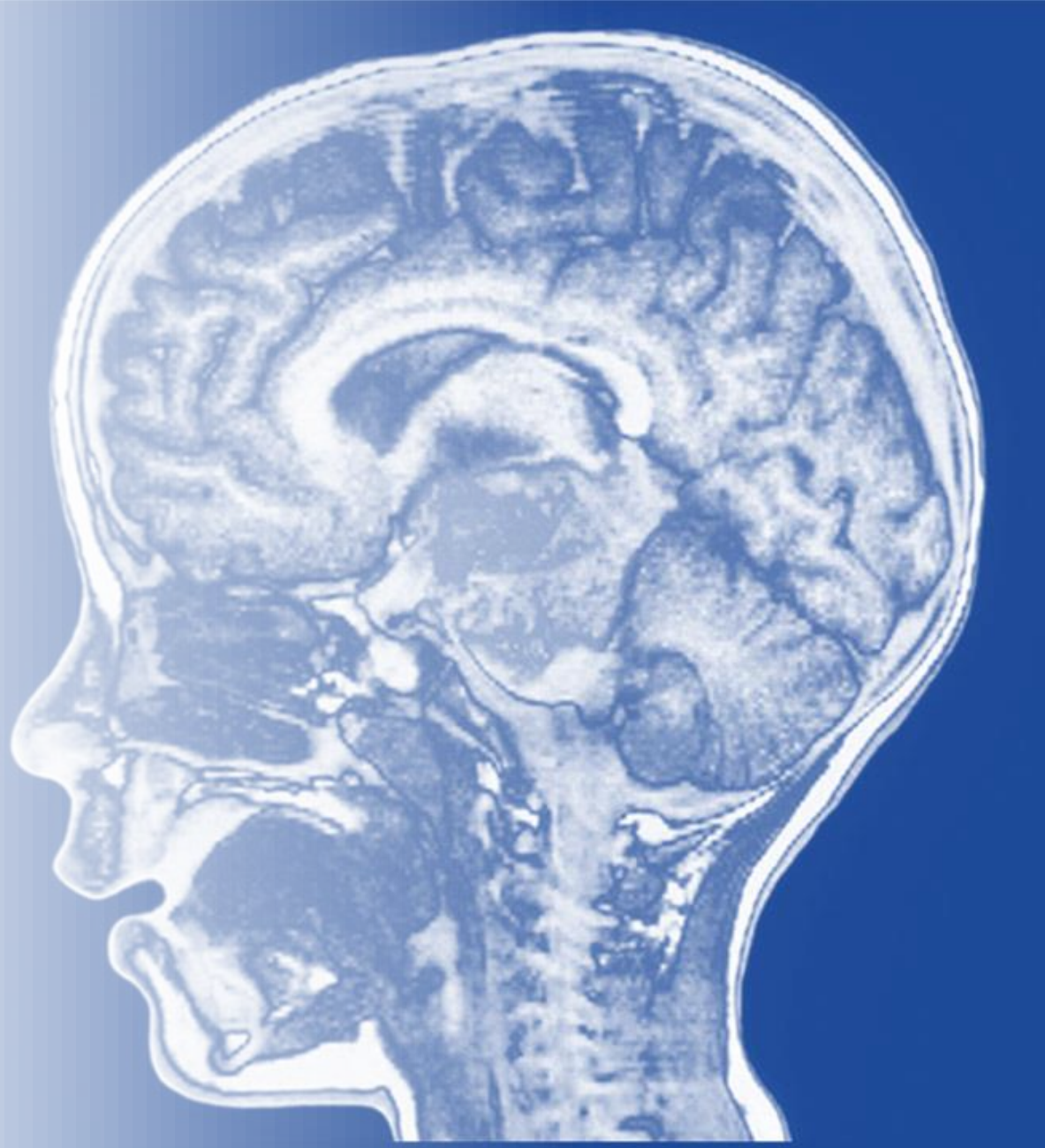
ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν Πανεπιστήμιον Αθηνών
ΙΔΡΥΘΕΝ ΤΟ 1837

Neurooncology:
Clinical presentation-Symptoms
Basic principles of treatment



Kleoniki Roka, MD, PhD

Senior Attending Physician

University Unit of Pediatric Oncology-Hematology (UPOHem)

1st Pediatric Clinic NKUA

"Aghia Sophia" Children's Hospital

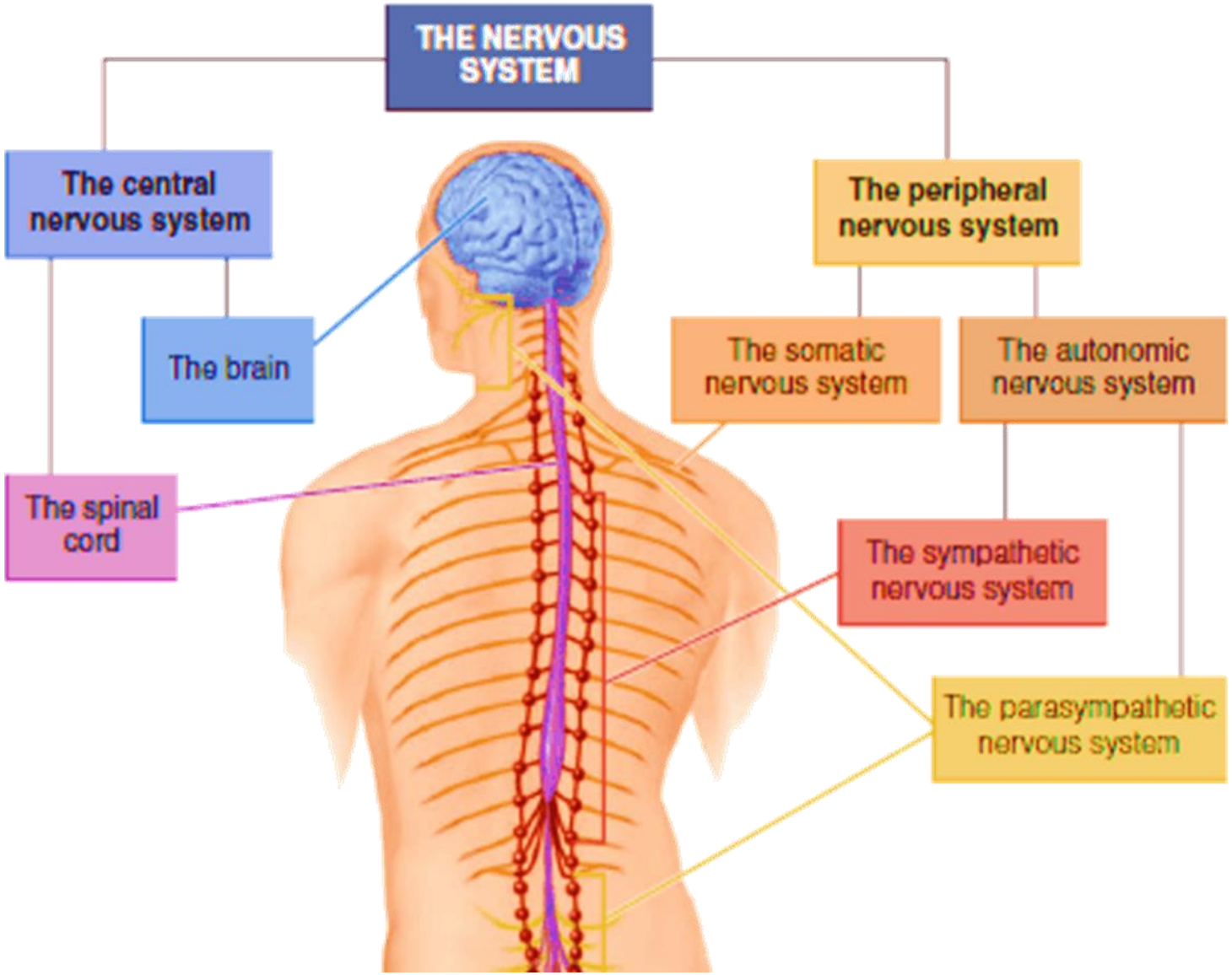
25.11.2025

Structure

- Introduction
- Clinical presentation
- Imaging studies
- Basic principles of treatment
- Conclusions

