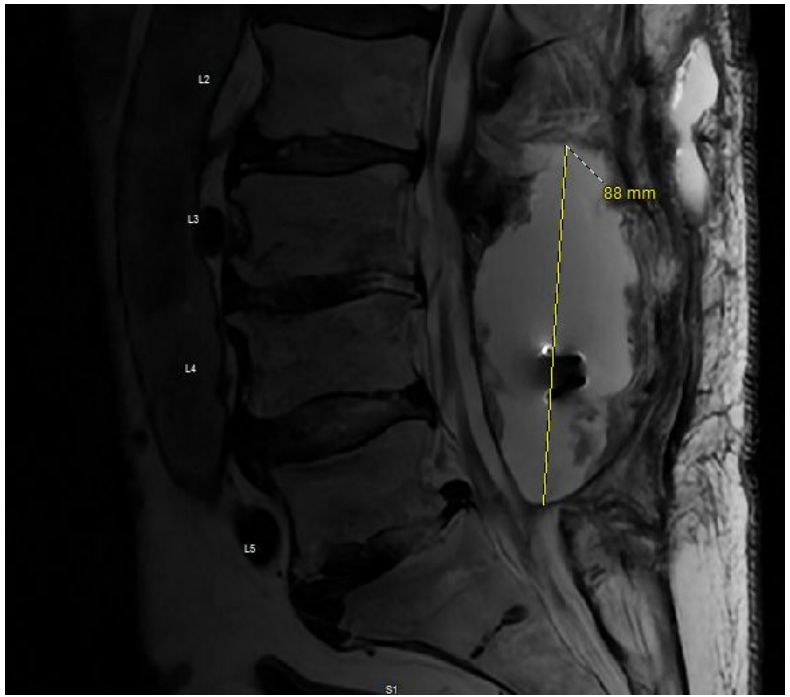
What is the diagnosis here?

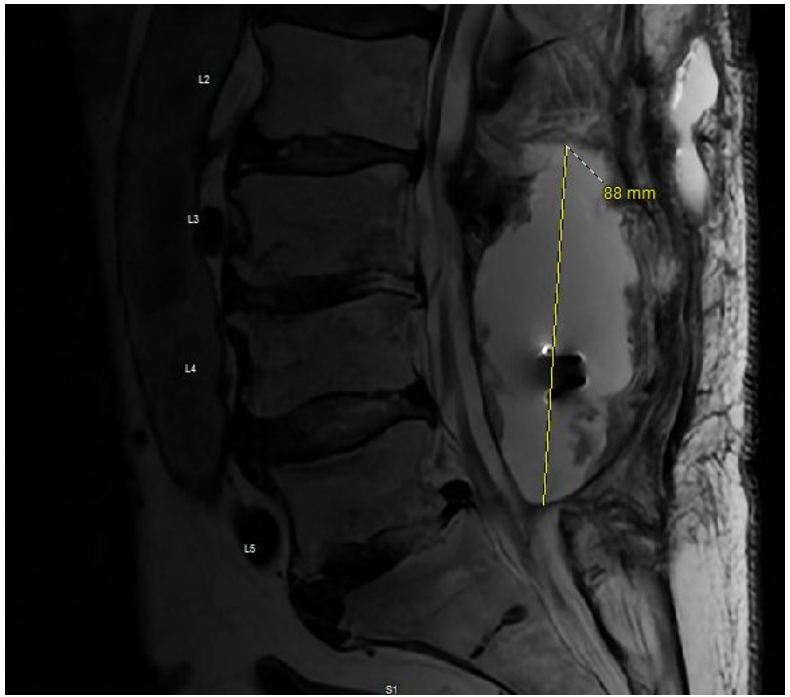
What caused that?

How is a pseudomeningocele related to the subdural hygromas?



Neurosurgical options?

Post operative management?



Discharge and Recovery

- Discharged to primary neurosurgeon for repair of pseudomeningocele
- Admitted to rehab 10 days later
- Recovered well

Case 3

71 yo WM with history of DMT2, HTN who presented to ED with ataxia, blurred and occasional diplopia, and nausea x 24 hours associated with elevated blood glucose of 305 on admission.

Where would you localize these symptoms in the brain?

