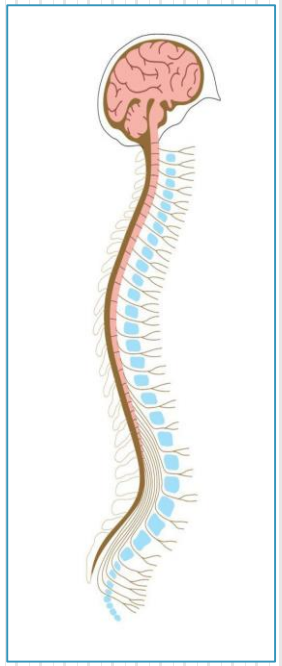
C470-C479, C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753

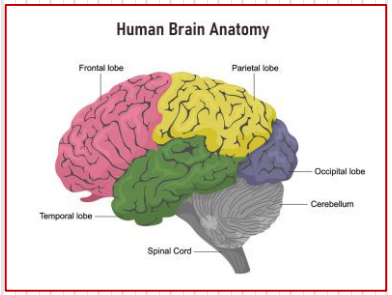
2022-2023 Neoplasms of the BRAIN & CNS



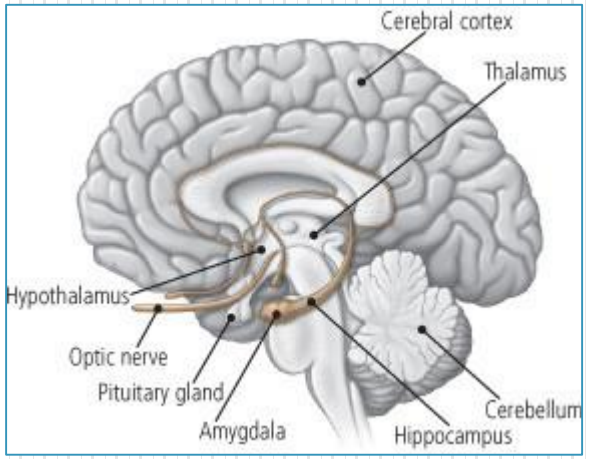
2022-2023 FCDS Educational Webcast Series

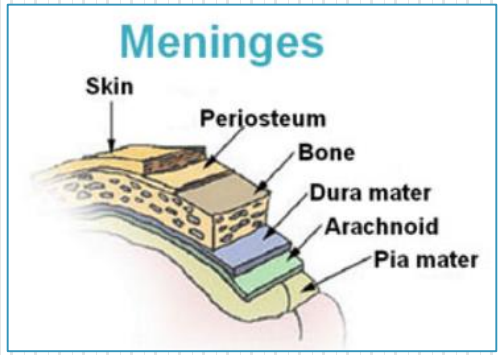
Steven Peace, CTR

November 17, 2022



World Health Organization





NBTS

CBTRUS
Central Brain Tumor Registry of the United States

https://braintumor.org/brain-tumors/about-brain-tumors/brain-tumor-facts/

CDC & Florida DOH Attribution

"Funding for this conference was made possible (in part) by the Centers for Disease Control and Prevention. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services, nor does the mention of trade names, commercial practices, or organizations imply endorsement by the US Government."

FCDS would also like to acknowledge the Florida Department of Health for its support of the Florida Cancer Data System, including the development, printing and distribution of materials for the 2018 FCDS Annual Conference and the 2018-2019 FCDS Webcast Series under state contract CODJU. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Florida Department of Health.

FLccSC LMS – CEU Quiz –FCDS IDEA

FLccSC
Fundamental Learning Collaborative for the Cancer Surveillance Community

NO CEU QUIZ FOR THIS WEBCAST

NCRA CEU# is 2022-160

2 CEUs AWARDED

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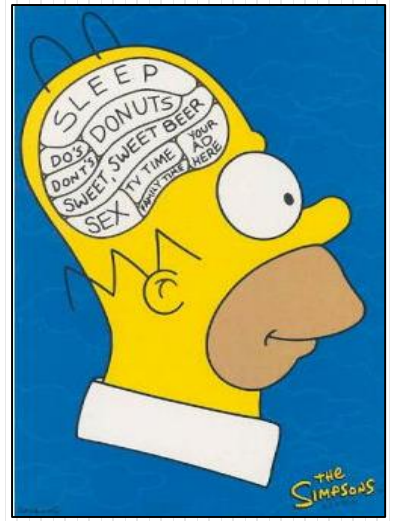
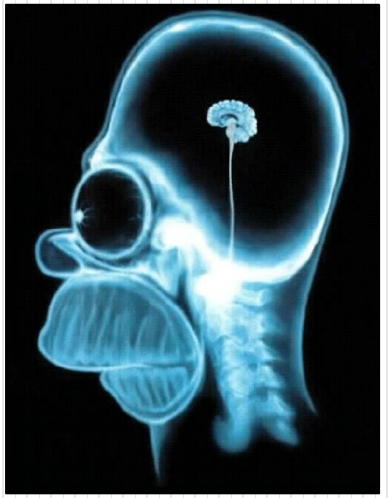
C470-C479, C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753

2022-2023 Neoplasms of the BRAIN/CNS

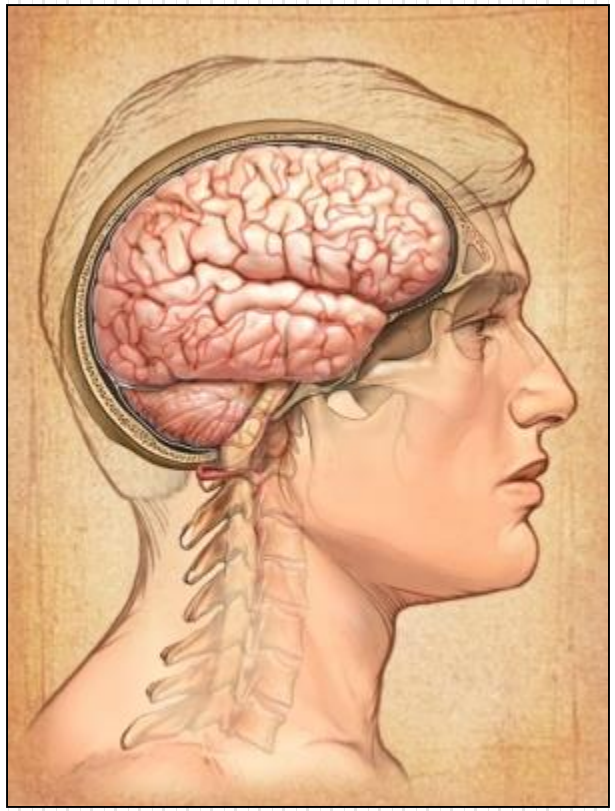
- Introduction to Neoplasms of the Brain and Central Nervous System
- Reporting Benign/Borderline/Malignant Tumors of the Brain & CNS
- Anatomy of the Human Brain & CNS
- Anatomy of the Cranial & Spinal Meninges
- Anatomy of the Intracranial Glands
- General Histologic Classification of Brain &CNS Neoplasms
- WHO Classification of Central Nervous System Tumors, 5th ed, Volume 6, 2021
- **2023** Updates to ICD-O-3 Histology Codes
- **2023** Solid Tumor MP/H Rules – published 11/10/2022
- Staging Brain & CNS Neoplasms
- SSDIs for Brain & CNS Neoplasms
- General Treatment Guidelines
- **2023** Surgery of Primary Site Codes
- Resources & References
- Questions

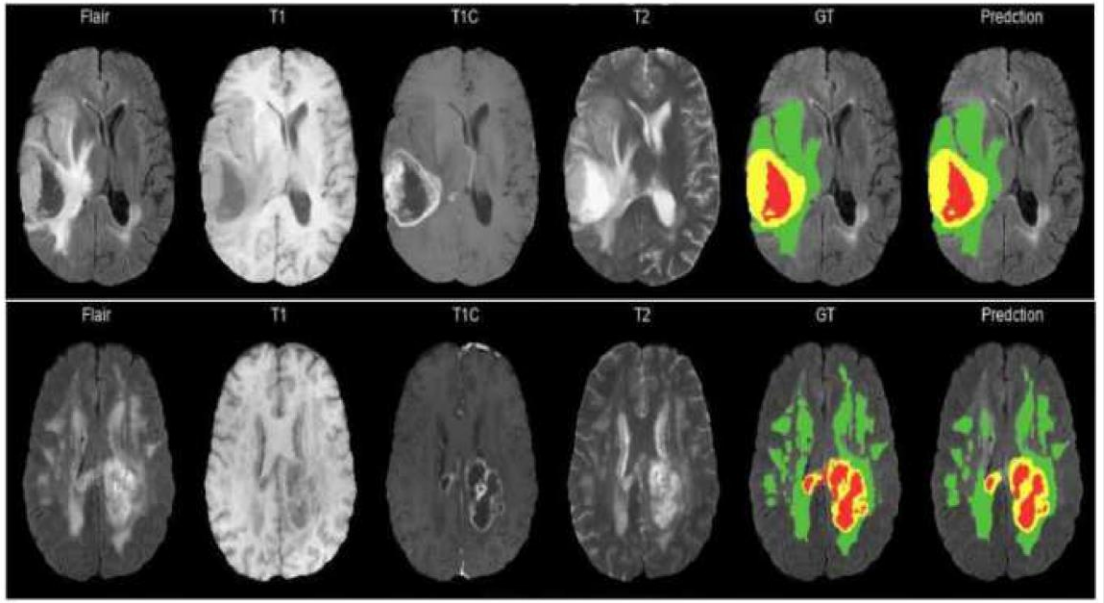




Homer J Simpson

Introduction to Neoplasms of the Brain and CNS





2021 RSNA-ASNR-MICCAI Brain Tumor or BRATS dataset

Brain Tumors are:

Primary "brain" tumors - those that begin in the brain *or central nervous system (or its supporting tissues)* and tend to stay in the brain - occur in people of all ages, but they are statistically more frequent in children and older adults.

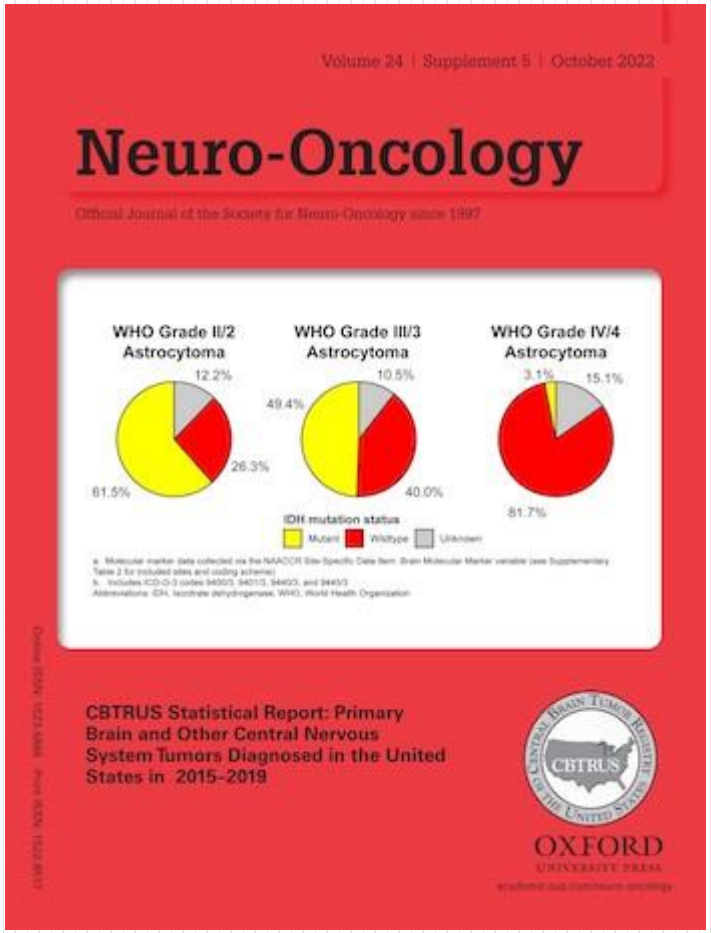
Metastatic "brain" tumors – those that begin as a cancer elsewhere in the body and spread to the brain – are more common in adults than in children.

Brain Tumors are:

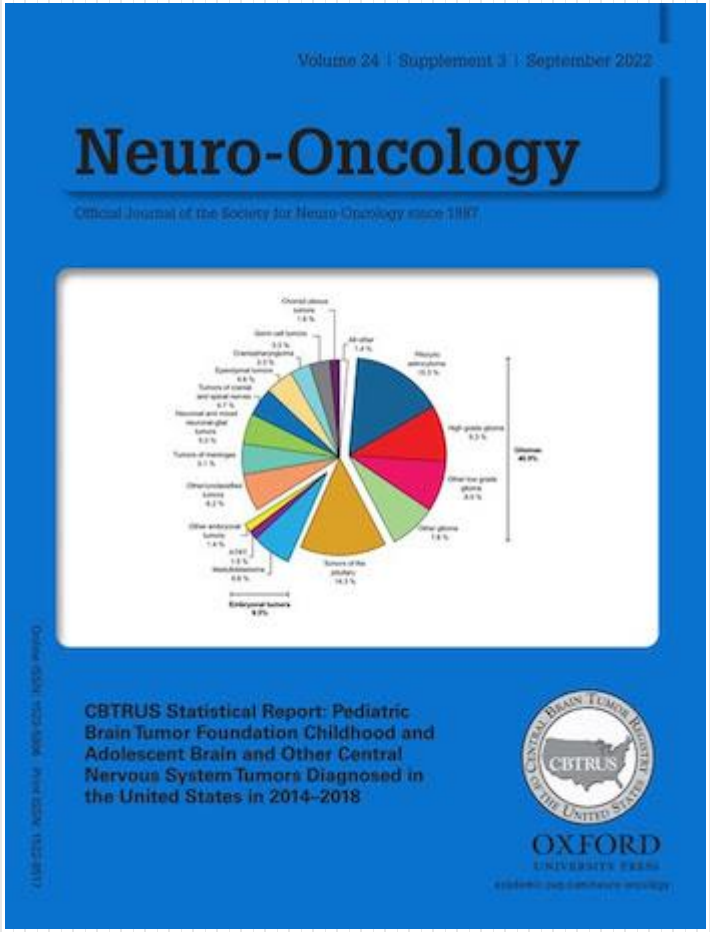
- **Benign** – "Benign" brain tumors are not cancer, although they often cause symptoms and will sometimes require treatment. We prefer to use the term "non-malignant" to describe brain tumors made up of noncancerous cells.
  - Behavior = 0
  - Sequence Number = 60>
  - Reportable for Cases Diagnosed 1/1/2004 and later - only
- **Malignant** – Malignant brain tumors are cancer. They generally grow faster and more aggressively than non-malignant tumors, invade other areas of the brain and spinal cord, and can be deadly.
  - Behavior = 3 and
  - Sequence Number = 00>
  - Reportable for All Cases Regardless of Diagnosis Date
- **Borderline** – Somewhere in-between having malignant potential.
  - Behavior = 1 and
  - Sequence Number = 60>
  - Reportable for Cases Diagnosed 1/1/2004 and later - only

CBTRUS

CENTRAL BRAIN TUMOR REGISTRY OF THE UNITED STATES



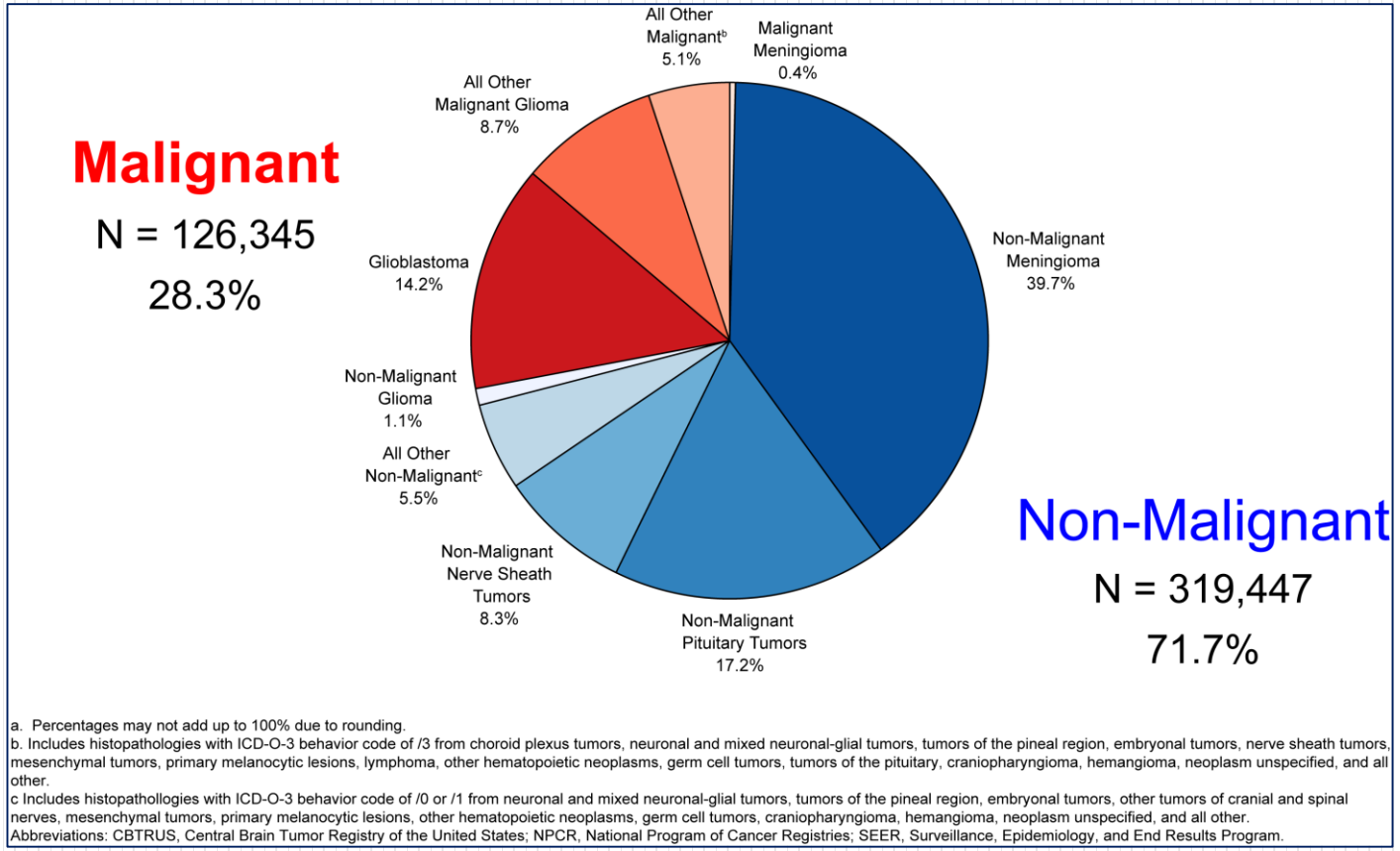
https://cbtrus.org/reports/



24(S5), v1–v95, 2022 | https://doi.org/10.1093/neuonc/noac202

All Primary Brain & CNS Tumors by Behavior

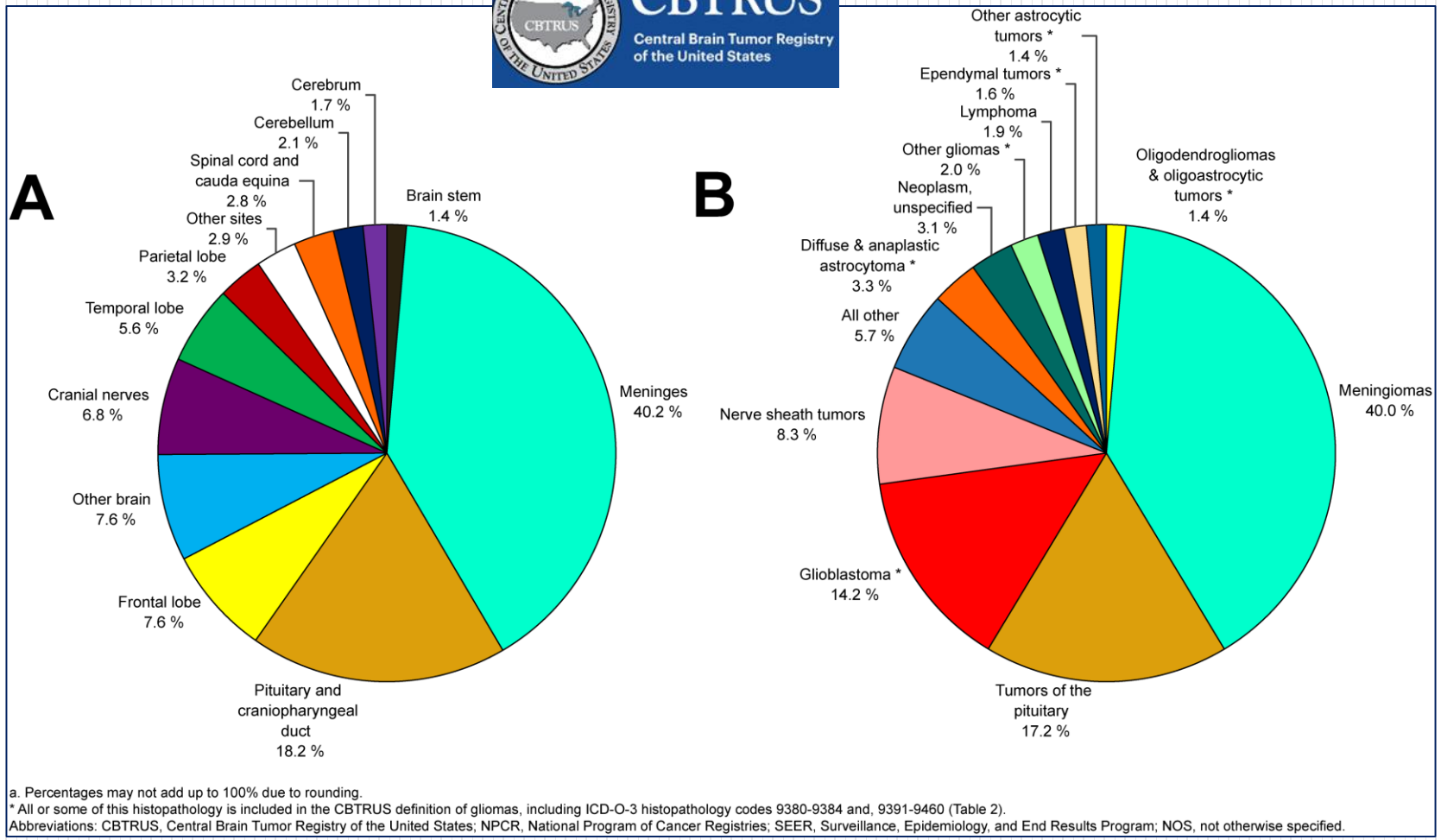
CBTRUS
Central Brain Tumor Registry of the United States



a. Percentages may not add up to 100% due to rounding.
b. Includes histopathologies with ICD-O-3 behavior code of /3 from choroid plexus tumors, neuronal and mixed neuronal-glial tumors, tumors of the pineal region, embryonal tumors, nerve sheath tumors, mesenchymal tumors, primary melanocytic lesions, lymphoma, other hematopoietic neoplasms, germ cell tumors, tumors of the pituitary, craniopharyngioma, hemangioma, neoplasm unspecified, and all other.
c Includes histopathollogies with ICD-O-3 behavior code of /0 or /1 from neuronal and mixed neuronal-glial tumors, tumors of the pineal region, embryonal tumors, other tumors of cranial and spinal nerves, mesenchymal tumors, primary melanocytic lesions, other hematopoietic neoplasms, germ cell tumors, craniopharyngioma, hemangioma, neoplasm unspecified, and all other.
Abbreviations: CBTRUS, Central Brain Tumor Registry of the United States; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program.

Neuro-Oncology - 24(S5), v1–v95, 2022 | https://doi.org/10.1093/neuonc/noac202

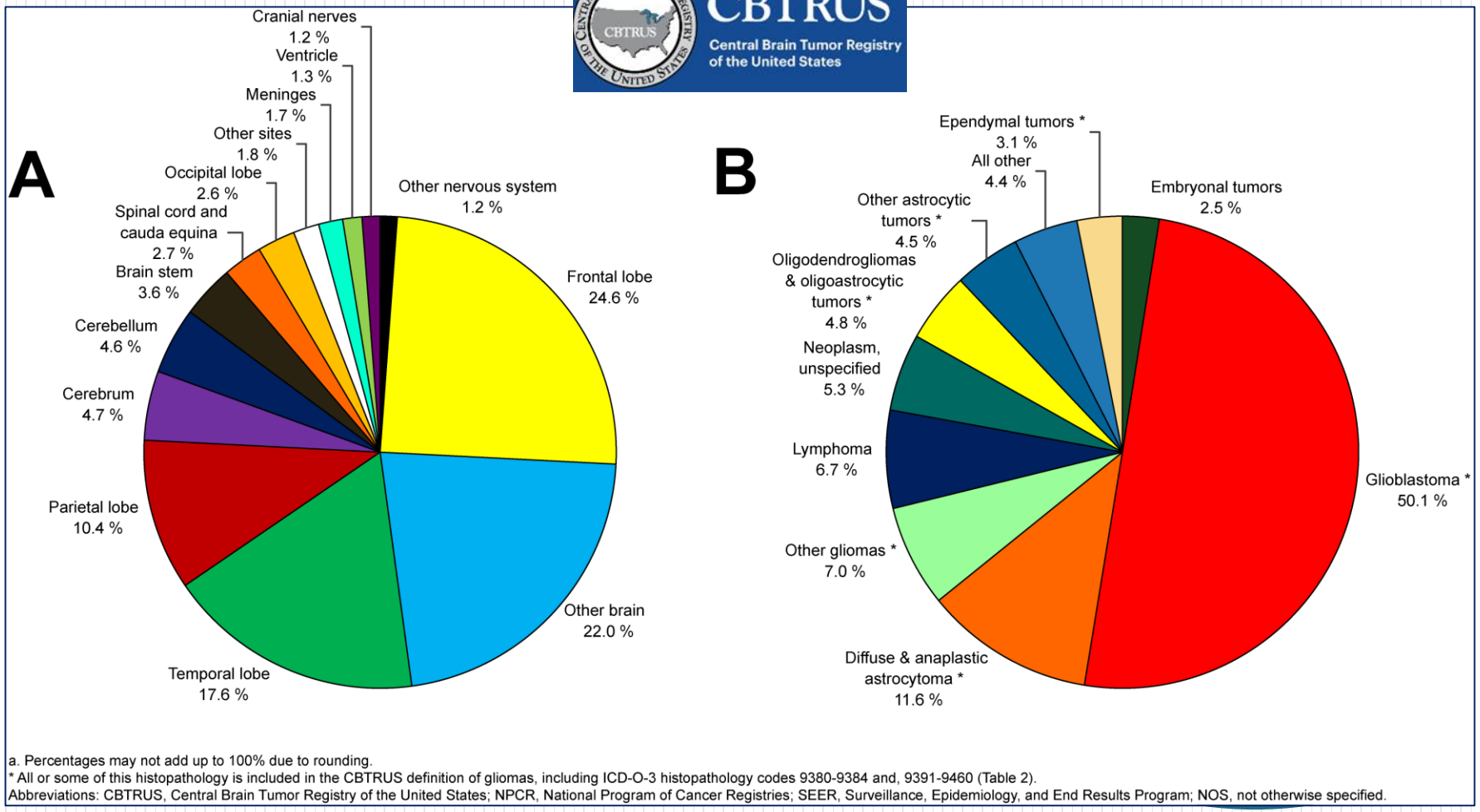
All Primary Brain & CNS Tumors by Site & Histology



a. Percentages may not add up to 100% due to rounding.
* All or some of this histopathology is included in the CBTRUS definition of gliomas, including ICD-O-3 histopathology codes 9380-9384 and, 9391-9460 (Table 2).
Abbreviations: CBTRUS, Central Brain Tumor Registry of the United States; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program; NOS, not otherwise specified.

Neuro-Oncology - 24(S5), v1–v95, 2022 | https://doi.org/10.1093/neuonc/noac202

Distribution of All Types of Malignant Brain Tumors



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Abbreviations: CBTRUS, Central Brain Tumor Registry of the United States; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program; NOS, not otherwise specified.

