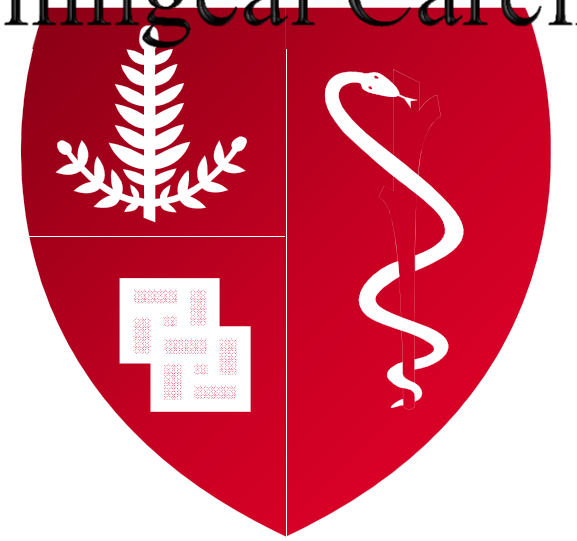
Brain Metastasis and Leptomeningeal Carcinomatosis



Anthony Simon RN, AGACNP-BC, AOCNS

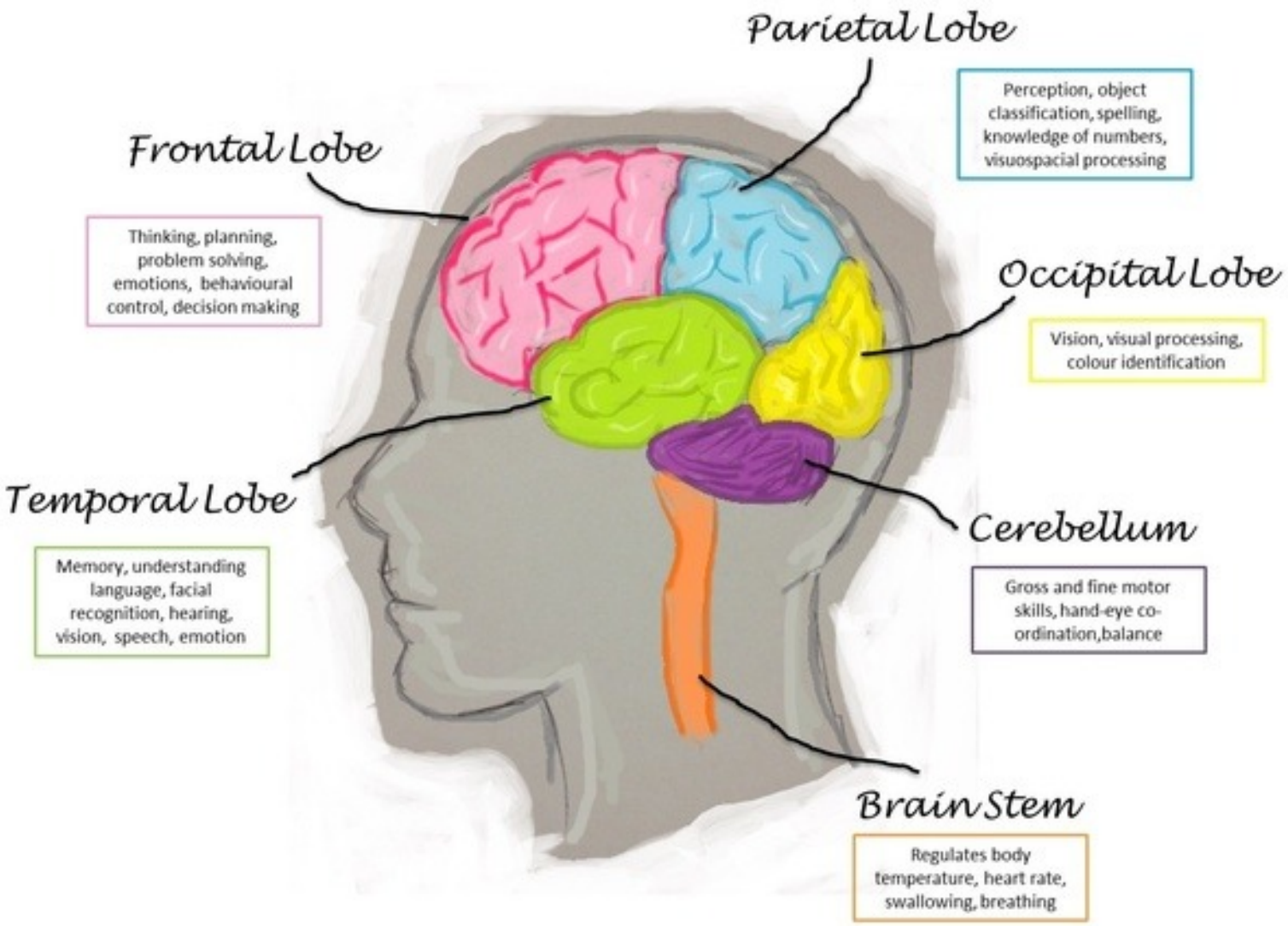
Objectives

- To be able to localize 3 symptoms, and their respective locations in the brain
- Name and understand the primary prognostic indicator for patients with brain metastasis and leptomeningeal disease
- Understand what differentiates the treatment goals for a patient with good prognosis vs a poor prognosis patient
- Name approaches to each form of treatment- Surgery, Radiation, and chemotherapy

Introduction

- Brain metastasis and leptomeningeal disease are lethal
- Untreated brain metastasis from solid tumors has a prognosis of 1-2 months
- Once diagnosed leptomeningeal disease has a prognosis of 2 weeks–2 months