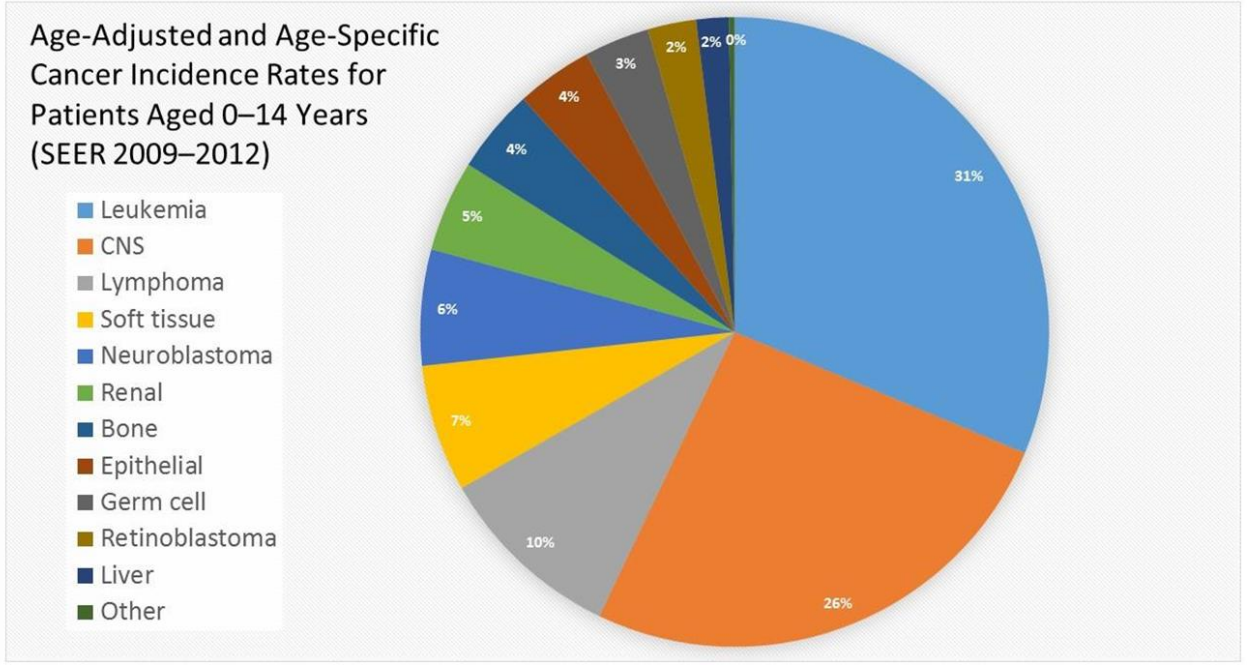
Introduction

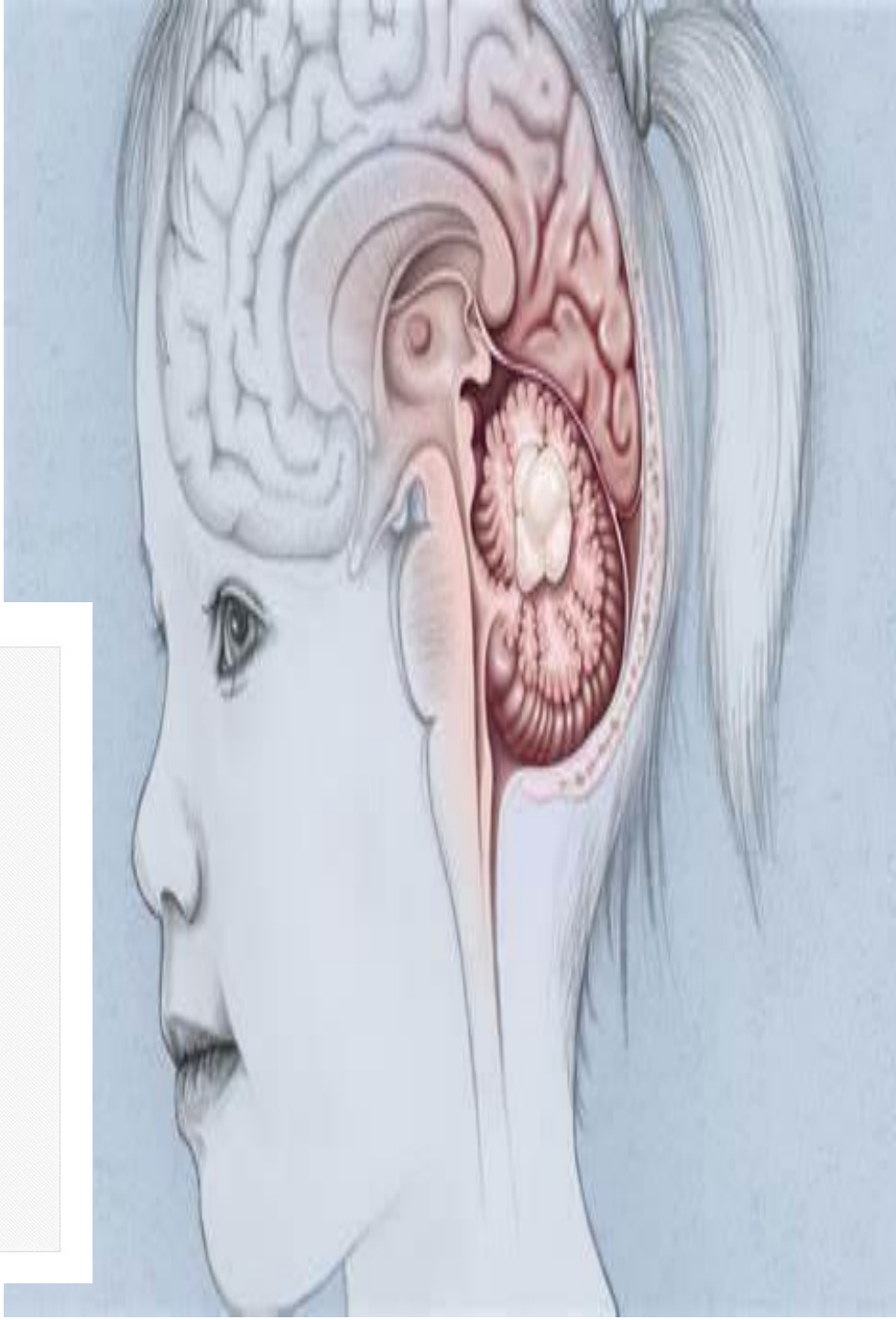
Nervous system



Epidemiology

- The 2nd most common neoplasm in childhhood





Epidemiology

- The 1st cause of cancer-related death in childhood
- The 2nd cause of death in childhood after accidents

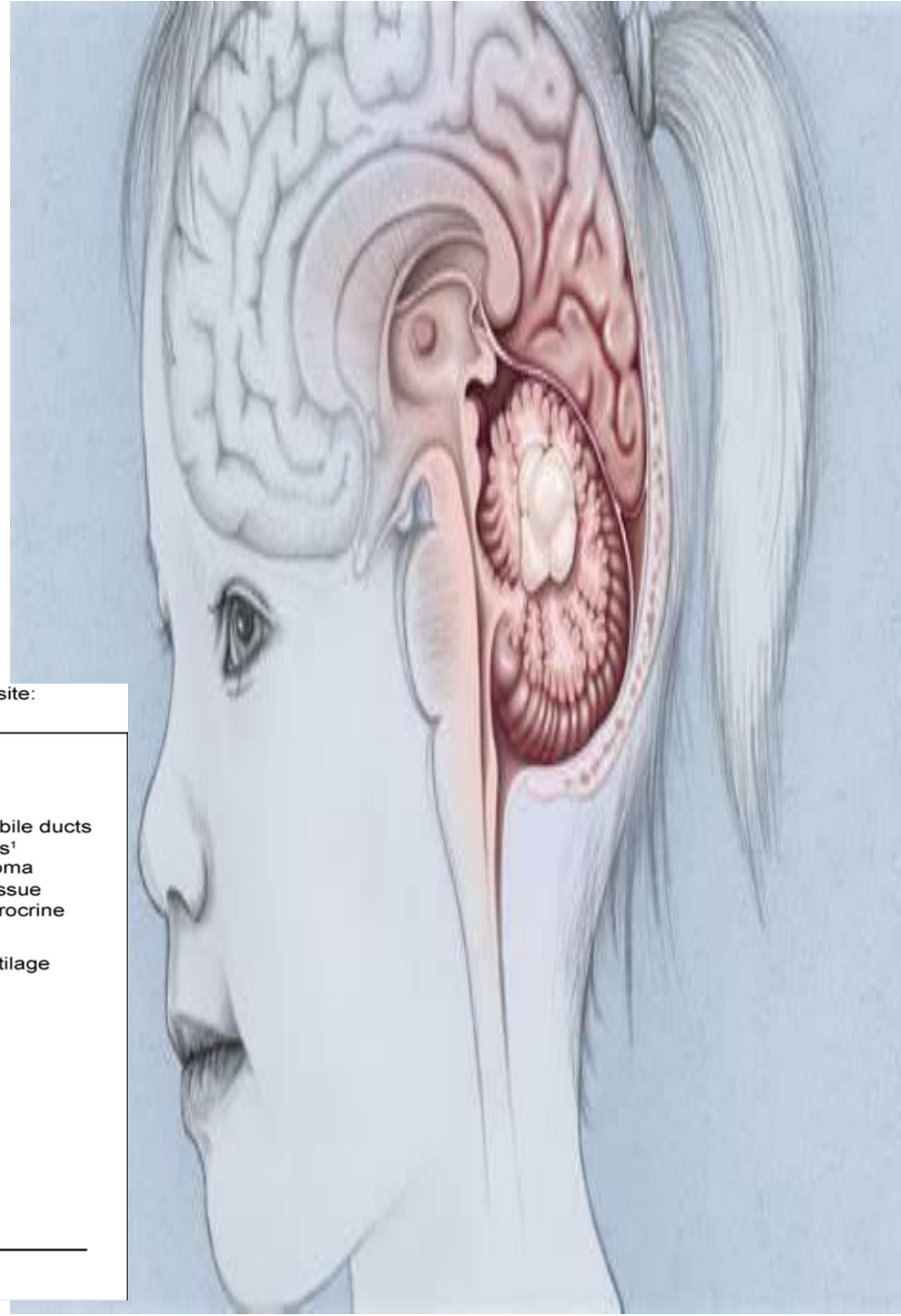
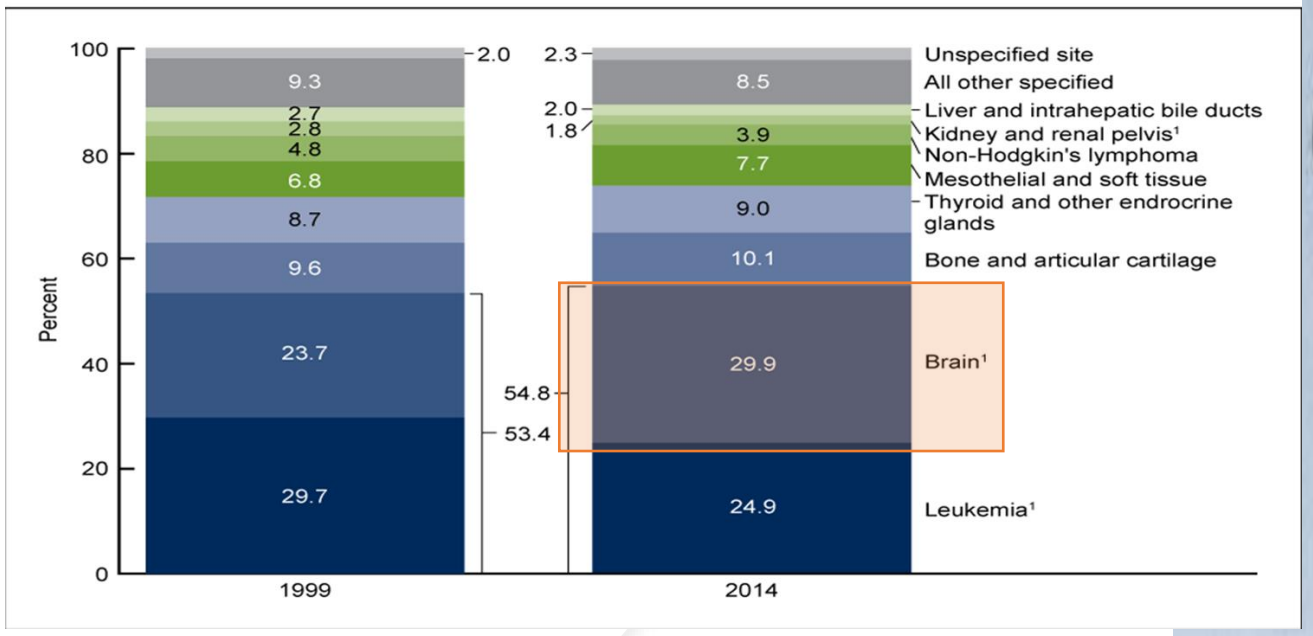


Figure 4. Percent distribution of cancer deaths for children and adolescents aged 1–19 years, by anatomical site: United States, 1999 and 2014



Epidemiology

- The estimated **5-year OS** for children diagnosed with CNS tumor in 2017 was **76%**

- There is a wide heterogeneity in survival, from **2-year OS** under **10%** in DIPGs to **5-year OS** of **95%** in pLGGs

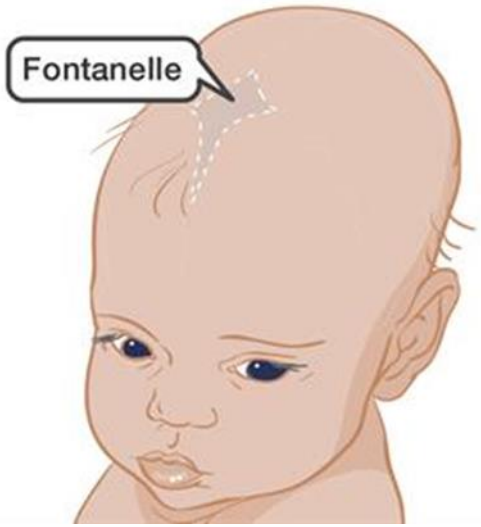
Qaddoumi et al, Cancer 2009,115(24):5761-70
Crotty et al. J Neurooncol 2020,148(3):607-617

Clinical presentation

SYMPTOMS

The symptoms differ according to:

- age

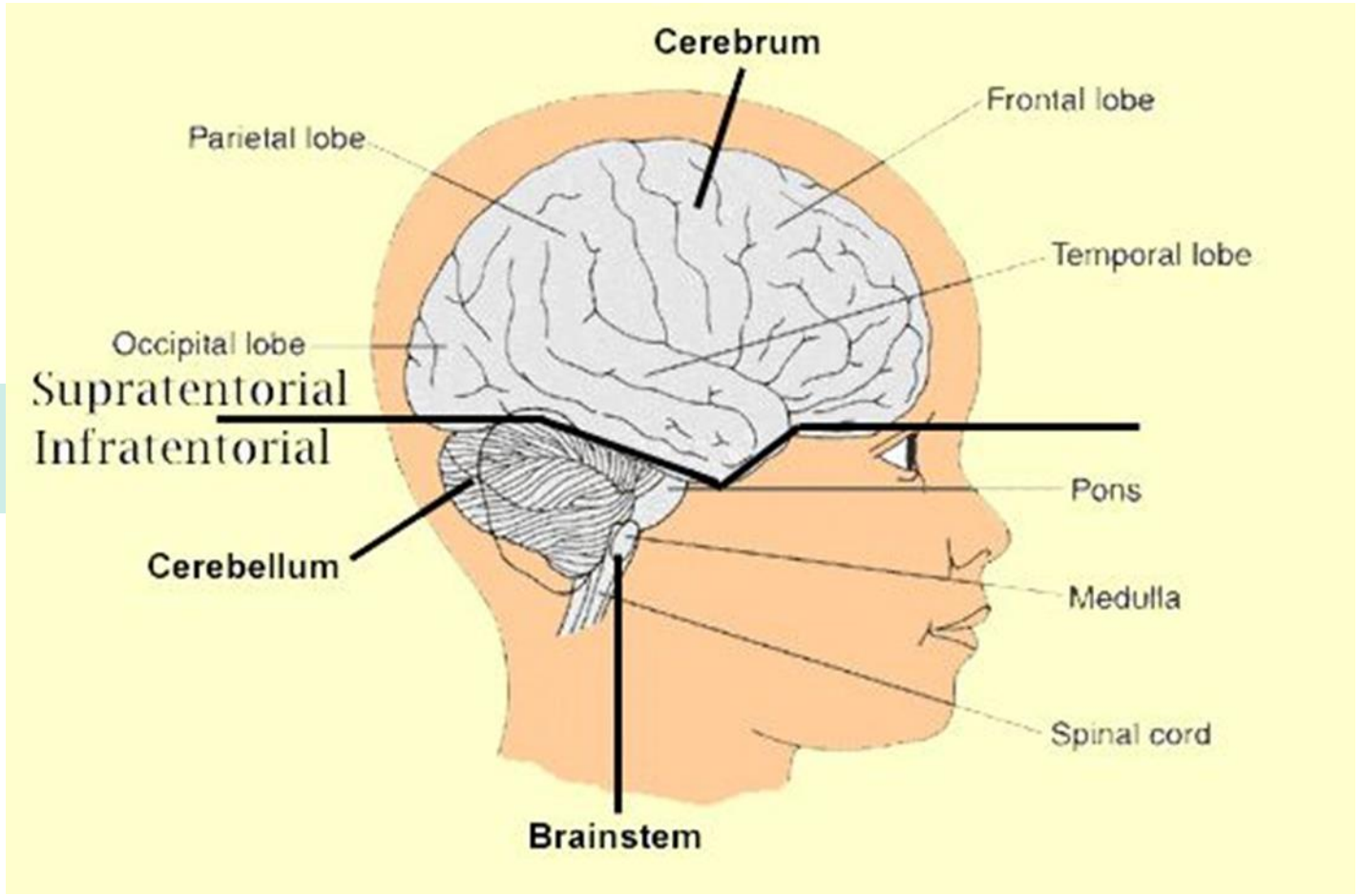


SYMPTOMS

The symptoms differ according to:

- age
- location

<3 years: supratentorial tumors
4-10 years: posterior fossa



SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

   - Headaches

✓ 1/3 of the patients
✓ They are usually described at night, wake up the child and are continuous
✓ Other concomitant symptoms are described

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

- Headaches
- Nausea and vomiting

✓ 1/3 of the patients
Differential diagnosis: viral gastroenteritis which is more usual

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

- Headaches
- Nausea and vomiting
- Irritability

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

   - Headaches
   - Nausea and vomiting
   - Irritability
   - Lethargy

SYMPTOMS

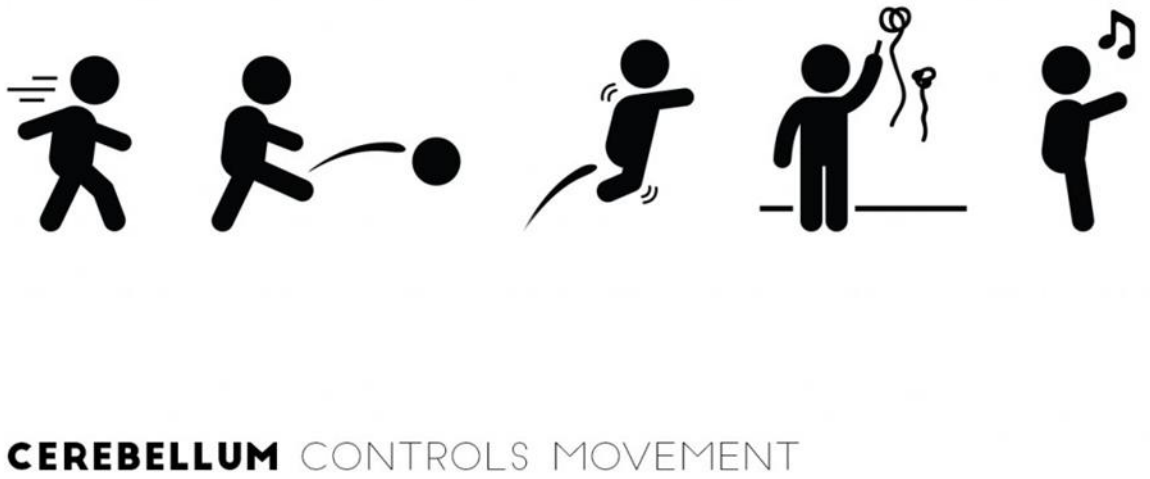
1. **<u>Signs of increased intracranial pressure</u>**

- Headaches
- Nausea and vomiting
- Irritability
- Lethargy, sleepiness
- Torticollis

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

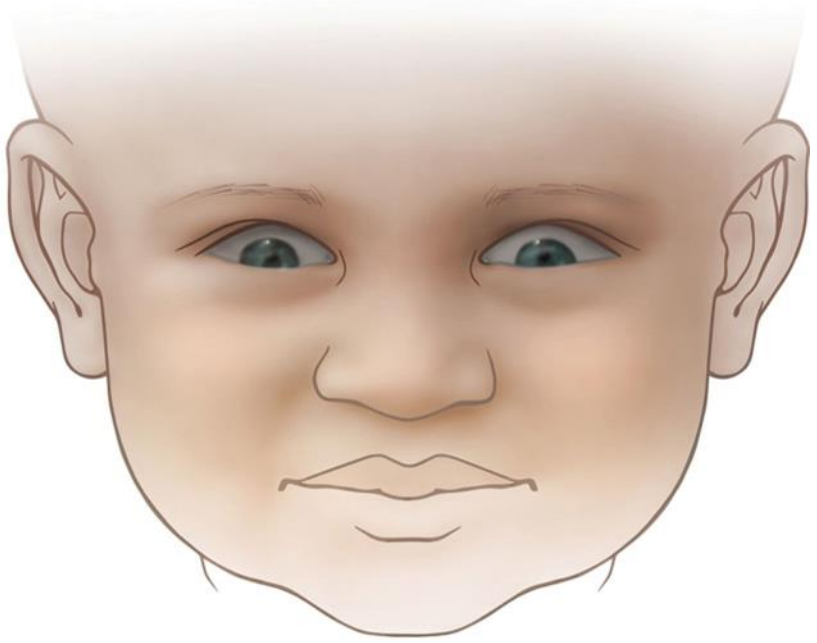
- Headaches
- Nausea and vomiting
- Irritability
- Lethargy, sleepiness
- Torticollis
- Ataxia



SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

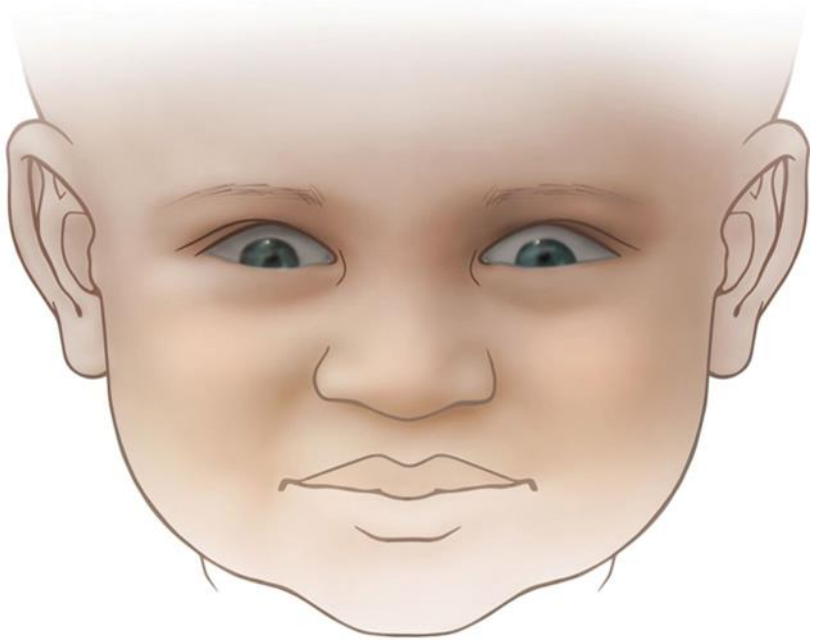
- Headaches
- Nausea and vomiting
- Irritability
- Lethargy, sleepiness
- Torticollis
- Ataxia
- Sunset eye sign



SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

- Headaches
- Nausea and vomiting
- Irritability
- Lethargy, sleepiness
- Torticollis
- Ataxia
- Sunset eye sign



!!! In infants, increased intracranial pressure may only cause increase of the head circumference due to open fontanelle

SYMPTOMS

1. **Signs of increased intracranial pressure**

2. **Focal symptoms**

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

2. **<u>Focal symptoms</u>**

    -hemiparesis

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

2. **<u>Focal symptoms</u>**

    -hemiparesis

    -paresis of the cranial nerves

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

2. **<u>Focal symptoms</u>**

    -hemiparesis

    -paresis of the cranial nerves

    -seizures

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**

2. **<u>Focal symptoms</u>**

    -hemiparesis

    -paresis of the cranial nerves

    -seizures

    -visual problems

SYMPTOMS

1. **Signs of increased intracranial pressure**
2. **Focal symptoms**
3. **General symptoms**

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**
2. **<u>Focal symptoms</u>**
3. **<u>General symptoms</u>**

    - body weight changes

SYMPTOMS

1. **Signs of increased intracranial pressure**
2. **Focal symptoms**
3. **General symptoms**

    - body weight changes

    - changes in behaviour or school performance

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**
2. **<u>Focal symptoms</u>**
3. **<u>General symptoms</u>**

    - body weight changes

    - changes in behaviour or school performance

    - endocrine disorders

SYMPTOMS

1. **<u>Signs of increased intracranial pressure</u>**
2. **<u>Focal symptoms</u>**
3. **<u>General symptoms</u>**

    - body weight changes

    - changes in behaviour or school performance

    - endocrine disorders

    - failure to thrive

SYMPTOMS

1. **Signs of increased intracranial pressure**
2. **Focal symptoms**
3. **General symptoms**
4. **Underlying cancer predisposition syndromes**

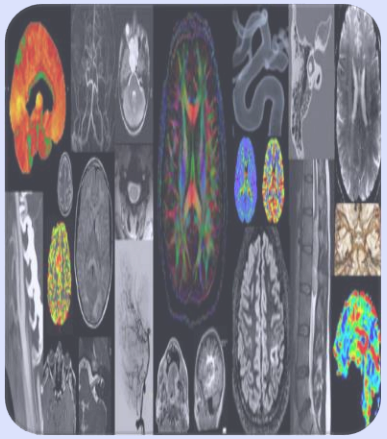
- Neurofibromatosis type 1 and 2
- Tuberous sclerosis
- Li Fraumeni syndrom

The clinical triad **headache, nausea,** and **instability/ataxia** are usually found in tumors located in the posterior cranial fossa