Neuro-Oncology - 24(S5), v1–v95, 2022 | https://doi.org/10.1093/neuonc/noac202

Figure 13. Most Common Brain and CNS Tumors by Age

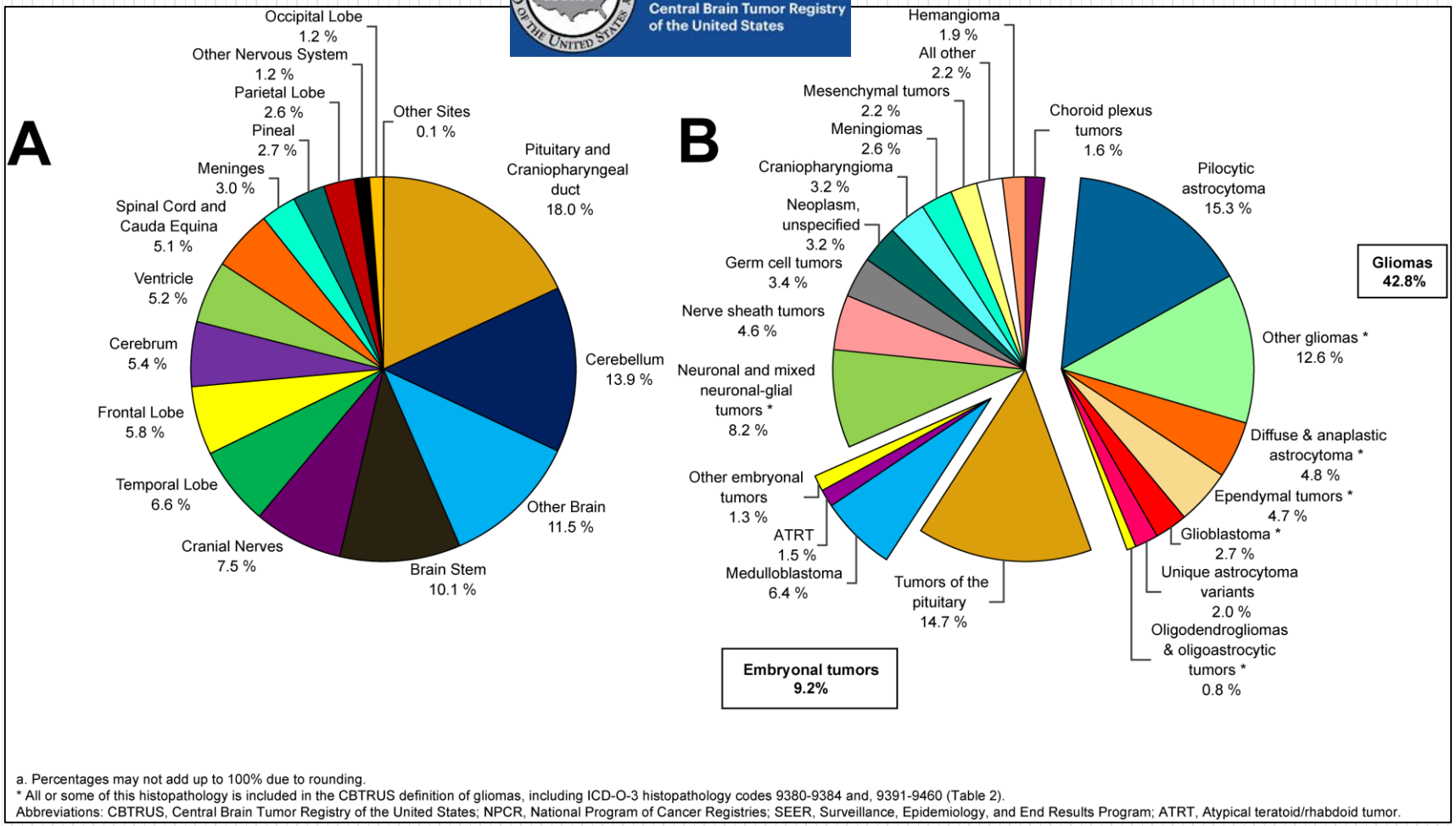
CBTRUS Statistical Report: NPCR and SEER Data from 2004-2007

Age (yr)	Most Common Histology	Second Most Common Histology
0-4	Embryonal/medulloblastoma	Pilocytic astrocytoma
5-9	Pilocytic astrocytoma	Malignant glioma, NOS
10-14	Pilocytic astrocytoma	Neuronal/glial
15-19	Pituitary	Pilocytic astrocytoma
20-34	Pituitary	Meningioma
35-44	Meningioma	Pituitary
45-54	Meningioma	Glioblastoma
55-64	Meningioma	Glioblastoma
65-74	Meningioma	Glioblastoma
75-84	Meningioma	Glioblastoma
85+	Meningioma	Neoplasm, unspecified

While brain/CNS tumors are not one of the top incidence tumors for adults, they are the most common solid tumor in children (0-19 years) (18%) second only to leukemias (26%).

(*ACS Cancer Facts and Figures 2014*).

Distribution in Children/Adolescents



a. Percentages may not add up to 100% due to rounding.
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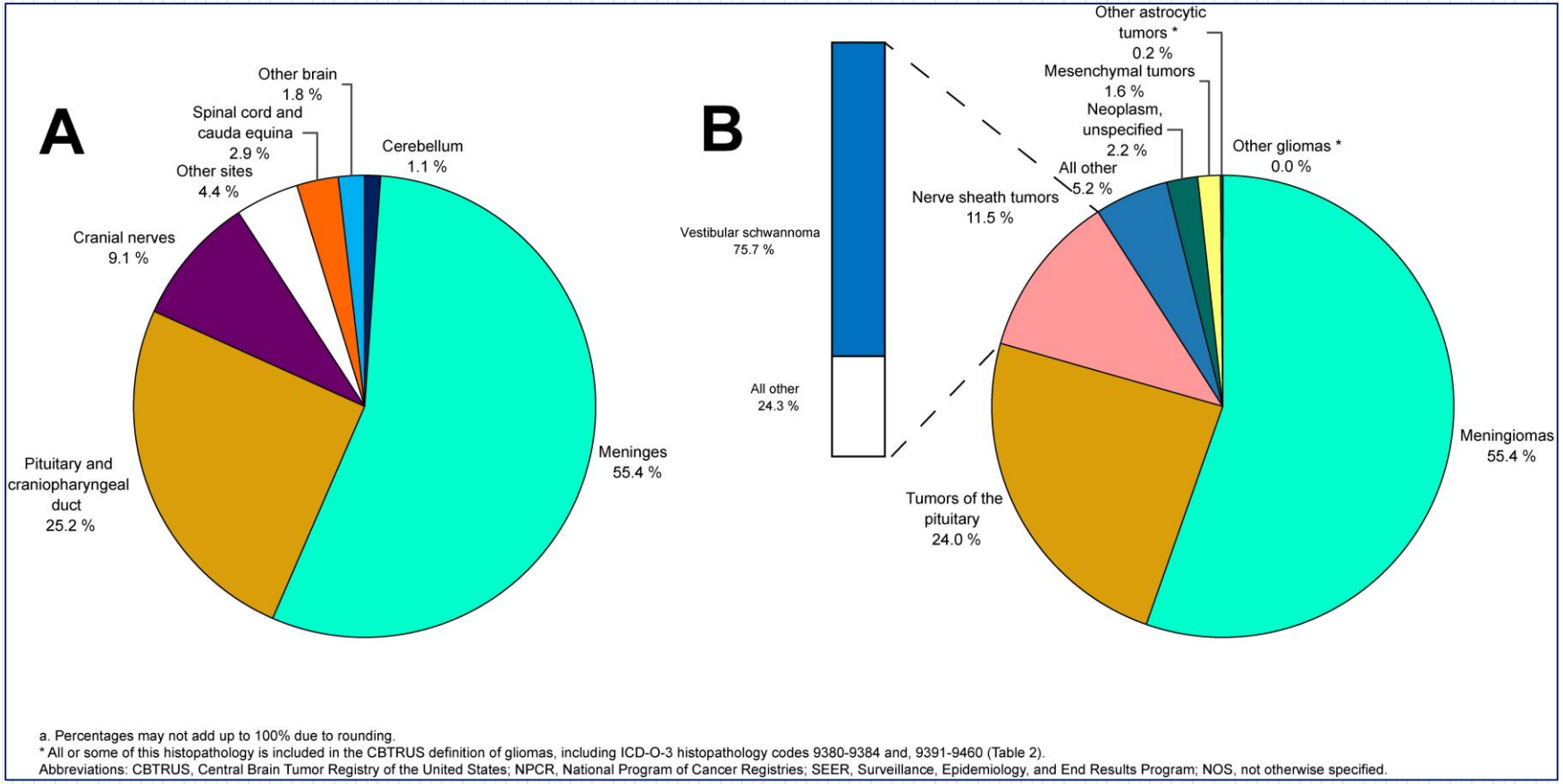
Abbreviations: CBTRUS, Central Brain Tumor Registry of the United States; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program; ATRT, Atypical teratoid/rhabdoid tumor.

http://neuro-oncology.oxfordjournals.org/20(S4), 1–86, 2018 | doi:10.1093/neuonc/noy131

Distribution of Non-Malignant Brain & CNS



a. Percentages may not add up to 100% due to rounding.
* All or some of this histopathology is included in the CBTRUS definition of gliomas, including ICD-O-3 histopathology codes 9380-9384 and, 9391-9460 (Table 2).
Abbreviations: CBTRUS, Central Brain Tumor Registry of the United States; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology, and End Results Program; NOS, not otherwise specified.

Neuro-Oncology - 24(S5), v1–v95, 2022 | https://doi.org/10.1093/neuonc/noac202

Brain Tumors are:

Malignant primary brain and CNS tumors are assigned **Sequence Codes 00-35**

- Sequence Chronologically 00-35
- Only count malignant tumors in the sequence
- If only one malignant tumor occurs, it is coded 00
- If subsequent (multiple) primary malignant and/or in situ neoplasms, the sequence number for the first tumor begins at 01, the sequence number for the second primary tumor is 02, and so forth.

Non-malignant primary brain and CNS tumors are assigned **Sequence Codes 60-87.**

- Sequence Chronologically 60-87
- Only count benign/borderline or reportable by agreement neoplasms in the sequence
- If only one non-malignant tumor occurs, it is coded 60.
- If subsequent (multiple) non-malignant neoplasms are diagnosed, the first tumor should be sequenced as 61, the second 62 and so forth.

Brain Tumors are:

Characterized by Anatomic Location, Histologic Type, Behavior, WHO CNS Tumor Grade, and the Tumor's Molecular Genetics Profile – what abnormalities are found in testing.

Grade I: These are the least malignant tumors and are usually associated with long-term survival. They grow slowly and have an almost normal appearance when viewed through a microscope.

Grade II: These tumors are slow growing and look slightly abnormal under a microscope. Some can spread into nearby normal tissue and recur, sometimes as a higher grade tumor.

Grade III: These tumors are malignant, although there is not always a significant difference between grade II and grade III tumors. The cells of a grade III tumor are actively reproducing abnormal cells, which grow into nearby normal brain tissue. These tumors tend to recur, often as a grade IV.

Grade IV: These are the most malignant tumors. They reproduce rapidly, can have a bizarre appearance when viewed under the microscope, and easily grow into nearby normal brain tissue. These tumors form new blood vessels so they can maintain their rapid growth.

Characteristics of Brain Tumors

- Start in the brain and grow steadily there.
- Very rarely spread to other organs through the bloodstream.
- Named for the anatomic location of tumor or the cells from which they arise, each having a certain function essential to normal physiological functioning of the brain.
- For example:
  - Brain Stem Glioma arises in the lowest part of the brain – the brain stem.
  - Meningioma arises in the meninges.
  - Glioma arises from glial cells that support the CNS.
  - Astrocytoma arises from astrocytes
  - Ependymoma arises from ependymal cells which line the ventricles
  - Oligodendrogliomas arise from oligodendrocyte cells which make up the fatty substance called myelin that covers nerves like electrical insulation.

Symptoms and Complications

- CNS tumors are associated with a range of symptoms and complications such as edema, seizures, endocrinopathy, fatigue, psychiatric disorder, venous thromboembolism that can seriously impact quality of life.

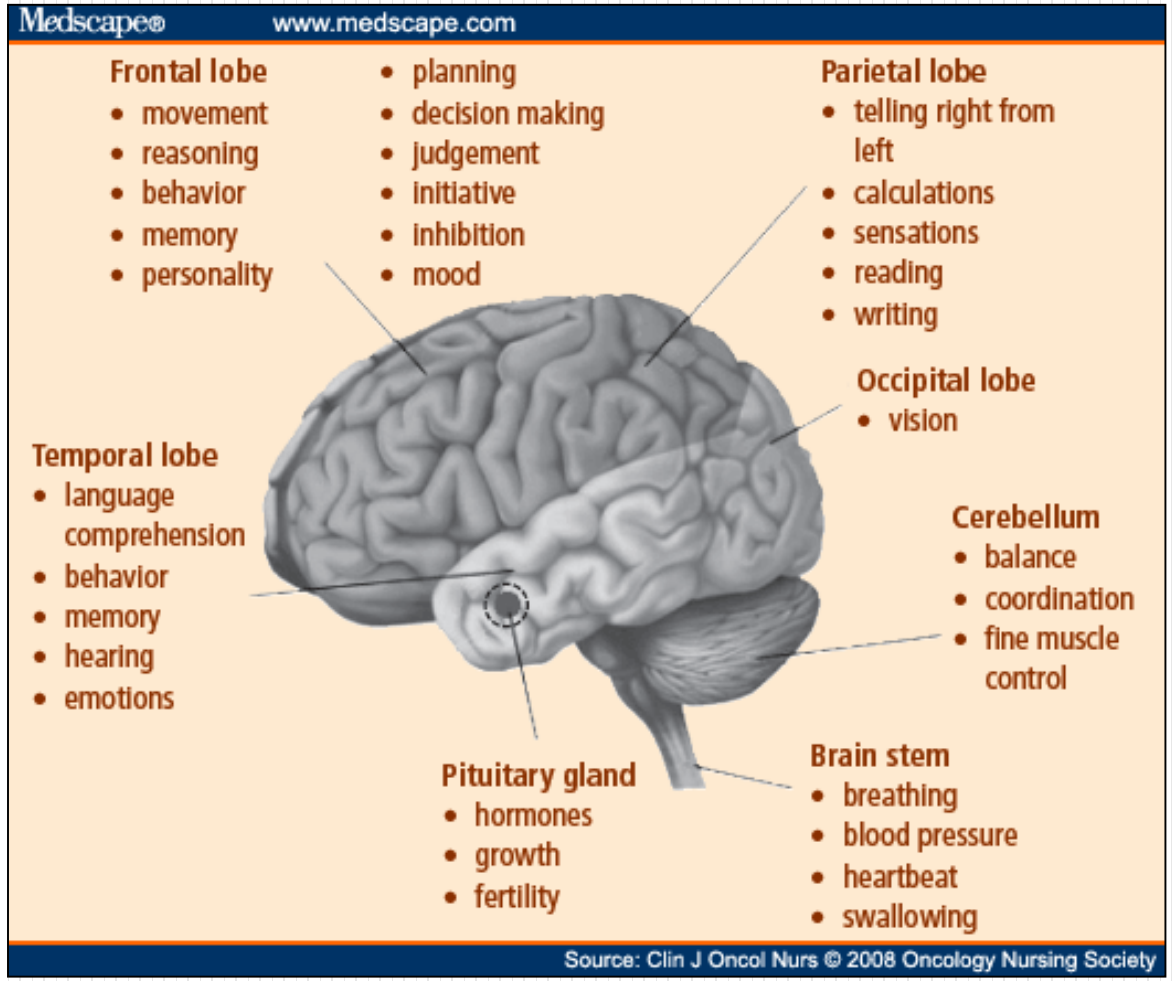
- Symptoms depend on the size and location of the tumor, growth of tumor, swelling in the brain (edema), or blockage in the flow of cerebrospinal fluid.

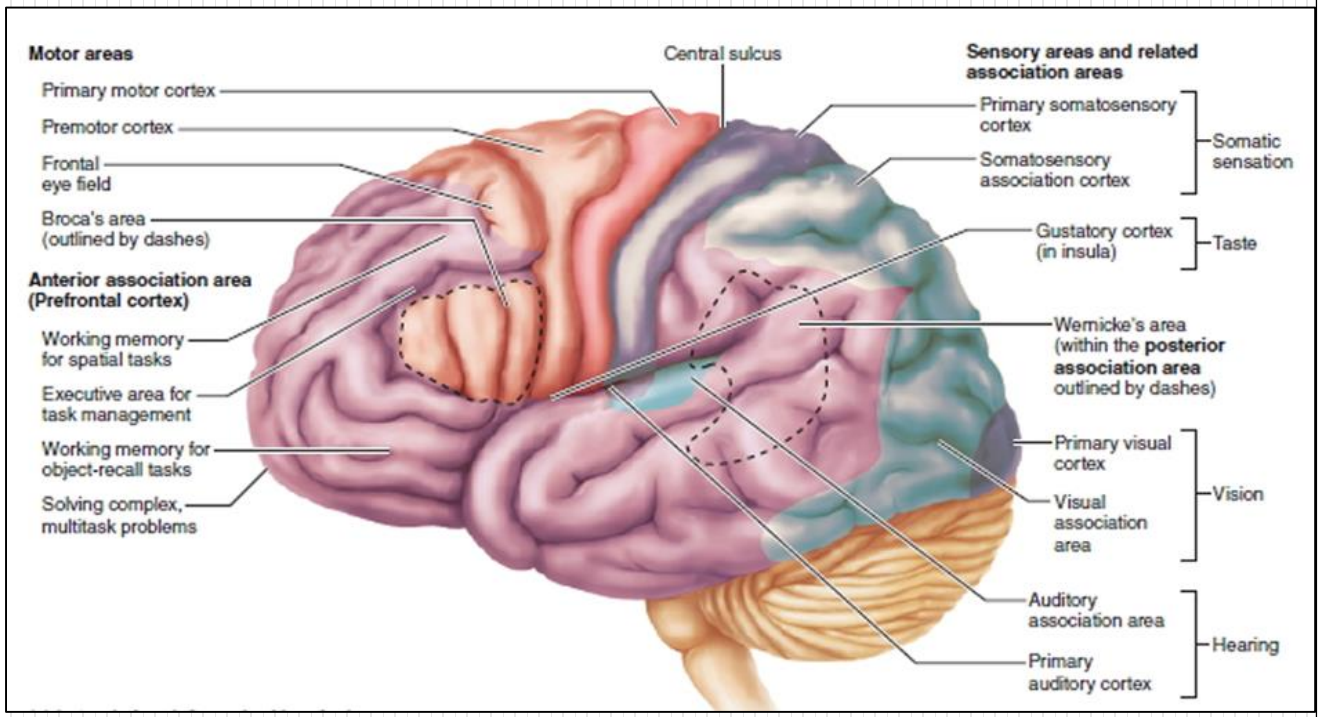
- Symptoms of increased intracranial pressure include headaches which tend to be worse with activity, at night or early in the morning, convulsions, vomiting, changes in personality, behavior, memory, mental ability, drowsiness, lethargy and coma.

Tumor Location and Symptoms

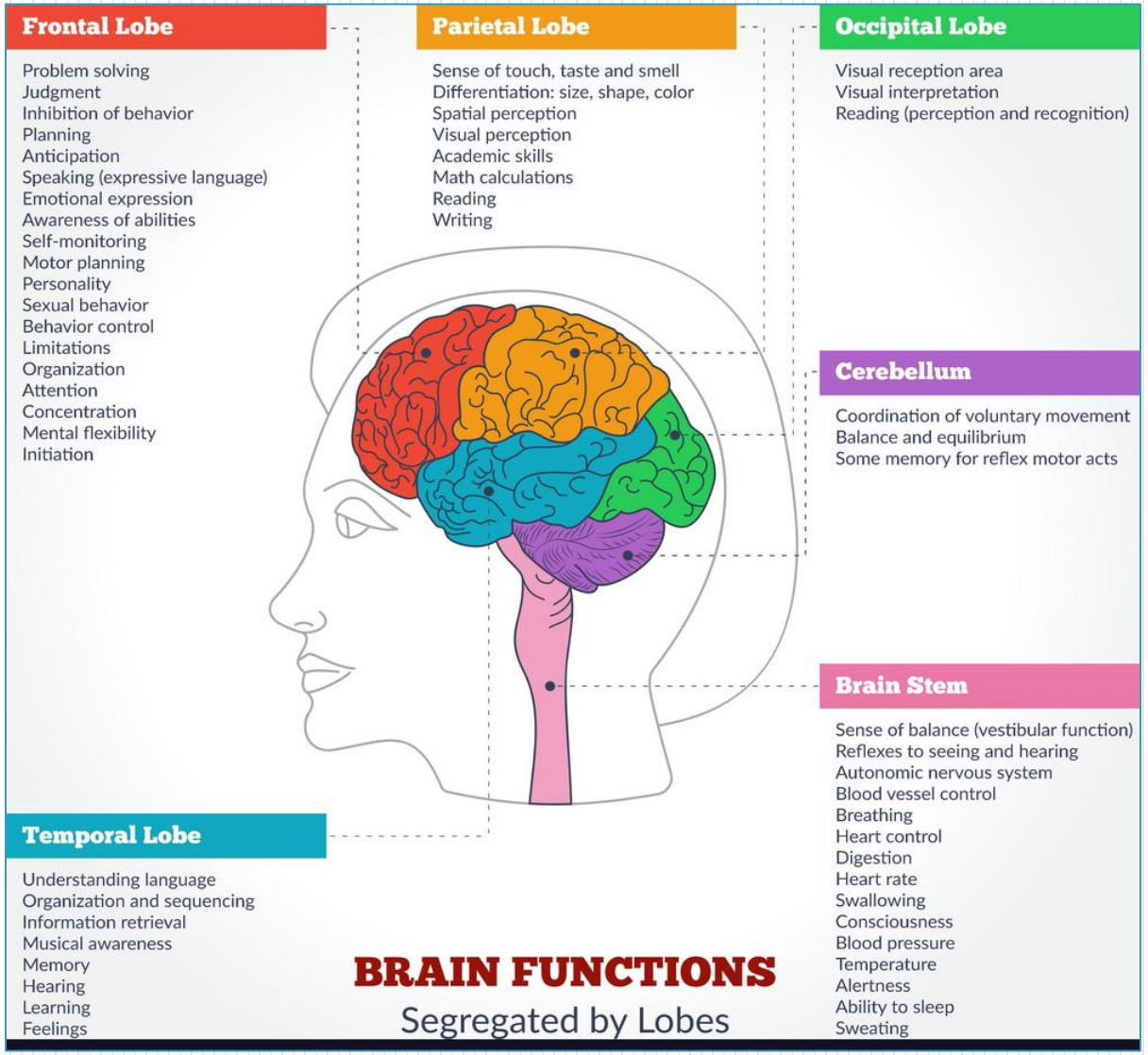
- Symptoms are often tumor location specific or provide clues
- Symptoms on the right side of the body may occur if the tumor is located on the left side of the brain and vice-versa.
  - The speech center in most people is on the left side of the brain. Symptoms of a tumor located here may include difficulty saying correct words while still capable of understanding what is being said.
  - If the tumor is located in the frontal lobe which controls intellectual function, thought process, behavior and memory, those activities may be affected.
  - Tumors in the cerebellum cause balance and motor function problems.
- Similarity to closed head injury victims (motorcycle crash).

Brain Anatomy and Function as Related to Symptoms





Brain Anatomy and Function as Related to Symptoms



VectorStock – Human Brain Anatomy and Functions – Vector Image

ALL Benign Brain & CNS Tumors are Reportable

C470-C479, C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753

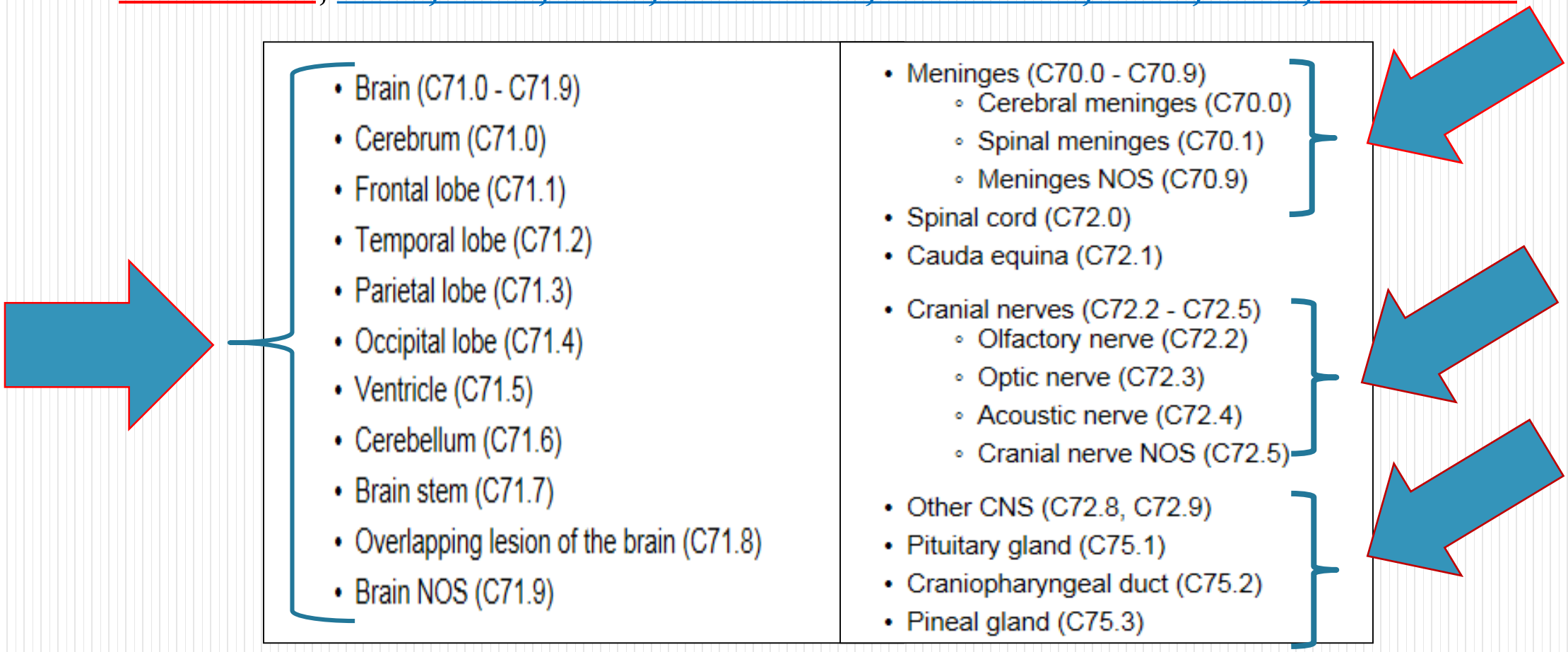
(MALIGNANT TUMORS HAVE ALWAYS BEEN REPORTABLE)

Public Law 107-260, the Benign Brain Tumor Cancer Registries Amendment Act, [PDF-185KB] requires programs participating in the National Program for Cancer Registries (NPCR) to collect data on benign and borderline tumors of the central nervous system in addition to the previously required data on malignant tumors.

In addition to NPCR, the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) program and the American College of Surgeons (ACoS) Commission on Cancer began requiring that these tumors be reported, starting with cases diagnosed on January 1, 2004.

ICD-O Topography Codes (Anatomic Site)

C470-C479, C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753



USE SOLID TUMOR RULES – NON-MALIGNANT BRAIN & CNS

- Benign/Borderline Neoplasms were added 1/1/2004
- Malignant Neoplasm of Peripheral Nerves (C47.0-C47.9) were added 1/1/2018

Not Reportable Neoplasms – Brain Not Malignant Only

Intracranial Cysts

Neuro-Fibromatosis

Table 4: Non-Reportable Neoplasms

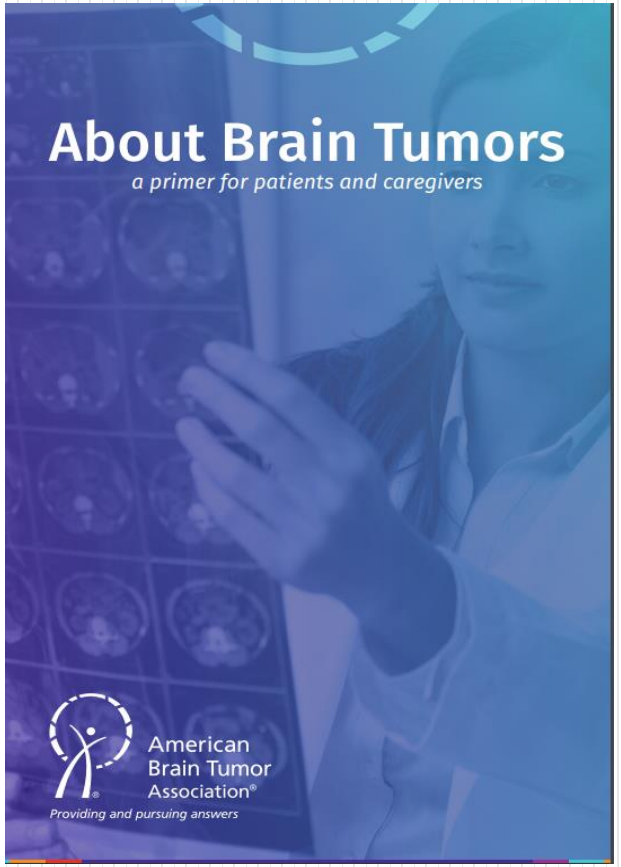
Use **Table 4** for **non-malignant neoplasms ONLY**. The table identifies **histology/site** combinations which are **not reportable.** This table was created from WHO with the cooperation of the Central Brain Tumor Registry of the United States (CBTRUS).