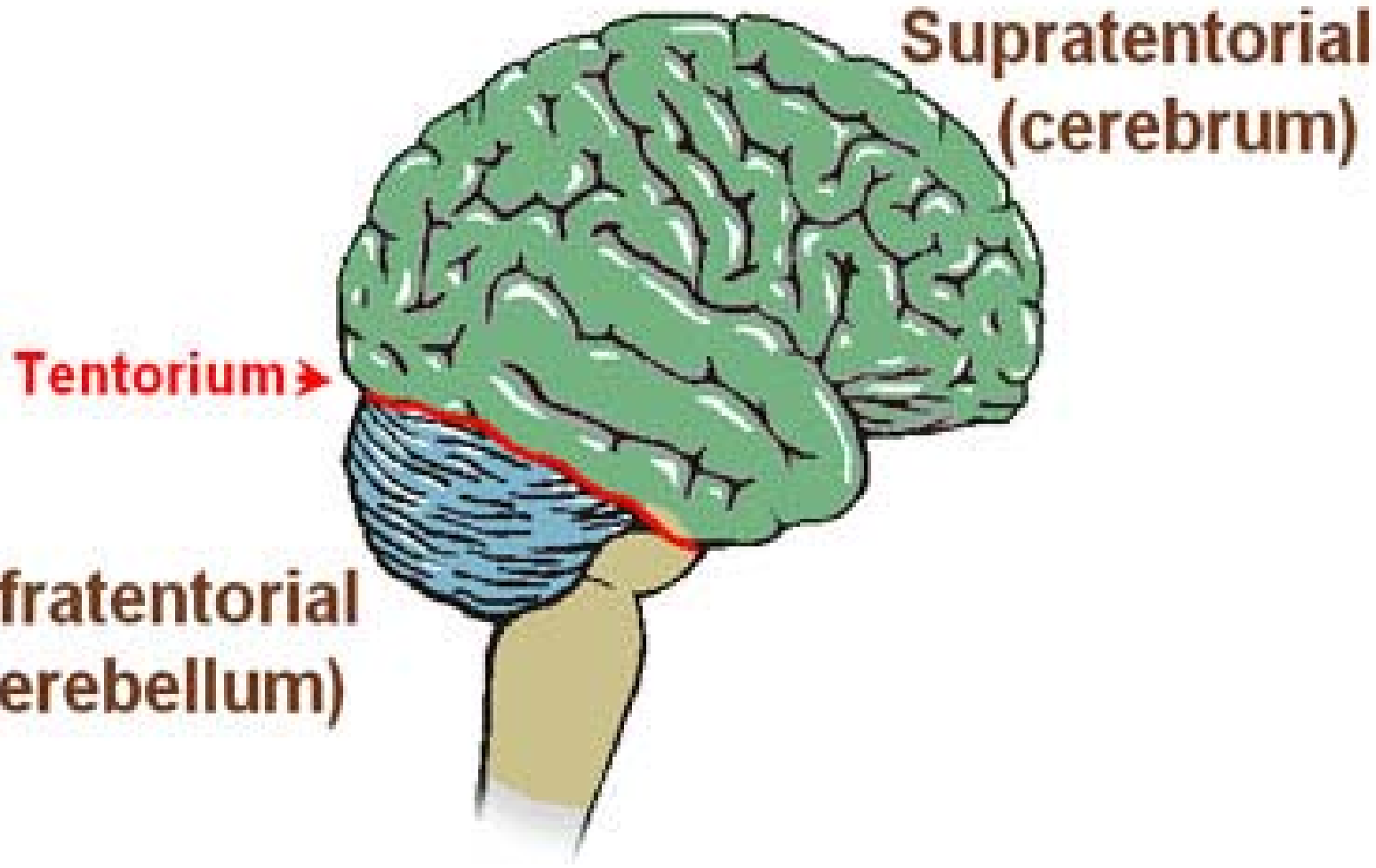
The Lobes of the Brain



Brain Metastasis

- Brain metastasis is the most common intracranial tumor in adults
- In systemic malignancy brain metastasis occurs in 10-30% of adults, and 6-10% of children
- Incidences increasing
  - Improved imaging with MRI
  - Improve control of extracranial disease

The Tentorium Cerebelli



Common Malignancies Responsible for Brain Metastasis

- Adults
  - Lung
  - Breast
  - Kidney
  - Colorectal
  - Melanoma
- Children
  - Sarcomas
  - Germ Cell tumors
  - Neuroblastoma

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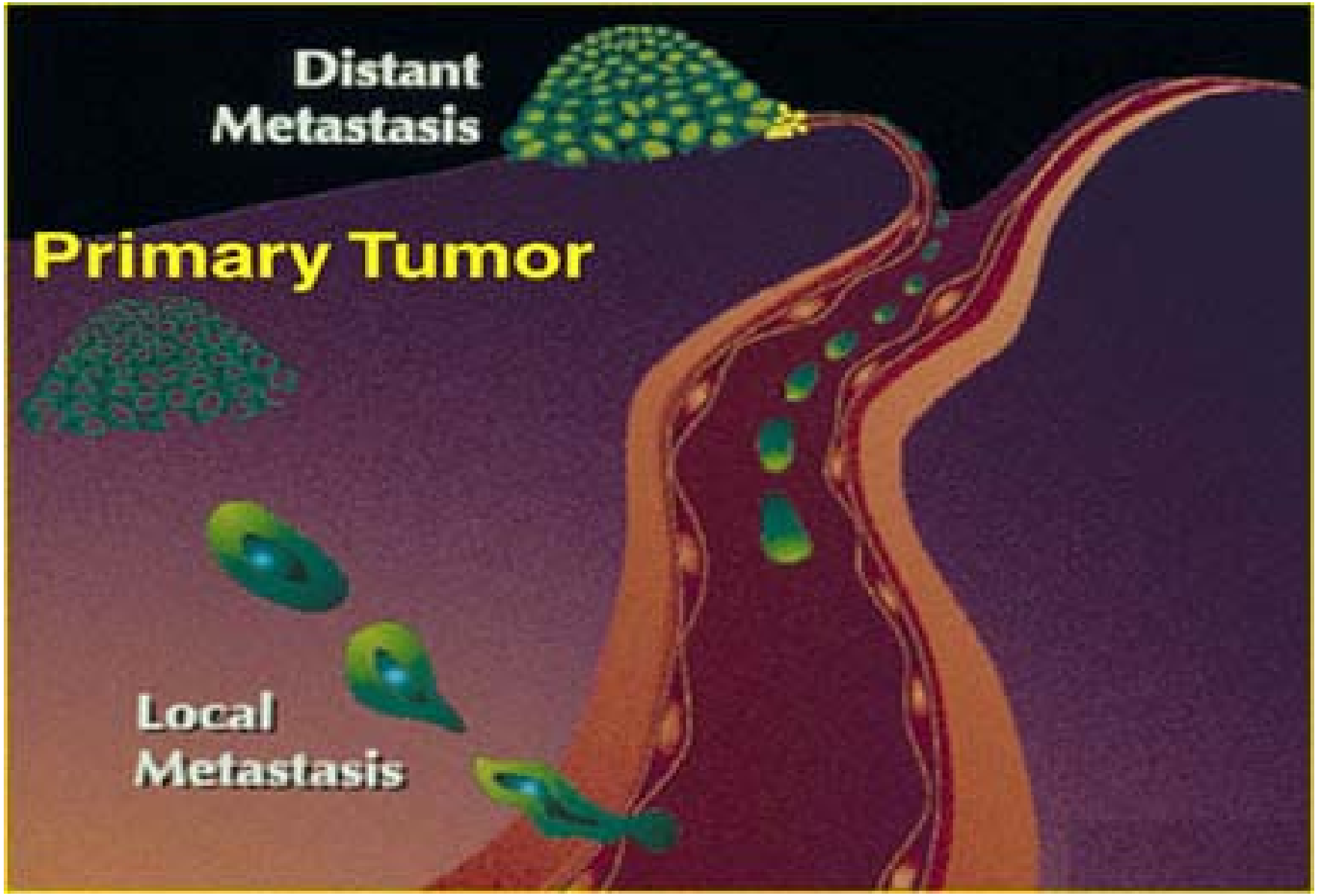

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Clinical Manifestations

- Headache
  - 40-50% of patients
  - Early morning headache
- Focal neurologic dysfunction
  - 20-40% pf patients
  - Hemiparesis most common
- Cognitive dysfunction
  - 30-35% of patients
- Seizures
- Stroke
- Others

Imaging

- Magnetic resonance imaging with contrast
- More sensitive than non contrast MRI or CT scan