1. Frontal lobe
2. Temporal lobe
3. Parietal lobe
4. Occipital lobe
5. Cerebellum

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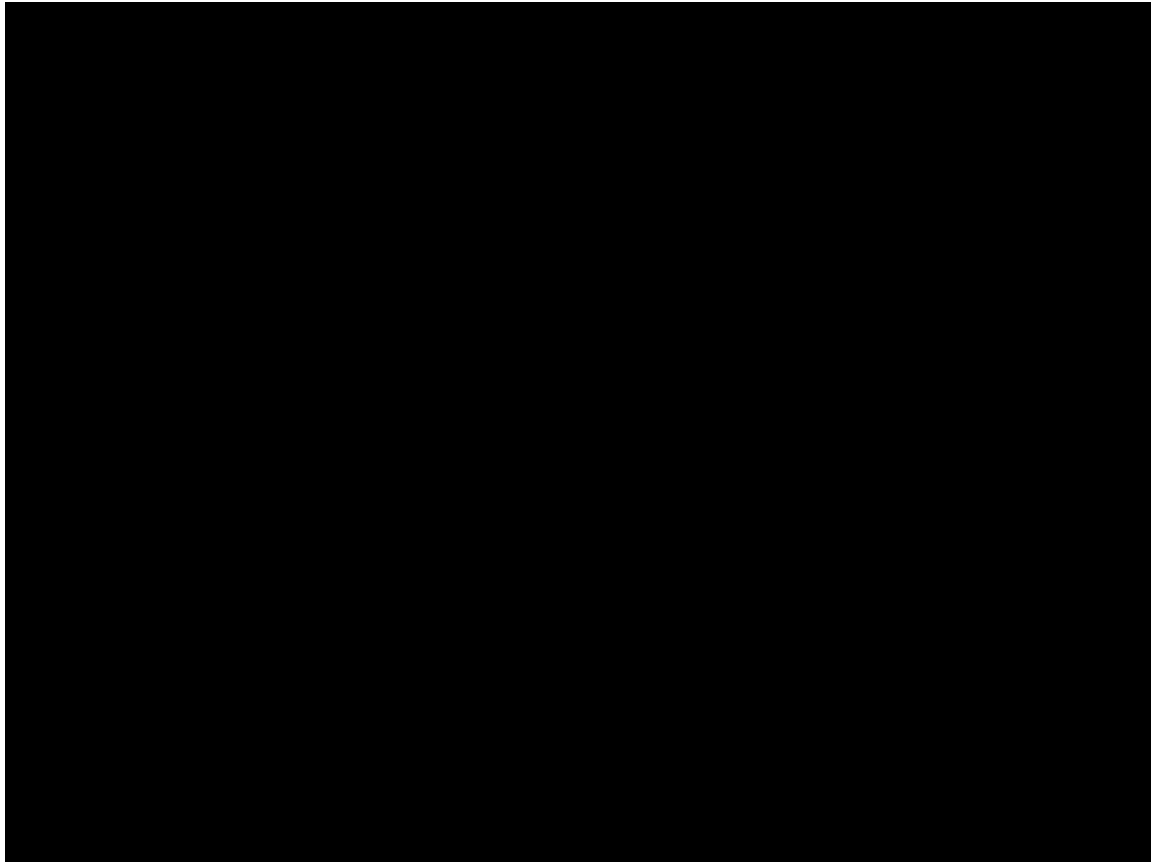
Case 3 - MRI



Case 3

He was out of the window for thrombolytics and not a thrombectomy candidate because there was no large vessel occlusion (LVO).

Why would neurosurgery be more concerned about a posterior circulation stroke, aka a cerebellar stroke?

a. Neurosurgery is not concerned about it at all
b. Concern for crowding the 4th ventricle causing acute hydrocephalus and brain stem compression
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What are our options??