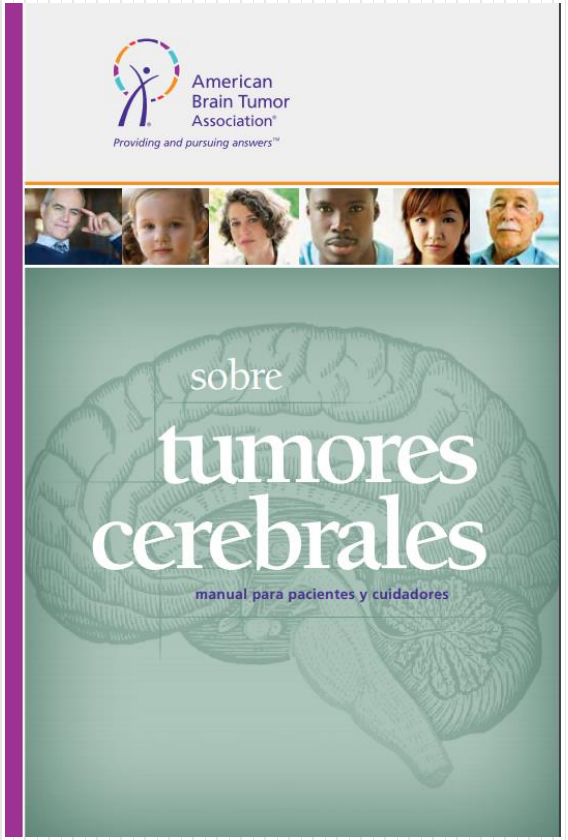
Non-reportable Histology Term	Non-reportable Histology Code	Definitions and Sites
Carcinomas	**8010-8060, 8071-8671, 8940-8941**	Brain C710-C719 **Site/histology edit** carcinomas/brain
Carcinomas	**8010-8671, 8940-8941**	Cerebral meninges, spinal meninges, meninges NOS C700-C709 **Site/histology edit** carcinomas/meninges
Carcinomas	**8010-8671, 8940-8941**	C721-C729 (Other central nervous system) **Site/histology edit** carcinomas/other CNS
Colloid cyst	**No code**	
Epidermoid tumor/cyst	**No code**	
Glomus tympanicum, glomus jugulare	**8690/1**	These tumors occur in the inner ear, the aortic body and other paraganglia respectively; these sites are **not reportable.**
Hygroma	**9173/0**	
Hypothalamic hamartoma	**No code**	Occurs in hypothalamus
Neurofibromatosis, NOS	**9540/1**	Genetic disease that produces non-malignant tumors in the skin, brain, CNS, and other sites. The brain and CNS tumors spawned by NF, NOS are reportable, the genetic disease is not.
Neurofibromatosis, type 1 (NF1)	**No code***	Genetic disease that produces non-malignant tumors in the skin, brain, CNS, and other sites. The brain and CNS tumors spawned by NF1 are reportable, the genetic disease is not.
Neurofibromatosis, type 2 (NF2)	**No code***	Genetic disease that produces non-malignant tumors in the skin, brain, CNS, and other sites. The brain and CNS tumors produced by NF2 are reportable, the genetic disease is not.
Neuroglial cyst	**No code**	Ventricles
Osteochondroma	**9210/0**	Originates in the cartilage around bone, site not reportable for non-malignant neoplasms
Rathke cleft cyst	**No code**	Sella turcica C751. This is a Rathke cleft CYST, not a Rathke cleft tumor.
Schwannomatosis	**No code***	A form of neurofibromatosis newly named/discovered

***The code which is currently in ICD-O-3 for neurofibromatosis will not be used in ICD-O updates or in future ICD-O editions**

Brain Tumor Characteristics

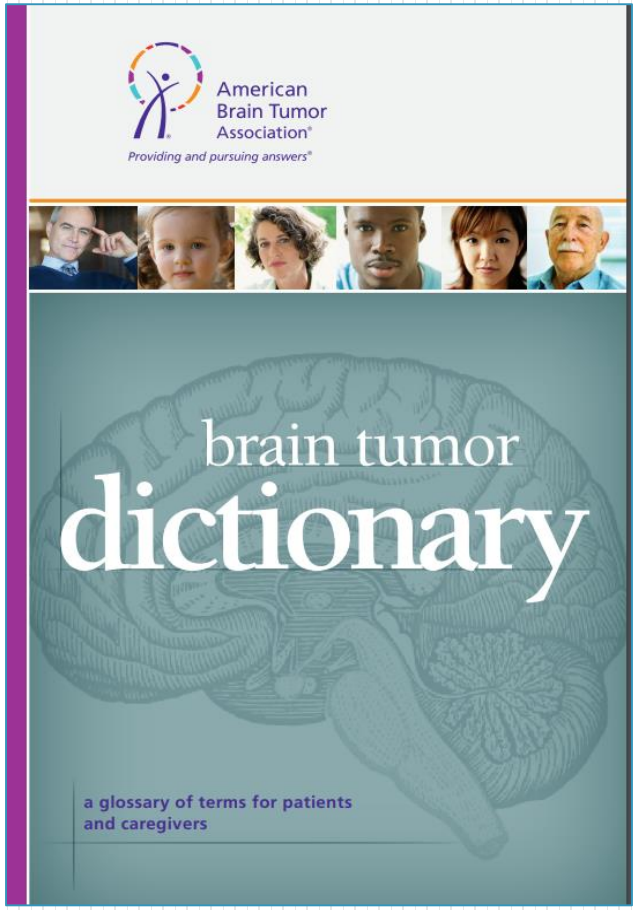
- **Patient Age**
- **Tumor Location**
- **Behavior**
- **Histologic Type**
- **WHO Grade of Primary Tumor**
- **Tumor Molecular Profile – DOCUMENT IT !!**





American Brain Tumor Association – http://www.abta.org/brochures

Brain Tumor Terminology



DOE **D**epartment **o**f **E**nergy (of the US government).

dose-rate The quantity of a treatment given over a period of time, e.g., 10cc per hour.

double-blind study A clinical trial where neither the doctor nor the patient knows which drug is being given. In a single-blind study, the patients don't know which treatment they are receiving but the doctors do.

doubling time The time it takes a cell to complete the cell cycle; the time it takes a cell to produce daughter cells.

drug delivery The method and route used to provide medication, for example, PO (by mouth), IV (intravenous), IM (intramuscular), intrathecal, intratumoral, spinal.

drug resistance Failure of cancer cells to respond to chemotherapy.

DSc **D**octor of **Sc**ience degree.

dura mater [du´ rah • ma´ tur] The outermost, toughest, and most fibrous of the three membranes (meninges) that cover the brain and spinal cord. *See* ***meninges***.

DVM **D**octor of **V**eterinary **M**edicine degree.

DX, dx Diagnosis.

dynamic CT or **dynamic MRI** CT or MRI

dysphagia [dis fay´ gee ah] Difficulty in swallowing or inability to swallow. This symptom usually indicates tumors involving the lower brain stem.

dysphasia [dis fay´ zee ah] Language disorder. Inability to speak words which one has in mind or to think of correct words, or the inability to understand spoken or written words. Symptom common to tumors of the dominant cerebral hemisphere, particularly the frontal, temporal, and parietal lobes.

dysplasia [dis play´ zee ah] Cells that are abnormal in size, shape and organization.

dyspnea [disp nee´ ah] Difficult, painful breathing or shortness of breath.

e.g. For example.

EBRT **E**xternal **B**eam **R**adiation **T**herapy. This acronym is used to distinguish the most common type of radiation, as opposed to interstitial radiation (which employs radiation implants), or radiosurgery.

echoplanar MRI This technique produces MRI images in a faster sequence than traditional MRIs. The increased speed permits the tumor's use of oxygen to be depicted. *Also called* ***functional, "real time," or fast MRI.***

edema [eh dee´ ma] Swelling caused by an

embolization [em bol ih zay´ shun] Used to reduce the amount of blood supply to a tumor, it involves blocking the flow of blood in selected arteries.

embryonal carcinoma [em bree on' al • kar sih no' ma] A germ cell tumor. Germ cell tumors begin in the cells that give rise to sperm or eggs. They can occur anywhere in the body. Germ cell tumors of the brain most commonly occur in the pineal or suprasellar regions.

embryonic [em bree on´ ik] Undeveloped, related to the embryo.

emesis [em´ ih sis] Vomiting.

encapsulated [en kap´ sue lay ted] Refers to a tumor that is wholly confined to a specific area, surrounded by a capsule. Localized.

encephalopathy [n seff ah lopp´ ah thee] A loss of function in tissue of the brain; can be due to a wide variety of causes. *See* ***leukoencephalopathy***.

endocrine dysfunction [en´ doe krin] With brain tumors, can refer to an increase, decrease or absence of hormone production by the pituitary gland. Symptoms depend on which hormone is affected and whether it is increased or decreased.

endocrine system [en´ doe krin] The tissues or glands in the body that secrete hormones into the circulatory system.

remove scar tissue blocking a shunt; or to remove intraventricular tumors. It is also useful during cyst removal.

enhancement Use of a dye that makes abnormal tissue more obvious during CT or MRI scans.

enteral [en´ tur al] Something which enters the body by way of the intestines such as by eating or drinking. When referring to medication, it is the opposite of parenteral, something that bypasses the intestines, e.g., medicine given through a vein.

entry criteria The conditions which must be met for a patient to enroll in a clinical trial. Usually includes the specific types of tumor, previous treatment allowable, age range and overall health requirements.

enzyme [en´ zime] A protein substance, secreted by certain cells, that stimulates chemical changes in the body without itself being changed. For example, the enzymes produced in the mouth and stomach are crucial for digestion.

EORTC **E**uropean **O**rganization for **R**esearch and **T**reatment of **C**ancer. A network of scientists and oncologists in the main cancer research institutions of the EU countries. They conduct clinical trials throughout Europe.

eosinophil [ee o sin´ o fil] The type of white blood cell (leukocyte) normally filled with granules

American Brain Tumor Association – http://www.abta.org

Histologic Type – Glioma/Glioneuronal

- Most common category of primary brain tumors. They begin in glial cells (supporting cells of the CNS) – can be Grade 1-4 not just 3-4. Some with good outcomes.
- Often spread into surrounding brain tissue along nerve fibers invading the spaces between nearby normal brain cells. Some invade the surrounding brain more than others.
- Difficulty obtaining complete surgical removal. MRI scans show the largest part of the glioma, but cannot reliably show areas of the brain where tumor cells have invaded. Aggressive efforts to remove small numbers of tumor cells within the brain could cause loss of neurologic function.
- When it is not possible to remove the entire glioma, post-op radiation therapy and chemotherapy may be advised.
- Even with maximum safe resection followed by radiation and chemotherapy, gliomas can grow back.

Glioma – 3 Main Histologic SubTypes

1. Astrocytoma: In adults most often arise in the cerebrum. In children they occur in the brain stem, cerebrum and cerebellum. Rarely in brain stem in adults.
2. Felt to be most aggressive of brain tumors.
3. Different outcomes based on molecular pathology traits and age
   - Pilocytic Astrocytoma - Grade 1 – was coded as 9421/1 – new behavior 9421/3
   - Diffuse Astrocytoma – Grade 2 – see Grade 2 clarifications – usually malignant
   - Anaplastic Astrocytoma – Grade 3 – Malignant Astrocytoma, Grade 3
   - Glioblastoma Multiforme - Grade 4 – now with IDH-mutant or IDH-wild type
   - Brain Stem Gliomas – hard to treat due to location in brainstem – DIPG

Glioma – 3 Main Histologic SubTypes

2. Oligodendroglioma: Rare tumor that usually occurs in the cerebrum, grows slowly and usually does not spread into surrounding brain tissue like astrocytoma does. Most common in middle-aged adults.

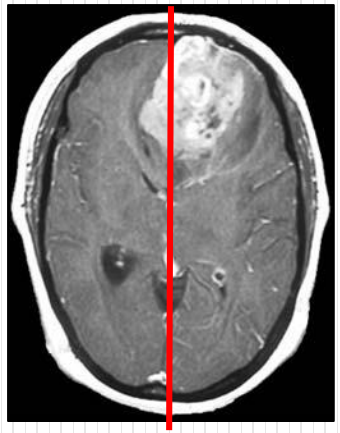
3. Ependymoma: Most commonly arise in children and young adults. They are also seen with neurofibromatosis Type II. Another kind of glioma that forms from the cells that make, support, nourish, and line the ventricles.
   - Check if neurofibroma or ependymoma

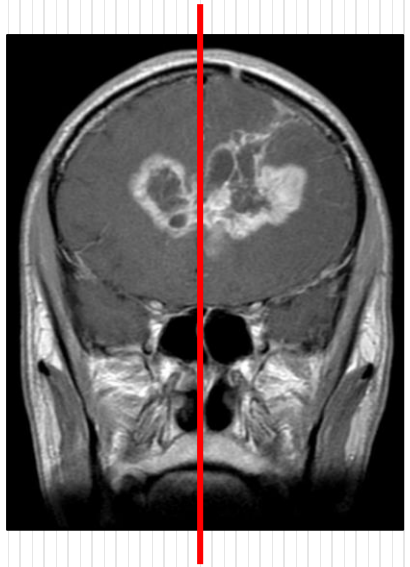
Note 2: For the Brain, CNS Other and Intracranial Schemas **ONLY**, Grade Clinical may be assigned without histologic confirmation if the histology is documented based on imaging.

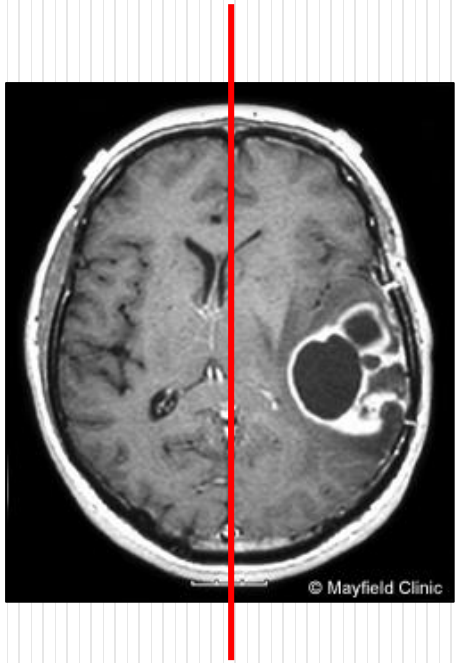
Glioma – Other Subtypes

There are other subtypes of gliomas, each with their own specific characteristics and modes of growth. These subtypes were reclassified into 6 'families' in 2022 by WHO

- Brain Stem Glioma
- Juvenile Pilocytic Astrocytoma
- Pleomorphic Xanthoastrocytoma
- Subependymoma
- Ganglioglioma

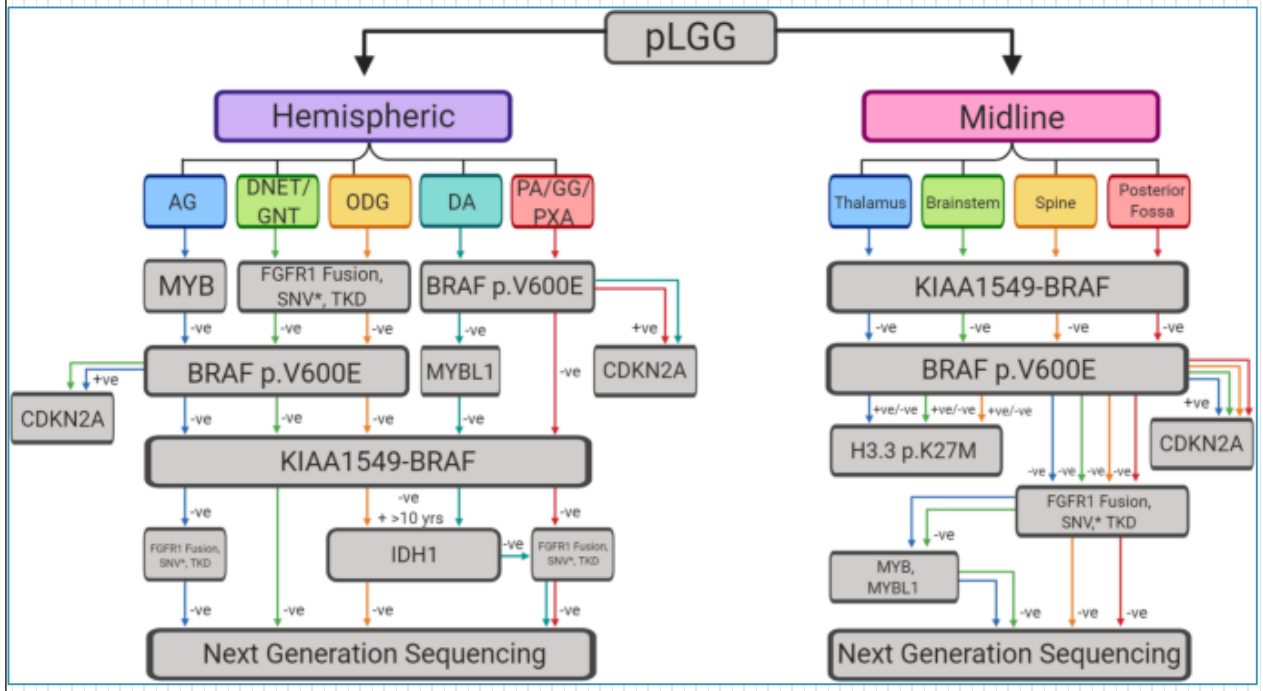


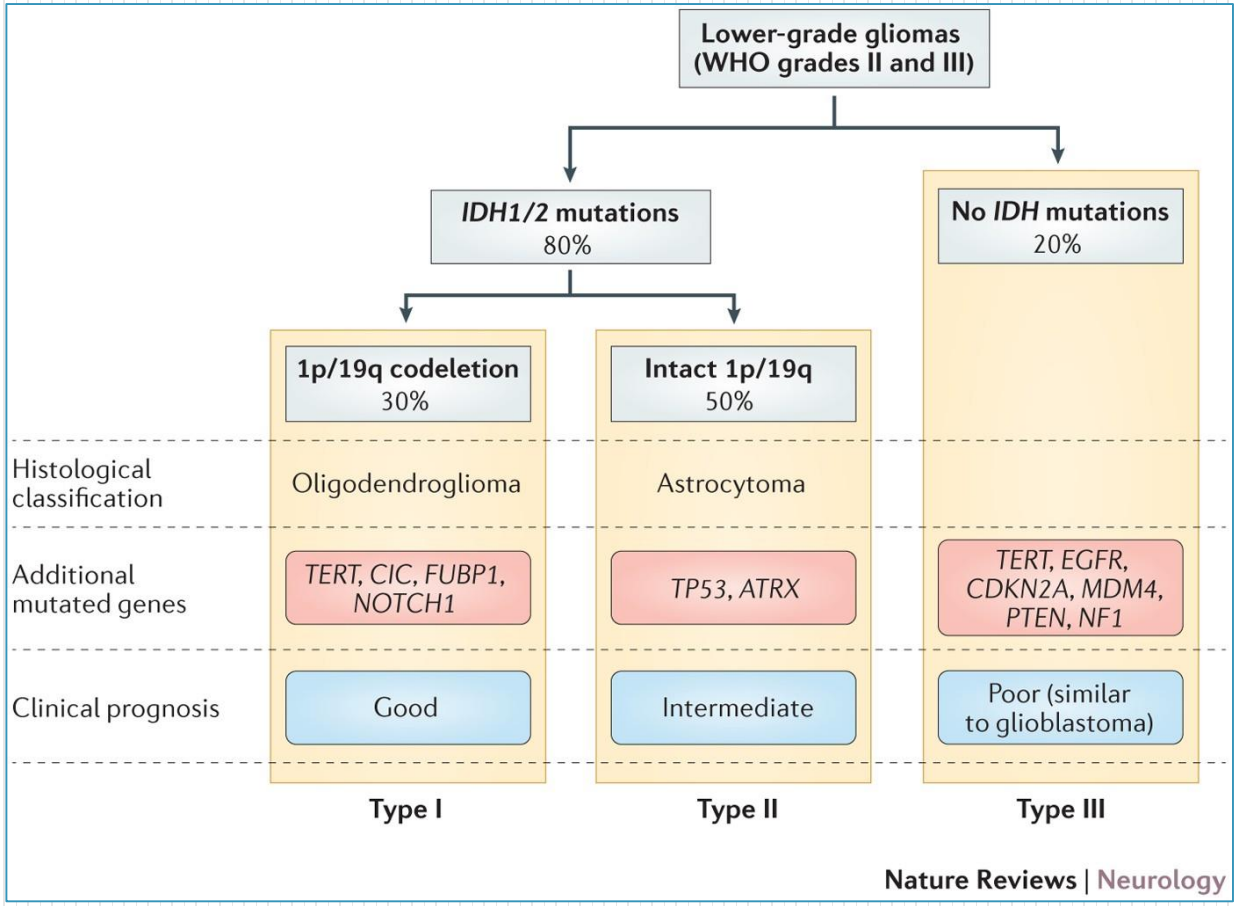




Glioma Molecular Pathology

Gliomas Reclassified into 6 Distinct Genetic "FAMILIES" as Part of the Reorganization of Glioma for the WHO 5th edition





Acta Neuropathologic Communications; https://doi.org/10.1186/s40478-020-00902-z

Glioma Molecular Pathology

Gliomas Reclassified into 6 Distinct Genetic "FAMILIES" as Part of the Reorganization of Glioma for the WHO 5th edition

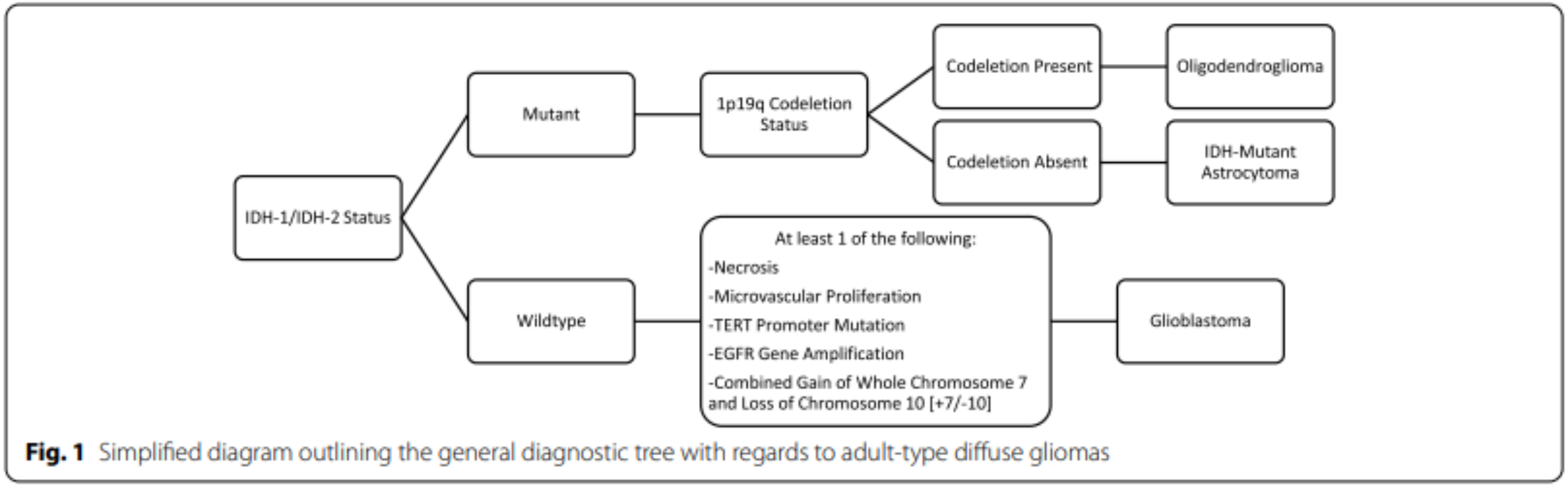
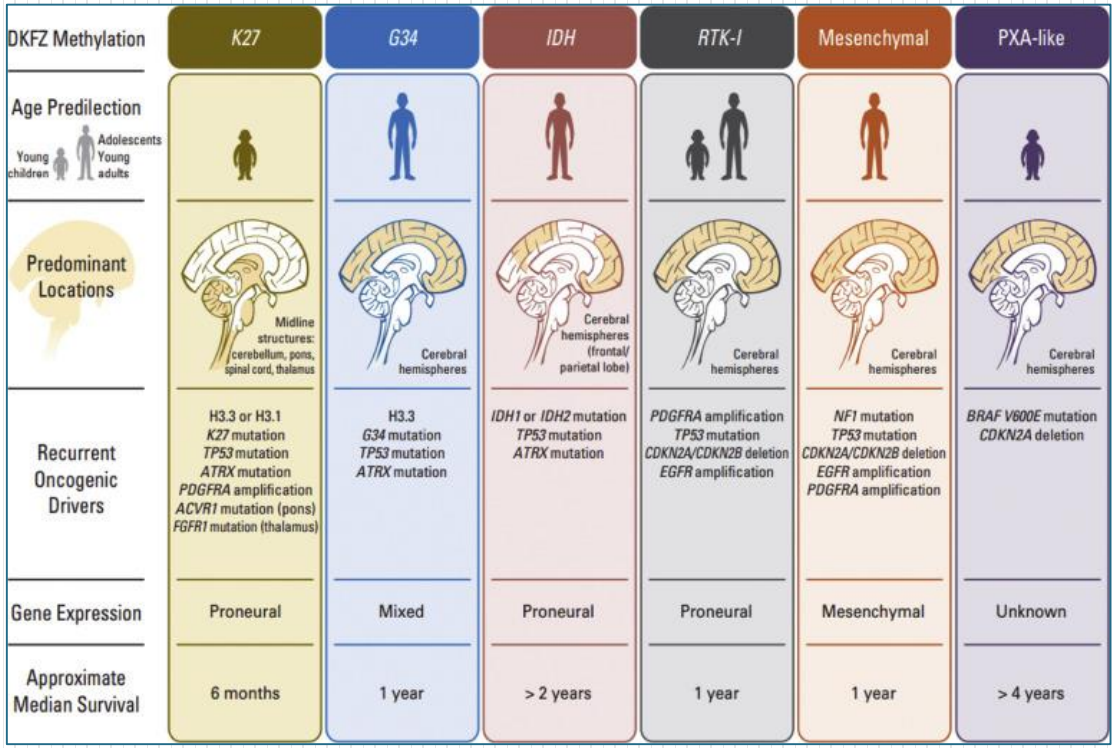


Fig. 1 Simplified diagram outlining the general diagnostic tree with regards to adult-type diffuse gliomas

Vagvala et al. Cancer Imaging (2022) 22:19; https://doi.org/10.1186/s40644-022-00455-5

Imaging/Labs/Path Reports

- Imaging continues to improve for brain diagnosis including improvements in identifying tumor location, size, spread
  - MRI – multiple new MRI Methods (DTI, MRSI, etc.)
- New Imaging techniques can identify tumors specific or absent with mutations in some instances – IDH mutation, EGFR mutant, FGFR3-TACC3 mutant, TERT promoter, etc.
- In recent years, researchers have found some changes in genes, chromosomes, and proteins inside brain tumor cells that can be used to help better classify the neoplasm, predict prognosis or guide treatment. Some examples include:
  - IDH1 or IDH2 gene mutations
  - Chromosomal 1p19q co-deletions
  - MGMT promoter methylation
  - MYB or MYBL1-alterations
  - MYCN-amplificaiton
  - ZFTA fusion gene
  - PATZ1 fusion gene
  - FOXR2-activation
  - BCOR tandem duplication
  - SMARCB1 mutation
  - H3K27 trimethylation
  - YAP1 fusion gene
  - WNT-activation
  - TP53 wild/mutant type
  - WNT activation
  - And MANY new ones defined in WHO 5th edition



Pediatric Neurology, Volume 104, March 2020, pages 3-12

Non-Glial Tumors

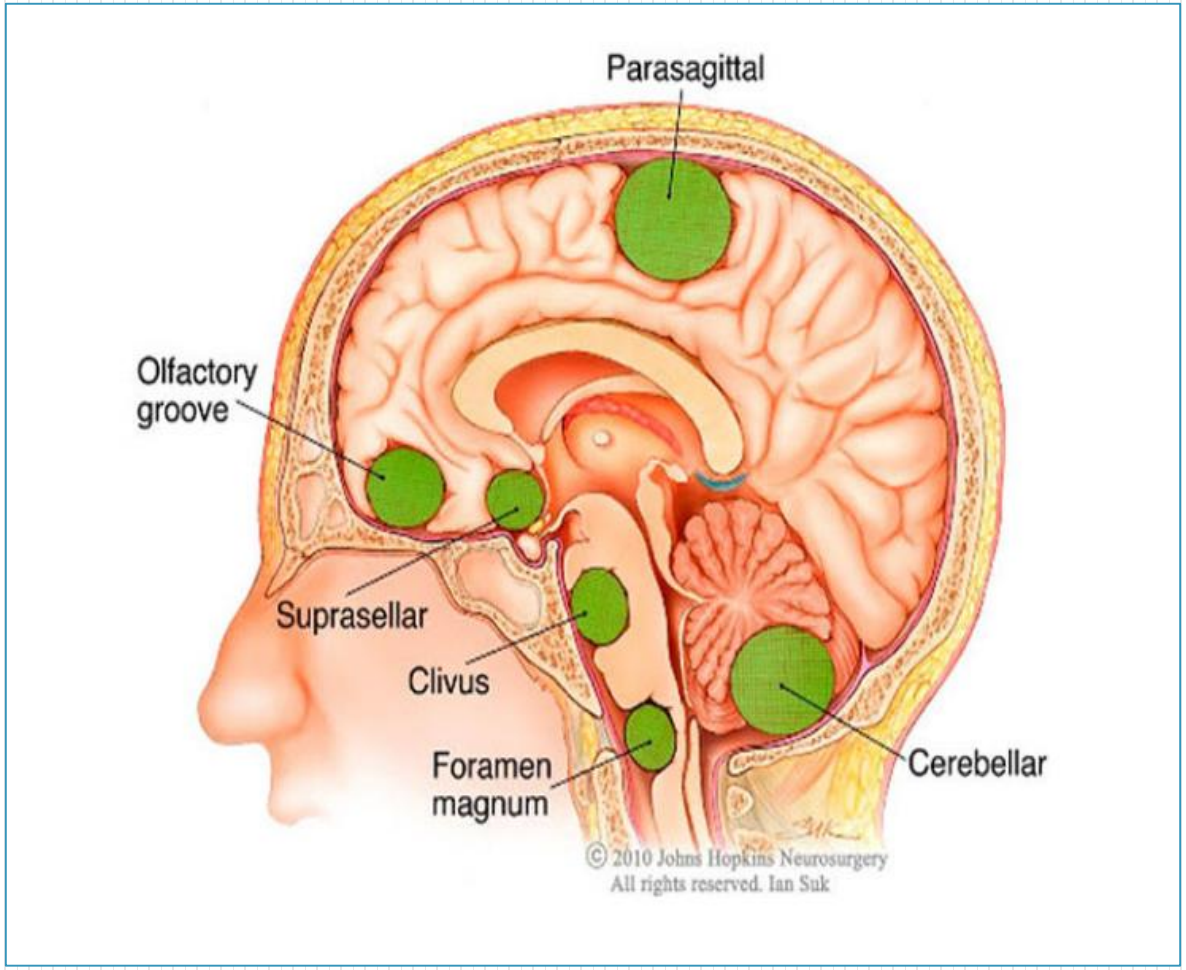
- Embryonal Tumors - Embryonal tumors of the central nervous system are cancerous (malignant) tumors that start in the fetal (embryonic) cells in the brain. Embryonal tumors can occur at any age, but most often occur in babies and young children.
  - Medulloblastoma: Usually arises in the cerebrum, is the most common brain tumor in children, and is sometimes called a "primitive neuroectodermal tumor" or PNET or extraosseous Ewing sarcoma.
  - Atypical Teratoid/Rhabdoid Tumor
- Neuronal and Mixed Neuronal-Glial Tumors - rare low grade malignant tumors that occur in the brain or spinal cord (DNET, PGT, MGT, DLGNT)
- Choroid Plexus Tumors - rare primary brain tumors arising from epithelial differentiated tissue – often benign tumors

Meningioma – benign/borderline/malignant

- Meningiomas are typically diagnosed by CT or MRI imaging
- Biopsy may be considered for confirmation
- Most meningioma are benign tumors.
- Options stratified by presence/absence of symptoms, tumor size and location
- Most asymptomatic patients with small tumors (<30mm) may just be observed.
- If neurological impairment is imminent - then surgery or radiotherapy (EBRT OR SRS)
- Asymptomatic tumors >30mm can be either resected or observed

Note 2: For the Brain, CNS Other and Intracranial Schemas **ONLY**, Grade Clinical may be assigned without histologic confirmation if the histology is documented based on imaging.