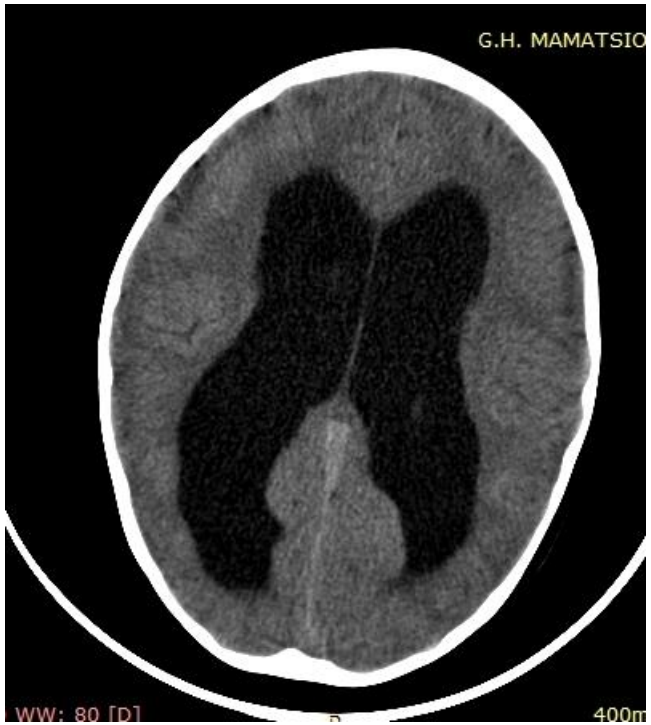
Imaging studies

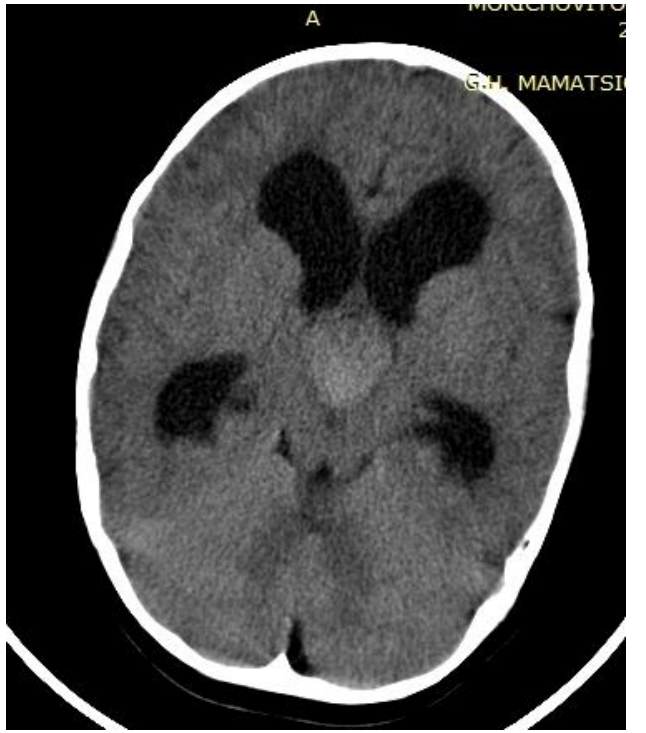
Imaging studies

1. In case of emergency: **CT scan**



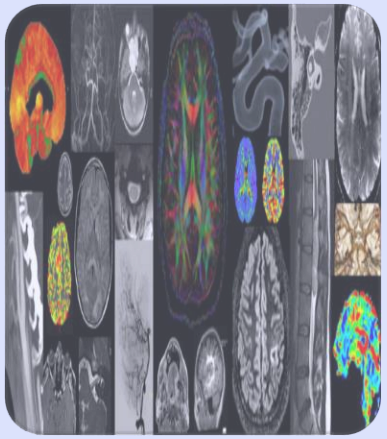
Imaging characteristics



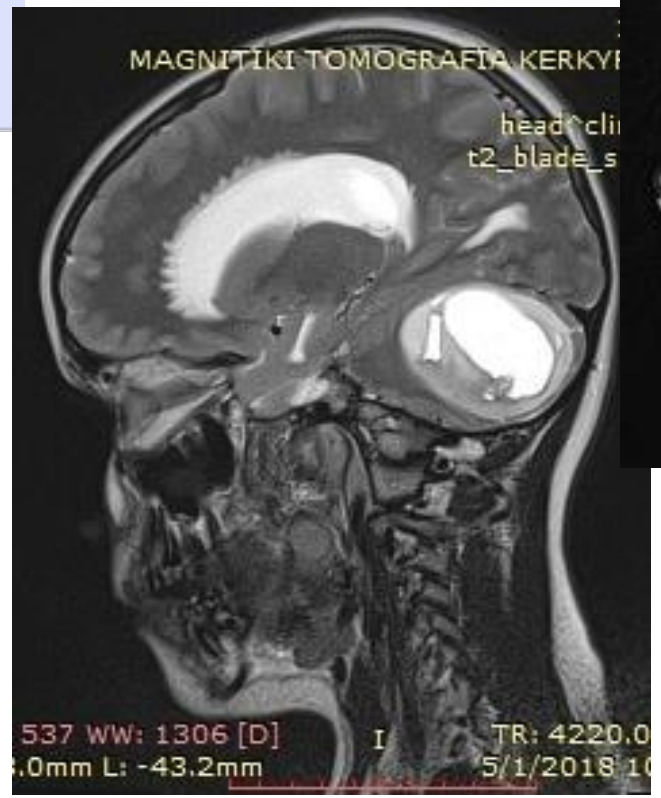


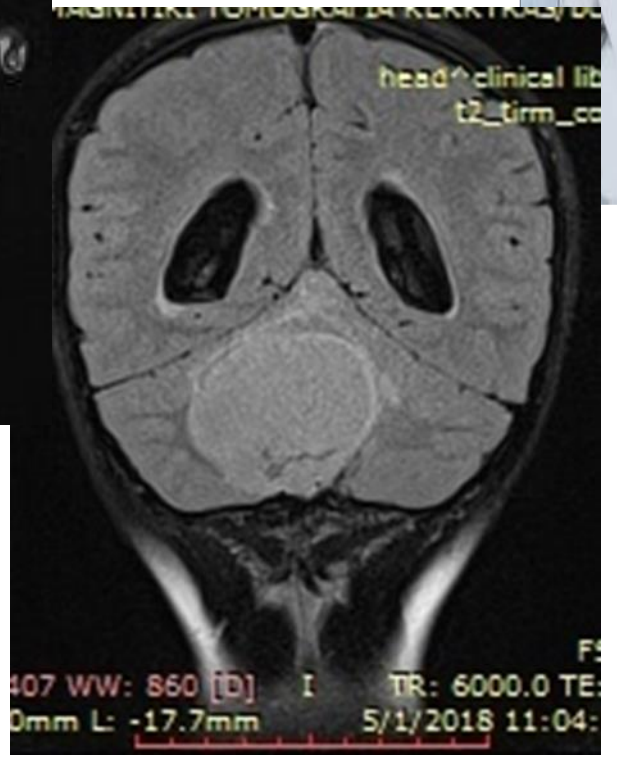
Imaging studies

2. Imaging modality of choice: **Magnetic resonance tomography**



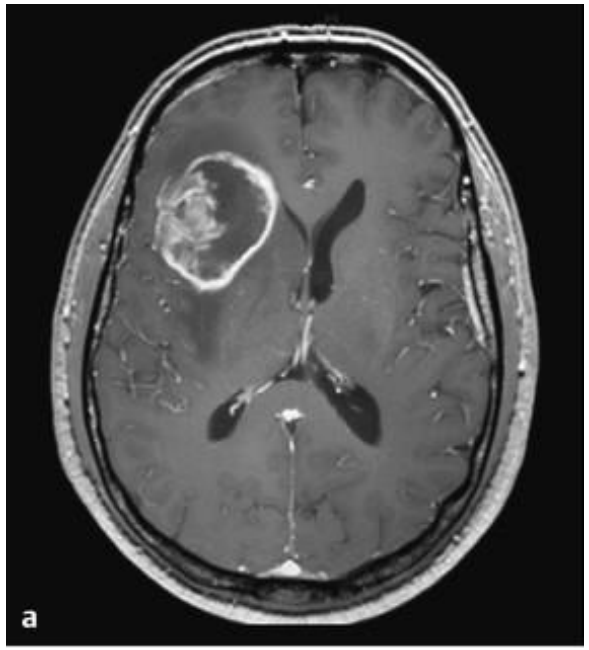
Imaging characteristics

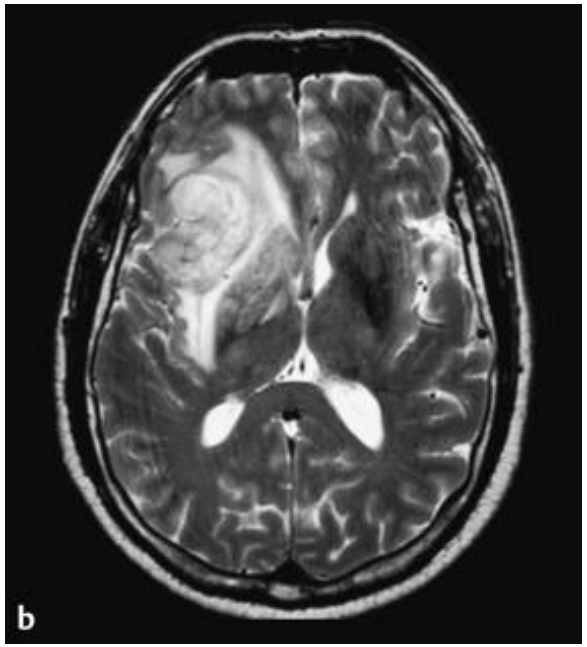


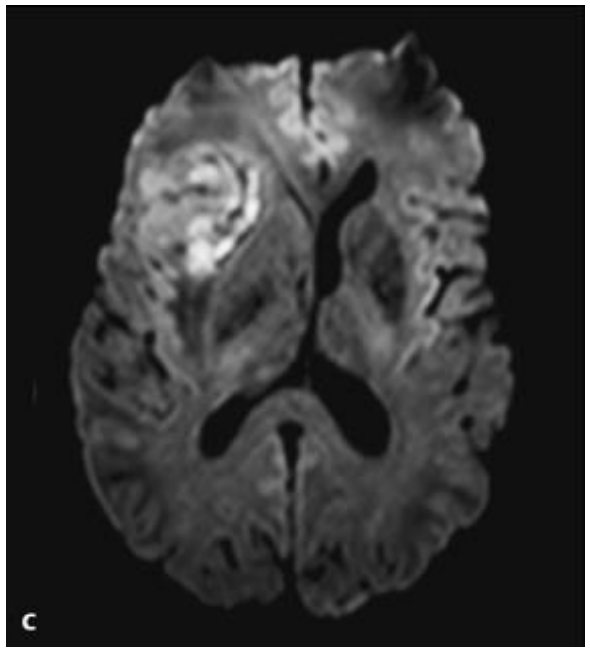


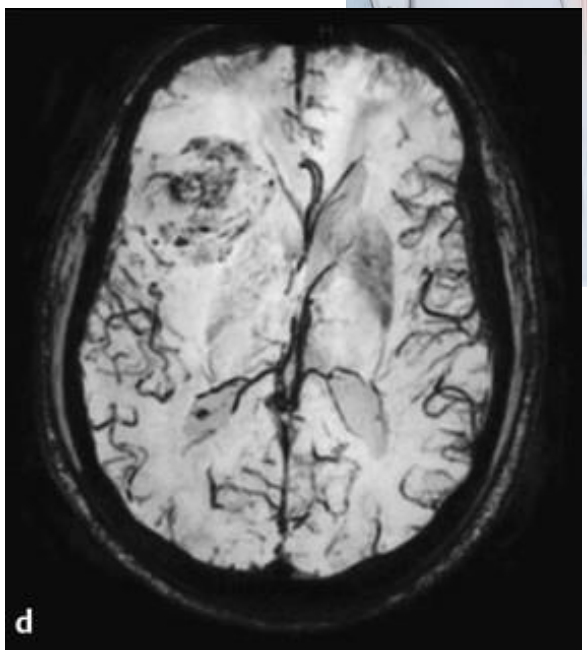
Imaging studies

2. Imaging modality of choice: **Magnetic resonance tomography and additional sequences**



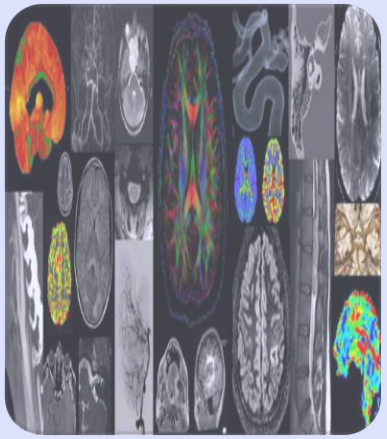




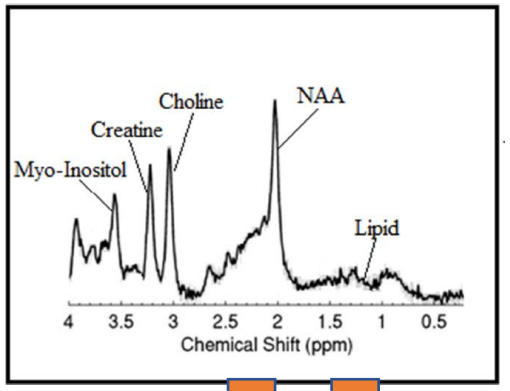


Imaging studies

3. Modern imaging techniques: **Magnetic Resonance Spectroscopy**



Imaging characteristics