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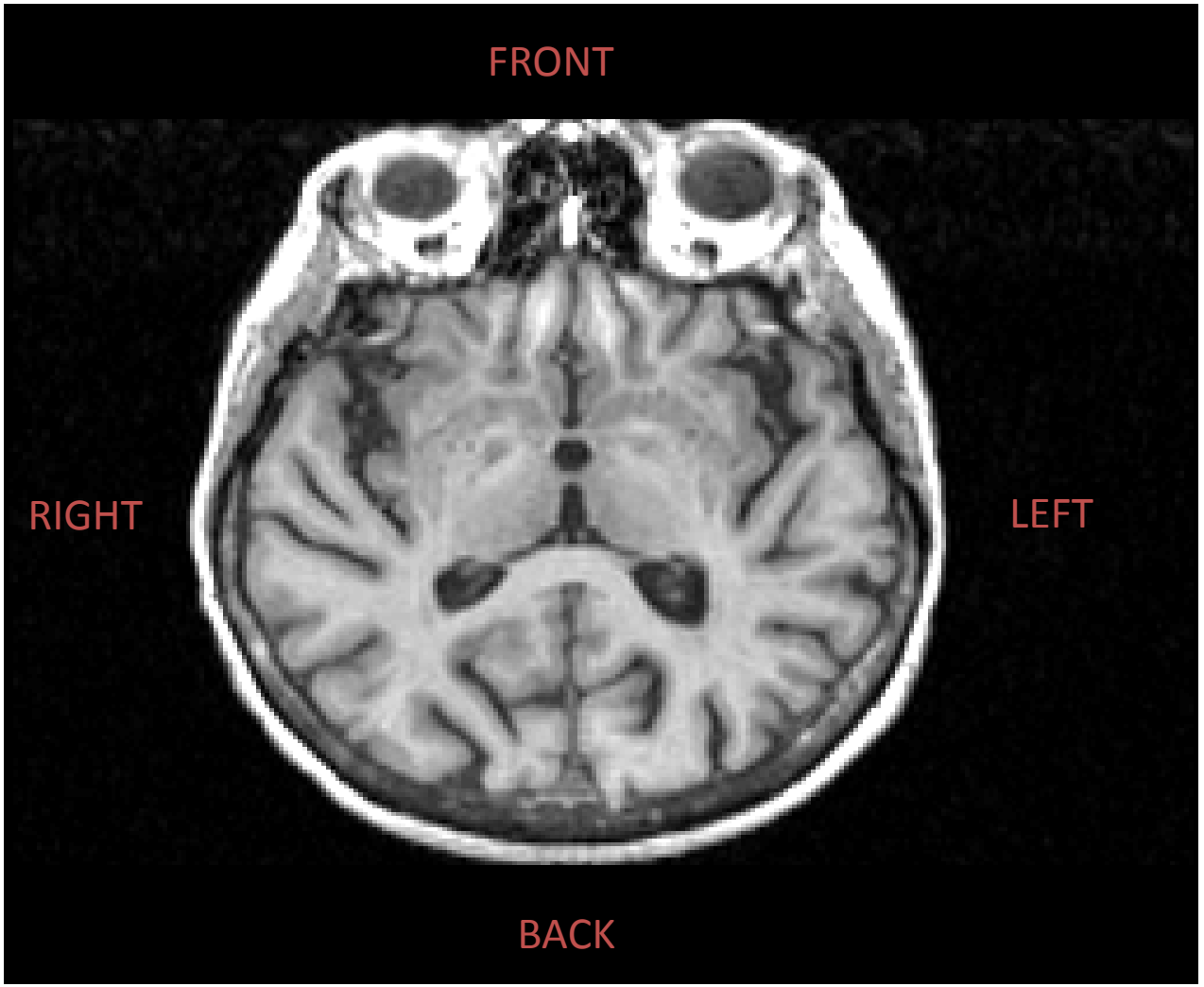

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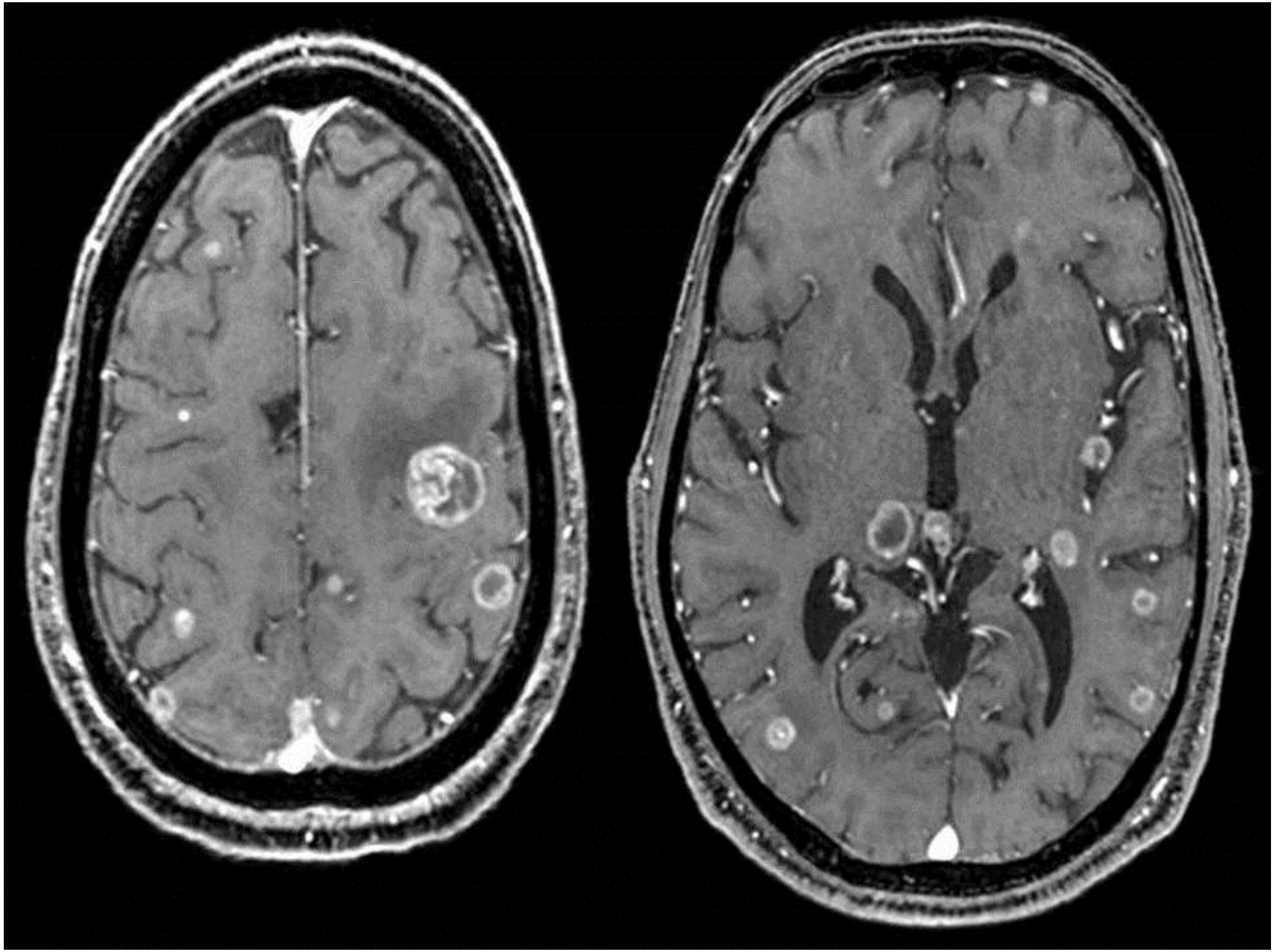