Meningioma


Parasagittal
Olfactory groove
Suprasellar
Clivus
Foramen magnum
Cerebellar
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Meningioma

- ***Note 1:*** The following non-malignant meningiomas are reportable:
- **Intraosseous**
  - ***Note:*** The **dura** layer of the meninges **contacts** the **endosteum** of the bones of the skull. The primary site for intraosseous meningioma is cranial meninges C700.
- **Sphenoid wing**
  - ***Note 1:*** Sphenoid wing meningiomas arise in the **cranial meninges** C700 which **covers** the bony structure called the sphenoid wing.
  - ***Note 2:*** The term "sphenoid wing meningioma" is used to identify the **location** of the meningioma because sphenoid wing meningiomas may be very **invasive**, spreading to the dura of the frontal, temporal and orbital regions.
- **Cavernous sinus**
- ***Note 1:*** Cavernous sinus is located between the endosteal and meningeal layers of the dura.
- ***Note 2:*** There is **no ICD-O site** code for cavernous sinus because tumors do not arise in the sinus itself; the primary sites are:
  - The **cranial nerves** passing through the sinus (trochlear, abducent **C725**) **OR**
  - The cerebral **meninges/dura C700** covering the cranial nerve
- ***Note 2:*** Cavernous sinus hemangiomas are reportable. Code primary site cerebral meninges C700.

Non-Glial Tumors

- Schwannoma: Arises from Schwann cells present in certain nerves, including those that control balance and hearing. May be called "neuroma".
- A common site is the vestibular or auditory nerve which carries signals from the inner ear to the brain stem.
- Tumors in this location are called "acoustic neuromas" (a.k.a. vestibular schwannoma), and occur most often in adults.

Non-Glial Tumors

- Craniopharyngioma: Grows at the base of the brain, arises from the tissue connecting the brain and the pituitary gland and occurs in both adults and children.

- Pituitary Adenoma: Arises from the pituitary gland and may cause compression of the optic nerves causing vision problems. Some produce excessive amounts of hormones that can disrupt the body's metabolism.

- Pineal Gland Tumors: Pineal region tumors are primary central nervous system (CNS) tumors. These tumors begin in the brain (in the pineal gland) but can spread to the spinal cord.

Neurofibromatosis

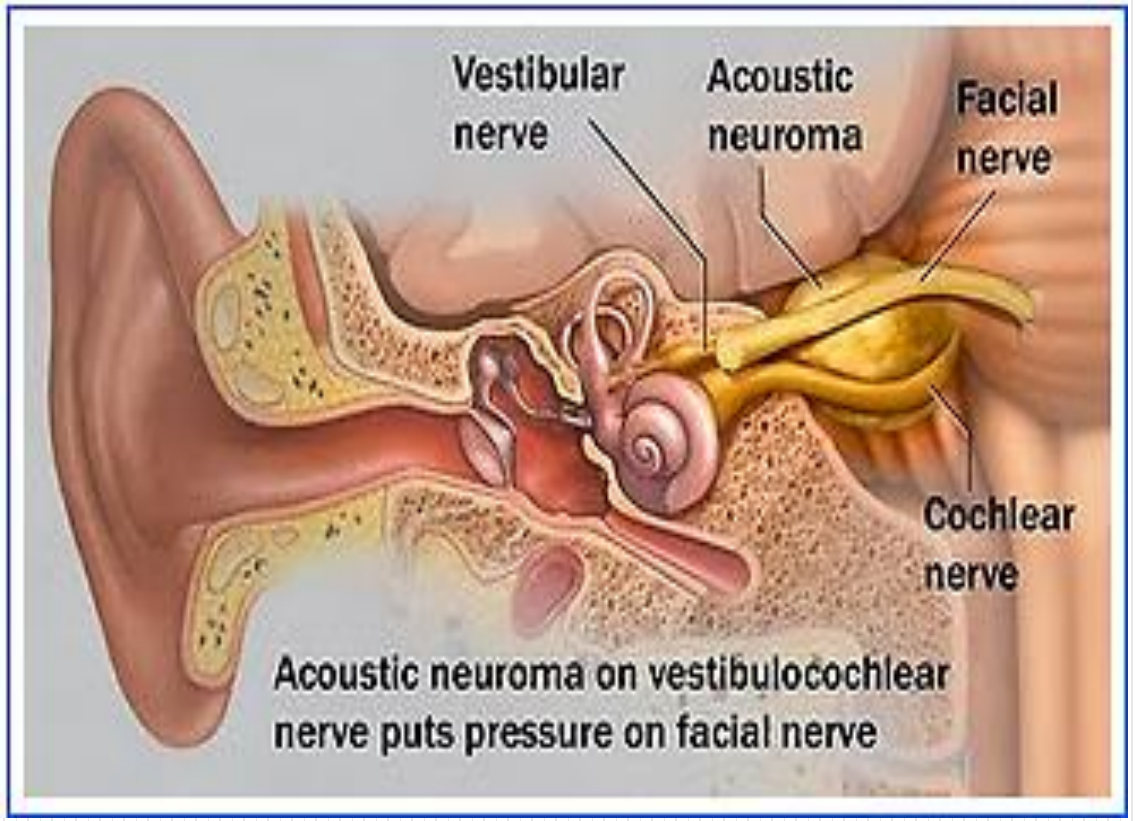
Table 4: Non-Reportable Neoplasms

Use **Table 4** for **non-malignant neoplasms ONLY**. The table identifies **histology/site** combinations which are **not reportable.** This table was created from WHO with the cooperation of the Central Brain Tumor Registry of the United States (CBTRUS).

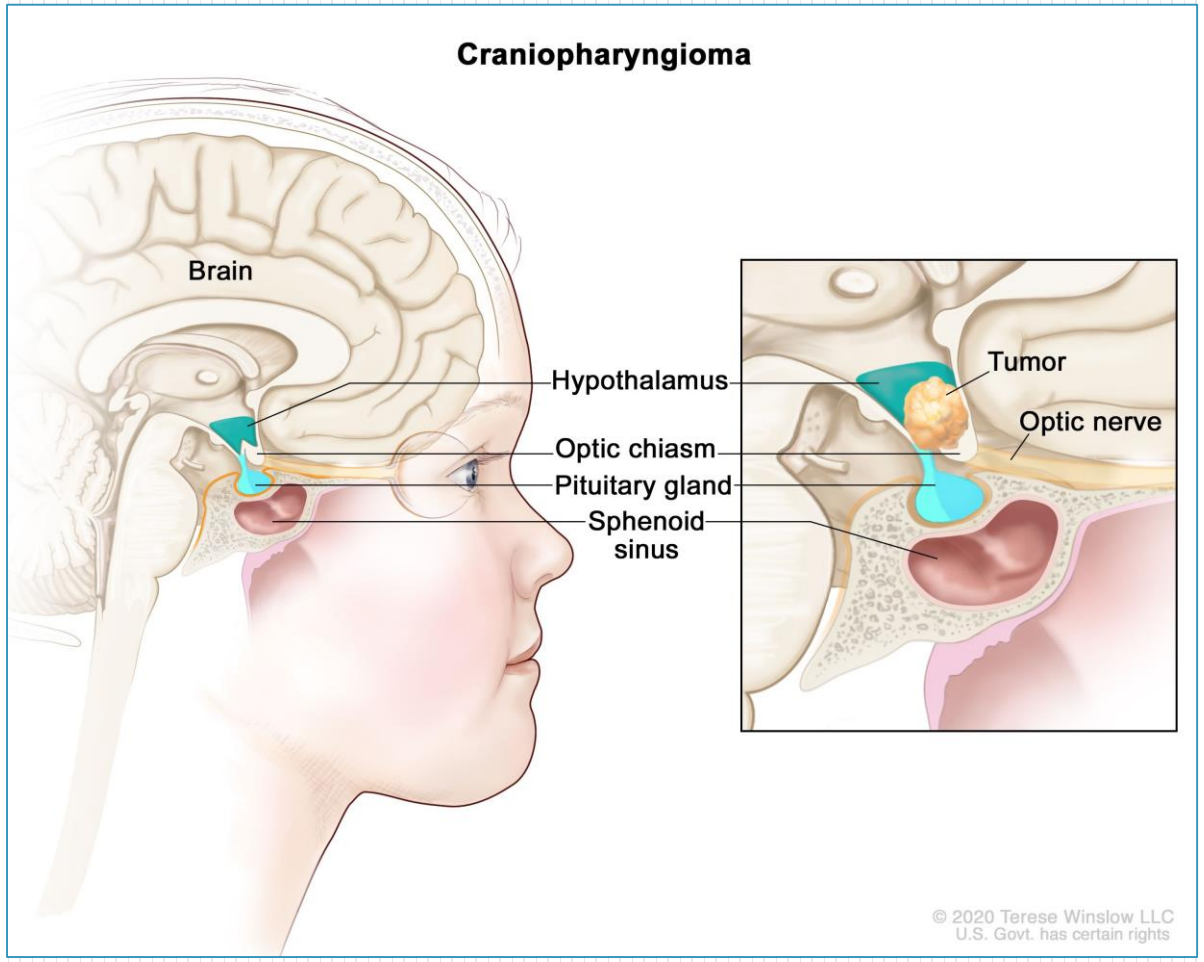
Non-reportable Histology Term	Non-reportable Histology Code	Definitions and Sites
Carcinomas	**8010-8060, 8071-8671, 8940-8941**	Brain C710-C719 **Site/histology edit** carcinomas/brain
Carcinomas	**8010-8671, 8940-8941**	Cerebral meninges, spinal meninges, meninges NOS C700-C709 **Site/histology edit** carcinomas/meninges
Carcinomas	**8010-8671, 8940-8941**	C721-C729 (Other central nervous system) **Site/histology edit** carcinomas/other CNS
Colloid cyst	**No code**	
Epidermoid tumor/cyst	**No code**	
Glomus tympanicum, glomus jugulare	**8690/1**	These tumors occur in the inner ear, the aortic body and other paraganglia respectively; these sites are **not reportable.**
Hygroma	**9173/0**	
Hypothalamic hamartoma	**No code**	Occurs in hypothalamus
Neurofibromatosis, NOS	**9540/1**	Genetic disease that produces non-malignant tumors in the skin, brain, CNS, and other sites. The brain and CNS tumors spawned by NF, NOS are reportable, the genetic disease is not.
Neurofibromatosis, type 1 (NF1)	**No code***	Genetic disease that produces non-malignant tumors in the skin, brain, CNS, and other sites. The brain and CNS tumors spawned by NF1 are reportable, the genetic disease is not.
Neurofibromatosis, type 2 (NF2)	**No code***	Genetic disease that produces non-malignant tumors in the skin, brain, CNS, and other sites. The brain and CNS tumors produced by NF2 are reportable, the genetic disease is not.
Neuroglial cyst	**No code**	Ventricles
Osteochondroma	**9210/0**	Originates in the cartilage around bone, site not reportable for non-malignant neoplasms
Rathke cleft cyst	**No code**	Sella turcica C751. This is a Rathke cleft CYST, not a Rathke cleft tumor.
Schwannomatosis	**No code***	A form of neurofibromatosis newly named/discovered

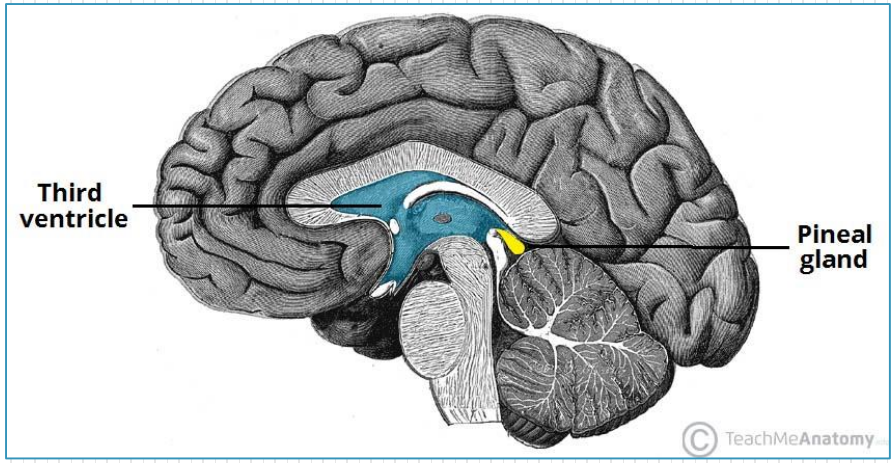
***The code which is currently in ICD-O-3 for neurofibromatosis will not be used in ICD-O updates or in future ICD-O editions**

Acoustic Neuroma/Schwannoma

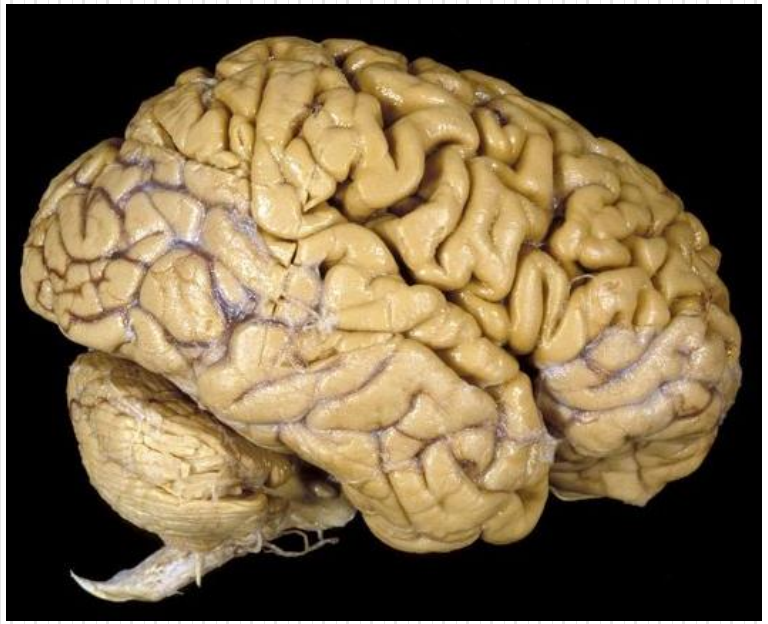


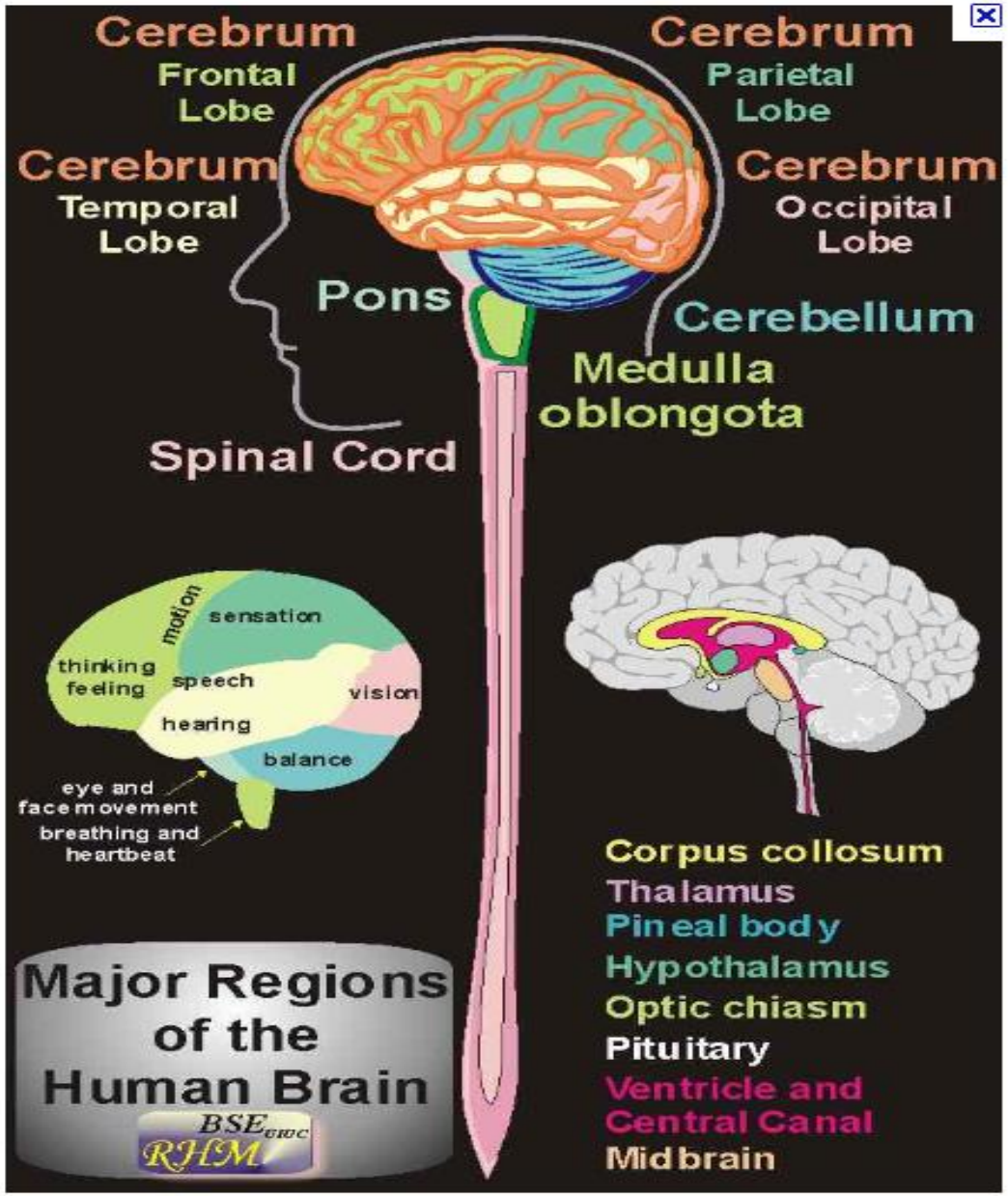
Pineal Gland Tumors and Craniopharyngioma



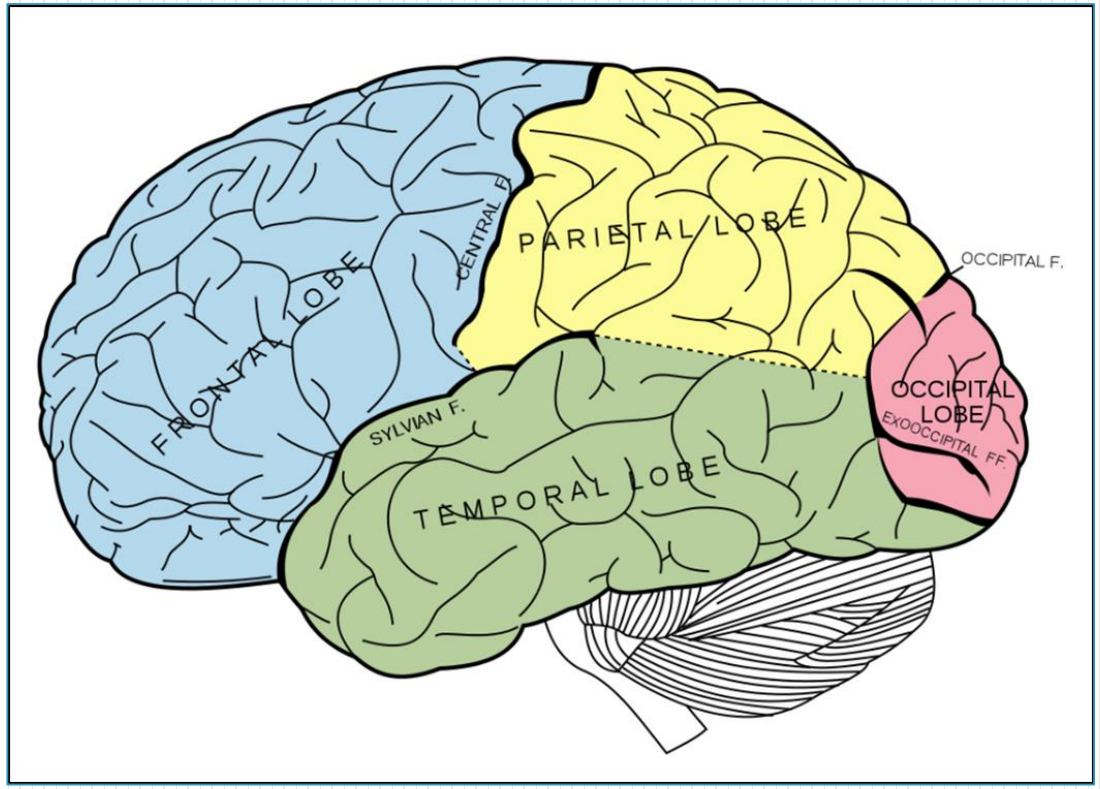


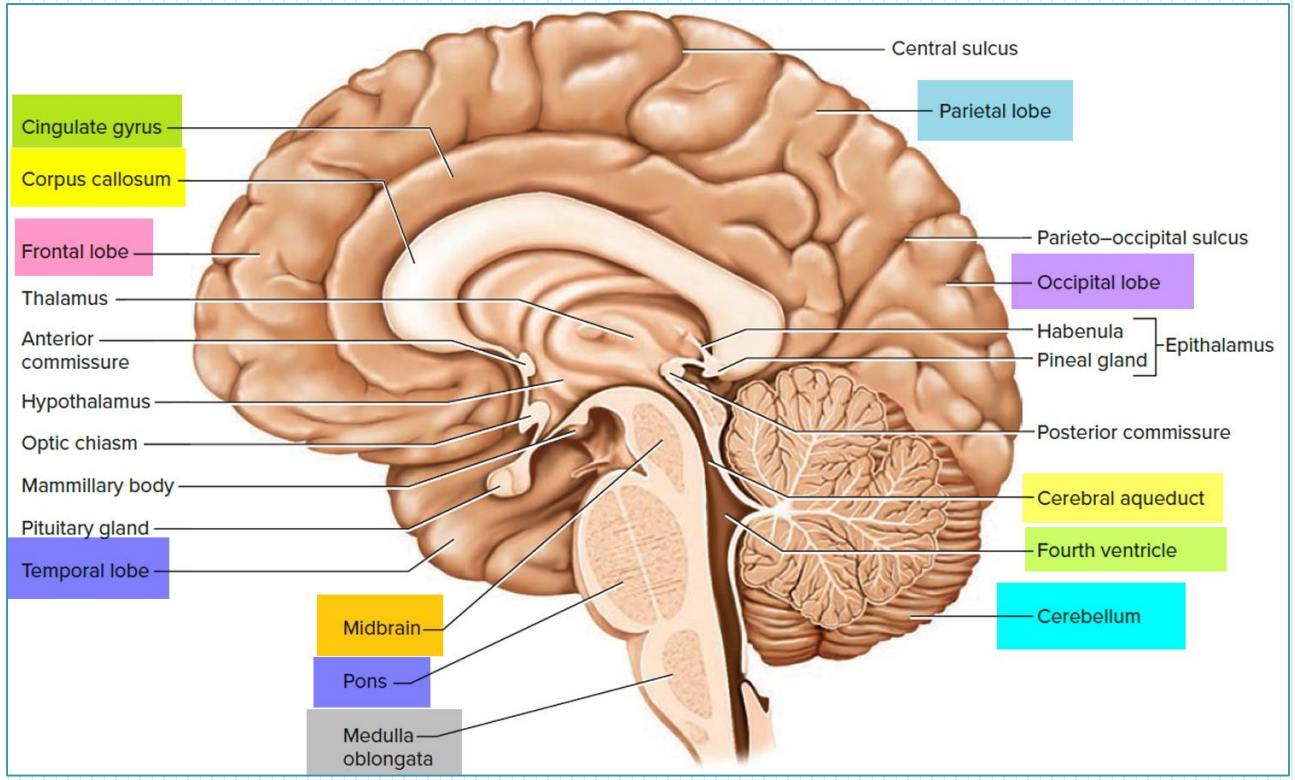
ANATOMY OF THE HUMAN BRAIN




Cerebrum
Frontal
Lobe
Cerebrum
Parietal
Lobe
Cerebrum
Temporal
Lobe
Cerebrum
Occipital
Lobe
Pons
Cerebellum
Medulla
oblongota
Spinal Cord
motion
sensation
thinking
feeling
speech
vision
hearing
balance
eye and
face movement
breathing and
heartbeat
Corpus collosum
Thalamus
Pineal body
Hypothalamus
Optic chiasm
Pituitary
Ventricle and
Central Canal
Midbrain
Major Regions
of the
Human Brain
BSE
RHM

Brain Lobes and Fissures





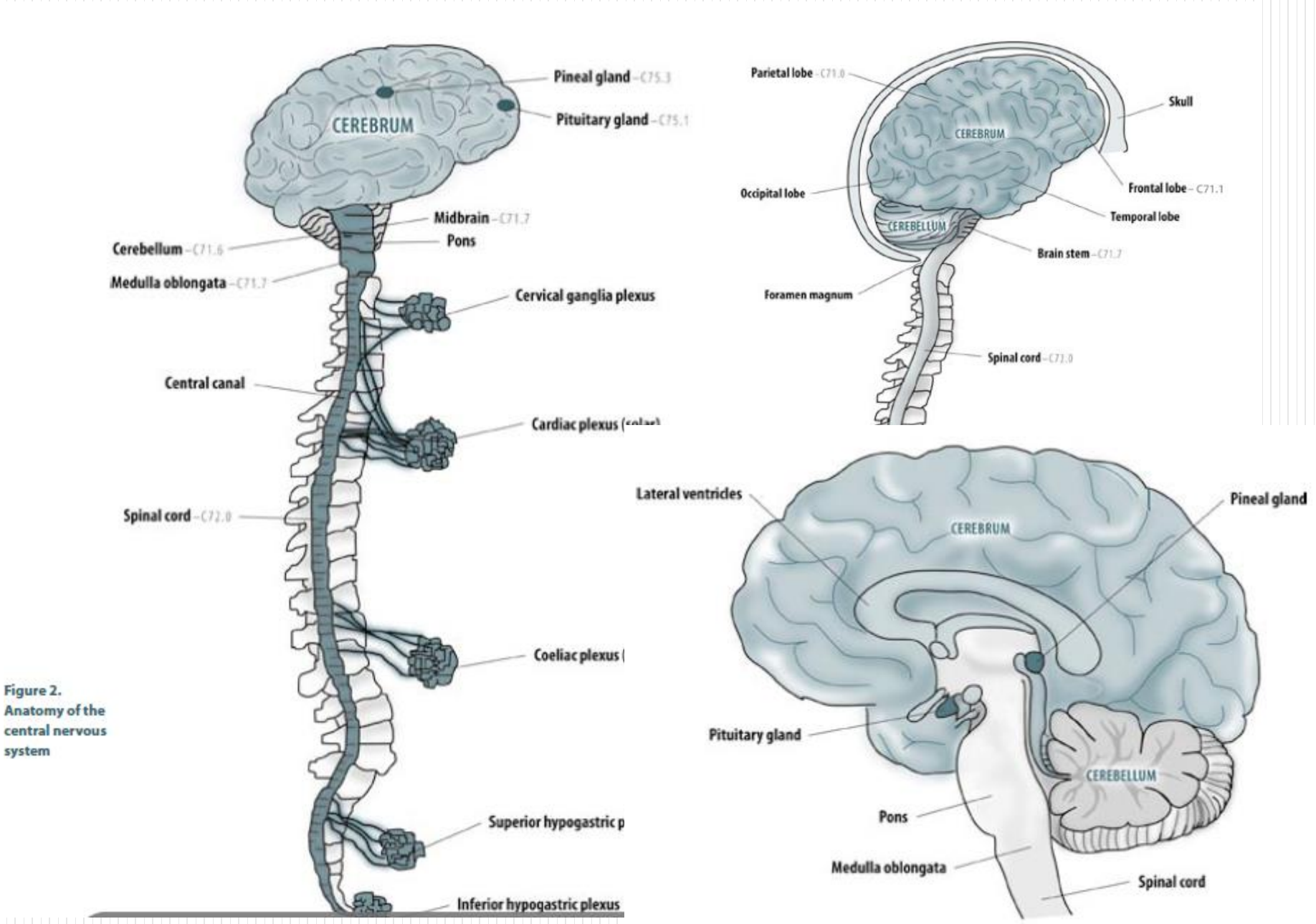
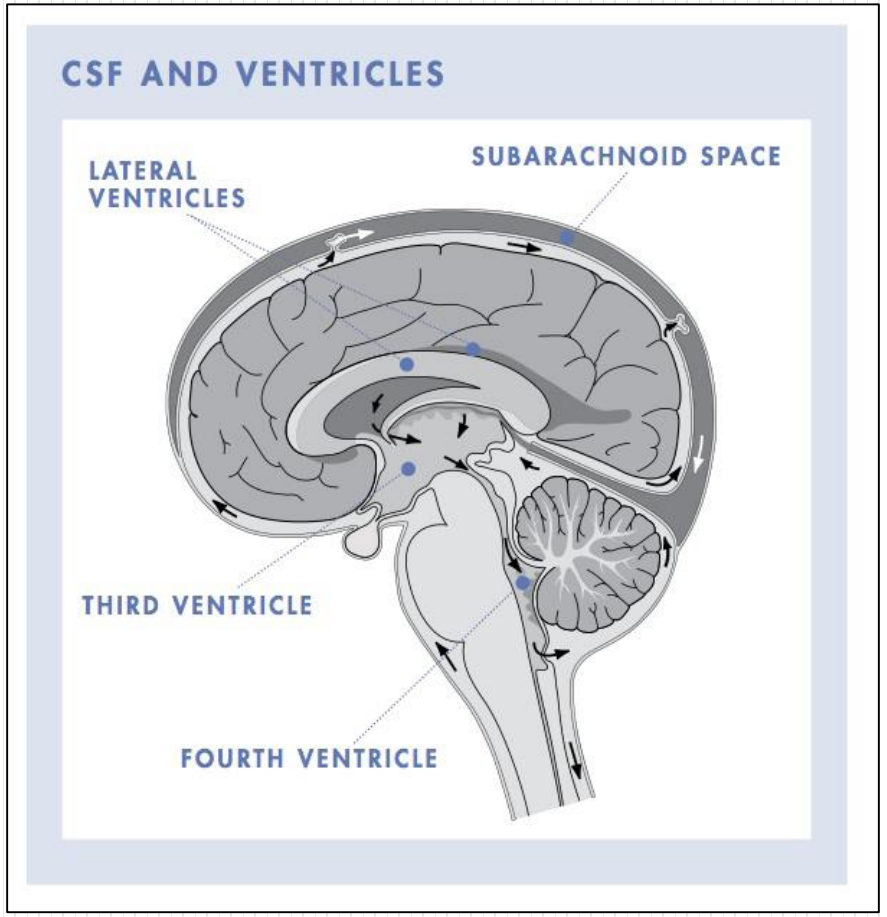