!! MRS **cannot be performed in** all CNS tumors

It depends on the **dimensions** and the **location** of the tumors

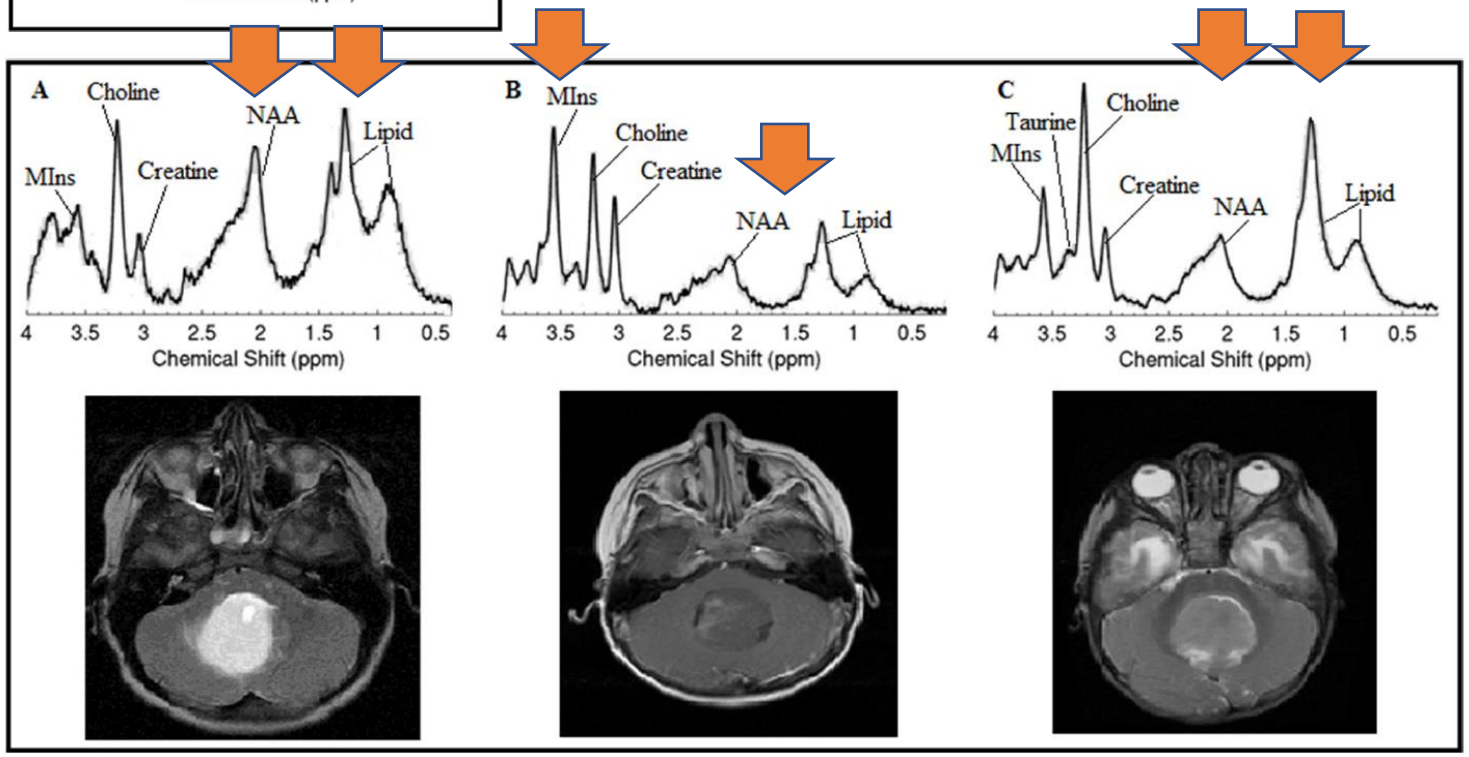
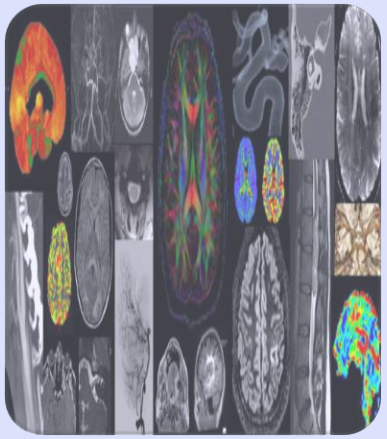


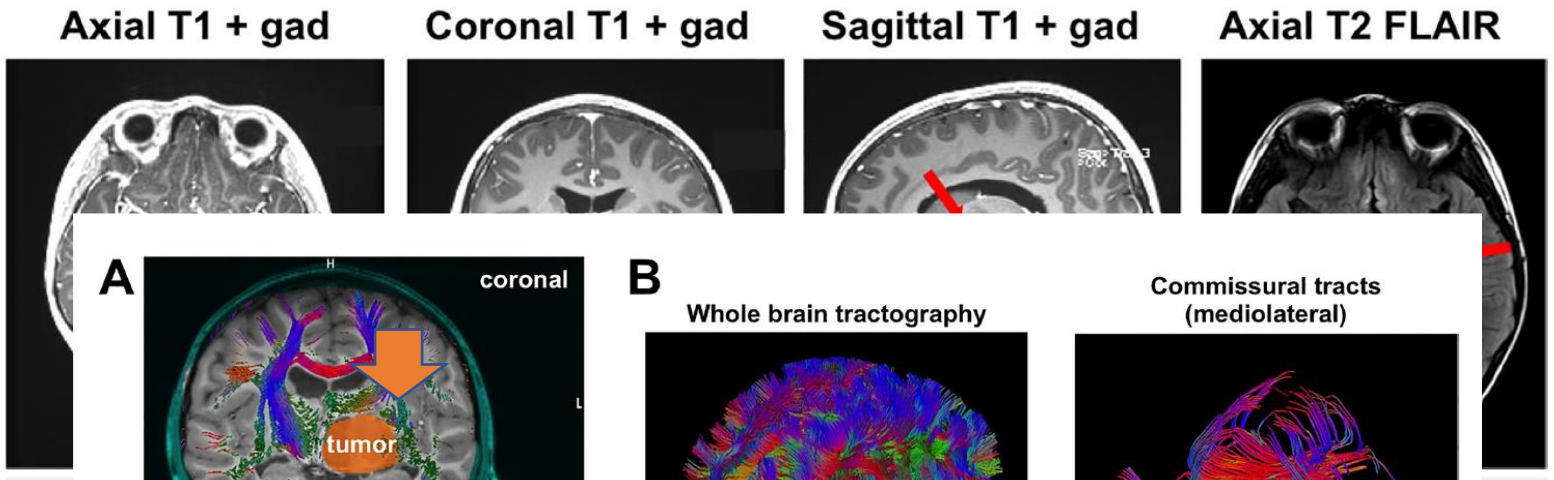
Figure 2 Magnetic resonance spectrum (MRS) profiles of cerebellar tumours. MR images and MRS profiles of (A) pilocytic astrocytoma, (B) ependymoma and (C) medulloblastoma. NAA, N-acetylaspartate.

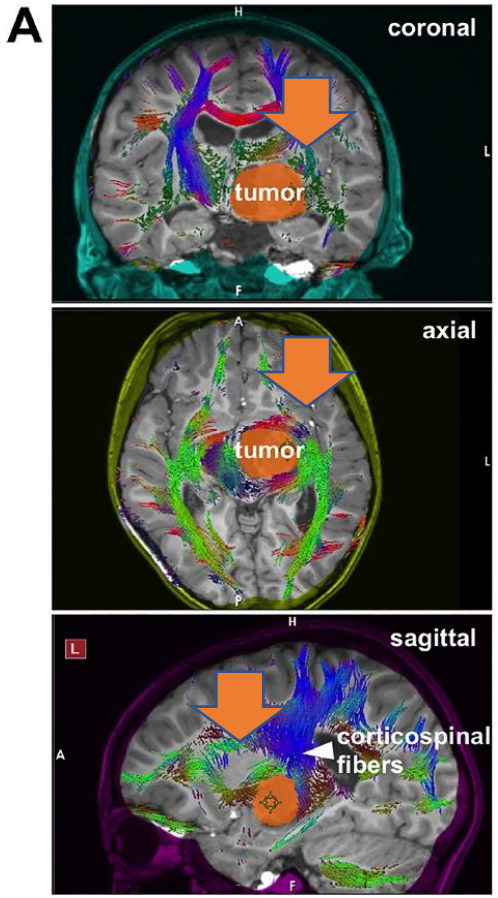
Imaging studies

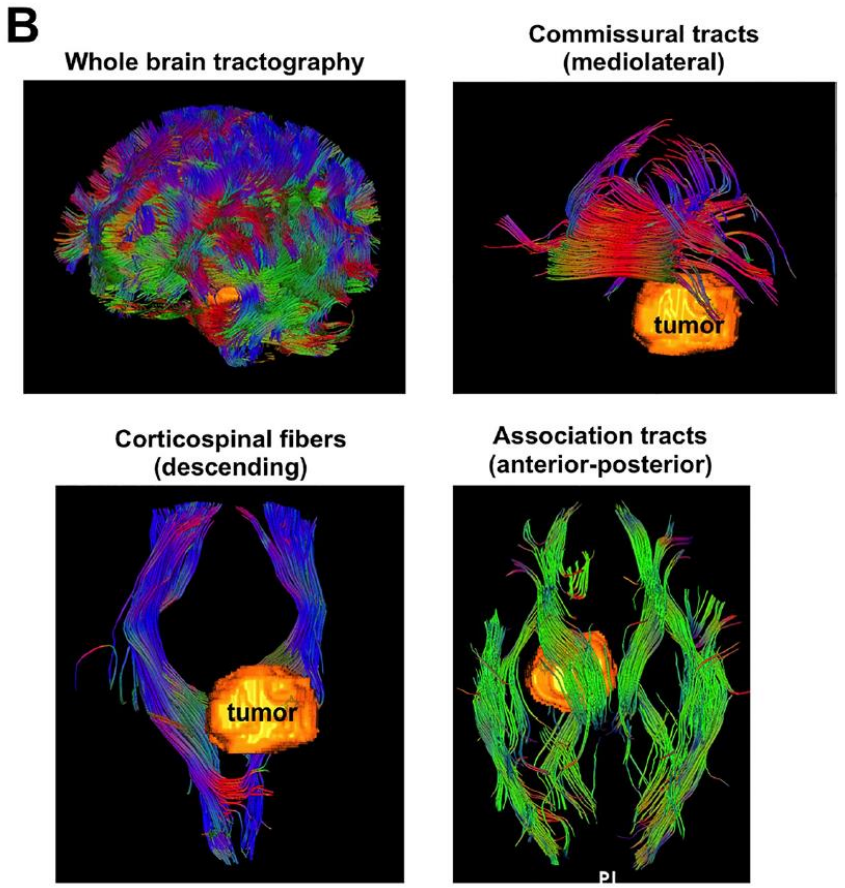
4. Modern imaging techniques: **Magnetic resonance tractography**



Imaging characteristics







Staging

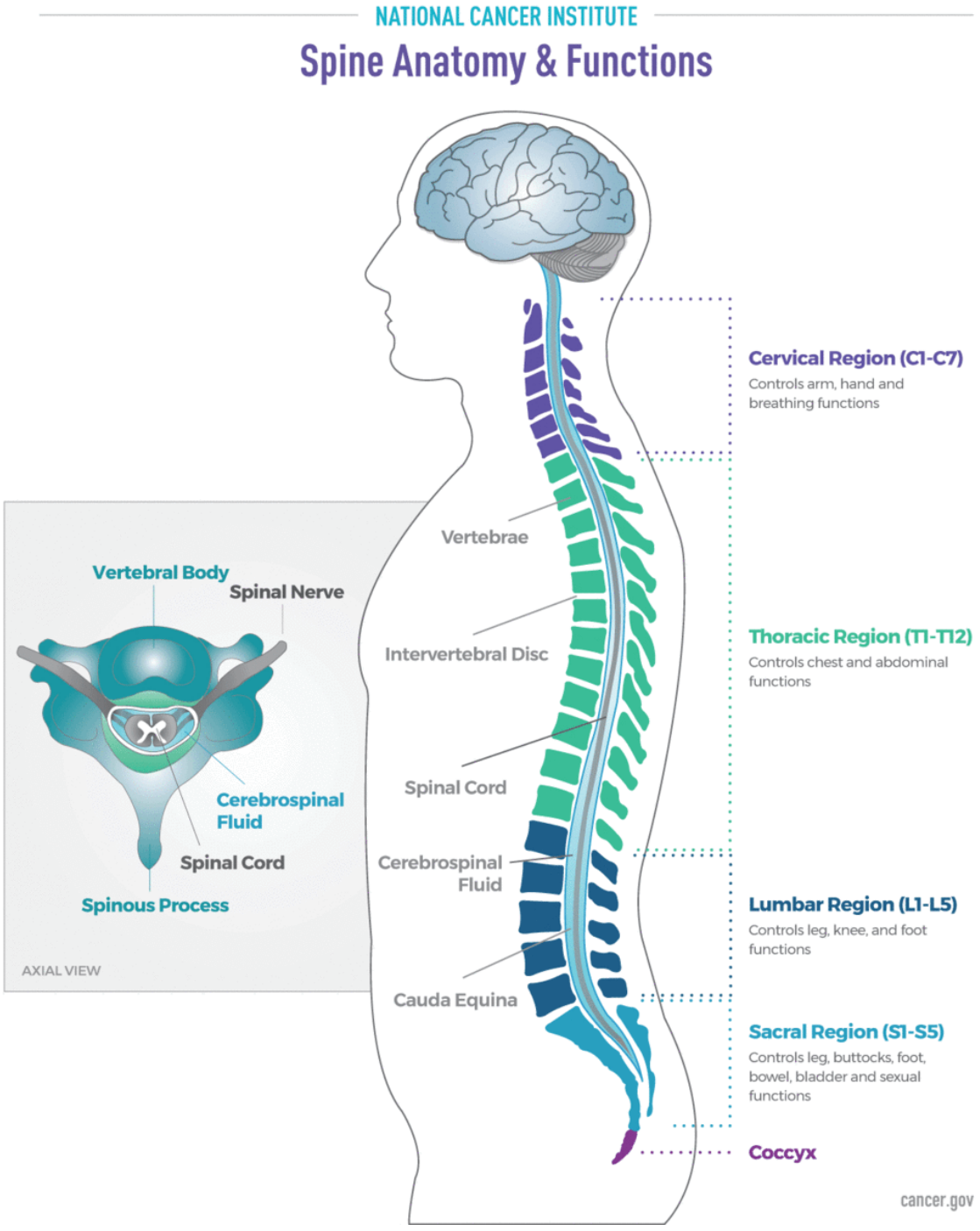
- **MRI of the spine**

If the location of the tumor is in the spine, additional brain MRI is needed

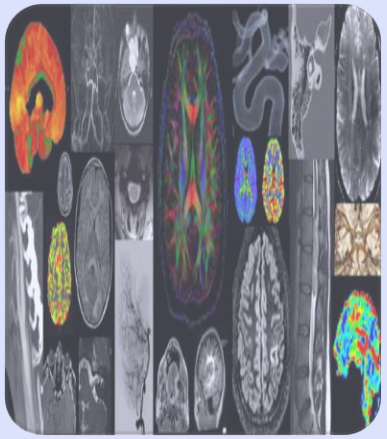
Spinal MRI is preferred to be performed preoperatively