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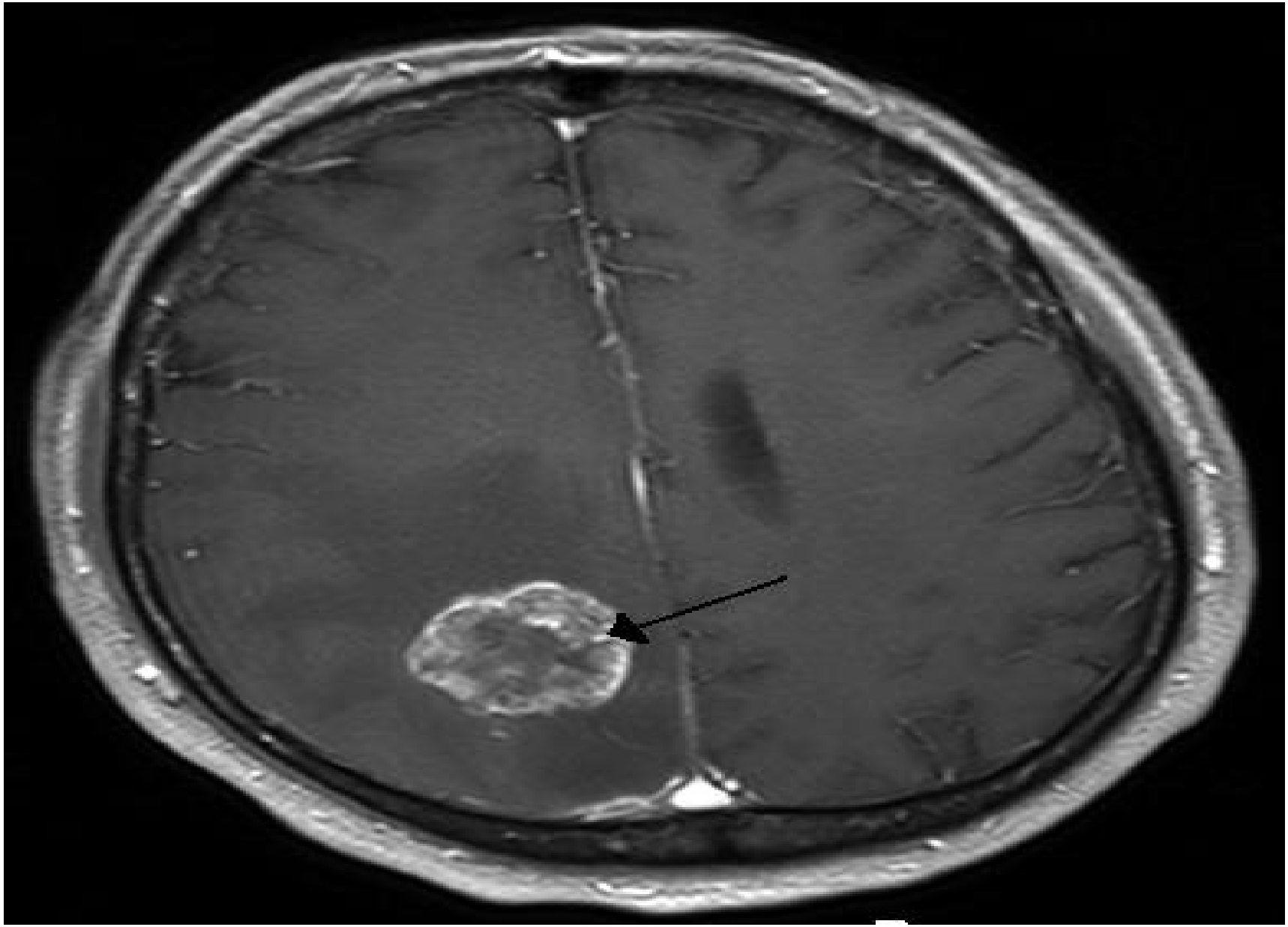

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Prognostic Indicators

- Performance status
- Age younger than 65
- Control of extracranial disease
- Underlying cancer histology and genealogy

Karnofsky Performance Scale

Karnofsky Performance Scale		
General category	%	Specific criteria
• Able to carry on normal activity • No special care needed	100	Normal general status - No complaint - No evidence of disease
	90	Able to carry on normal activity - Minor sign of symptoms of disease.
	80	Normal activity with effort, some signs or symptoms of disease.
• Unable to work • Able to live at home and care for most personal needs • Various amount of assistance needed	70	Able to care for self, unable to carry on normal activity or do work
	60	Requires occasional assistance from others, frequent medical care
	50	Requires considerable assistance from others; frequent medical care.
• Unable to care for self • Requires institutional or hospital care or equivalent • Disease may be rapidly progressing	40	Disabled, requires special care and assistance
	30	Severely disabled, hospitalization indicated, death not imminent
	20	Very sick, hospitalization necessary, active supportive treatment necessary
• Terminal states	10	Moribund
	0	Dead

Treatments

- Surgery
- Radiation
- Chemotherapy

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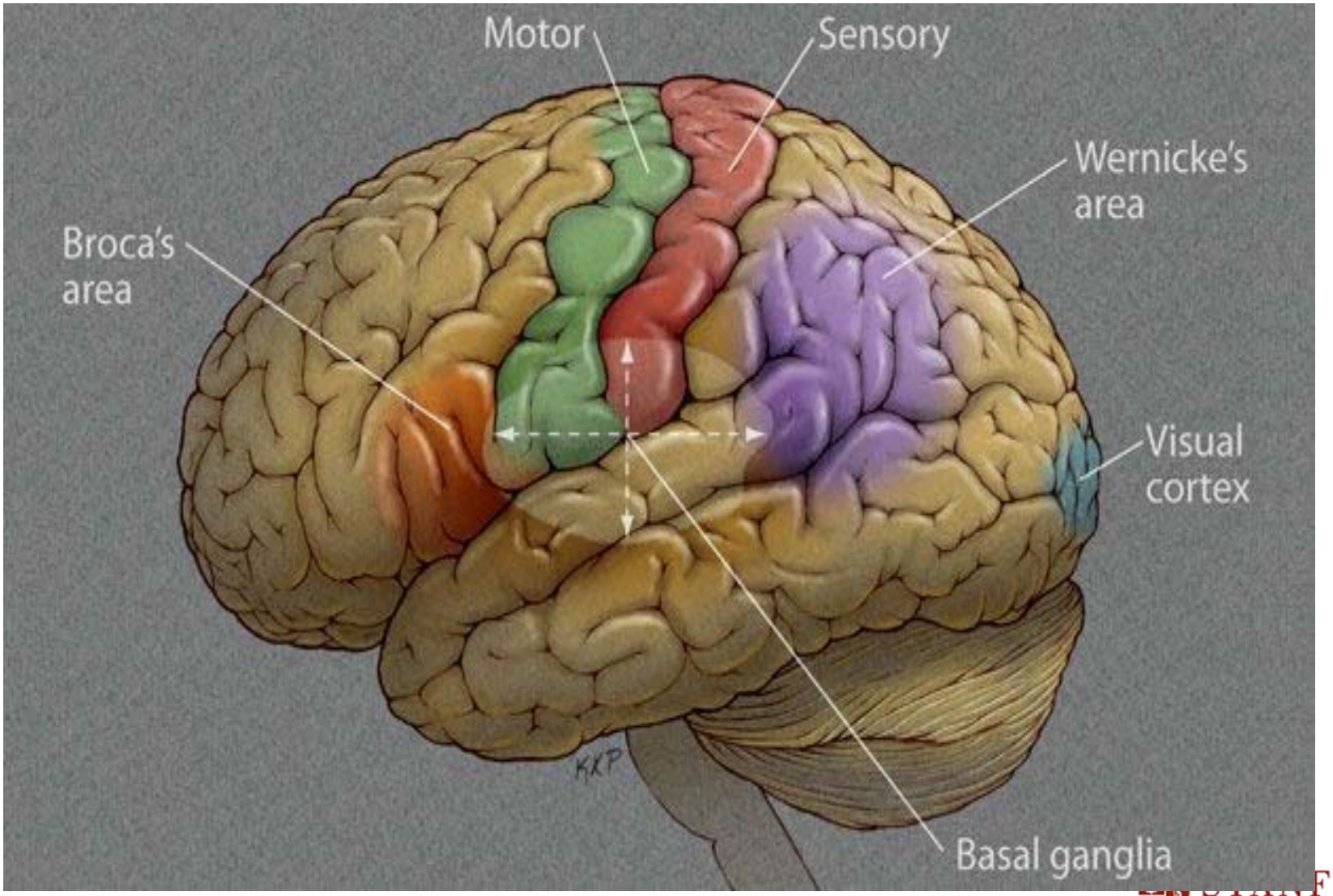
Surgery

- There is a single metastatic lesion
- Large symptom producing tumors
- Or if there is a uncertain diagnosis, excisional biopsy is considered

Eloquent Areas of the Brain



Radiation Therapy

- Many who undergo surgery get local radiation therapy to the surgical bed
- For those with a limited number of small brain metastasis, they may have stereotactic radiosurgery alone
- Whole brain radiation therapy

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Chemotherapy

- Chemotherapy is based on the primary site of cancer
  - Breast
  - Lung
  - Melanoma

Surveillance

- Imaging
  - 1 month after initial therapy, and then every 2-3 months after
  - Up to 50% progress within the first 6 months to one year