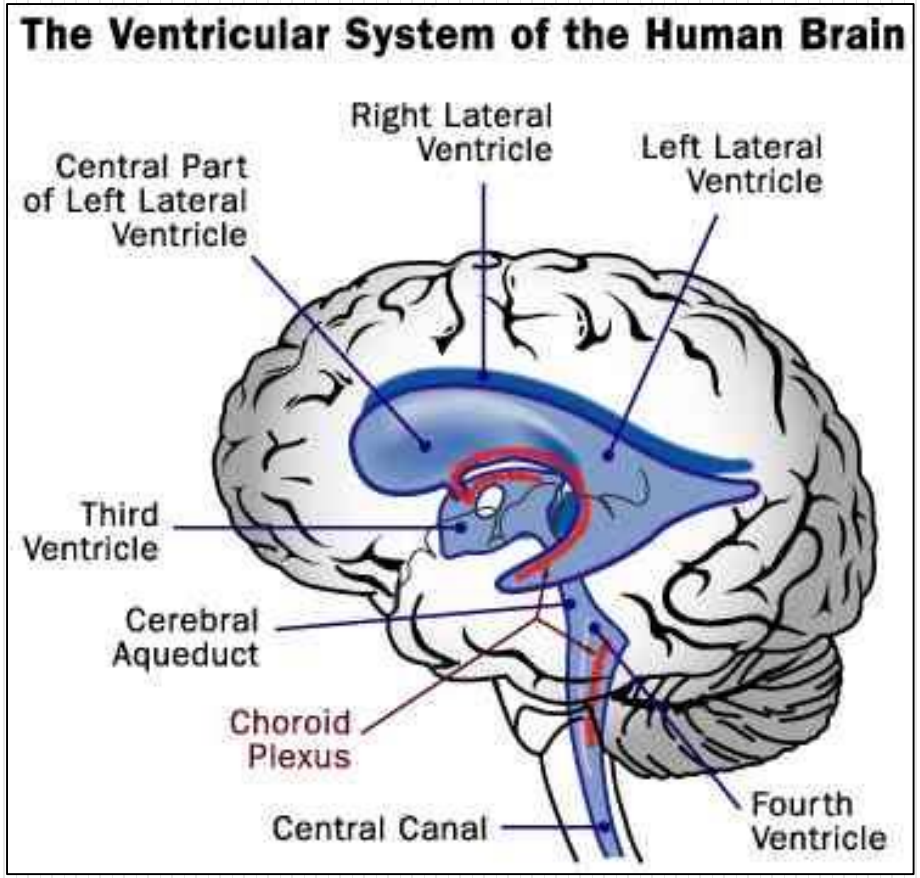
Figure 2.
Anatomy of the central nervous system

Ventricular System of the Brain



http://www.abta.org/brain-tumor-information/brain-anatomy/structure.html

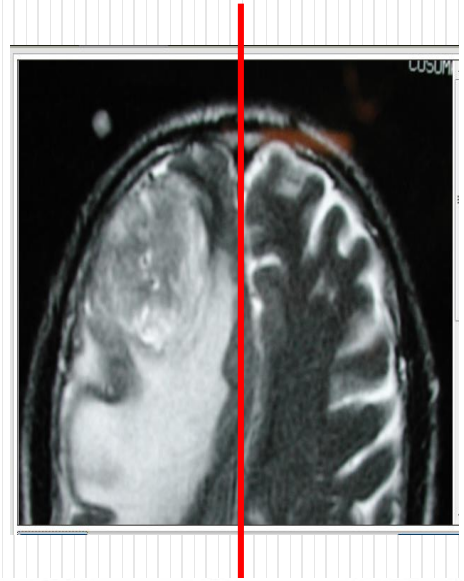
Ventricular System of the Brain

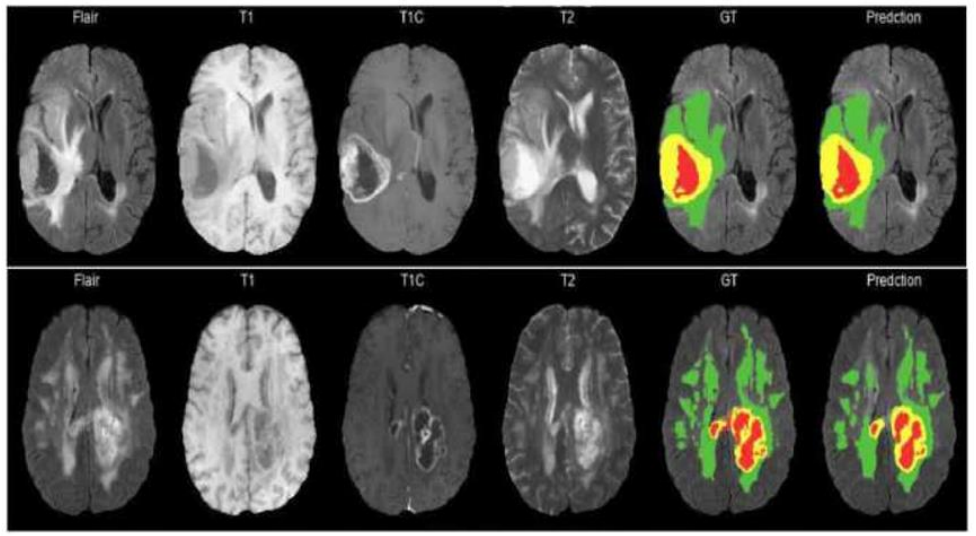


Source: solarnavigator.net/human_brain

Midline Shift and Mass Effect

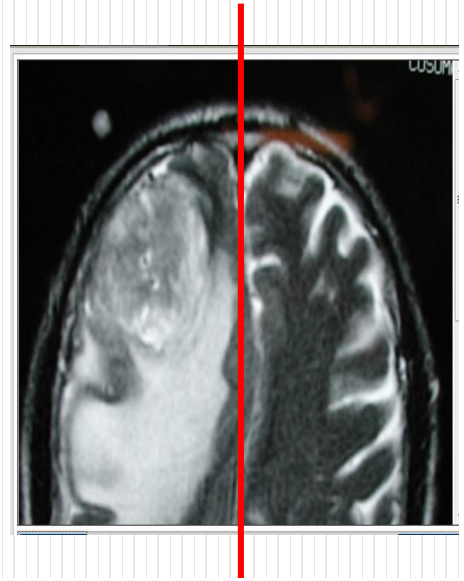
- The bony cranium protects the brain from outside impacts to the head. When swelling occurs in the brain, there isn't much "give".
- The swelling results in intracranial pressure and can cause a number of effects that begin to impact quality of life and comfort for the patient.
- The easiest way to describe midline shift is to bring to mind siting in a movie theater. As soon as the person to one side of you puts his elbow onto the shared armrest between you, you tend to shift away.

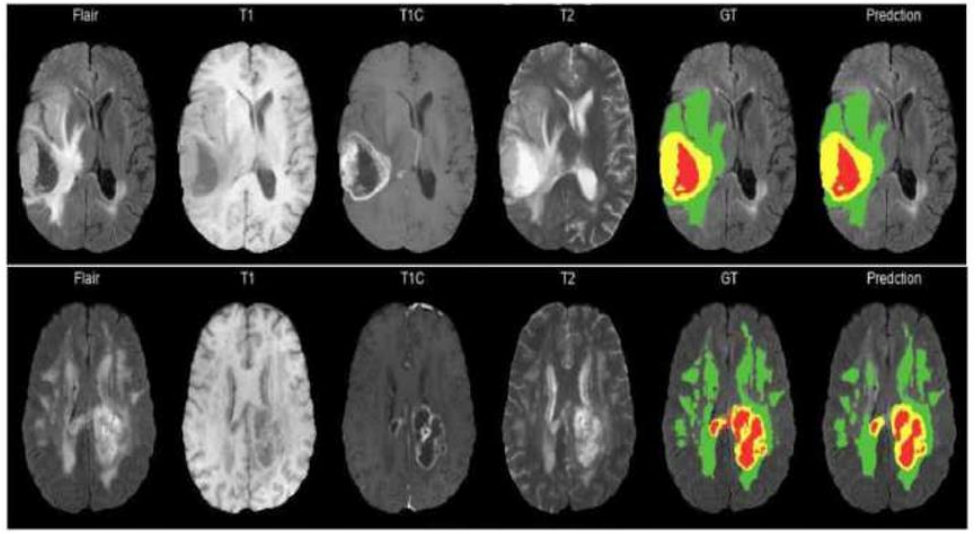




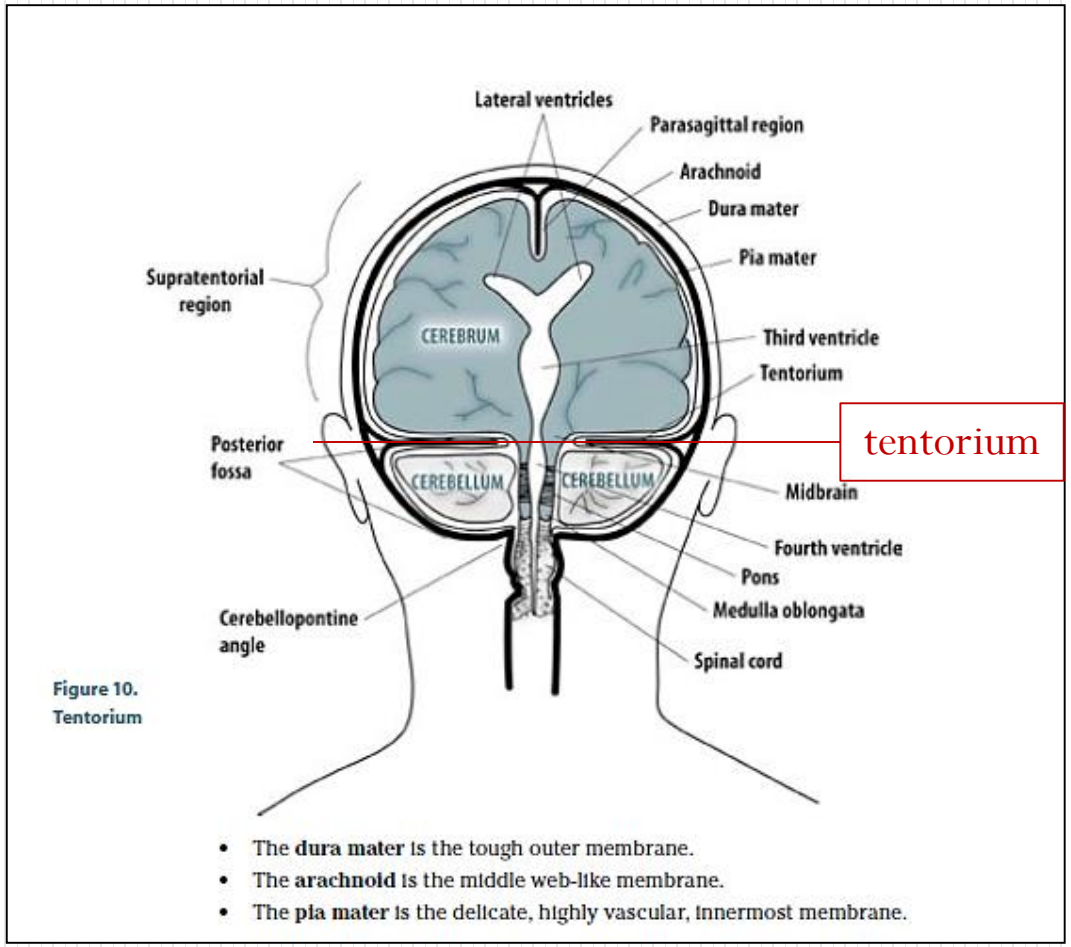
Midline Shift and Mass Effect

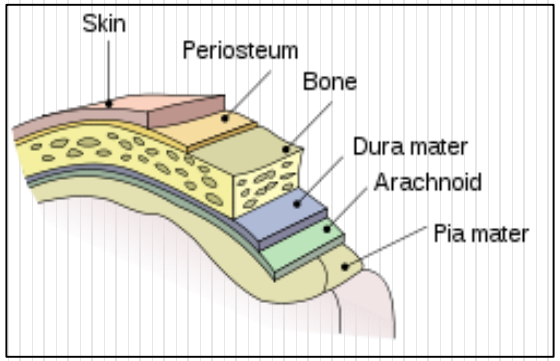
- Midline is a central boundary separating the left and right hemispheres.
- Midline Shift – Tumor crosses the brain to shift across the center line
- Mass Effect is – Edema or swelling causes the brain to shift across center line
- Both create new symptoms at cross-over
  - Depends on the size and location of he tumor and level of spread
  - Edema caused by many things
  - Either cause pushes midline out of alignment

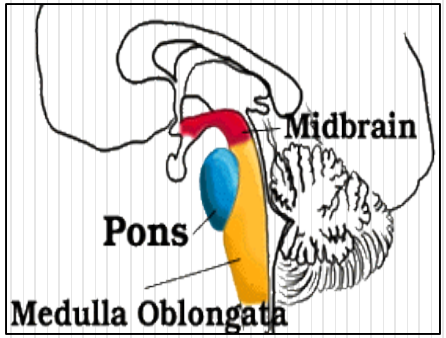




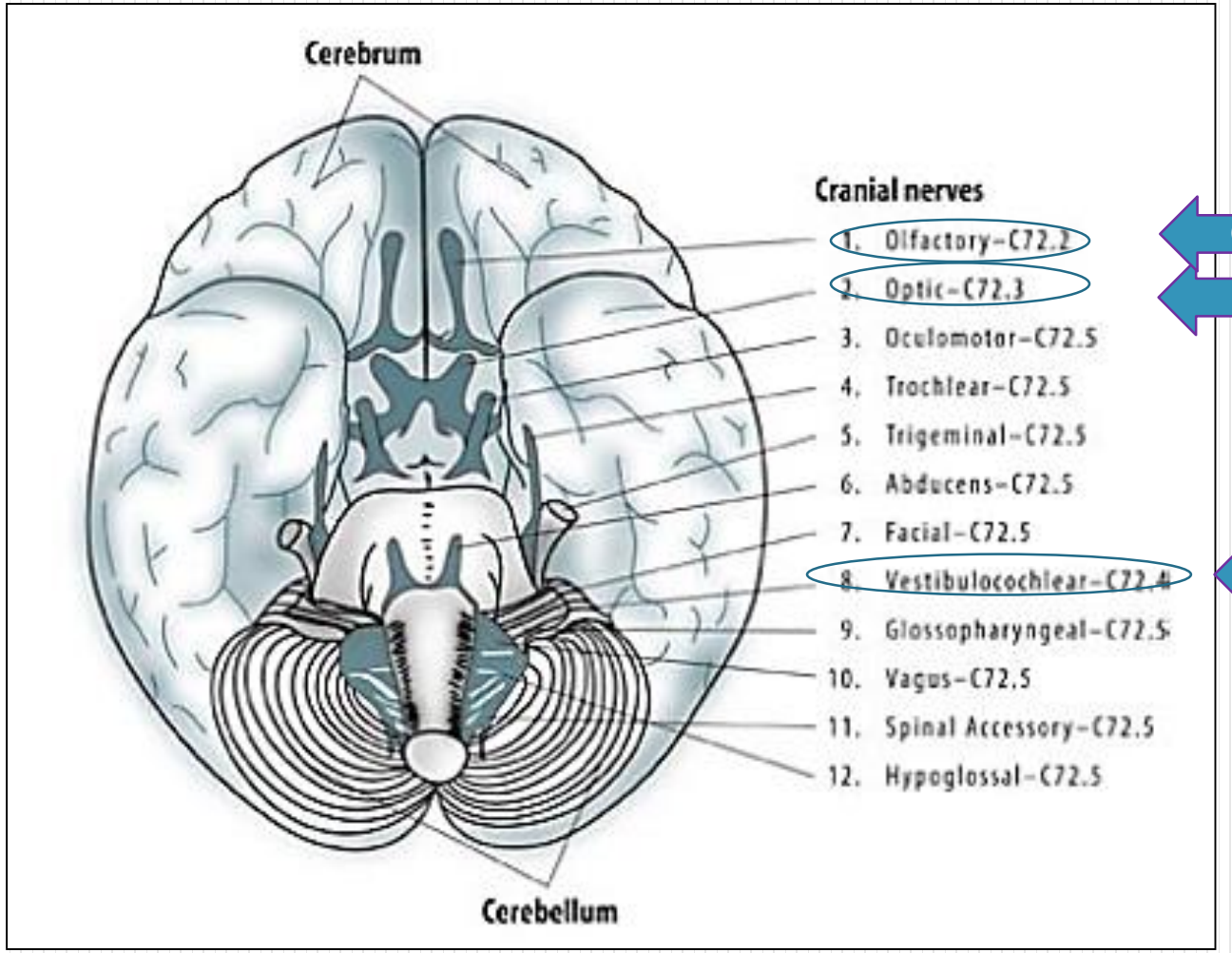
Meninges and Brain Stem







Cranial Nerves



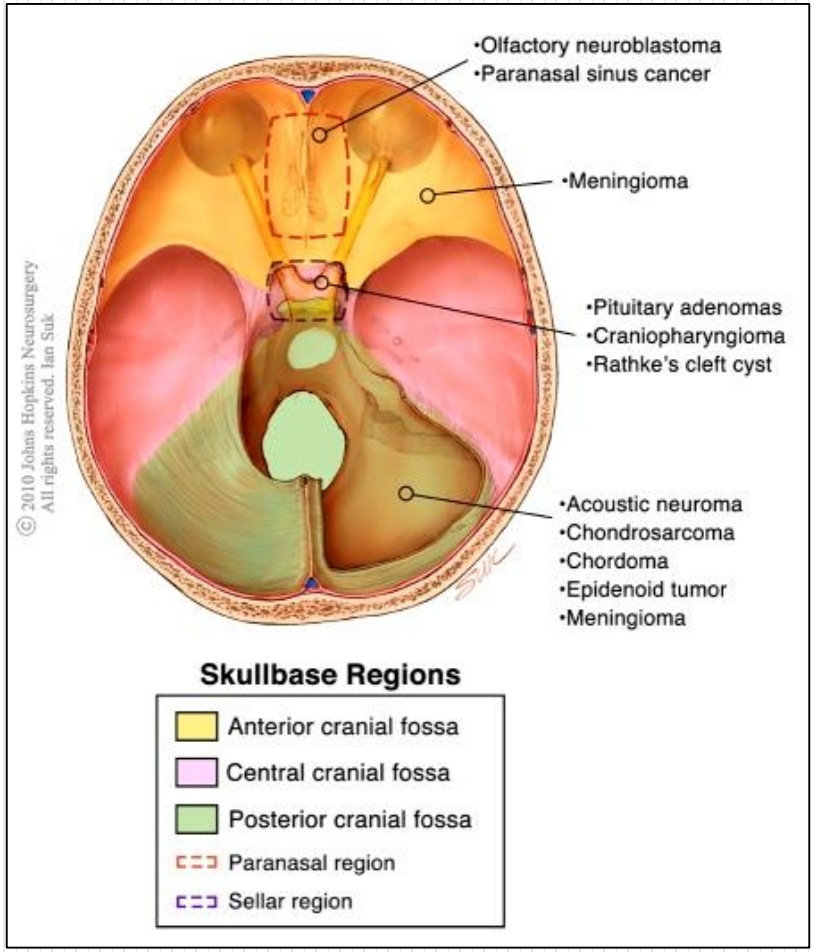
Cranial Nerve Functions

Cranial Nerve:	Major Functions:
I Olfactory	smell
II Optic	vision
III Oculomotor	eyelid and eyeball movement
IV Trochlear	turns eye downward and laterally, controls superior oblique muscles
V Trigeminal	chewing, face & mouth touch & pain
VI Abducens	turns eye laterally
VII Facial	facial expressions, taste, tears, saliva
VIII Vestibulocochlear	Also referred to as Auditory Nerve: hearing, equilibrium sensation
IX Glossopharyngeal	Taste, senses carotid blood pressure
X Vagus	aortic blood pressure, heart rate, stimulates digestive organs, taste
XI Spinal Accessory	controls trapezius & sternocleidomastoid muscles, controls swallowing
XII Hypoglossal	controls tongue movements

Sinus, Olfactory, Base of Skull Tumors

- Cancer Registries see many of these as Head & Neck Neoplasms
- Some are intra-cranial but many are not intra-cranial or CNS
- Primary Site of Tumor Critical for Stage, Treatment, and Prognosis
- Histology is used to identify which are abstracted as Brain/CNS
- Highly specialized surgical procedures – location of tumor
- Some Prognostic Factors Overlap

Sinus, Olfactory, Base of Skull Tumors

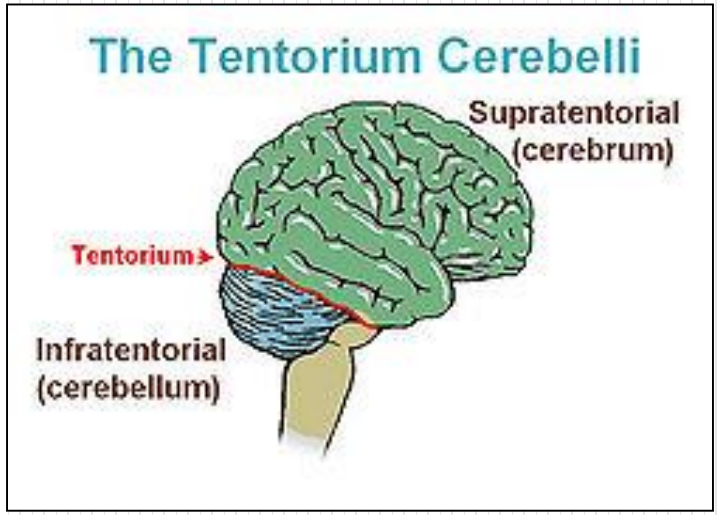


http://www.hopkinsmedicine.org/sebin/d/w/skull-base-ian-suk-sml.jpg

Childhood Brain Tumors

Tentorium - separates the cerebellum from the occipital lobes

- 50% of childhood brain and CNS tumors are infratentorial, originating below the tentorium
- 20+% of childhood CNS tumors are located in the sellar or suprasellar region around the sella turcica (the bone that contains the pituitary gland)
- Remainder of tumors occur in spinal cord, brain stem, cranial nerves, etc.



Childhood Brain Tumors

Tentorium – separates the cerebellum from the occipital lobes

Note 6: The following subsites code to C710 are INFRAtentorial:

- Hypothalamus
- Pallium
- Thalamus

Note 7: The following subsites coded to C718 are SUPRAtentorial

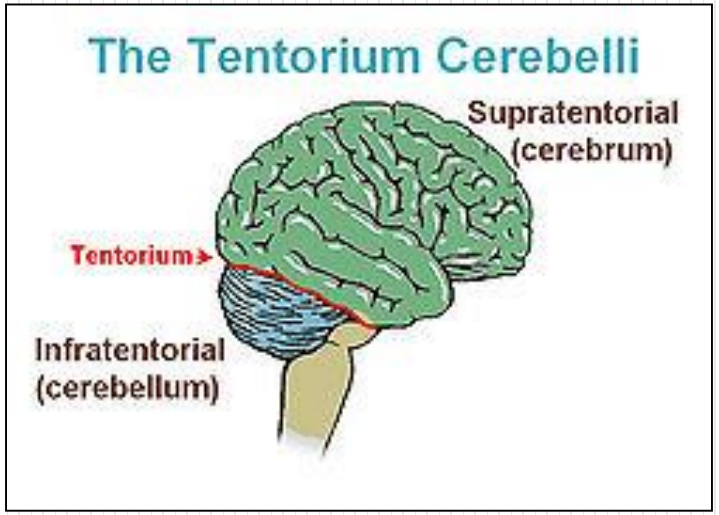
- Corpus callosum
- Tapetum

Note 8: The following sites coded to C719 are SUPRAtentorial

- Anterior cranial fossa
- Middle cranial fossa
- Suprasellar

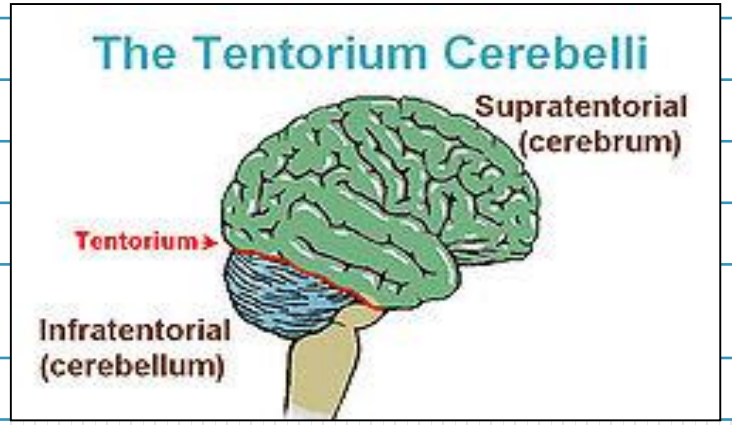
Note 9: The following subsites coded to C719 are INFRAtentorial

- Posterior cranial fossa

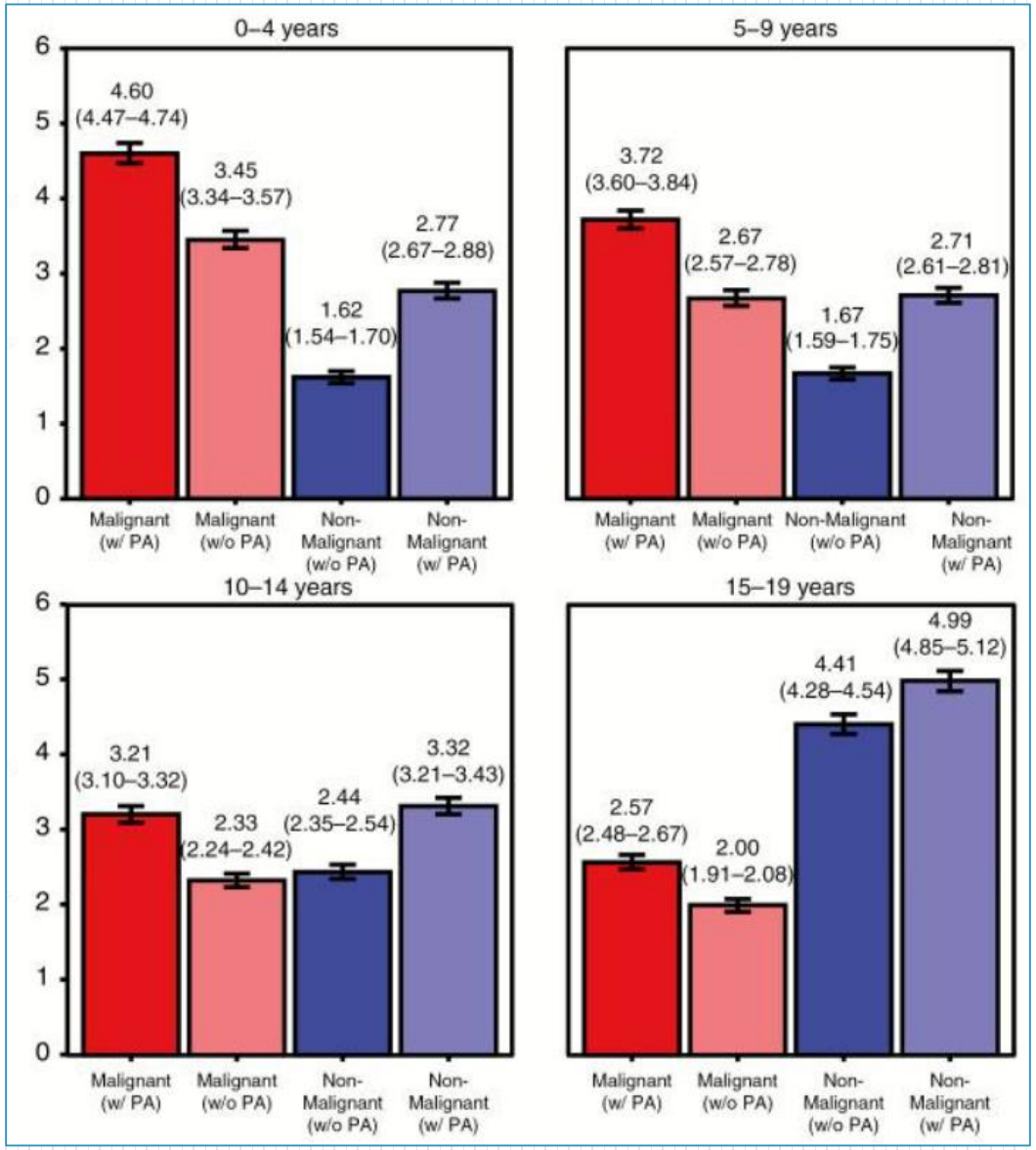


Childhood Brain Tumors

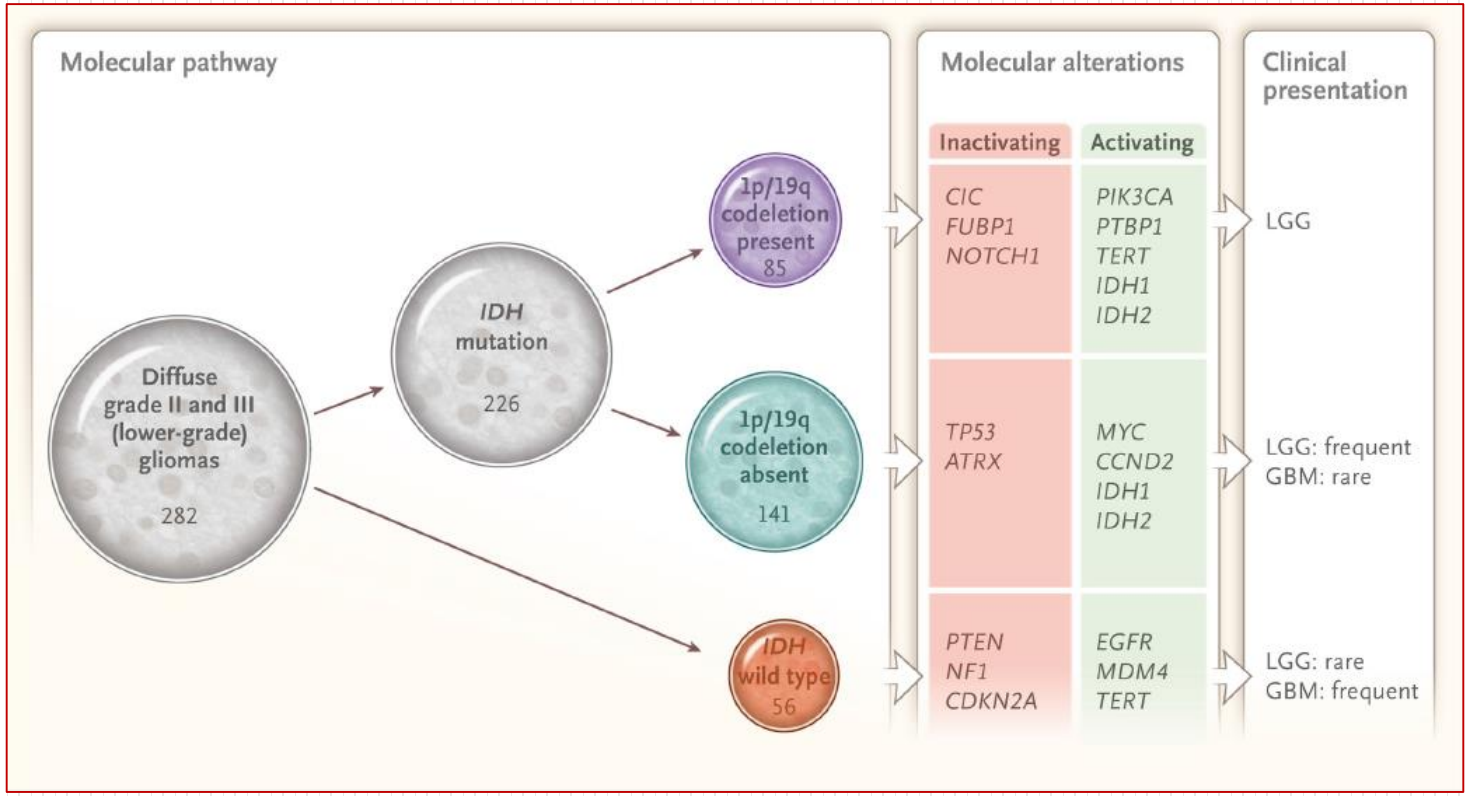
Supratentorial - childhood	Infratentorial - childhood
• Craniopharyngiomas.	• Cerebellar astrocytomas (usually high-grade).
• Diencephalic and hypothalamic gliomas.	• Medulloblastomas (primitive neuroectodermal tumors).
• Germ cell tumors.	• Ependymomas (low-grade or anaplastic).
• Low-grade astrocytomas.	• Brain stem gliomas (high-grade or low-grade).
• Anaplastic astrocytomas.	• Atypical teratoid tumors
• Glioblastoma multiforme.	
• Mixed gliomas.	
• Oligodendrogliomas.	
• Primitive neuroectodermal tumors.	
• Low-grade or anaplastic ependymomas.	
• Meningiomas.	
• Choroid plexus tumors.	