- **CSF for cytological examination**

It should be performed during surgery or on day 15 after surgery**



Imaging studies



Imaging characteristics

After surgery, postoperative MRI should be performed **within 24-72h to detect** residual mass

Imaging studies

4.4. Conventional RT, enhanced dose (35.2 Gy CSI + posterior fossa boost) with Maintenance chemotherapy

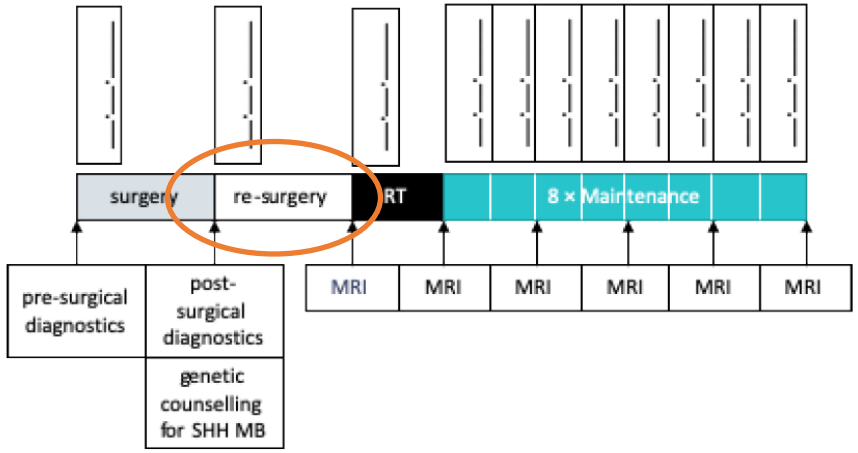
Indications

Age	Histo-logically defined	MYC/ MYCN	Genetically defined	Methylation class	Staging
4–21 y	CMB	Neg nor NA	WNT SHH-TP53wt non-WNT/non-SHH	WNT SHH-A (child/adult) Group 3/4	M0R+, or M1
4-21 y	CMB	pos.	WNT	WNT	M0R0, M0R+, M1
4-21 y	CMB	MYCN pos	SHH-TP53wt	SHH-A (child/adult)	M0R0, M0R+, M1
4-21 y	CMB	MYC pos	non-WNT/non-SHH	Group 3	M0R0, M0R+, M1
4-21 y	CMB	MYCN pos	non-WNT/non-SHH	Group 4	(M0R0), M0R+, M1
4-21 y	LCA	any	WNT SHH-TP53wt non-WNT/non-SHH	WNT SHH-A (child/adult) Group 3/4	M0R0, M0R+; M1
5-21 y	DMB	neg	SHH-TP53wt	SHH-A (child/adult)	M0R+ or M1
5-21 y	DMB,	MYCN pos.	SHH-TP53wt	SHH-A (child/adult)	M0R0, M0R+, M1

DMB: desmoplastic medulloblastoma, CMB: classical medulloblastoma, LCA: large cell anaplastic medulloblastoma, Medulloblastom: MYC/N neg: no MYC and no MYCN amplification, MYCN pos: MYCN amplification, no MYC amplification; MYC pos: MYC amplification, no MYCN amplification; NA: not available; post: MYC or MYCN amplification; R+≥1,5cm².

Notes

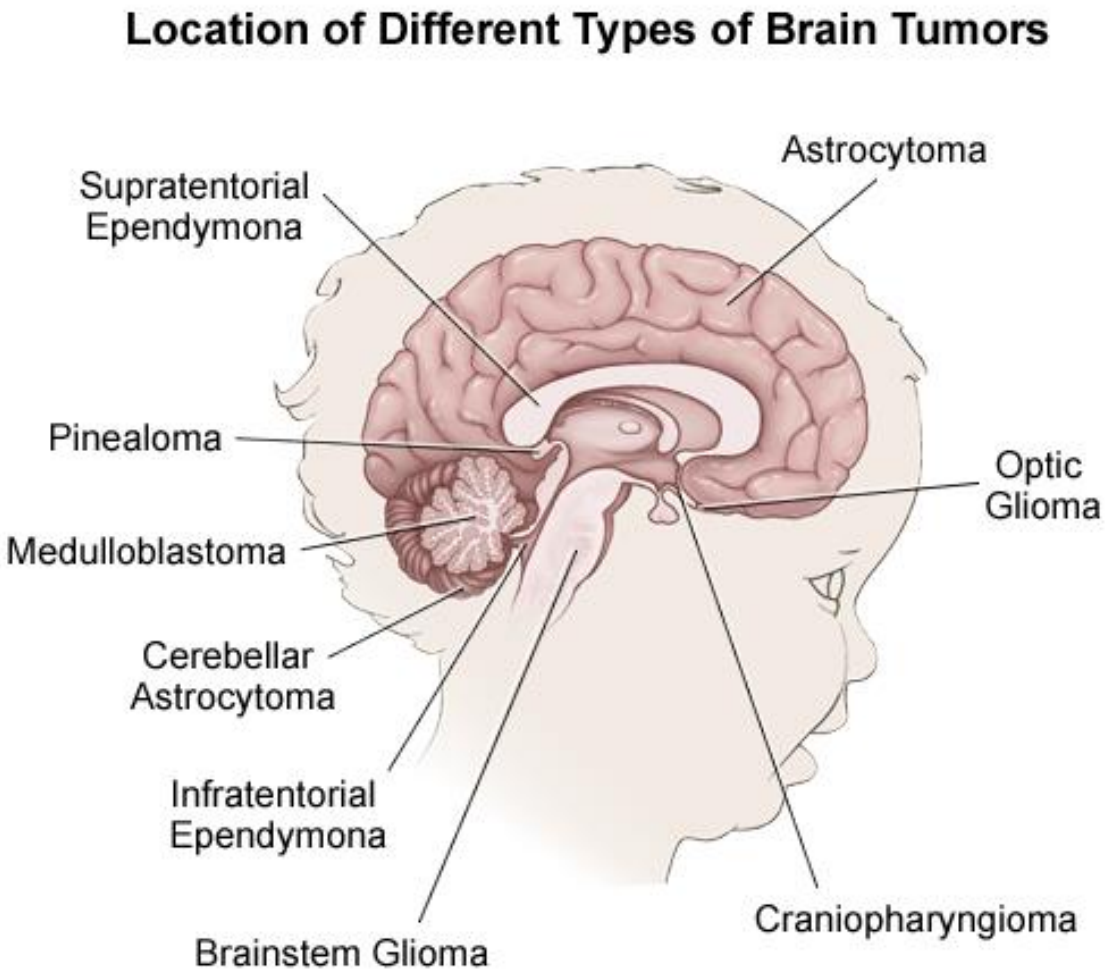
- In case of WNT-pathway-activation, please check eligibility for trials (e. g. PNET 5 MB)!
- Optimal time for second surgery is before radiotherapy. Evaluate re-surgery in patients not in CR at every staging
- Maintenance chemotherapy may be toxic. Monitoring of toxicity is crucial and dose modifications are frequently required (see guidelines). Dose reduction was not associated with inferior prognosis in HIT'91 (von Hoff Eur J Cancer 2009). Maintenance chemotherapy according to POG9031 (Tarbell JCO 2013) or Packer JCO 2006 may be alternatives.
- Evidence for efficacy of vincristine during RT is limited.
- **Please consider genetic counselling in case of SHH-pathway-activation before radiotherapy (esp- Gorlin-Goltz and Li-Fraumeni syndrome).**
- Presence of large residual tumour is associated with higher risk of relapse. Evidence for higher efficacy of a higher CSI dose in this condition is limited. Alternatively, 23,4 Gy CSI can be considered.

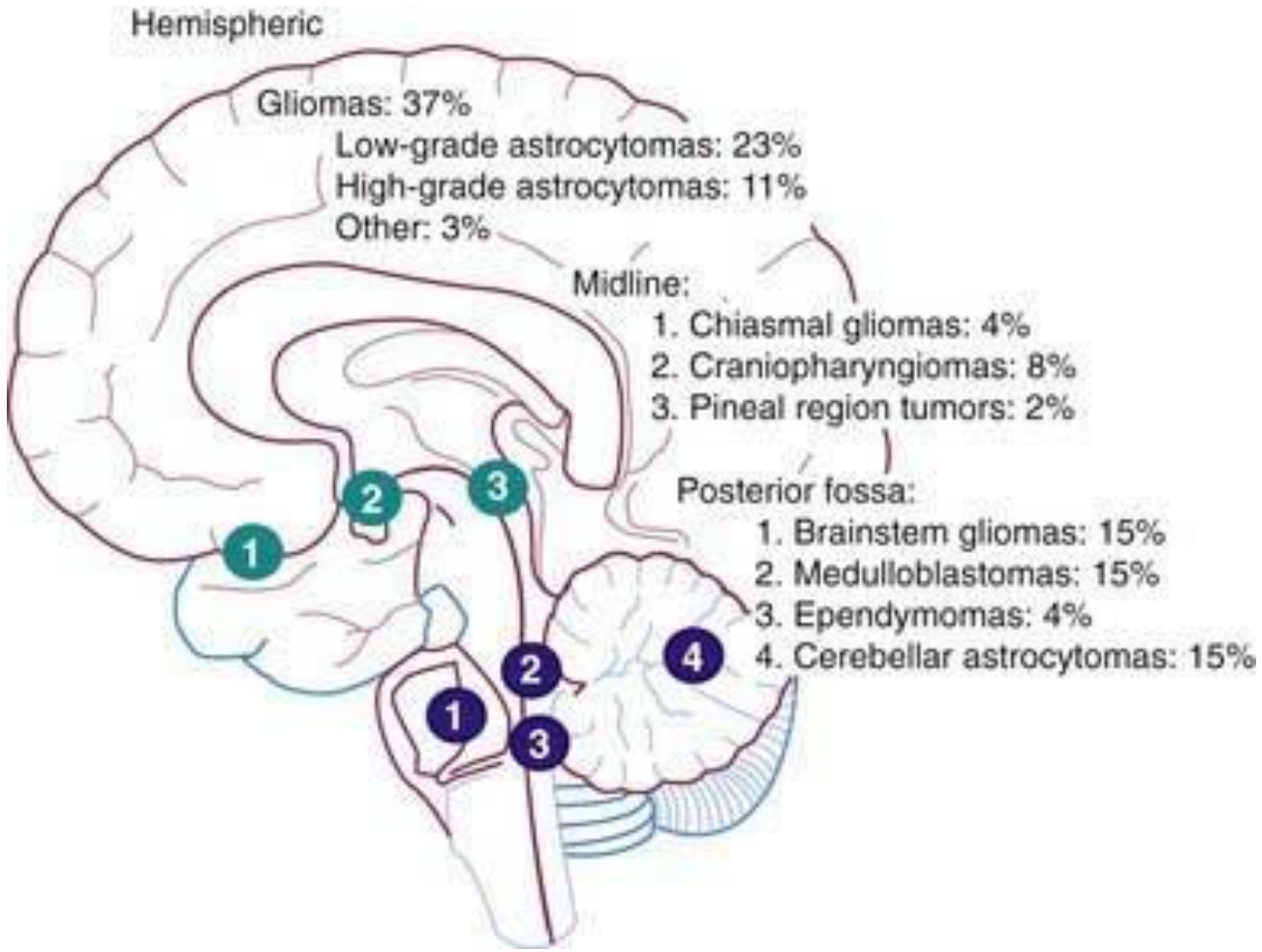


Maintenance (5.3)	Cisplatin/Lomustine/Vincristine Alternative maintenance chemotherapy regimens: - Cyclophosphamide: POG9031 (Tarbell JCO 2013) - Cyclophosphamide/Cisplatin/Vincristine (Packer JCO 2006) - Cisplatin/Lomustin/Vincristin alternating with Cyclophosphamide/Vincristine: ACNS-0331
Radiotherapy	CSI 35.2 Gy (consider 23.4Gy in R+ as only risk factor) posterior fossa boost 19.8 Gy (30.6 Gy) (total 55.0 Gy) Vincristine

All treatment regimens have been developed for primary treatment only. Neither whole regimens nor parts of them should be used for salvage therapy.