Recurrence

- Pseudo-progression
- Recurrence
  - Additional surgery a possible option
  - Additional radiation therapy is unlikely
  - Chemotherapy

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Leptomeningeal Disease

- Malignant cancer cells in the CSF
- Rare and devastating complication of advanced cancer
- Diagnosed in approximately 5% of patients with metastatic cancer
- Most common cancers to result in leptomeningeal disease–breast, lung, melanoma, GI cancers
- Primary brain tumors may also lead to the leptomeningeal disease- high-grade astrocytomas, oligodendroglioma, medulloblastoma, , pineoblastoma
- The development may be influenced by treatment

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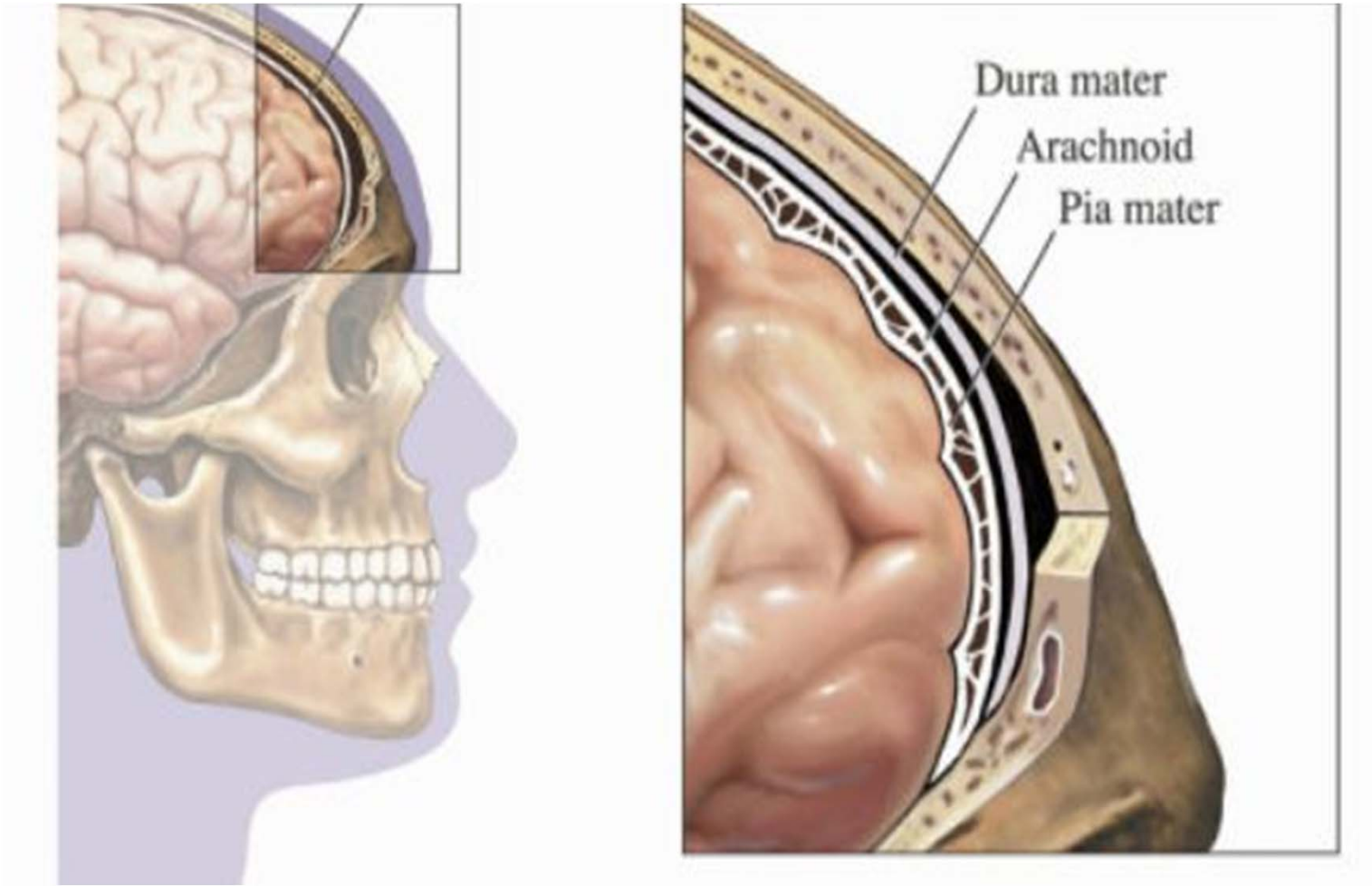
Pathophysiology/review



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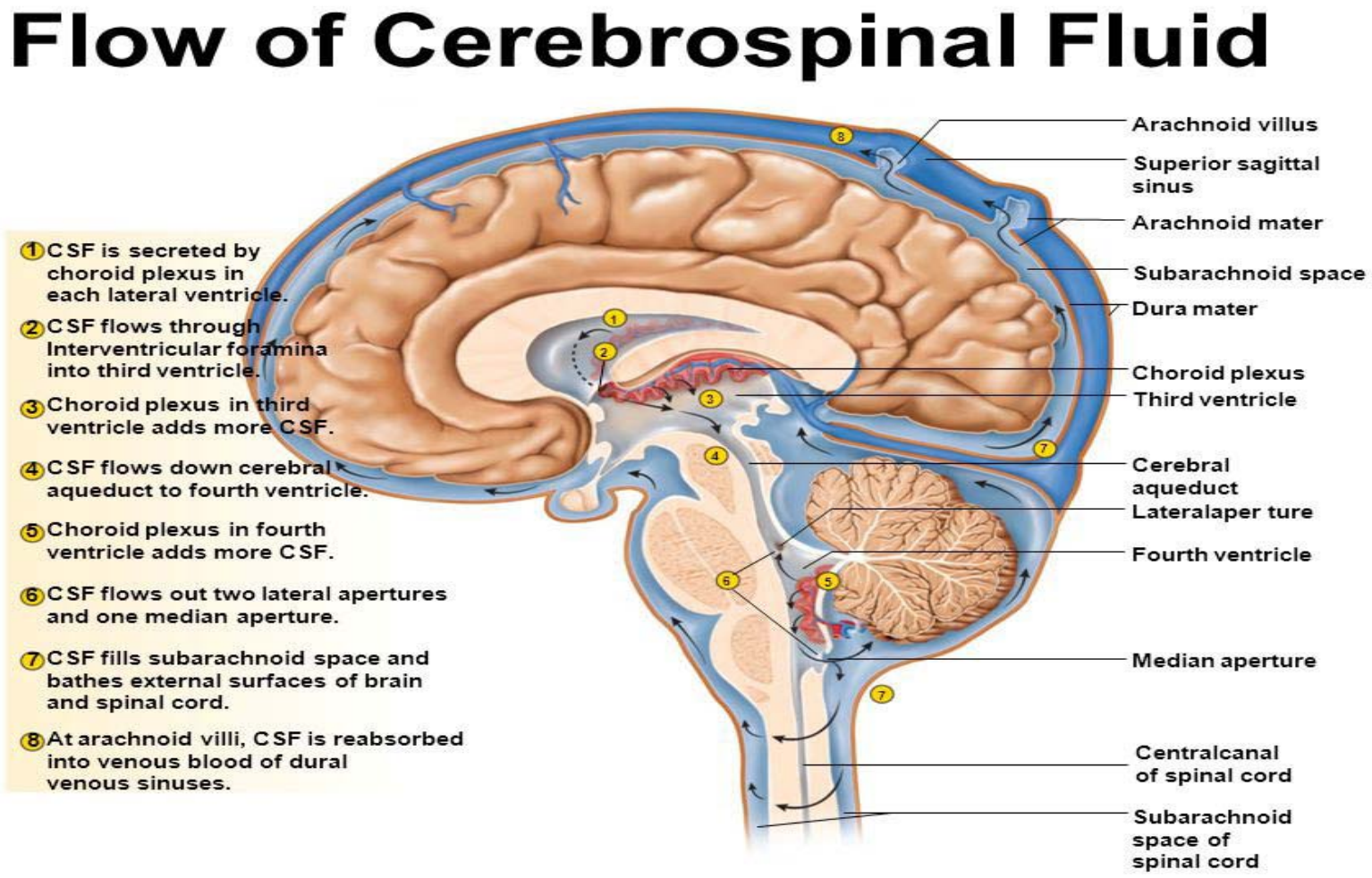
Cerebrospinal fluid