Pilocytic Juvenile Astrocytoma

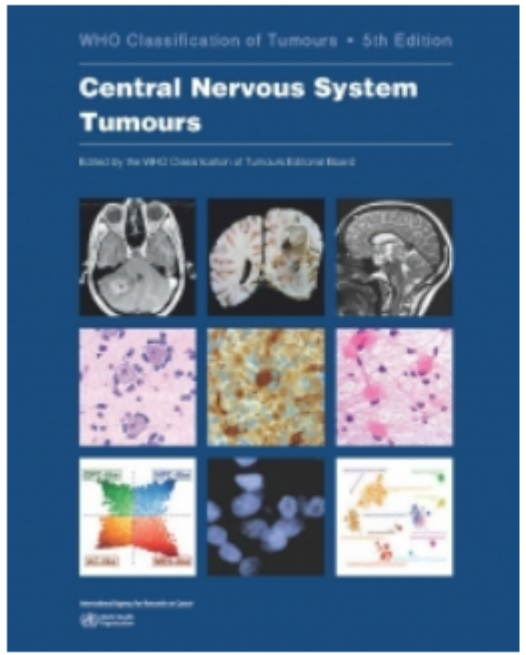


Diagnoses are based on Combination of Histology, Behavior, Tumor Genetic Profile or Makeup, and WHO CNS Grade



The NEW ENGLAND JOURNAL of MEDICINE

2021 WHO Classification of CNS Tumors



Central Nervous System Tumours

WHO Classification of Tumours, 5th Edition, Volume 6

WHO Classification of Tumours Editorial Board

2021

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WHO Classification of CNS Tumors – 5th ed, 7th vol

- **The WHO 5th edition incorporates 10 Basic Principles**
  - Histogenetic vs. Molecular Classification
  - Integrated Diagnosis
  - Essential and Desirable Diagnostic Criteria
  - NOS and NEC Diagnoses
  - Grading Across vs. Grading Within Types
  - Combined Histological and Molecular Grading
  - Pediatric-Type vs. Adult-Type Diffuse Gliomas
  - Use of Type/Subtype instead of Entity/Variant
  - Gene and Protein Nomenclature
  - DNA Methylation Profiling and Newly Recognized Tumor Types

2021 WHO Classification of CNS Tumors

Highlights of 2021 WHO Brain tumor Classification

- Adult diffuse low-grade gliomas
- Pediatric diffuse low-grade gliomas

- New entries-22
- Revised terminology-13

- Essential diagnostic criteria
- Desirable diagnostic criteria

Arabic numerals are employed (rather than Roman numerals)

***Gliomas*, *Glioneuronal Tumors*, and *Neuronal Tumors*, and dividing them into 6 different families**

Term "type" is used instead of "entity" and "subtype" is used instead of "variant."

- NOS -- **N**ot **O**therwise **S**pecified
  - An NOS suffix indicates that the diagnostic information (histological or molecular) necessary to assign a specific WHO diagnosis is not available, providing an alert to the oncologist that a molecular work-up has not been undertaken or failed technically
- NEC -- **N**ot **E**lsewhere **C**lassified
  - NEC suffix, on the other hand, indicates that the necessary diagnostic testing has been successfully performed but that the results do not readily allow for a WHO diagnosis; for example, if there is a mismatch between clinical, histological, immunohistochemical, and/or genetic features.

2021 WHO Classification of CNS Tumors

Table 7 Newly Recognized Tumor Types in the 2021 WHO Classification of Tumors of the Central Nervous System

Newly Recognized Tumor Types
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered
Polymorphous low-grade neuroepithelial tumor of the young
Diffuse low-grade glioma, MAPK pathway-altered
Diffuse hemispheric glioma, H3 G34-mutant
Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype
Infant-type hemispheric glioma
High-grade astrocytoma with piloid features
Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (provisional type)
Myxoid glioneuronal tumor
Multinodular and vacuolating neuronal tumor
Supratentorial ependymoma, *YAP1* fusion-positive
Posterior fossa ependymoma, group PFA
Posterior fossa ependymoma, group PFB
Spinal ependymoma, *MYCN*-amplified
Cribriform neuroepithelial tumor (provisional type)
CNS neuroblastoma, *FOXR2*-activated
CNS tumor with *BCOR* internal tandem duplication
Desmoplastic myxoid tumor of the pineal region, *SMARCB1*-mutant
Intracranial mesenchymal tumor, FET-CREB fusion positive (provisional type)
CIC-rearranged sarcoma
Primary intracranial sarcoma, *DICER1*-mutant
Pituitary blastoma

New entries-22

- 7 Gliomas
- 3 Glioneuronal
- 4 Ependymomas
- 4 Embryonal
- 3 Sarcomas
- 1 Pituitary

David N. Louis,/ Neuro Oncology/2021

14th DEC 2021/BRAIN

2021 WHO Classification of CNS Tumors

Table 1 Diffuse gliomas in WHO CNS 5

	CNS WHO grade
Adult-type diffuse gliomas	
Astrocytoma, IDH-mutant	2/3/4
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	2/3
Glioblastoma, IDH-wildtype	4
Pediatric-type diffuse low-grade gliomas	
Diffuse astrocytoma, *MYB*-or *MYBL1*-altered	1
Angiocentric glioma	1
Polymorphous low-grade neuroepithelial tumor of the young	1
Diffuse low-grade glioma, MAPK pathway-altered	NA
Pediatric-type diffuse high-grade gliomas	
Diffuse midline glioma, H3 K27-altered	4
Diffuse hemispheric glioma, H3 G34-mutant	4
Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype	4
Infant-type hemispheric glioma	NA

NA not assigned

Changes in glial tumor classification- WHO 5th edition

1. Taken a new approach to classify the Gliomas, Glioneuronal Tumors, and Neuronal Tumors and dividing them into 6 different families:
   1. **Adult-type diffuse gliomas** (the majority of primary brain tumors in neuro-oncology practice of adults, eg, glioblastoma, IDH wild type);
   2. **Pediatric-type diffuse low-grade gliomas**(expected to have good prognoses);
   3. **Pediatric-type diffuse high-grade gliomas** (expected to behave aggressively);
   4. **Circumscribed astrocytic gliomas** ("circumscribed" referring to their more solid growth pattern, as opposed to the inherently "diffuse" tumors in groups 1, 2, and 3);
   5. **Glioneuronal and neuronal tumors** (a diverse group of tumors, featuring neuronal differentiation);
   6. **Ependymomas** (now classified by site as well as histological and molecular features).
2. Choroid Plexus Tumors, with their marked epithelial characteristics, are separated from the category of Gliomas, Glioneuronal Tumors, and Neuronal Tumors.
3. **Fourteen** newly recognized types have been added to the classification of *Gliomas*, *Glioneuronal Tumors*, and *Neuronal Tumors*
4. Nearly all these newly recognized types can be diagnosed based on standard histological, immunohistochemical, and molecular analyses
5. Importantly, WHO CNS5 recognizes the clinical and molecular distinctions between those diffuse gliomas that primarily occur in adults (termed "adult-type") and those that occur primarily in children (termed "pediatric-type").

2021 WHO Classification of CNS Tumors

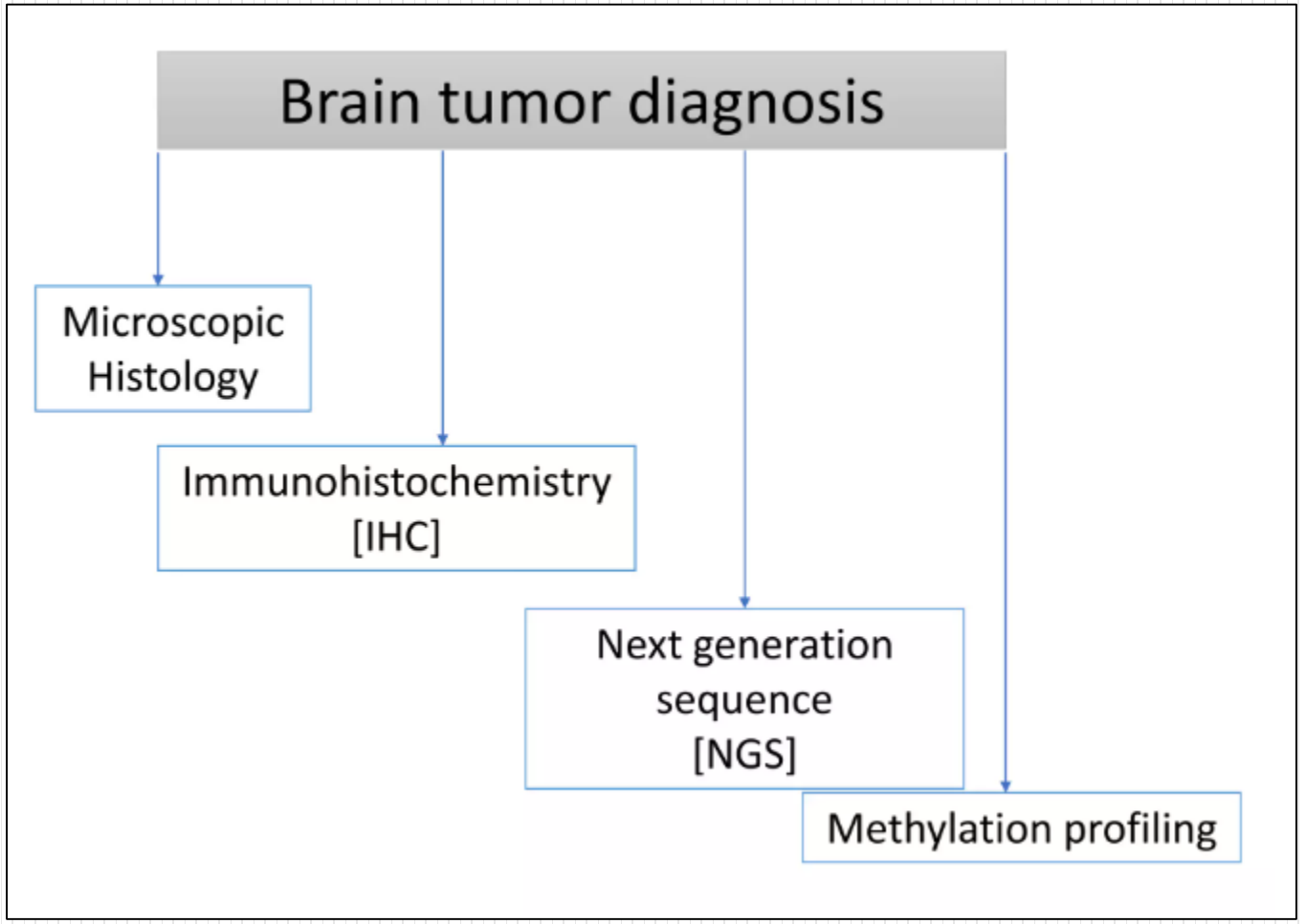
New entry of pediatric glial tumor classification- WHO 5th edition

1. Two new families of tumor types have been added to the classification to reflect the practical and conceptual importance of separating pediatric-type gliomas from other diffuse gliomas:
2. One for Pediatric-type diffuse low-grade gliomas and one for Pediatric-type diffuse high-grade gliomas
3. The low-grade group includes 4 entities that feature diffuse growth in the brain but with sometimes overlapping and less specific histological features; in all, molecular work-up helps to characterize the lesion as one type or the other.
4. The high-grade family also comprises 4 types

Pediatric-type diffuse low-grade gliomas
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered
Angiocentric glioma
Polymorphous low-grade neuroepithelial tumor of the young
Diffuse low-grade glioma, MAPK pathway-altered
Pediatric-type diffuse high-grade gliomas **LOCATION BASED**
Diffuse midline glioma, H3 K27-altered
Diffuse hemispheric glioma, H3 G34-mutant
Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype
Infant-type hemispheric glioma

2021 WHO Classification of CNS Tumors

DNA Methylation Profiling and Newly Recognized Tumor Types



2021 WHO Classification of CNS Tumors

When will we call as glioblastoma?

- Diffuse astrocytoma IDH wild type with
- TERT promoter mutation
- Necrosis
- Microvascular proliferation
- EGFR gene amplification
- Combined entire gain of chromosome 7 and entire loss of chromosome 10[+7/-10]

Table 6 Layered Report Example Illustrating: (1) A Tumor Type With a Subtype; (2) Lack of a Definite Grade; and (3) That the Integrated Diagnosis Does Not Necessarily Have the Histological Designation Included

Cerebrum	
Integrated diagnosis	Diffuse low-grade glioma, MAPK pathway-altered *Subtype: Diffuse low-grade glioma, FGFR1 TKD-duplicated*
Histopathological classification	Oligodendroglioma
CNS WHO grade	Not assigned
Molecular information	Duplication of the *FGFR1* tyrosine kinase domain (next-generation sequencing)

Cerebrum	
Integrated diagnosis	Supratentorial ependymoma, NOS
Histopathological classification	Ependymoma
CNS WHO grade	3
Molecular information	Derivatives extracted from FFPE tissue were of insufficient quality for sequencing and insufficient tissue remained for FISH studies

Abbreviations: CNS, central nervous system; FFPE, formalin-fixed paraffin-embedded; FISH, fluorescence in situ hybridization; NOS, not otherwise specified.

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2021 WHO Classification of CNS Tumors

Molecular Alteration Decides the Behavior of the Tumor – NOT Histopathology

Table 2 Key Diagnostic Genes, Molecules, Pathways, and/or Combinations in Major Primary CNS Tumors

Tumor Type	Genes/Molecular Profiles Characteristically Altered[a]
Astrocytoma, IDH-mutant	*IDH1, IDH2, ATRX, TP53, CDKN2A/B*
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	*IDH1, IDH2*, 1p/19q, *TERT* promoter, *CIC, FUBP1, NOTCH1*
Glioblastoma, IDH-wildtype	IDH-wildtype, *TERT* promoter, chromosomes 7/10, *EGFR*
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered	*MYB, MYBL1*
Angiocentric glioma	*MYB*
Polymorphous low-grade neuroepithelial tumor of the young	*BRAF*, FGFR family
Diffuse low-grade glioma, MAPK pathway-altered	*FGFR1, BRAF*
Diffuse midline glioma, H3 K27-altered	H3 K27, *TP53, ACVR1, PDGFRA, EGFR, EZHIP*
Diffuse hemispheric glioma, H3 G34-mutant	H3 G34, *TP53, ATRX*
Diffuse pediatric-type high-grade glioma, H3-wildtype, and IDH-wildtype	IDH-wildtype, H3-wildtype, *PDGFRA, MYCN, EGFR* (methylome)
Infant-type hemispheric glioma	NTRK family, *ALK, ROS, MET*
Pilocytic astrocytoma	*KIAA1549-BRAF, BRAF, NF1*
High-grade astrocytoma with piloid features	*BRAF, NF1, ATRX, CDKN2A/B* (methylome)
Pleomorphic xanthoastrocytoma	*BRAF, CDKN2A/B*
Subependymal giant cell astrocytoma	*TSC1, TSC2*
Chordoid glioma	*PRKCA*
Astroblastoma, *MN1*-altered	*MN1*
Ganglion cell tumors	*BRAF*
Dysembryoplastic neuroepithelial tumor	*FGFR1*
Diffuse glioneuronal tumor with oligodendroglioma-like features and	Chromosome 14, (methylome)

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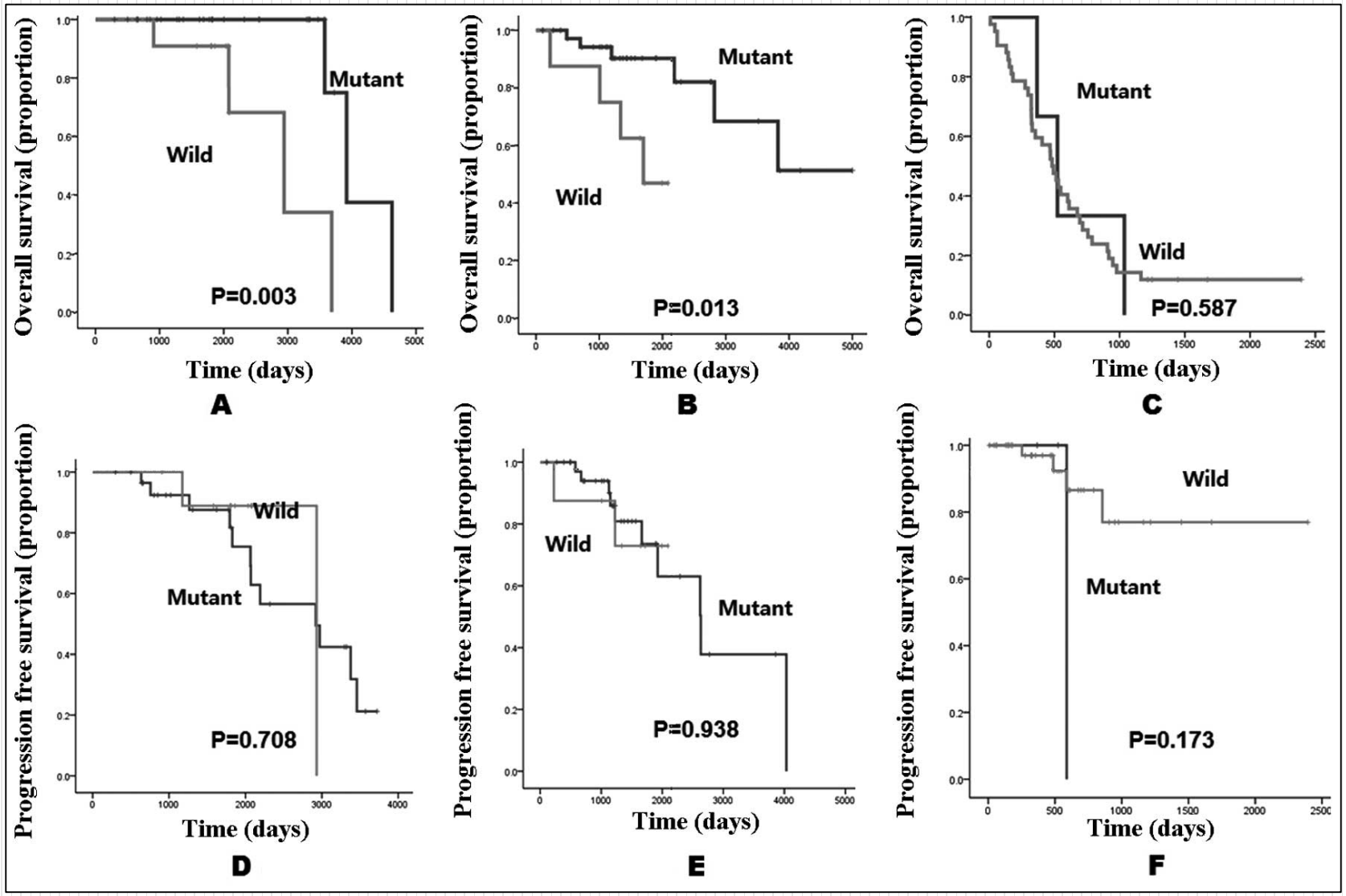
2021 WHO Classification of CNS Tumors

Molecular Alteration Decides the Behavior of the Tumor – NOT Histopathology

Table 2 Key Diagnostic Genes, Molecules, Pathways, and/or Combinations in Major Primary CNS Tumors

Tumor Type	Genes/Molecular Profiles Characteristically Altered*
Papillary glioneuronal tumor	*PRKCA*
Rosette-forming glioneuronal tumor	*FGFR1, PIK3CA, NF1*
Myxoid glioneuronal tumor	*PDFGRA*
Diffuse leptomeningeal glioneuronal tumor	*KIAA1549-BRAF* fusion, 1p (methylome)
Multinodular and vacuolating neuronal tumor	MAPK pathway
Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)	*PTEN*
Extraventricular neurocytoma	FGFR (*FGFR1-TACC1* fusion), IDH-wildtype
Supratentorial ependymomas	*ZFTA, RELA, YAP1, MAML2*
Posterior fossa ependymomas	H3 K27me3, *EZHIP* (methylome)
Spinal ependymomas	*NF2, MYCN*
Medulloblastoma, WNT-activated	*CTNNB1, APC*
Medulloblastoma, SHH-activated	*TP53, PTCH1, SUFU, SMO, MYCN, GLI2* (methylome)
Medulloblastoma, non-WNT/non-SHH	*MYC, MYCN, PRDM6, KDM6A* (methylome)
Atypical teratoid/rhabdoid tumor	*SMARCB1, SMARCA4*
Embryonal tumor with multilayered rosettes	C19MC, *DICER1*
CNS neuroblastoma, *FOXR2*-activated	*FOXR2*
CNS tumor with *BCOR* internal tandem duplication	*BCOR*
Desmoplastic myxoid tumor of the pineal region, *SMARCB1*-mutant	*SMARCB1*
Meningiomas	*NF2, AKT1, TRAF7, SMO, PIK3CA; KLF4, SMARCE1, BAP1* in subtypes; H3K27me3; *TERT* promoter, *CDKN2A/B* in CNS WHO grade 3
Solitary fibrous tumor	*NAB2-STAT6*
Meningeal melanocytic tumors	*NRAS* (diffuse); *GNAQ, GNA11, PLCB4, CYSLTR2* (circumscribed)

IDH Mutant/Wild Type Survival Comparison



Pediatric Brain/CNS Tumors – Molecular Groups

Gliomas, glioneuronal, and neuronal tumors
- *Pediatric-type diffuse low-grade gliomas*
  - Diffuse astrocytoma, *MYB* or *MYBL1*-altered new
  - Angiocentric glioma
  - Polymorphous low-grade neuroepithelial tumor of the young new
  - Diffuse low-grade glioma, MAPK pathway-altered new
- *Pediatric-type diffuse high-grade gliomas defined by H3 status*
  - Diffuse midline glioma, H3 K27-altered
  - Diffuse hemispheric glioma, H3 G34-mutant new
  - Diffuse pediatric-type high-grade glioma, H3-wild-type and IDH-wild-type new
  - Infant-type hemispheric glioma new
- *Circumscribed astrocytic gliomas*
  - Pilocytic astrocytoma
  - High-grade astrocytoma with piloid features new
  - Pleomorphic xanthoastrocytoma
  - Subependymal giant cell astrocytoma
  - Astroblastoma, *MN1*-altered
- *Glioneuronal and neuronal tumors*
  - Ganglioglioma
  - Desmoplastic infantile ganglioglioma/Desmoplastic infantile astrocytoma
  - Dysembryoplastic neuroepithelial tumor
  - Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (DGONC)* new
  - Diffuse leptomeningeal glioneuronal tumor
  - Multinodular and vacuolating neuronal tumor new
- *Ependymal tumors*
  - Supratentorial ependymoma
  - Supratentorial ependymoma, *ZFTA* fusion-positive
  - Supratentorial ependymoma, *YAP1* fusion-positive new
  - Posterior fossa ependymoma
  - Posterior fossa ependymoma, Group PFA new
  - Posterior fossa ependymoma, Group PFB new
  - Spinal ependymoma, *MYCN*-amplified new
  - Myxopapillary ependymoma

Choroid plexus tumors
- Choroid plexus papilloma
- Atypical choroid plexus papilloma
- Choroid plexus carcinoma

CNS embryonal tumors
- *Medulloblastomas, molecularly defined*
  - Medulloblastoma, WNT-activated
  - Medulloblastoma, SHH-activated & TP53-wild-type
  - Medulloblastoma, SHH-activated & TP53-mutant
  - Medulloblastoma, non-WNT/non-SHH
- *Medulloblastoma, histologically defined*
  - Medulloblastoma, histologically defined
- *Other CNS embryonal tumors*
  - Atypical teratoid/rhabdoid tumor
  - Cribriform neuroepithelial tumor* new
  - Embryonal tumor with multilayered rosettes
  - CNS neuroblastoma, *FOXR2*-activated new
  - CNS tumor with *BCOR* internal tandem duplication new
  - CNS embryonal tumor NEC/NOS