CNS tumor types





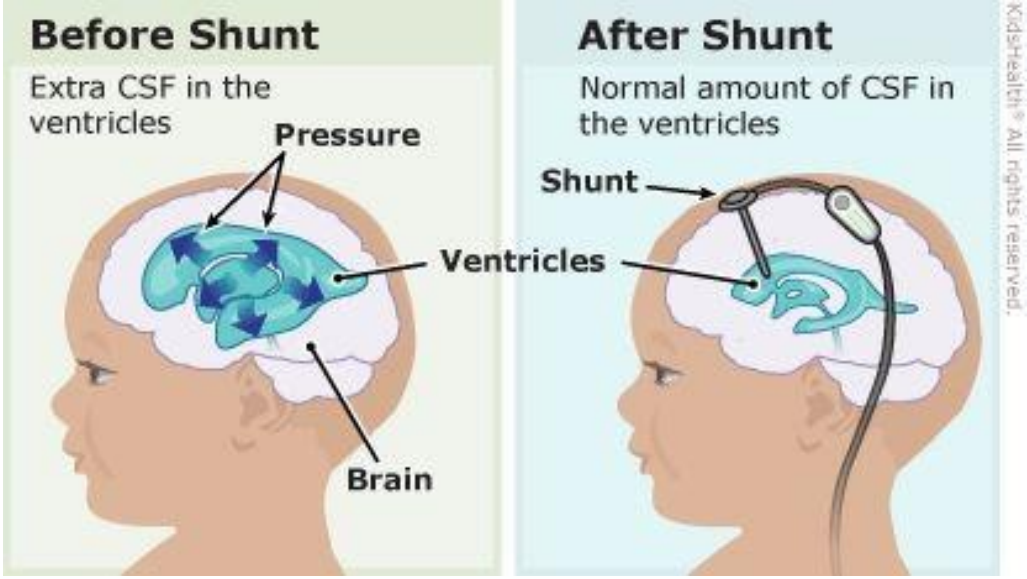
Structure

- Introduction
- Clinical presentation
- Imaging studies
- Basic principles of treatment
- Conclusions

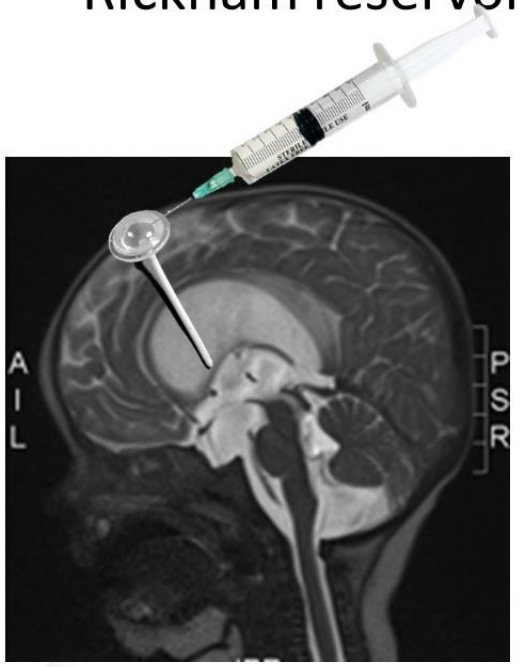
Basic principles of treatment

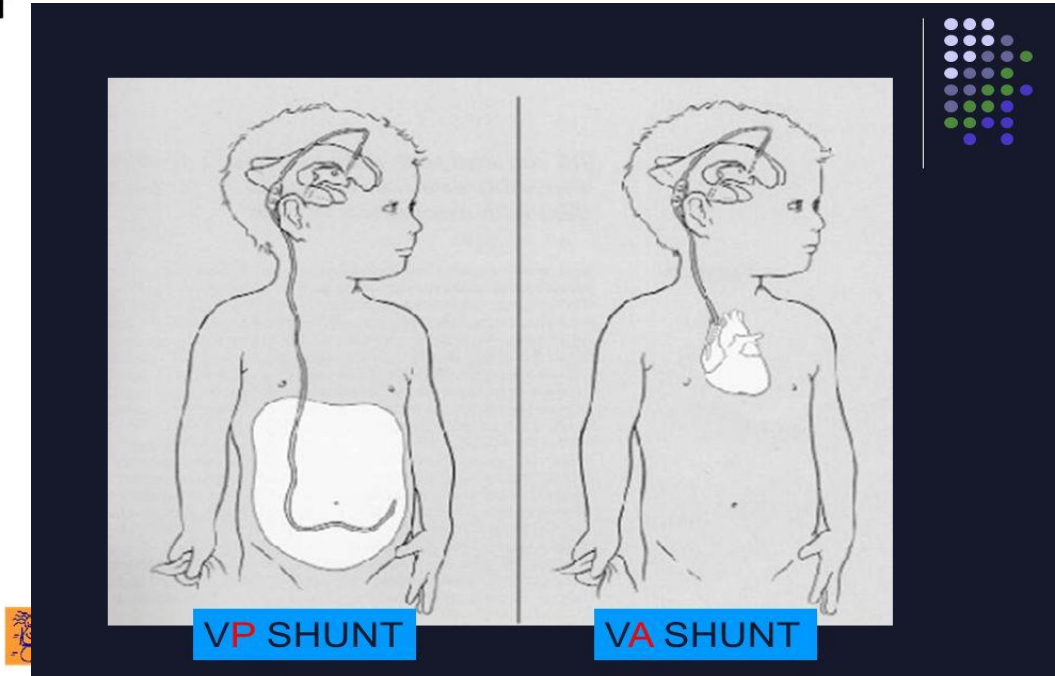
Initially treat the emergency

- **Acute obstructive hydrocephalus**

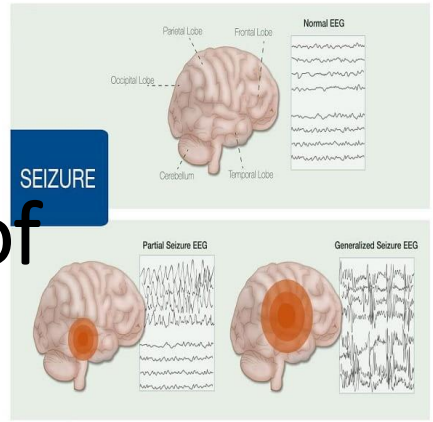


Rickham reservoir





Basic principles of treatment



Initially treat the emergency

- **Acute obstructive hydrocephalus**
- **Seizures**

- ✓ Patients with HGG are usually under **valproate sodium** because of its antineoplastic action
- ✓ **Certain histological subtypes** are correlated with increased risk of seizures **(long-term epilepsy associated tumors)**
- ✓ **Levatiracetam:** effectiveness, absence of significant interactions with other drugs, absence of hematological toxicity

REVIEW

OPEN

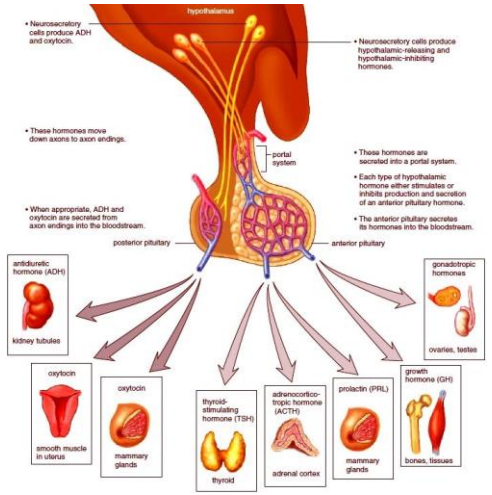
CURRENT OPINION

Management of epilepsy in brain tumor patients

Pim B. van der Meer[a], Martin J.B. Taphoorn[a,b], and Johan A.F. Koekkoek[a,b]

Van der Meer, Curr Opin in Oncol 2022;34(6):685-690

Basic principles of treatment



Initially treat the emergency

- **Acute obstructive hydrocephalus**
- **Seizures**
- **Endocrinological disorders**

✓ At diagnosis, **all patients** require an endocrine assessment of the function of the hypothalamic-pituitary axis

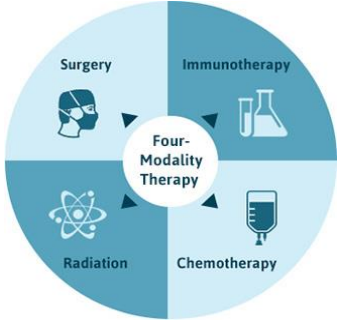
✓ Treatment with **hydrocortisone** is recommended at a stress dose pre- and postoperatively

✓ Postoperatively, homeostasis disorders and mainly **diabetes insipidus** may occur

✓ They are common as **late effects**, especially if the location is in the midline or if radiotherapy has been preceded

Claude F, Children 2022;9:1617

Basic principles of treatment



The treatment plan is based in the diagnosis (histological and molecular)

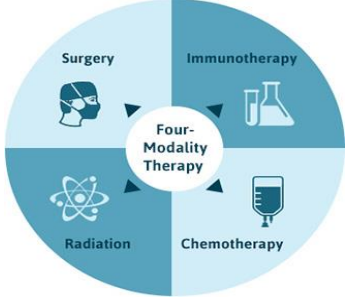
Surgery

1. In case of obstructive hydrocephalus, an insertion of VP shunt might be needed

2. **Surgical excision** is the treatment of choice if the tumor is neurosurgically accessible

3. Nowadays, it is considered necessary at least to take **a biopsy** for the histological and molecular classification of the tumor, with a few exceptions, e.g. in optic glioma (?)

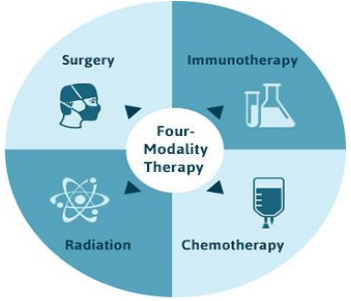
Basic principles of treatment



The treatment plan is based in the diagnosis (histological and molecular)

- Surgery
- Chemotherapy

Basic principles of treatment

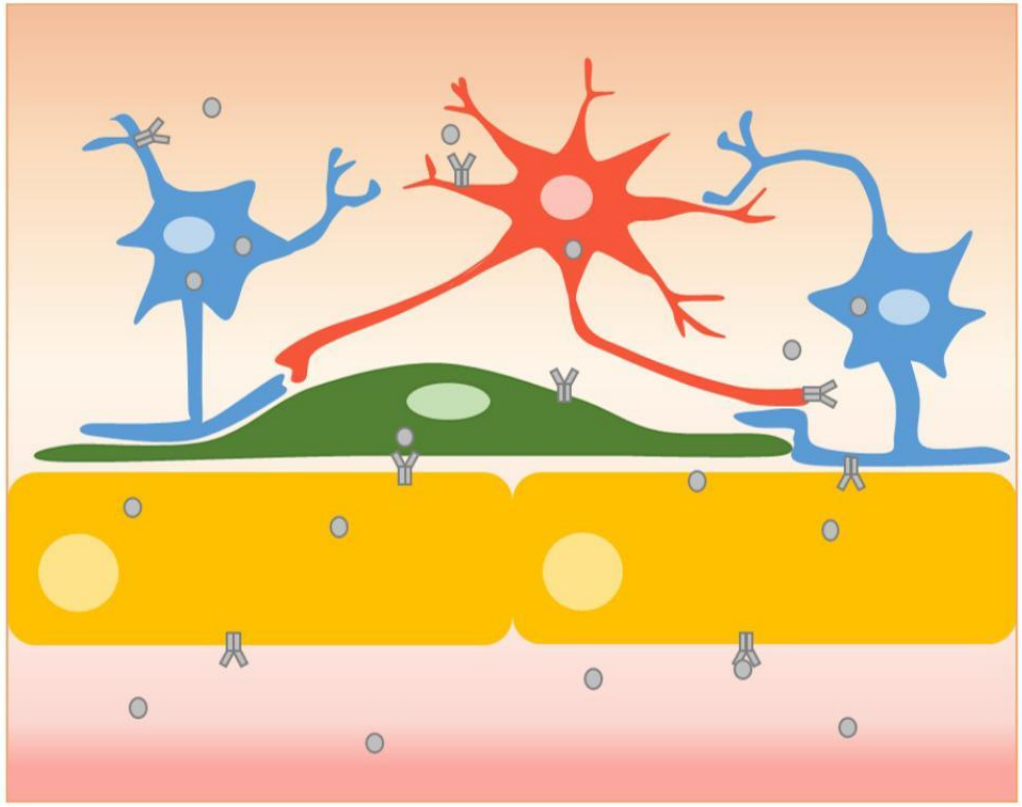


Neuron

- Peripheral metabolism
- Dopamine signaling
- Mitochondrial function
- Synapse density
- Supports cognition
- Tau phosphorylation
- IDE expression
- Aβ Interactions