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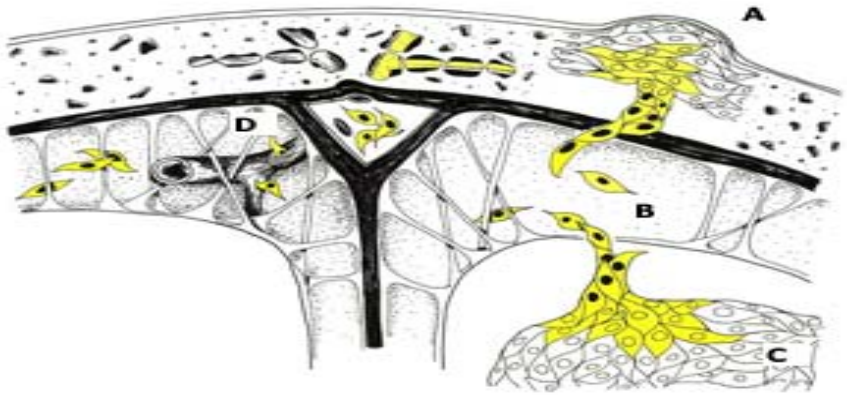
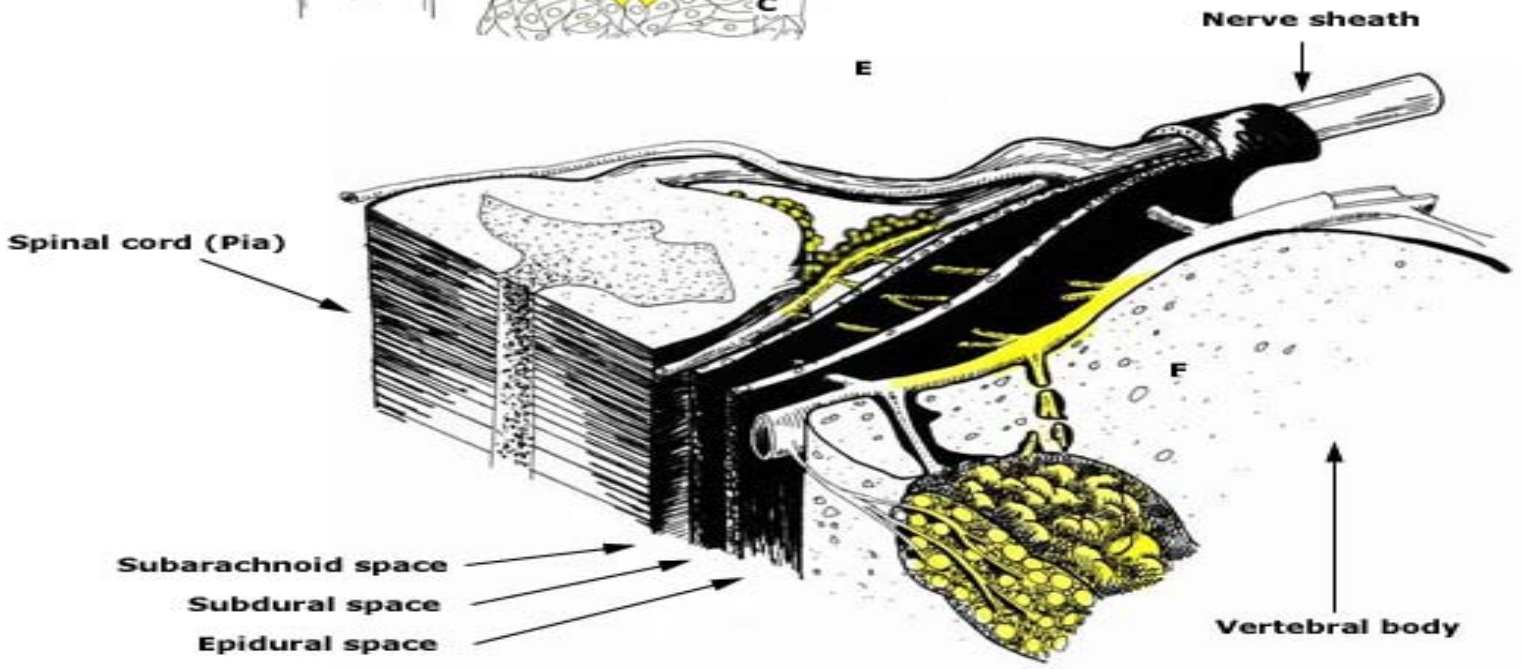
Pathogenesis





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Clinical Manifestations

- Mass effect
- Cranial nerves and spinal root dysfunction
- Invasion of the brain parenchyma
- Disruption of the blood brain barrier