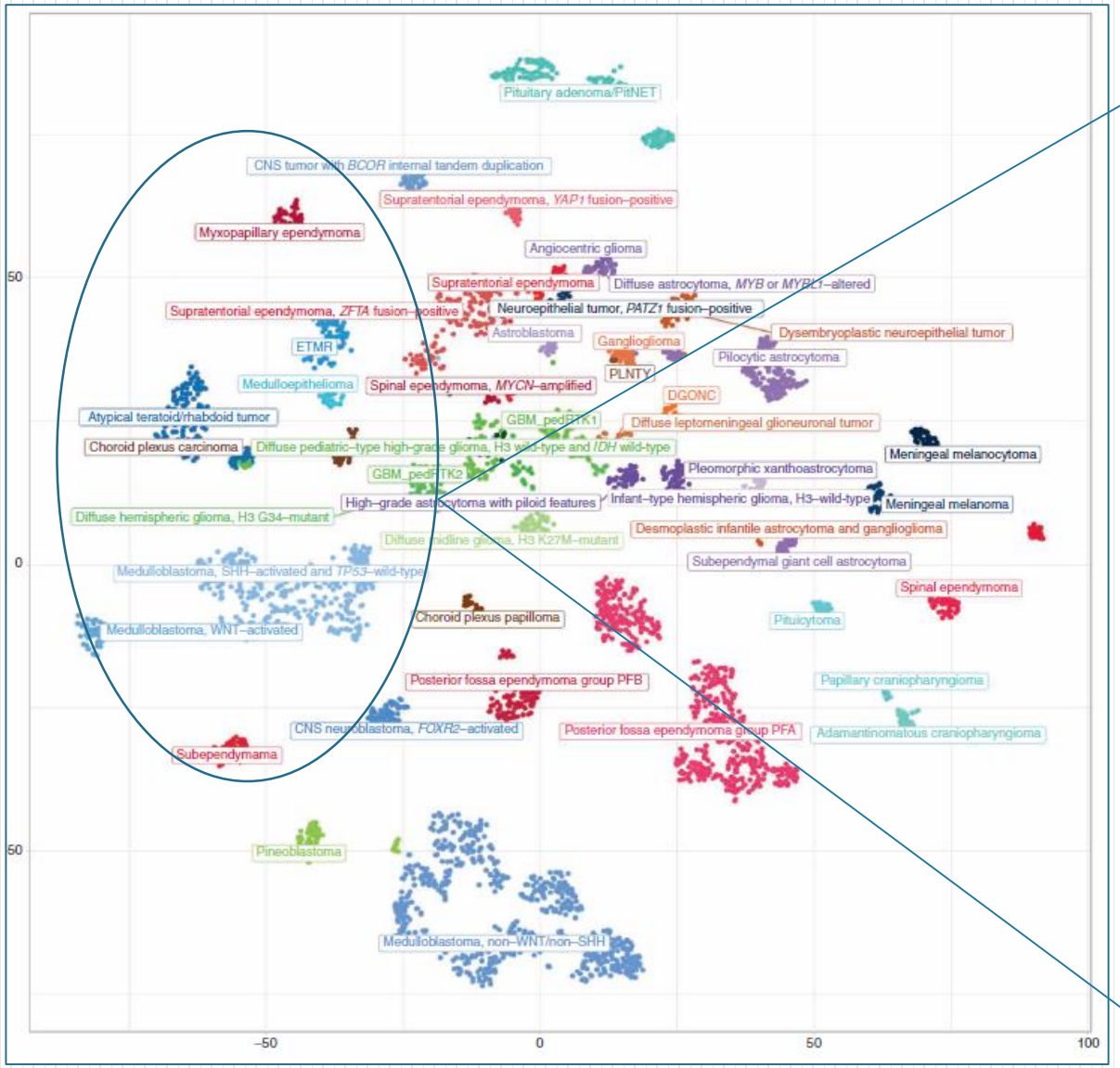
Pineal region tumors
- Pineoblastoma

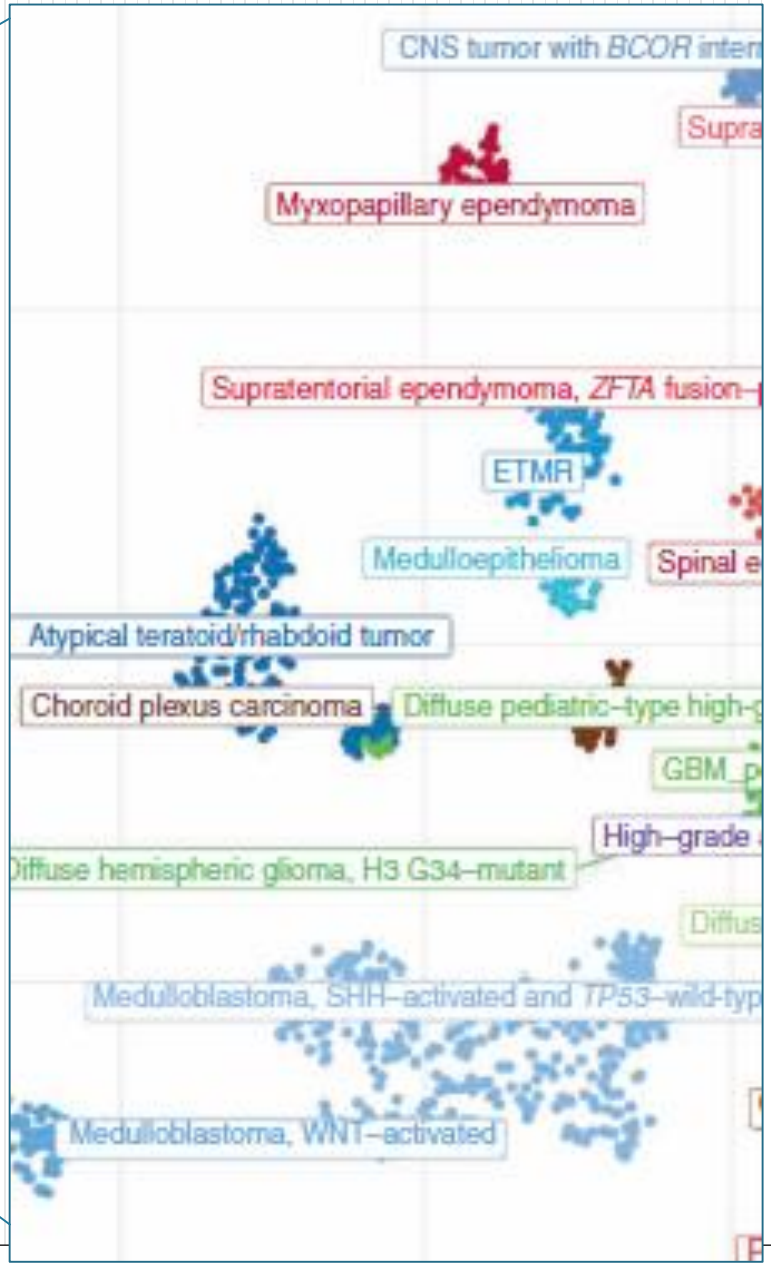
Melanocytic tumors
- Meningeal melanocytosis and melanomatosis

Tumors of the sellar region
- *Pituitary endocrine tumors*
  - Pituitary adenoma/PitNET
  - Pituitary blastoma new
- *Craniopharyngiomas*
  - Adamantinomatous craniopharyngioma

Inaugural WHO Classification of Pediatric Tumors, 2022

Pediatric Brain/CNS Tumors – Molecular Groups





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2023 New ICD-O-3 Histology Codes/Behavior

ICD-O Code	Term	Remarks
9509/3	Diffuse leptomeningeal glioneuronal tumor	New code/new term/new behavior
9421/3	**High-grade astrocytoma with piloid features (HGAP)**	New code/new term. **Beginning 1/1/2023, cases diagnosed as *high-grade astrocytoma with piloid features (HGAP)* are coded 9421/3.** Beginning 1/1/2023,
9749/1	Juvenile xanthogranuloma **(C71.5)**	New code/new term/new behavior
9509/0	Multinodular and vacuolating neuronal tumor	New code/new term/new behavior. Cases diagnoses prior to 1/1/2023 use code 9505/0. Cases diagnosed 1/1/2023 forward use code 9509/0.

2023 Changes to Pilocytic Astrocytoma

ICD-O Code	Term	Remarks
9421/1	**Diffuse astrocytoma, *MYB*- or *MYBL1*-altered**	New preferred term for "pilocytic astrocytoma" **Beginning with cases diagnosed 1/1/2023, pilocytic astrocytoma are coded 9421/1. Cases diagnosed prior to 1/1/2023 are coded 9421/3.**
9421/1	Diffuse low-grade glioma, MAPK pathway–altered†	Related term for "pilocytic astrocytoma" **Beginning with cases diagnosed 1/1/2023, pilocytic astrocytoma are coded 9421/1. Cases diagnosed prior to 1/1/2023 are coded 9421/3.**

2023 New Histology Terms

ICD-O Code	Term	Remarks
9430/3	Astroblastoma, MN1-altered	New term
9400/3	Astrocytoma, IDH-mutant, grade 2	New term
9401/3	Astrocytoma, IDH-mutant, grade 3	New term
9445/3	Astrocytoma, IDH-mutant, grade 4	New term
9473/3	CNS embryonal tumor, NEC/NOS	New term
9500/3	CNS tumor with BCCR internal tandem duplication	New term
9500/3	CNS neuroblastoma, FOXR2-activated	New term
9385/3	Diffuse hemispheric glioma, H3 G34-mutant	New term
9385/3	Diffuse midline glioma, H3 K27-altered	New term
9385/3	Diffuse pediatric-type glioma, H3-wildtype and IDH-wildtype	New term
9385/3	Infant-type hemispheric glioma	New term
9540/3	Malignant melanotic nerve sheath tumor	New term
9699/3	MALT lymphoma of the dura	New term
9470/3	Medulloblastoma, histologically defined **(C71.6)**	New term
9509/1	Myxoid glioneuronal tumor	New term
9450/3	Oligodendroglioma, IDH-mutant and 1p/19q-codeleted, grade 2	New term
9451/3	Oligodendroglioma, IDH-mutant and 1p/19q-codeleted, grade 3	New term
9413/0	Polymorphous low-grade neuroepithelial tumor of the young	New term
9391/3	Posterior fossa ependymoma, NOS	New term
9396/3	Posterior fossa group A (PFA) ependymoma	New term
9396/3	Posterior fossa group B (PFB) ependymoma	New term
9480/3	Primary intracranial sarcoma, DICER1-mutant	New term
9391/3	Spinal ependymoma, NOS **(C72.0)**	New term
9396/3	Spinal ependymoma, MYCN-amplified **(C72.0)**	New term
9391/3	Supratentorial ependymoma, NOS	New term
9396/3	Supratentorial ependymoma, YAP1 fusion-positive	New term
9396/3	Supratentorial ependymoma, ZFTA fusion-positive	New term

2023 Other Histology Term Changes

ICD-O Code	Term	Remarks
8693/3	Cauda equina neuroendocrine tumor (cranial and paraspinal nerves)	New related term
8272/3	Pituitary adenoma/pituitary neuroendocrine tumor (PitNET) **(C75.1)**	New term. Per WHO, both terms may be used in the diagnosis or pituitary neuroendocrine tumor, or PitNET. All are coded 8272/3. Pituitary adenoma, NOS is coded 8272/0

Tumor Grade – CNS WHO Grade 1, 2, 3, 4

Table 3 CNS WHO Grades of Selected Types, Covering Entities for Which There Is a New Approach to Grading, an Updated Grade, or a Newly Recognized Tumor That Has an Accepted Grade

CNS WHO Grades of Selected Types	
Astrocytoma, IDH-mutant	2, 3, 4
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	2, 3
Glioblastoma, IDH-wildtype	4
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered	1
Polymorphous low-grade neuroepithelial tumor of the young	1
Diffuse hemispheric glioma, H3 G34-mutant	4
Pleomorphic xanthoastrocytoma	2, 3
Multinodular and vacuolating neuronal tumor	1
Supratentorial ependymoma[a]	2, 3
Posterior fossa ependymoma[a]	2, 3
Myxopapillary ependymoma	2
Meningioma	1, 2, 3
Solitary fibrous tumor	1, 2, 3

Grade is based on natural history and for some tumor types, definite grading criteria and understanding of natural history are not yet known. Note the use of Arabic numerals.
[a]For morphologically defined ependymomas.

Grade Coding Instructions

Note 2: For the Brain, CNS Other and Intracranial Schemas **ONLY**, Grade Clinical may be assigned without histologic confirmation if the histology is documented based on imaging.

Code	Grade Description
1	WHO Grade I: Circumscribed tumors of low proliferative potential associated with the possibility of cure following resection
2	WHO Grade II: Infiltrative tumors with low proliferative potential with increased risk of recurrence
3	WHO Grade III: Tumors with histologic evidence of malignancy, including nuclear atypia and mitotic activity, associated with an aggressive clinical course
4	WHO Grade IV: Tumors that are cytologically malignant, mitotically active, and associated with rapid clinical progression and potential for dissemination
L	Stated as "low grade" NOS
H	Stated as "high grade" NOS
A	Well differentiated
B	Moderately differentiated
C	Poorly differentiated
D	Undifferentiated, anaplastic
9	Grade cannot be assessed; Unknown

2023 Solid Tumor Rules:
Non-Malignant Brain and CNS Tumors
Malignant Brain and CNS Tumors

The Wizard of Oz

Different Rules for Benign and Malignant

Non-Malignant CNS Equivalent Terms and Definitions
C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Introduction

Note 1: Central nervous system (**CNS**) **includes** the following **primary sites**: Cere[illegible]meninges C70[illegible]nal meninges C701; meninges NOS C709; brain C710-C719; spinal cord C720; cauda equina C[illegible] olfactory [illegible] C722; optic nerve C723; acoustic nerve C724; cranial nerve NOS C725; overlapping lesion of b[illegible] and cent[illegible]us system C728; nervous system NOS C729; pituitary gland C751; craniopharyngeal duct C752; [illegible] gland C753.

Note 2: **Malignant CNS** neoplasms have a separate set of rules.

Note 3: 2007 MPH Rules and 2018 Solid Tumor Rules are used bas[illegible]n **date of [illegible]is**.

- Tumors diagnosed 01/01/2007 through 12/31/2017: [illegible]007 MPH Ru[illegible]
- Tumors diagnosed 01/01/2018 and later: Use 201[illegible]d Tum[illegible] Ru[illegible]
- The original tumor diagnosed before 1/1/201[illegible]nd a subseque[illegible]mor diagnosed 1/1/2018 or l[illegible] **site**: Use the 2018 Solid Tumor Rules.

Note 4: Non-malignant central nervous system (C[illegible] [illegible]plasms ([illegible]iously called benign and borderline **diagnosed 1/1/2004** and later.

Note 5: **Pilocytic astrocytoma/juvenile [illegible]l[illegible]c astrocyt[illegible]**

- For cases diagnosed prior t[illegible]/2023, thes[illegible]plasms are reportable in North American as n[illegible] CNS sites with the exception of the [illegible]ve:
  - WHO Classification Tumors of the [illegible]entral Nervous System and IARC designate pilocytic for optic glioma
  - When the primary site is optic nerve and the diagnosis is either optic glioma or pilocytic a[illegible] non-malignant and coded 9421/1
  - Beginning with cases diagnosed 1/1/2023 forward, pilocytic astrocytoma/juvenile pilocyti[illegible] reported as 9421/1 for *all* CNS sites.

Benign and Borderline Brain and CNS Rules

Malignant CNS and Peripheral Nerves Equivalent Terms and Definitions
C470-C479, C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Introduction

Note 1: This section includes the following **primary sites**: P[illegible]eral nerve[illegible]479; cerebral meninges C700; spinal meninges C701; meninges NOS C709; brain C710-C719; [illegible]cord C720; c[illegible]equina C721; olfactory nerve C722; optic nerve C723; acoustic nerve C724; cranial nerv[illegible]25; overl[illegible]lesion of brain and central nervous system C728; nervous system NOS C729; pituitary gland C7[illegible]harynx C752; pineal gland C753.

Note 2: Non-malignant intracranial and C[illegible]ors have a [illegible]epara[illegible] set of rules.

Note 3: 2007 MPH Rules and 2018 S[illegible]or Rules [illegible]e us[illegible]based on **date of diagnosis**.

- Tumors diagnosed 01/01/20[illegible]hrough 12/31/20[illegible]7: Use 2007 MPH Rules
- Tumors diagnosed 01/01/2018 and later: [illegible]2018 Solid Tumor Rules
- The original tumor diagnosed before [illegible]2018 and a subsequent tumor diagnosed 1/1/2018 or later **in the same primary site**: Use the 2018 Solid Tu[illegible]or Rules.

Note 4: There **must be** a histologic, [illegible]c, radiographic, or clinical **diagnosis** of a **malignant** neoplasm /3.

Note 5: Tumors from a number of [illegible]ary sites metastasize to the brain. Do not use these rules for tumors described as metastases; report metastatic tu[illegible]ing the rules for that primary site.

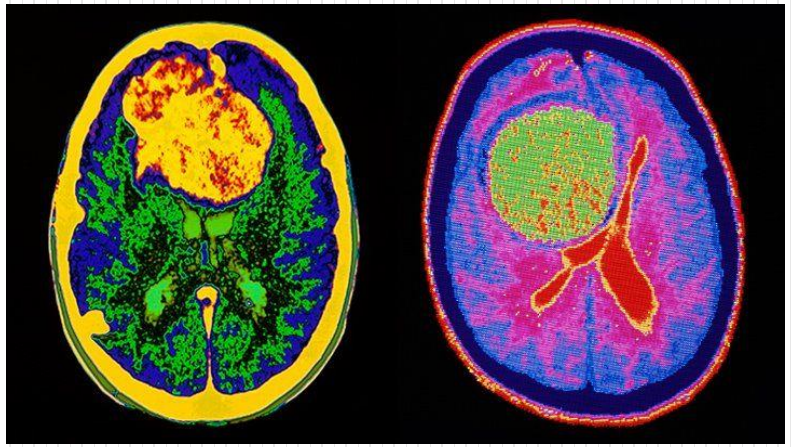
Note 6: **Pilocytic astrocytoma/juvenile pilocytic astrocytoma** is reportable in North America as a **malignant** neoplasm 9421/3.

- See the Non-malignant CNS Rules when the primary site is optic nerve and the diagnosis is either optic glioma or pilocytic astrocytoma. The behavior for these tumors is non-malignant and coded 9421/1.
- **IMPORTANT FOR 2023 FORWARD: Beginning 1/1/2023, all cases diagnosed with pilocytic astrocytoma/juvenile pilocytic astrocytoma and new related terminology are to be reported with behavior /1. They will no longer be collected with malignant behavior (/3). See the Non-malignant CNS Rules.**

Malignant Brain and CNS Rules

Benign and Borderline Tumor Rules

- **Non-malignant central nervous system (CNS) neoplasms are reportable for cases diagnosed 1/1/2004 and later**
- When multiple tumors are present registrars should document tumor characteristics for MPH Rules Text
  - Date of Diagnosis (Timing is not used to determine number of abstracts or primary neoplasms to abstract)
  - Method and Details of Diagnosis (some are never resected)
  - Location of Tumor
  - Bilaterality is NOT used to determine multiple primaries
    - Acoustic neuroma/vestibular schwannoma (9560/0)
    - Optic glioma/pilocytic astrocytoma (9421/1)
  - Laterality indicates multiple primaries for
    - Any lobe of the brain (C71.0-C71.9) and any other part of CNS
    - Cerebral meningioma (9530/0) and Spinal meningioma (9530/0)
    - Cranial Nerves and other Parts of CNS
  - Laterality is NOT used to determine multiple primaries when all tumors are in the cranial meninges
  - Histologic Type – you must refer to Tables in Module – not just Histology Pick List in Software
  - Tumor Behavior – behaviors have been changed for some tumors over time – be aware of changes



Benign and Borderline Tumor Rules

- ***Note 5:* Pilocytic astrocytoma/juvenile pilocytic astrocytoma:**
- **For cases diagnosed prior to 1/1/2023**, these neoplasms are reportable in North American as **malignant 9421/3** for all CNS sites with the exception of the optic nerve:
  - WHO Classification Tumors of the Central Nervous System and IARC currently designate pilocytic astrocytoma as a synonym for optic glioma
  - When the primary site is optic nerve and the diagnosis is either optic glioma or pilocytic astrocytoma, the behavior is non-malignant and coded 9421/1
- **For cases diagnosed 1/1/2023 forward, pilocytic astrocytoma/juvenile pilocytic astrocytoma are 9421/1 for *all* CNS sites.**

New for 2023

Beginning with cases diagnosed 1/1/2023, pilocytic astrocytoma/juvenile pilocytic astrocytoma will **no longer be reported as malignant (9421/3)**. These neoplasms will continue to be reportable as a benign CNS tumor with a behavior of /1. Historically, pilocytic astrocytomas were coded as 9421/3 from 1976-2000. Beginning in 2001 with the release of ICD-O-3, WHO changed the behavior to /1, however, the standard setters opted to continue collecting these cases using malignant /3 behavior. This practice will continue through 12/31/2022.

Benign and Borderline Tumor Rules

- **Clarifications**:
  - The following meningiomas **are reportable**:
    - **Intracranial, intraosseous, cavernous sinus, sphenoid wing and spinal meninges.**
  - Multiple cerebral meningiomas are a single primary.
  - Multiple brain tumors (same histology) are a single primary.
  - Bilateral optic nerve gliomas/pilocytic astrocytoma are a single primary.
  - Laterality is not used to determine multiple primaries.
  - Timing is not used to determine multiple primaries.
  - The brain C710-C719 is a single primary site.
  - Neurofibromatosis NOS, Neurofibromatosis 1 (NF1), Neurofibromatosis 2 (NF2), and schwannomatosis are familial tumor syndromes and are not reportable conditions.
    - The brain and CNS tumors spawned by NF are reportable, the genetic disease is not.
    - ONLY abstract reportable tumors such as:
      - Plexiform neurofibroma (usually NF1)
      - Tumors of brain and spinal cord, meningiomas of cranial or spinal dura, glioma (usually NF2)

Benign and Borderline Tumor Rules

Non-Malignant CNS Equivalent Terms and Definitions
C700, C701, C709, C710-C719, C720-C725, C728, C729, C751-C753
(Excludes lymphoma and leukemia M9590 – M9993 and Kaposi sarcoma M9140)

Table 5: Histologic Types of Non-Malignant Intracranial (Brain and Glands) Tumors

Because non-malignant brain and gland tumors are **less common**, this table identifies histologies which occur in the brain C710-C719 and the glands within the cranium C751-C753. These histologies also appear in Table 6.

IMPORTANT: This table does not list ALL PRIMARY SITES that are possible for a histology. It only includes sites where the histology can occur INTRACRANIALLY.

Use **Table 5** to:

- **Code primary site** when the instructions in **Section 2**: **Reportable Primary Sites and Histologies** do not apply
- **Confirm** that a **histology** can/should be coded to brain or intracranial glands

Column 1 contains **histology terms and codes** that occur in the **brain**, **ventricles** of the brain, and **intracranial glands**
Column 2 contains the **site code** for the most common **intracranial** primary site(s) for that specific histology

Histology Term and Code	Most Common Intracranial Primary Site
Angiocentric glioma 9431/1*	Cerebrum **C710**
Choroid plexus papilloma 9390/0	Intraventricular site (lateral/third ventricle **C715** and IV ventricle **C717**)
(Capillary) hemangioblastoma 9161/1	Cerebellum **C716**, cerebrum (rare) **C710**
Craniopharyngioma 9350/1	Craniopharyngeal duct **C752**, pituitary gland, sella turcica **C751**
Dermoid cyst 9084/0	Pineal gland **C753**, suprasellar **C719**
Desmoplastic infantile astrocytoma and ganglioglioma 9412/1	Cerebrum/supratentorial brain NOS **C710**
Dysembryoplastic neuroepithelial tumor (DNT) 9413/0	Cerebrum **C710**, temporal lobe **C712**

Benign and Borderline Tumor Rules

NOS/Specific Histology Term and Code	Synonyms	Subtypes/Variants Histology Term and Codes
Diffuse astrocytoma, MYB- or MYBL1 altered 9421/1 *Note 1:* Beginning 1/1/2023, diffuse astrocytoma, MYB- or MYBL1 altered is the preferred term for 9421/1. *Note 2:* Beginning 1/1/2023, pilocytic astrocytoma/juvenile pilocytic astrocytoma are coded 9421/1. Cases diagnosed prior to 1/1/2023 are coded 9421/3.	Angiocentric glioma Diffuse low-grade glioma, MAPK pathway-altered Juvenile pilocytic astrocytoma Pilocytic astrocytoma	
Dysembryoplastic neuroepithelial tumor 9413/0 *Note:* DNET and PLNTY have the same ICD-O code but are distinctly different histologies. Because they are different, they are on separate rows in column 1.	DNET	
Gangliocytoma 9492/0		Dysplastic cerebellar gangliocytoma/Lhermitte-Duclos disease **9493/0**
Ganglioglioma 9505/1		
Granular cell tumor of the sellar region 9582/0		
Hemangioblastoma 9161/1	Capillary hemangioblastoma	
Hemangioma 9120/0		Cavernous hemangioma **9121/0**
Juvenile xanthogranuloma 9749/1		
Leiomyoma 8890/0		
Lipoma 8850/0		Hibernoma **8880/0**
Meningeal melanocytosis 8728/0		Meningeal melanocytoma **8728/1**

Tumors with Potential to Transform

Table 8: Non-Malignant CNS Tumors with the Potential of Transforming to Malignant Behavior

The word "**transformation**" as used in this table means that:

- Residual tumor becomes more aggressive /3 **OR**
- The tumor **recurs** as a **more aggressive /3 histology**

The table identifies non-malignant tumors that have the **potential** of **transforming to** a malignant tumor (**new primary**).

Column 1 is the **non-malignant** ICD-O histology term and code.
Column 2 is the **malignant** /3 ICD-O histology term and code to which the non-malignant tumor can transform.

Original Histology and Code	Transformed Histology and Code
Chondroma **9220/0**	Chondrosarcoma **9220/3**
Ganglioglioma **9505/1**	Anaplastic ganglioglioma **9505/3**
Hemangioma **9120/0**	Angiosarcoma **9120/3**
Hemangiopericytoma **9150/1**	Anaplastic hemangiopericytoma **9150/3**
Leiomyoma **8890/0**	Leiomyosarcoma **8890/3**
Lipoma **8850/0**	Liposarcoma **8850/3**
Osteoma **9180/0**	Osteosarcoma **9180/3**
Perineurioma **9571/0**	Malignant perineurioma **9571/3**
Rhabdomyoma **8900/0**	Rhabdomyosarcoma **8900/3**
Teratoma **9080/1**	Immature teratoma **9080/3**
Teratoma, mature **9080/0**	Immature teratoma **9080/3**

Do not report a **malignant** /3 meningioma based on:

- **Invasion** of the **skull** bone
- Tumor **extension through the foramina at the base of the skull**
- Do not report a malignant /3 meningioma based on tumor extension to brain

Malignant Tumor Rules

New for 2023

1. Beginning with cases diagnosed 1/1/2023, pilocytic astrocytoma/juvenile pilocytic astrocytoma will **no longer be reported as malignant (/3)**. These neoplasms will continue to be reportable with a behavior of /1. Historically, pilocytic astrocytomas were coded as 9421/3 from 1976-2000. Beginning in 2001 with the release of ICD-O-3, WHO changed the behavior to /1, however, the standard setters opted to continue collecting these cases using malignant /3 behavior. This practice will continue through 12/31/2022.
2. WHO 5th Ed CNS Tumors has assigned a new histology to 9421/3. Beginning with cases diagnosed 1/1/2023, for surveillance purposes, code 9421/3 will be valid for the following histology *only:*
    a. High Grade astrocytoma with piloid features (HGAP)

CNS neoplasms must meet all **three of the conditions below** to be **reported as malignant /3**:

1. The **behavior** must be malignant /3:
    A. Pathology designates the behavior as malignant/invasive, /3 **OR**
    B. The tumor is a WHO Grade 3 or 4 (See **Section 1: Table 1**)

    Note 1: WHO Grade 2 tumors may be non-malignant or malignant.
    Note 2: **Always** code the behavior as designated by the **pathologist.**
    Note 3: **Never report** a **malignant** /3 behavior code for a meningioma **based on tumor extension** to brain, skin of scalp, or other regional organs/tissue. Non-malignant CNS tumors can extend to the regional tissue and bone.

2. The **primary site** must be reportable (See **Section 2: Table 2**) **AND**
3. The **histology** must be reportable (See **Section 2: Table 3**)

WHO Grade for Brain/CNS Tumors

- **WHO CNS Grade is no longer entirely histological in the 5th edition classification.**
- WHO CNS Grade can be based on the absence of microvascular proliferation or necrosis (traditional histology-based grading), or it can be based on the presence of certain gene mutations present or absent and/or other factors beyond histologic grade
- **WHO Tumor Grades are NOW Arabic Numbers – Grade 1, 2, 3, and 4**
- The higher the grade – the more malignant the tumor behavior
- A tumor can contain more than one grade
- Always record the highest WHO Tumor Grade noted

WHO Grade for Brain/CNS Tumors
Histogenic Grade – Traditional WHO Grade

WORLD HEALTH ORGANIZATION (WHO) GRADING SYSTEM

Grade I Tumor

- *Slow-growing cells*
- *Almost normal appearance under a microscope*
- *Least malignant*
- *Usually associated with long-term survival*

Grade II Tumor

- *Relatively slow-growing cells*
- *Slightly abnormal appearance under a microscope*
- *Can invade adjacent normal tissue*
- *Can recur as a higher grade tumor*

Grade III Tumor

- *Actively reproducing abnormal cells*
- *Abnormal appearance under a microscope*
- *Infiltrate adjacent normal brain tissue*
- *Tumor tends to recur, often as a higher grade*

Grade IV Tumor

- *Abnormal cells which reproduce rapidly*
- *Very abnormal appearance under a microscope*
- *Form new blood vessels to maintain rapid growth*
- *Areas of dead cells (necrosis) in center*

http://www.abta.org/brain-tumor-information/diagnosis/grading-staging.html

WHO Grade for Brain/CNS Tumors

Note 2: For the Brain, CNS Other and Intracranial Schemas **ONLY**, Grade Clinical may be assigned without histologic confirmation if the histology is documented based on imaging.

Table Instructions

1. Use the **malignant CNS** rules for all **WHO Grade 3, 4, and WHO Grade 2 neoplasms with malignant /3 behavior.**
2. Go to **Section 1: Behavior Code** to determine whether **WHO Grade 2** neoplasms are non-malignant or malignant.
3. Use **non-malignant CNS** rules for **all WHO Grade I** (always non-malignant).

Column 1 contains the **histology** term.
Column 2 contains the **WHO Grade** assigned **based** on the **molecular features** of the histology.

Histology	WHO Grade
Anaplastic (malignant) meningioma	3
Anaplastic astrocytoma, IDH-mutant	3
Anaplastic ependymoma	3
Anaplastic ganglioglioma	3
Anaplastic oligodendroglioma IDH-mutant and 1p/19q-codeleted	3
Anaplastic pleomorphic xanthroastrocytoma	3
Angiocentric glioma	1
Atypical choroid plexus papilloma	2

WHO Grade for Brain/CNS Tumors

Histology	WHO Grade
Atypical meningioma	2
Atypical teratoid/rhabdoid tumor	4
Central neurocytoma	2
Cerebellar liponeurocytoma	2
Chordoid glioma of third ventricle	2
Choroid plexus carcinoma	3
Choroid plexus papilloma	1
CNS embryonal tumor NOS	4
CNS embryonal tumor with rhabdoid features	4
Craniopharyngioma	1
Desmoplastic infantile astrocytoma and ganglioglioma	1
Diffuse astrocytoma, IDH-mutant	2
Diffuse midline glioma, H3K27M-mutant	4
Dysembryoplastic neuroepithelial tumor	1
Dysplastic gangliocytoma of cerebellum (Lhemitte-Duclos)	1
Ependymoma	2
Ependymoma, RELA fusion-positive *Note:* Tissue/pathology reports or CAP protocol/summary will specify whether this is WHO Grade 2 or 3	2 or 3
Extraventricular neurocytoma	2
Gangliocytoma	1
Glioblastoma, IDH-mutant	4
Glioblastoma, IDH-wildtype	4
Granular cell tumor	1
Hemangioblastoma	1

WHO Grade for Brain/CNS Tumors

Histology	WHO Grade
Malignant peripheral nerve sheath tumor (MPNST) *Note:* Tissue/pathology reports or CAP protocol/summary will specify whether this is WHO Grade 2, 3, or 4	2, 3, or 4
Medulloblastoma (including all subtypes)	4
Medulloepithelioma	4
Meningioma	1
Myxopapillary ependymoma	1
Neurofibroma	1
Oligodendroglioma IDH-mutant and 1p/19q deleted	2
Papillary glioneuronal tumor	1
Papillary tumor of the pineal region *Note:* Tissue/pathology reports or CAP protocol/summary will specify whether it is WHO Grade 2 or 3	2 or 3
Perineuroma	1
Pilocytic astrocytoma *Note:* Collected as malignant /3 in North America	1
Pineal parenchymal tumor of intermediate differentiation *Note:* Tissue/pathology reports or CAP protocol/summary will specify WHO Grade 2 or 3	2 or 3
Pineoblastoma	4
Pineocytoma	1
Pituicytoma	1
Pleomorphic xanthroastrocytoma	2
Rosette-forming glioneuronal tumor	1
Schwannoma	1

2023 Solid Tumor Rules – Brain & CNS – WHO Grade Table

WHO Grade for Brain/CNS Tumors

Histology	WHO Grade
Solitary fibrous tumor/hemangiopericytoma *Note:* Tissue/pathology reports or CAP protocol/summary will specify WHO Grade 1, 2, or 3	1, 2, or 3
Spindle cell oncocytoma	1
Subependymal giant cell astrocytoma	1
Subependymoma	1

Also Remember that these tables are the same for non-malignant and malignant in case you get mixed up – they are identical.