Pericyte

- Proliferation
- Not involved in glucose uptake
- Hyperpolarization
- Protects endothelial cells
- Neuronal insulin sensitivity
- Vascular development



Astrocyte

- Morphology and circuit connectivity
- Mitochondrial function
- Dopamine and ATP release
- ApoE and GLUT1 expression levels
- Glucose BBB Transport

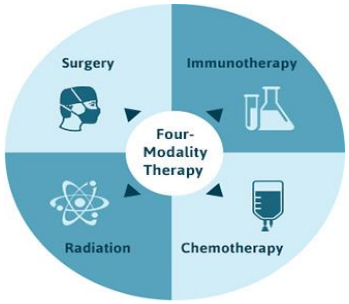
Endothelial Cell

- Vaso-regulation
- Potential role in tight junction structure
- Independent of insulin transport
- Regional CNS insulin signaling
- Aβ Transport

Blood brain barrier

Intraventricular chemotherapy

Basic principles of treatment

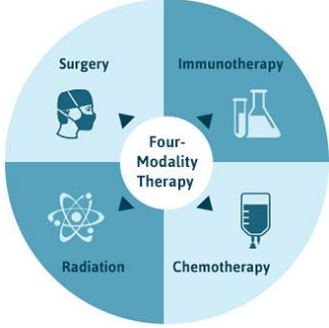


Surgery

Chemotherapy

1. It is used in tumours considered **chemosensitive**
2. It can be used in patients who **due to age** cannot receive radiation therapy.
3. It can be used in patients with partial surgical excision who show symptoms or disease progression or in diagnoses where surgical excision alone does not provide cure
4. **High dose chemotherapy** and **autologous transplantation**
5. Immunocompromise

Basic principles of treatment



The treatment plan is based in the diagnosis (histological and molecular)

Surgery

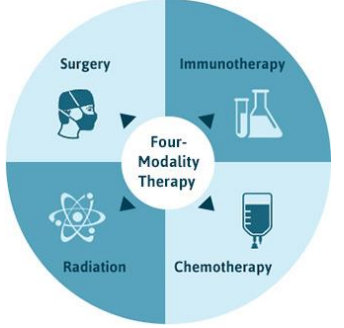
Chemotherapy

Radiotherapy

1. It is used in tumours considered **radiosensitive**

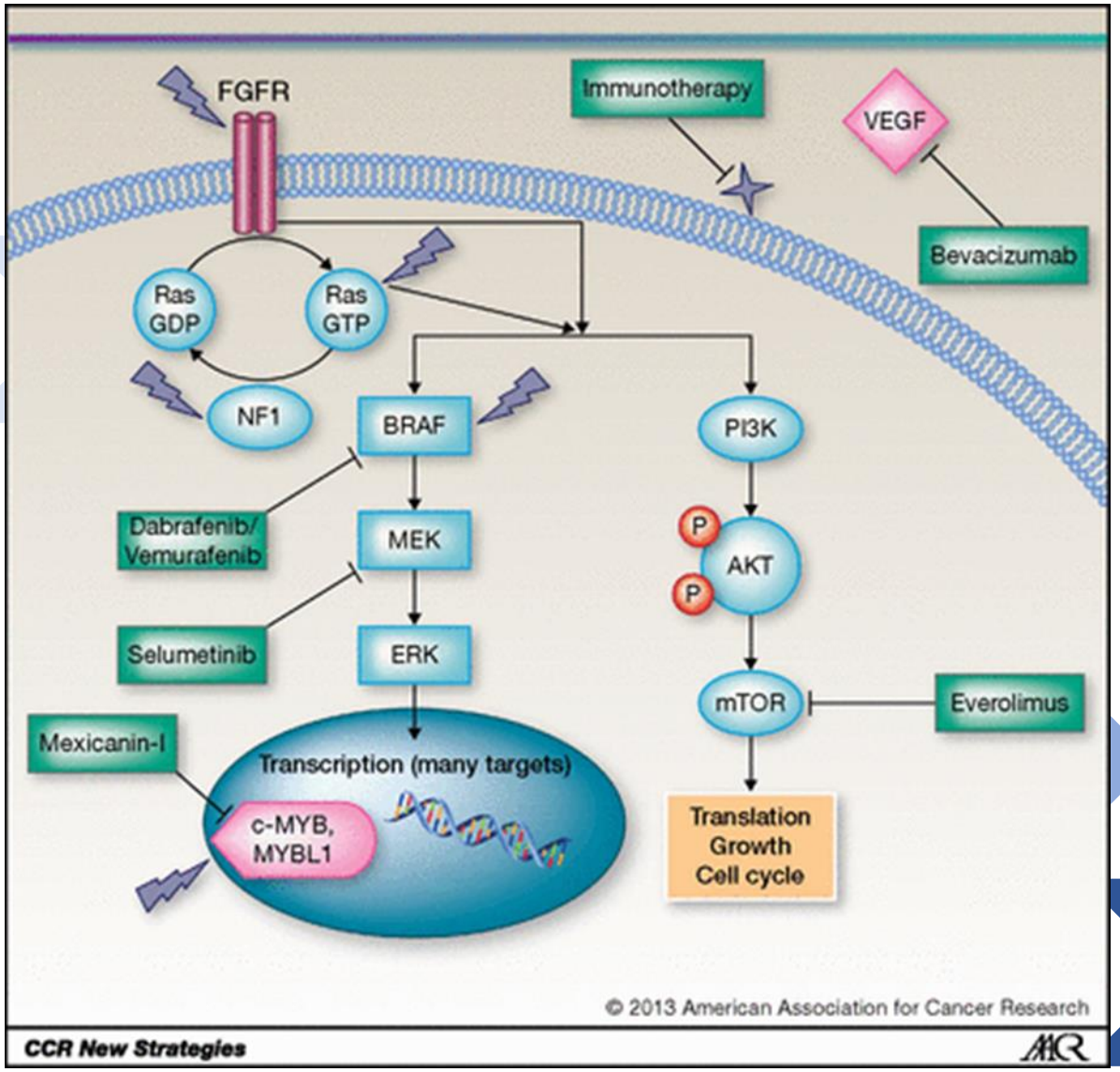
2. It can be administered to patients after a certain different age depending on each disease

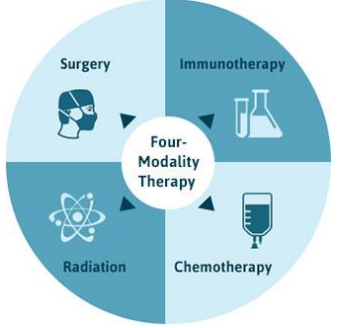
Basic principles of treatment



- Surgery
- Chemotherapy
- Radiotherapy
- Targeted Therapy

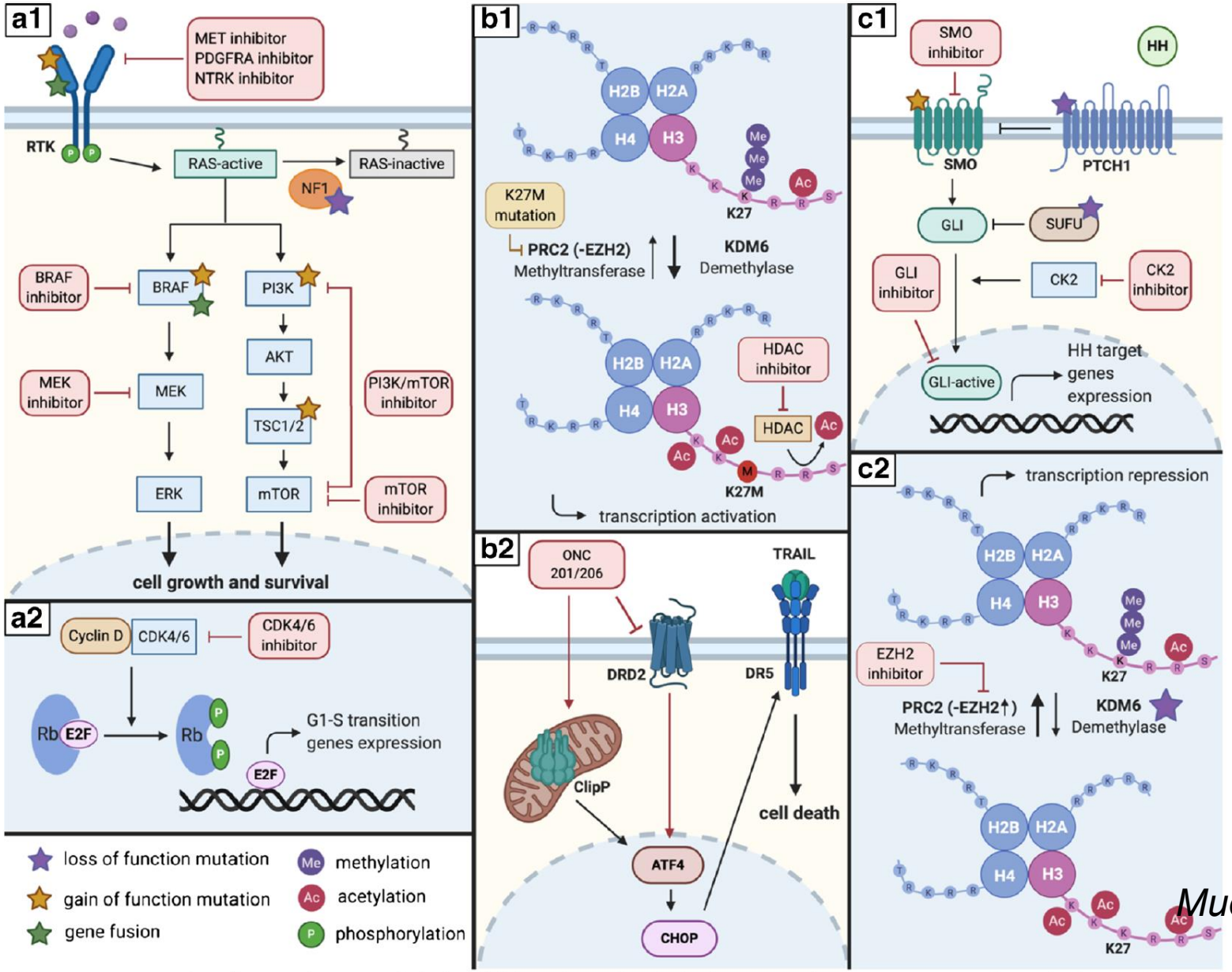
Basic principles of treatment

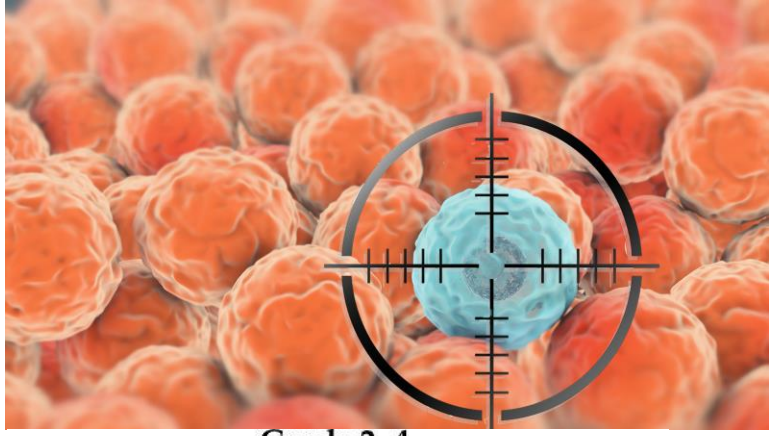




Targeted Therapy

Targeted therapies





Grade 2–4
Skin
Changes in how the skin feels
Increase of photosensitivity
Rash (scalp, face, neck, chest, upper back
Dry skin
Itching
Red, sore cuticles (the areas around the nails)
Hand-foot syndrome, painful
Changes in hair growth
Changes in hair or skin color
Changes in and around the eyes
Common and serious side effects
High blood pressure
Bleeding or blood clotting problems
Slow wound healing
Heart damage
Swelling
Diarrhea
Hepatitis

Mueller T,Curr Treat Options Neurol 2020;22(43)
https://doi.org/10.1007/s11940-020-00651-3

Structure

- Introduction
- Clinical presentation
- Imaging studies
- Basic principles of treatment
- Conclusions