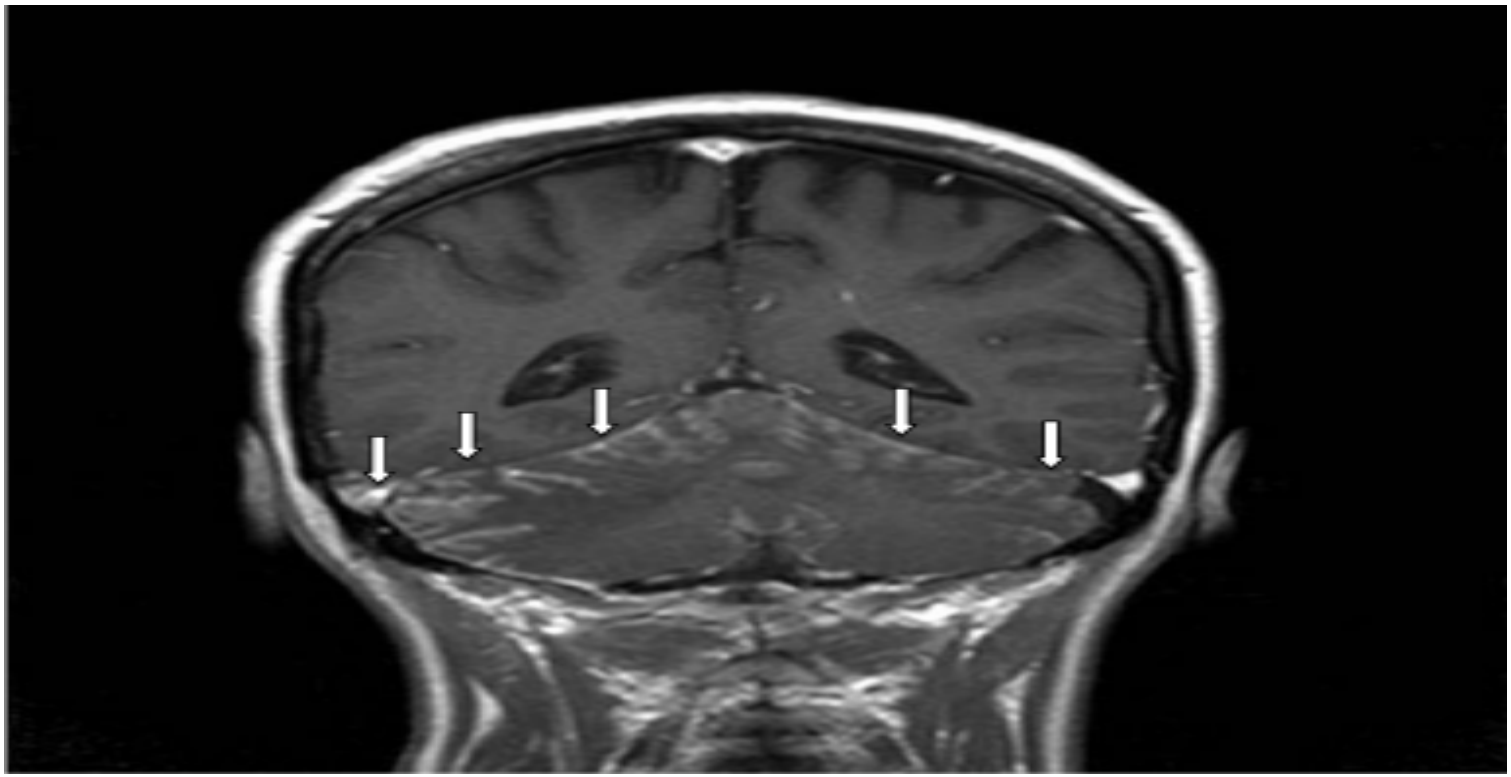
Signs and symptoms

- Any neurological symptom may be related to LM
- Symptoms present acutely and progress within days to weeks
- Multifocal neurological signs and symptoms
- Be aware of those that present with a single symptom

Diagnostics

- Brain MRI
- CSF analysis through lumbar puncture

Leptomeningeal contrast enhancement



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Leptomeningeal Contrast Enhancement

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Treatment Goals

- Stabilizing or improving neurological function
- Prolonging survival
- Palliation of symptoms

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	0	Dead

Poor Risk Patients

- Patients with multiple serious/fixed neurological deficits
- Extensive systemic disease even with active treatment
- Focus is largely on palliation of symptoms

Treatments

- Radiation therapy
- Analgesics for pain
- Corticosteroids
- Anticonvulsants
- VP shunting
- SSRIs

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Good Risk Patients

- Those without fixed neurological deficits
- Minimal systemic disease
- Cancer with reasonable treatment options
- Goal is direct tumor control

Treatments

- Surgery
- Radiation
- Chemotherapy

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Surgery

- Treatment of increased intracranial pressure
  - For signs of increased intracranial pressure initially treat with steroids
  - VP shunting

Radiation Therapy

- Used to treat bulkier symptomatic areas of disease
- Appears to be more effective at relieving symptoms when compared to chemotherapy
- Standard radiation dose for leptomeningeal disease includes 30-36 Gy, in 3 Gy daily fractions
- Major adverse effects during or after focal radiation therapy unusual
- With large extension radiation fields common adverse effects include myelosuppression, mucositis, esophagitis, leukoencephalopathy

Intrathecal chemotherapy

- Mainstay of treatment with leptomeningeal metastasis
- It may be delivered via lumbar puncture versus Ommaya reservoir
- Methotrexate is the chemotherapy most often used for the leptomeningeal disease

Systemic Chemotherapy

- There are several therapeutic chemotherapy agents provide therapeutic concentration within the CSF when given at appropriate doses
- Advantages
  - Surgery risks
  - Obstruction normal CSF flow
  - Increased availability of cytotoxic agents
  - Uniform drug distribution

Common Systemic Chemotherapy Agents

- High-dose methotrexate with leucovorin rescue
- High-dose cytarabine
- Capecitabine
- Tyrosine kinase inhibitors such as erlotinib
- Anaplastic lymphoma kinase inhibitors such as Crizotinib

Investigational Therapies

- IT etoposide
- Intrathecal trastuzumab
- Intrathecal rituximab

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Prognosis

- Despite aggressive therapy even good risk patients with leptomeningeal disease have limited survival
- Average survival with aggressive treatment is 3-4 months
- Tumor histology and molecular subtype may influence prognosis
- Performance status and control of systemic disease are important factors

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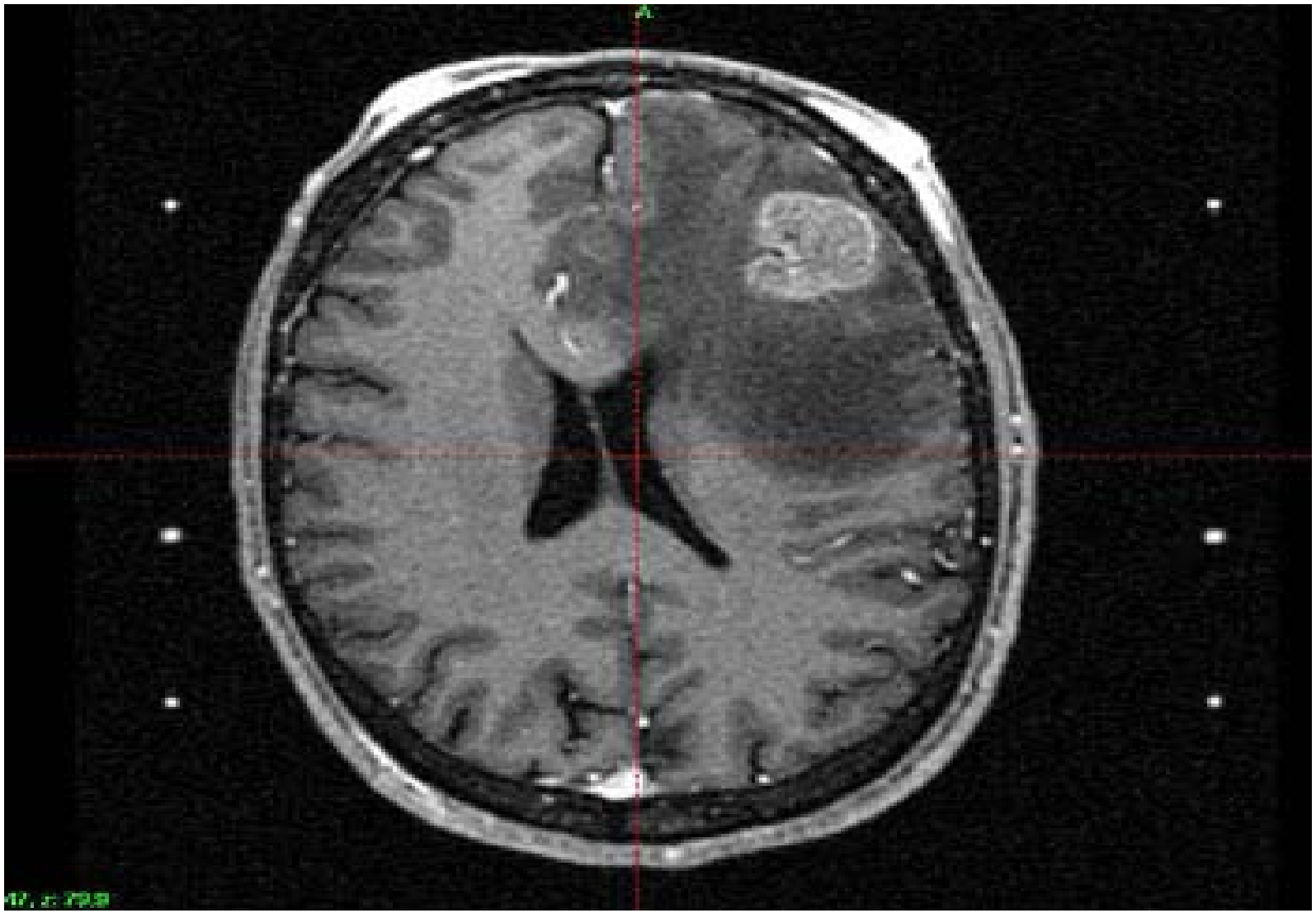
QUIZ

- Questions to ask yourself
  - What lobe of the brain is this lesion in?
  - Would you resect the tumor?
  - What part of the brain would receive radiation?
  - Name 2 symptoms the patient may experience with a metastatic lesion in this area.