A. Comfort Care
B. Medical management
C. CSF diversion with EVD
D. Suboccipital decompression

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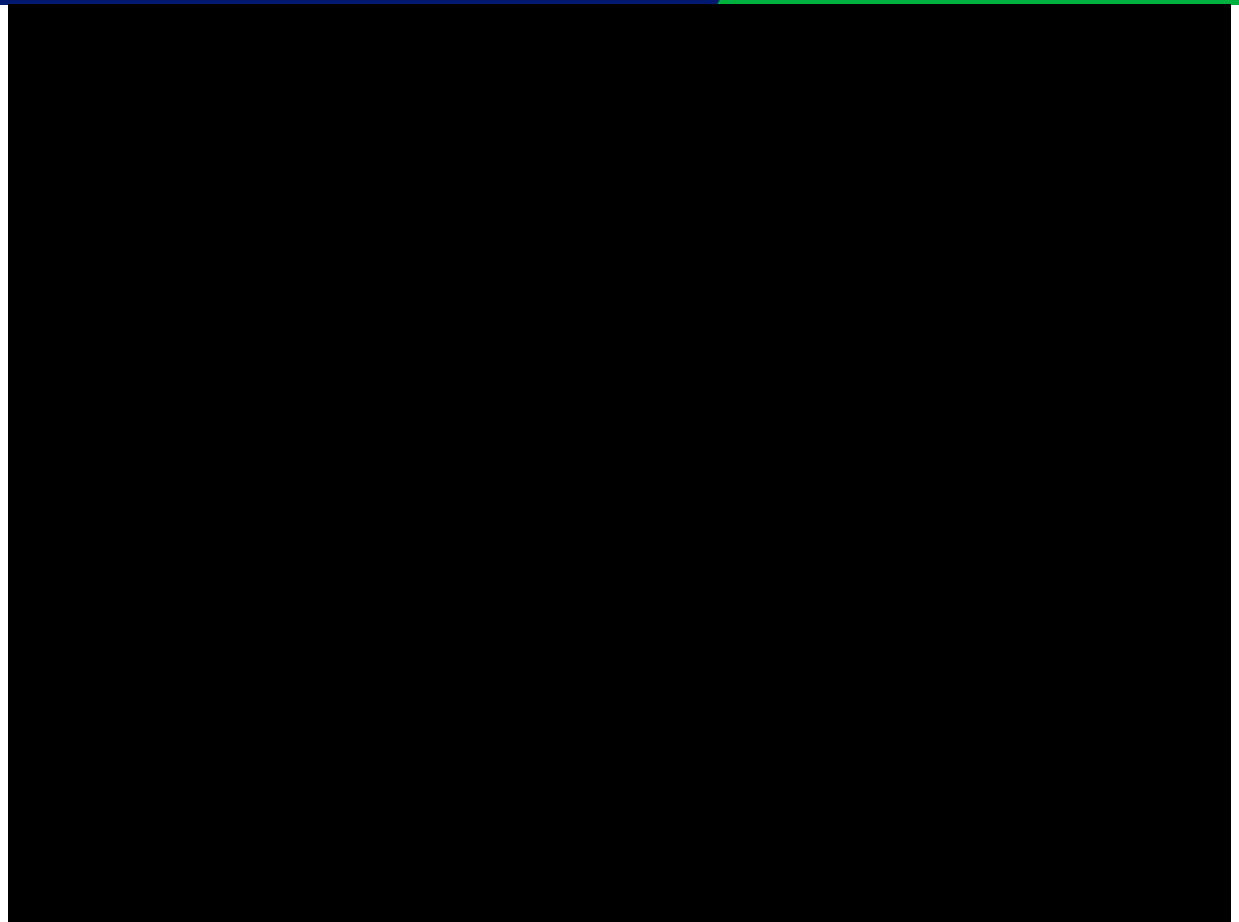

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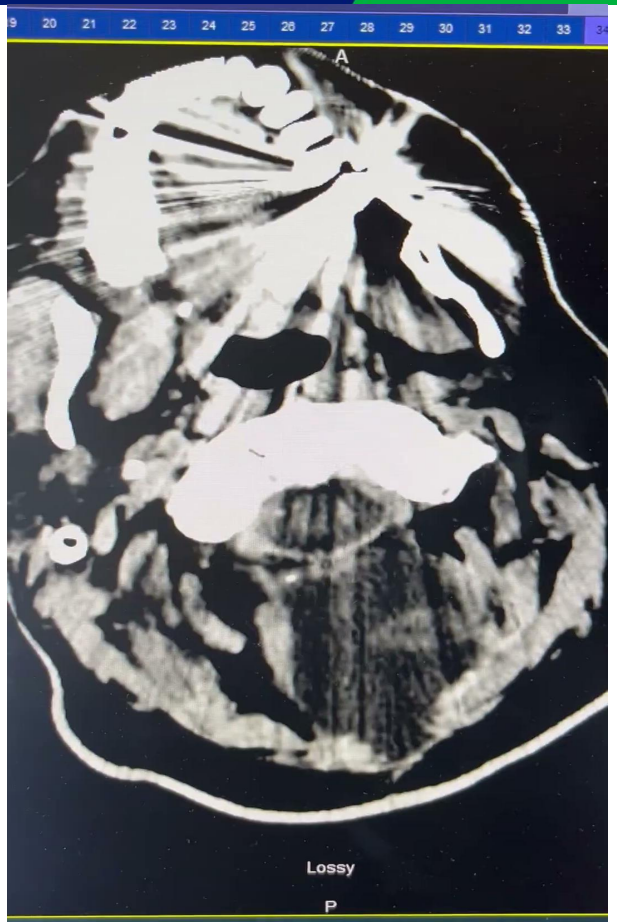

Questions

- Do you need to put the bone back on after a suboccipital decompression?
- Do these patients need a helmet?

How well did this patient do?

Down to the Wire

- Refers to an outcome that is not decided until the last minute

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- Refers to an outcome that is not decided until the last minute
- These cases demonstrate vigilant care throughout the hospitalization and rehabilitation process to obtain the best outcomes
- That’s why YOU are important in the continuum of care


Thank you

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References

Saposnik, G. (2024). Diagnosis and management of cerebral venous thrombosis: A scientific statement from the American Heart Association. *Stroke,* 55(3). https://doi.org/10.1161/STR.0000000000000456

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BREAK TIME!

RETURN TO MAIN ROOM AT 2:05PM

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FOR YOU. FOR LIFE.