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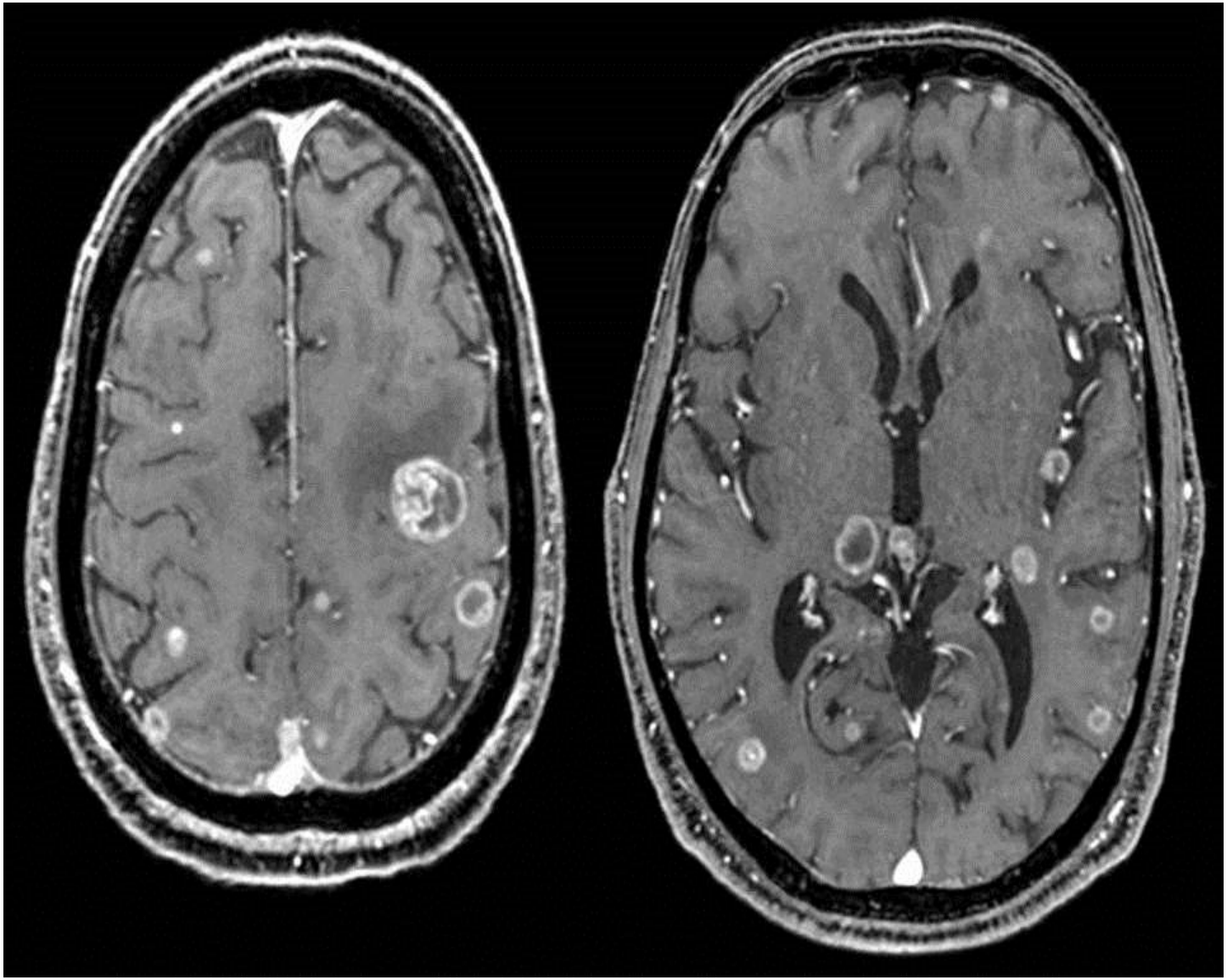

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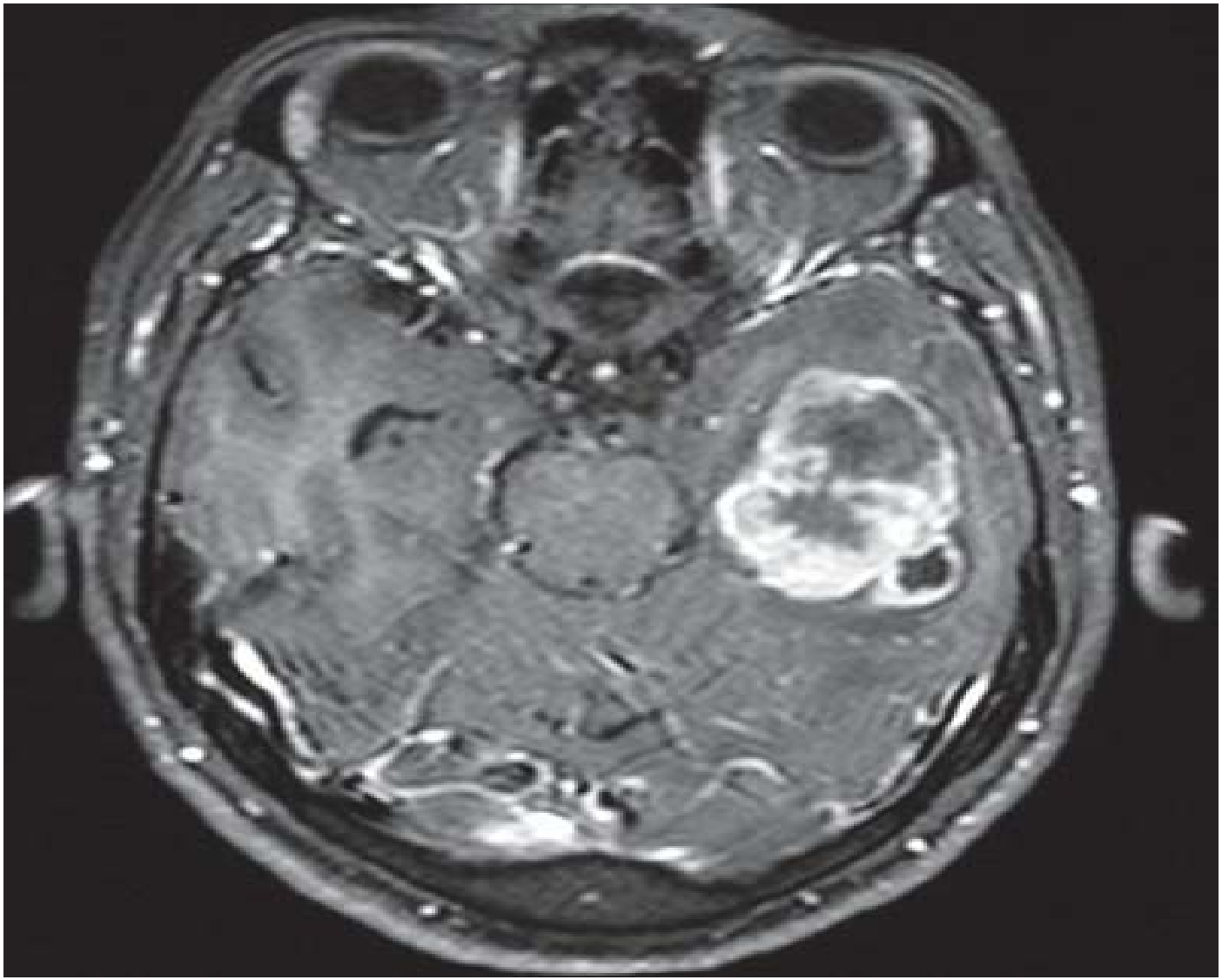

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