Malignant Tumor Rules

Table 3: Specific Histologies, NOS, and Subtypes/Variants

Specific and NOS Histology Codes	Synonyms	Subtypes/Variants
Anaplastic ganglioglioma **9505**		
Astroblastoma **9430**	Astroblastoma, MN1-altered	
Astrocytoma NOS **9400**	Astrocytoma, IDH-mutant, grade 2 Diffuse astrocytoma IDH-mutant Diffuse astrocytoma IDH-wildtype Diffuse astrocytoma NOS	Anaplastic astrocytoma IDH-mutant/wildtype; anaplastic astrocytoma NOS **9401** Astrocytoma, IDH-mutant, grade 3 **9401** Astrocytoma, IDH-mutant, grade 4 **9445** Gemistocytic astrocytoma IDH-mutant **9411** Pleomorphic xanthroastrocytoma /anaplastic pleomorphic xanthroastrocytoma **9424**
Choriocarcinoma **9100**		
Choroid plexus carcinoma **9390**		
CNS embryonal tumor with rhabdoid features **9508**	Atypical teratoid/rhabdoid tumor Embryonal tumor with rhabdoid features	
CNS ganglioneuroblastoma **9490**		CNS embryonal tumor, NEC/NOS **9473**
CNS neuroblastoma **9500**	CAN neuroblastoma, FOXR2-activated CNS Tumor with BCCR internal tandem duplication	
Diffuse leptomeningeal glioneuronal tumor **9509*** *Note 1*: Cases diagnosed prior to 1/1/2023 are coded 9509/1. See the non-malignant CNS rules. *Note 2:* Cases diagnosed 1/1/2023 forward are coded 9509/3	DLGNT	
Diffuse midline glioma H3 K27M mutant **9385***	Diffuse intrinsic pontine glioma Diffuse hemispheric glioma, H3 G34-mutant	

*** These new codes were approved by the IARC/WHO Committee for ICD-O**

Malignant Tumor Rules

Specific and NOS Histology Codes	Synonyms	Subtypes/Variants
	Diffuse pediatric-type high grade glioma, H3-wildtype and IDH-wildtype DIPG Infant-type hemispheric glioma	
Embryonal carcinoma **9070**		Yolk sac tumor **9071**
Embryonal tumor with multilayered rosettes C19MC-altered **9478***	Embryonal tumor with multilayered rosettes, NOS ETMR	
Ependymoma **9391** *Note:* The following terms are synonyms of ependymoma, RELA fusion-positive 9396, and are NOT subtypes/variants of it. They are all coded 9396. • Posterior fossa group A (PFA) ependymoma • Posterior fossa group B (PFB) ependymoma • Spinal ependymoma, MYCN-amplified • Supratentorial ependymoma, YAP1 fusion-positive • Supratentorial ependymoma, ZFTA fusion-positive	Clear cell ependymoma Posterior fossa ependymoma, NOS Spinal ependymoma, NOS Supratentorial ependymoma, NOS Tanycytic ependymoma	Anaplastic ependymoma **9392** Ependymoma, RELA fusion-positive **9396*** Posterior fossa group A (PFA) ependymoma Posterior fossa group B (PFB) ependymoma Spinal ependymoma, MYCN-amplified Supratentorial ependymoma, YAP1 fusion-positive Supratentorial ependymoma, ZFTA fusion-positive Papillary ependymoma **9393**
Epithelioid hemangioendothelioma **9133**		
Germinoma **9064**		
Glioblastoma NOS **9440**	Glioblastoma multiforme GBM Glioblastoma, IDH wild-type	Giant cell glioblastoma **9441** Glioblastoma IDH-mutant **9445*** Gliosarcoma **9442**

*** These new codes were approved by the IARC/WHO Committee for ICD-O**

Malignant Tumor Rules

Specific and NOS Histology Codes	Synonyms	Subtypes/Variants
	Epithelioid glioblastoma	
High-grade astrocytoma with piloid features 9421/3 Note: This term is reportable for cases diagnosed 1/1/2023 forward	HGAP	
Immature teratoma **9080**		Mixed germ cell tumor **9085** Teratoma with malignant transformation **9084**
Malignant meningioma **9530**	Anaplastic meningioma	Papillary/rhabdoid meningioma **9538**
Malignant peripheral nerve sheath tumor **9540**	Malignant melanotic nerve sheath tumor Malignant perineurioma MPNST MPNST with perineural differentiation	Epithelioid malignant peripheral nerve sheath tumor **9542**
Medulloblastoma NOS **9470**	Classic medulloblastoma Medulloblastoma, histologically defined	Anaplastic/large cell medulloblastoma **9474** Medulloblastoma described as one of the following **9471** Desmoplastic SHH-activated and TP53-wildtype With extensive nodularity Nodular Medulloblastoma non-WNT/non-SHH; medulloblastoma group 3 or group 4 **9477*** Medulloblastoma SHH-activated and TP53-mutant **9476*** Medulloblastoma WNT-activated **9475***
Medulloepithelioma **9501**		
Meningeal melanoma **8720**		Meningeal melanomatosis **8728**

*** These new codes were approved by the IARC/WHO Committee for ICD-O**

Malignant Tumor Rules

Specific and NOS Histology Codes	Synonyms	Subtypes/Variants
Neuroepithelial tumor, malignant 8000/3		
Oligoastrocytoma NOS **9382**	Anaplastic oligoastrocytoma NOS	
Oligodendroglioma NOS **9450** *Note:* Oligodendroglioma NOS is used when molecular markers cannot fully be determined	Oligodendroglioma 1p/19q-codeleted Oligodendroglioma IDH-mutant Oligodendroglioma IDH-mutant and 1p/19q-codeleted, grade 2	Anaplastic oligodendroglioma NOS **9451** IDH-mutant 1p/19q-codeleted IDH-mutant and 1p/19q-codeleted Oligodendroglioma, IDH-mutant and 1p/19q-codeleted, grade 3
Peripheral primitive neuroectodermal tumor **9364**	Ewing sarcoma pPNET	
Pilocytic astrocytoma **9421** *Note 1:* ICD-O-3 lists a behavior code of /1. It is collected as /3 in North America for cases diagnosed prior to 1/1/2023. *Note 2*: Beginning with cases diagnosed 1/1/2023 forward, pilocytic astrocytoma will no longer be reported with /3 behavior. Pilocytic astrocytoma and the related terms listed below are to be reported as a /1 • Diffuse astrocytoma, MTB- or MYBL1-alterd • Diffuse low-grade glioma, MAPK pathway- altered+		Pilomyxoid astrocytoma **9425**
Pineal parenchymal tumor of intermediate differentiation **9362**	Pineoblastoma	Papillary tumor of the pineal region **9395**
Pituitary adenoma/pituitary neuroendocrine tumor **8272/3**	PitNET	

*** These new codes were approved by the IARC/WHO Committee for ICD-O**

Malignant Tumor Rules

Specific and NOS Histology Codes	Synonyms	Subtypes/Variants
Sarcoma NOS **8800** *Note 1:* **Chondrosarcoma 9220** has the following subtype/variant: Mesenchymal chondrosarcoma **9240** *Note 2:* **Leiomyosarcoma 8890** has the following subtypes/variants: Epithelioid leiomyosarcoma **8891** Myxoid leiomyosarcoma **8896**		Angiosarcoma **9120** Chondrosarcoma **9220** Mesenchymal chondrosarcoma **9240** Leiomyosarcoma/granular cell leiomyosarcoma/inflammatory leiomyosarcoma **8890** Epithelioid leiomyosarcoma **8891** Myxoid leiomyosarcoma **8896** Osteosarcoma **9180** Primary intracranial sarcoma, DICER1-mutant **9480** Undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma **8802**
Solitary fibrous tumor grade 3 **8815**	Hemangiopericytoma grade 3 Solitary fibrous tumor/Hemangiopericytoma grade 3 (CNS)	

*** These new codes were approved by the IARC/WHO Committee for ICD-O**

Malignant Tumor Rules

- When multiple tumors are present registrars should identify and **document specific characteristics for MPH Rules Text**
  - Non-malignant intracranial and CNS tumors have separate sets of rules
  - Laterality is not used to determine multiple primaries for CNS tumors
  - Date of Diagnosis (Timing is not used to determine number of abstracts or primary neoplasms to abstract)
  - Method and Details of Diagnosis (most attempt resection)
  - Location of Tumor (not spread or invasion – but bulk of tumor)
  - Histologic Type / Synonyms / Subtype or Combination – Table 3
  - Separate GBM following an astrocytic or glial tumor is a multiple primary.

Malignant Tumor Rules

Rule M6 Abstract **multiple primaries**[ii] when a patient has a glial tumor and is subsequently diagnosed with a **glioblastoma multiforme 9440** (GBM).

Note 1: Definition of a glial tumor: Any tumor arising from the CNS glial cells. The following is simply a list of all tumors which would be classified as glial.

- Astroblastoma **9430**
- Astrocytomas **9400** and all subtypes
  - Anaplastic astrocytoma IDH-mutant/wildtype; anaplastic astrocytoma NOS **9401**
  - Gemistocytic astrocytoma IDH-mutant **9411**
- Diffuse midline glioma H3 K27M Mutant **9385**
- Ependymoma **9391** and all subtypes
  - Anaplastic ependymoma **9392**
  - Ependymoma, RELA fusion-positive **9396**
  - Papillary ependymoma **9393**
- Glioblastoma **9440** and all subtypes **(this is a glial tumor; however do not apply this rule to a GBM followed by a GBM)**
  - Giant cell glioblastoma **9441**
  - Glioblastoma IDH-mutant **9445**
  - Gliosarcoma **9442**
- Oligodendroglioma and all subtypes **9450**
  - Anaplastic oligodendroglioma; IDH-mutant; 1p/19q-codeleted; IDH-mutant and 1p/19q-codeleted **9451**
- Pleomorphic xanthroastrocytoma **9424**

Note 2: This is a change from the 2007 Rules.

Note 3: Abstracting GBM as a new primary will allow analysis of:

- The number of tumors that recur as a more aggressive histology (GBM)
- The time interval between occurrence of the glial or astrocytic tumors and a GBM
- Which histologies are more likely to recur as a GBM

Note 4: This rule applies to multiple tumors. A glioblastoma multiforme (GBM) that is subsequently diagnosed in residual tumor from a glial tumor is a single primary. See previous rules.

Malignant Tumor Rules

Rule H4 Code the **subtype/variant** when there is a **NOS** and a **single** **subtype/variant** of that NOS such as the following:

Note: All tumors are malignant/invasive /3.

- Astrocytoma **9400** and a subtype/variant of astrocytoma
- CNS ganglioneuroblastoma **9490** and a subtype/variant of CNS ganglioneuroblastoma
- Embryonal carcinoma **9070** and a subtype/variant of embryonal carcinoma
- Ependymoma **9391** and a subtype/variant of ependymoma
- Glioblastoma **9440** and a subtype/variant of glioblastoma
- Immature teratoma **9080** and a subtype/variant of immature teratoma
- Malignant meningioma **9530** and a subtype/variant of malignant meningioma
- Malignant peripheral nerve sheath tumor **9540** and a subtype/variant of malignant peripheral nerve sheath tumor
- Medulloblastoma **9470** and a subtype/variant of medulloblastoma
- Meningeal melanoma **8720** and a subtype/variant of meningeal melanoma
- Oligodendroglioma **9450** and a subtype/variant of oligodendroglioma
- Pilocytic astrocytoma **9421** and a subtype/variant of pilocytic astrocytoma
- Pineal parenchymal tumor of intermediate differentiation **9362** and a subtype/variant of pineal parenchymal tumor of intermediate differentiation
- Sarcoma **8800** and a subtype/variant of sarcoma

Note: See Table 3 in the Equivalent Terms and Definitions to find NOS and subtypes/variants.

Staging Brain and CNS Neoplasms

Mars Attacks

AJCC TNM, 8th edition

"Attempts to develop a TNM-based classification and staging system for central nervous system tumors have been neither practical nor pertinent. Early editions of this manual proposed a system that was used with poor compliance and was not useful as a predictor of outcome, neither in practice nor in clinical trials for patients with primary CNS Tumors."

"The CNS expert panel continues to recommend that a formal TNM-based classification not be attempted. We continue to incorporate the WHO CNS tumor nomenclature and classification, which were revised in 2016, and the ICD topography system for location of the lesions."

AJCC Stage = 88 (Not Applicable)

Includes: ANY Benign
or ANY Malignant Neoplasm

AJCC TNM, 8th edition

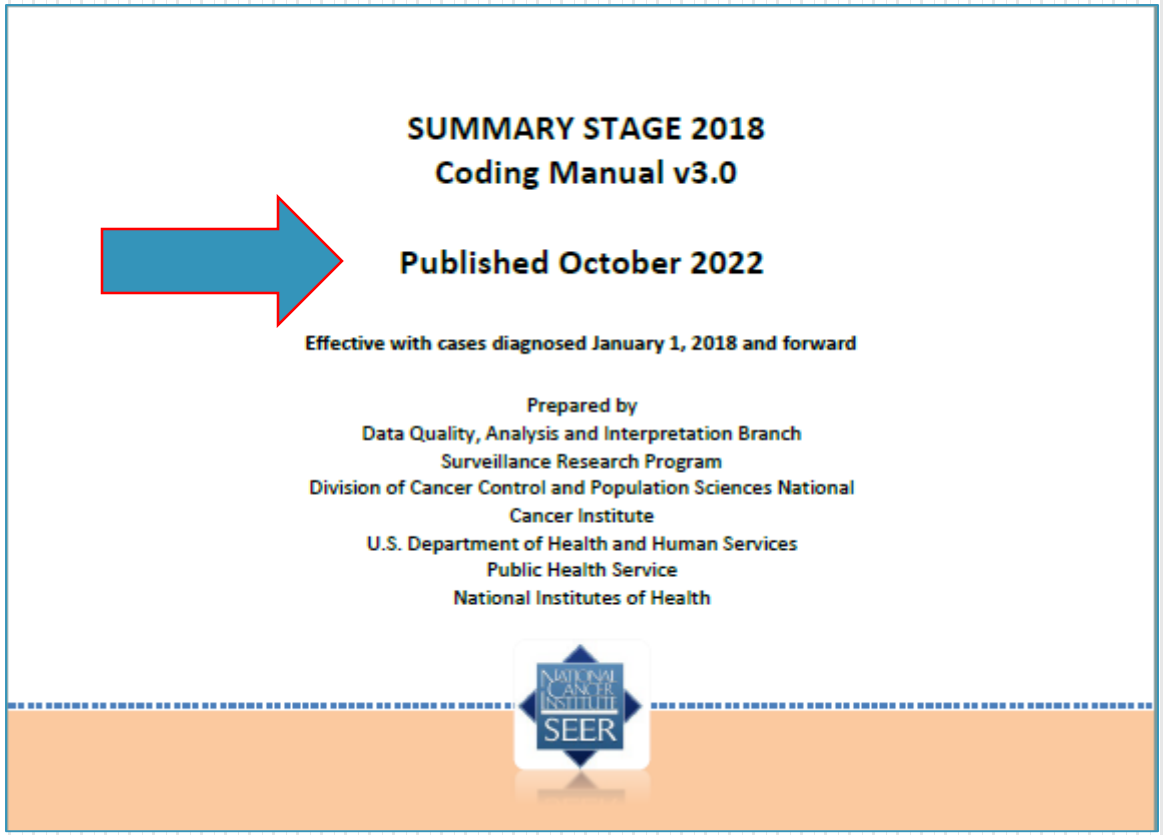
Factors Felt to be of Prognostic and/or Clinical Significant Include:

- Tumor Histology
- Location of Tumor
- Unifocal or Multifocal
- WHO Grade of Tumor
- Patient Age at Diagnosis
- Functional Neurologic Status (Karnofsky Score, QOL)
- Primary or Recurrent Tumor
- Extent of Resection
- Molecular Aspects
  - IDH Mutation for gliomas
  - 1p, 19q deletions for gliomas
  - MGMT methylation status for gliomas

SEER Summary Stage 2018 version 3 for 2022

To obtain a FREE electronic copy of the SS2018Manual version 3 for 2022

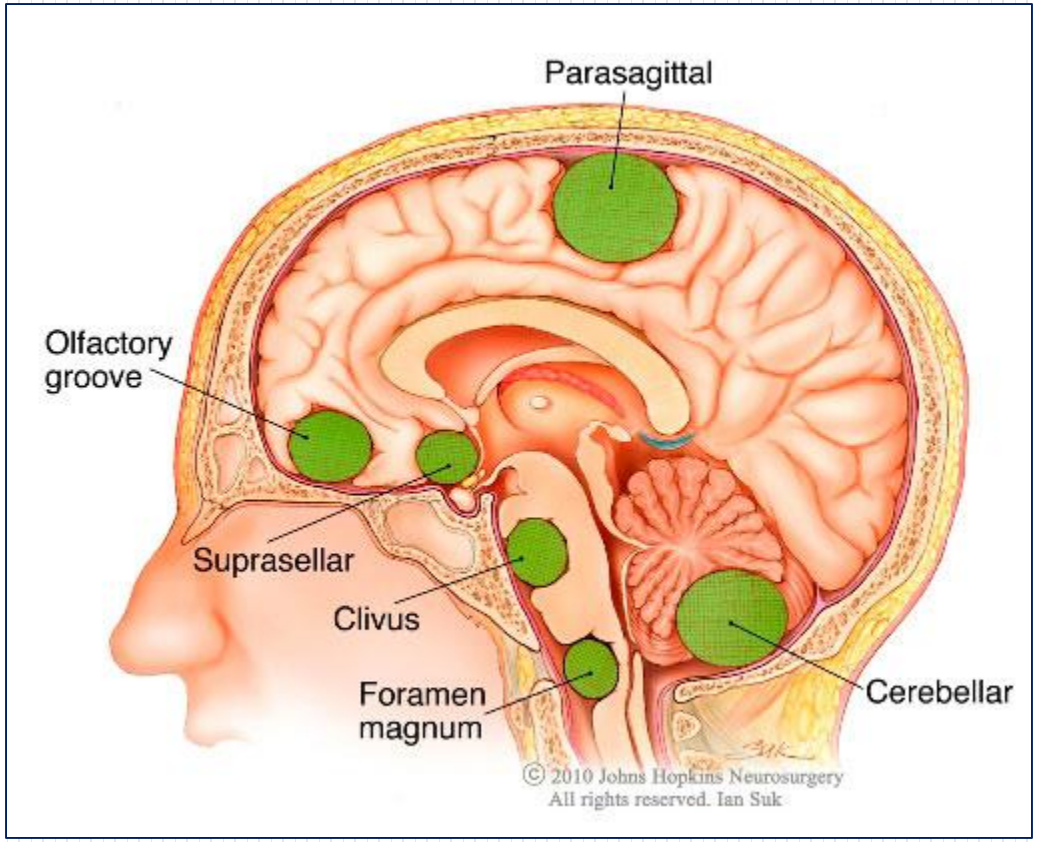
https://seer.cancer.gov/tools/ssm/2018-Summary-Stage-Manual.pdf



ALL Benign/Borderline – Summary Stage = 8

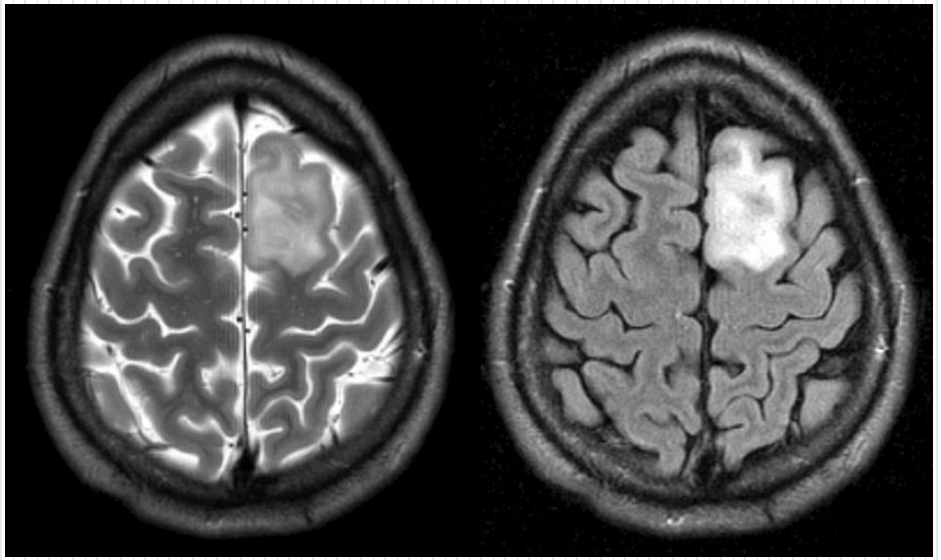
Meningioma, Pituitary Adenoma, Optic Neuroma, Neurofibroma, Vestibular Schwannoma/Acoustic Neuroma, DNET, Hemangioma, Chondroma, Cysts, Craniopharyngioma, Pineal Tumor, etc.

SS2018 = 8



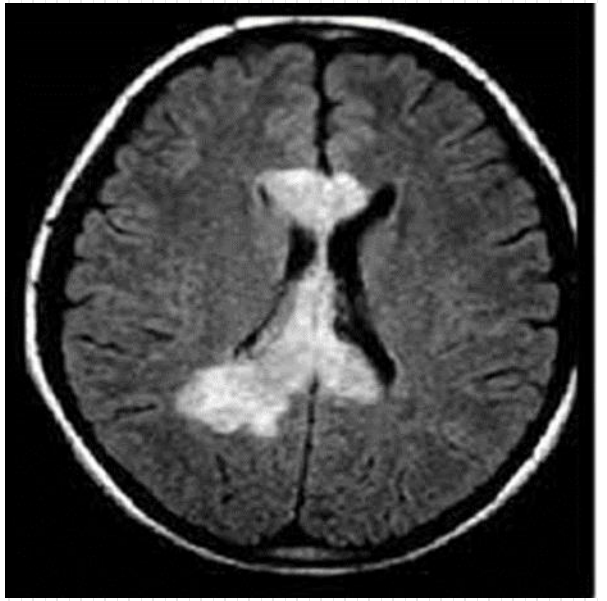
Localized Brain/CNS Tumor

- Confined to brain, NOS
- Confined to meninges, NOS
- Confined to ventricles
  - Tumor invades or encroaches upon ventricular system
- Infratentorial tumor confined to
  - Brain stem or meninges of brain stem (one side)
    - Medulla oblongata
    - Midbrain (mesencephalon)
    - Pons
  - Cerebellum or meninges of cerebellum (one side or midline)
    - Lateral lobes
    - Median lobe of cerebellum
    - Vermis
  - Hypothalamus
  - Thalamus
- Infratentorial tumor
  - Both cerebellum and brain stem involved with tumor on one side
- Supratentorial tumor confined to
  - Cerebral hemisphere (cerebrum) or meninges of cerebral hemisphere (one side)
    - Frontal lobe
    - Occipital lobe
    - Parietal lobe
    - Temporal lobe



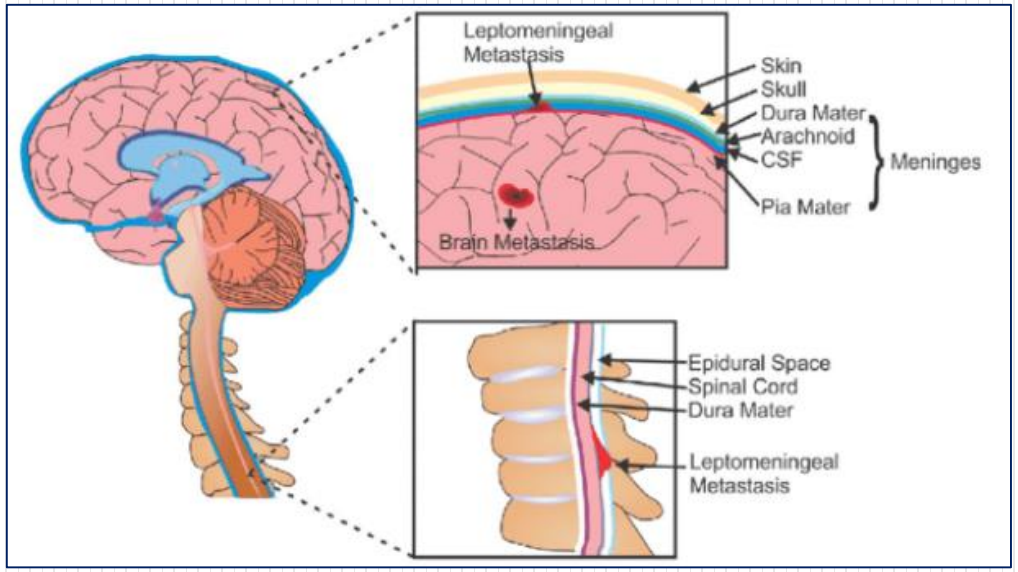
Regional Direct Extension of Brain/CNS Tumor

- Bone (skull)
- Contralateral hemisphere
- Corpus callosum (including splenium)
- Major blood vessel(s)
- Meninges (e.g., dura)
- Nerves (cranial, NOS)
- Spinal cord/canal
- Supratentorial tumor extends infratentorially to involve
    - Brain stem
    - Cerebellum
    - Hypothalamus
    - Pallium
    - Posterior cranial fossa
    - Thalamus
- Infratentorial tumor extends supratentorially to involve
    - Anterior cranial fossa
    - Cerebrum (cerebral hemisphere) (excluding hypothalamus, pallium, thalamus)
    - Corpus callosum
    - Middle cranial fossa
    - Suprasellar brain
    - Tapetum
- Tumor crosses the midline



Distant

- Distant site(s) (including further contiguous extension)
  - Circulating cells in cerebral spinal fluid (CSF)
  - Nasal cavity
  - Nasopharynx
  - Other direct extension outside CNS
  - Posterior pharynx
- Distant lymph node(s), NOS
- Distant metastasis, NOS
  - Carcinomatosis
  - Distant metastasis WITH or WITHOUT distant lymph node(s)
  - Metastasis within CNS and CSF pathways
    - "Drop" metastasis
    - Extra-neural metastasis
    - Metastasis outside the CNS



2022 Site Specific Data Items

- **Brain Molecular Markers** - Multiple brain molecular markers have become standard pathology components necessary for diagnosis. This data item captures clinically important brain cancer subtypes identified by molecular markers that are not distinguishable by ICD-O-3 codes.
- This data item applies only to ICD-O-3 histology codes: 9400/3, 9401/3, 9440/3, 9450/3, 9451/3, 9471/3 and 9478/3.
- If a microscopically confirmed histology is not included in this list, assign, code 85.
- If the case is not microscopically confirmed, code 99.

Code	Description
01	Diffuse astrocytoma, IDH-mutant (9400/3)
02	Diffuse astrocytoma, IDH-wildtype (9400/3)
03	Anaplastic astrocytoma, IDH-mutant (9401/3)
04	Anaplastic astrocytoma, IDH-wildtype (9401/3)
05	Glioblastoma, IDH-wildtype (9440/3)
06	Oligodendroglioma, IDH-mutant and 1 p/19q co-deleted (9450/3)
07	Anaplastic oligodendroglioma, IDH-mutant and 1p/19q co-deleted (9451/3)
08	Medulloblastoma, SHH-activated and TP53-wildtype (9471/3)
09	Embryonal tumor with multilayered rosettes, C19MC-altered (9478/3)
85	Not applicable: Histology not 9400/3, 9401/3, 9440/3, 9450/3, 9451/3, 9471/3, 9478/3
86	Benign or borderline tumor
87	Test ordered, results not in chart
88	Not applicable: Information not collected for this case (If this item is required by your standard setter, use of code 88 will result in an edit error.)
99	Not documented in medical record No microscopic confirmation Brain molecular markers not assessed or unknown if assessed

2022 Site Specific Data Items

- **Loss of Heterozygosity: Chromosome 1p and Chromosome 19q**
  - Other names allelic loss, gene deletion, 1p/19q fragment analysis
  - LOH for chromosome 1p and 19q is tested primarily for oligodendroglioma, anaplastic oligodendroglioma, oligoastrocytoma, and anaplastic oligoastrocytoma.
  - It is infrequently tested for other gliomas, such as glioblastoma multiforme.

Coding guidelines

- Code 0 when the 1p/19q is not identified/not present
- Code 1 when the 1p/19q is present
- Code 7 when the 1p/19q test was ordered but the results are not in the medical record
- Code 9 when
  - No documentation in the medical record
  - 1p/19q test not done (not assessed)
  - Unknown if 1p/19q test was performed (unknown if assessed)

2022 Site Specific Data Items

- **Chromosome 1p: Loss of Heterozygosity**

Code	Description
0	Chromosome 1p deletion/LOH not identified/not present
1	Chromosome 1p deletion/LOH identified/present
6	Benign or borderline tumor
7	Test ordered, results not in chart
8	Not applicable: Information not collected for this case (If this item is required by your standard setter, use of code 8 will result in an edit error.)
9	Not documented in medical record Cannot be determined by the pathologist Chromosome 1p deletion/LOH not assessed or unknown if assessed

2022 Site Specific Data Items

- **Chromosome 19q: Loss of Heterozygosity**

Code	Description
0	Chromosome 19q deletion/LOH not identified/not present
1	Chromosome 19q deletion/LOH present
6	Benign or borderline tumor
7	Test ordered, results not in chart
8	Not applicable: Information not collected for this case (If this item is required by your standard setter, use of code 8 will result in an edit error.)
9	Not documented in medical record Cannot be determined by the pathologist Chromosome 19q: LOH not assessed or unknown if assessed

2022 Site Specific Data Items

- **Methylation of O6-Methylguanine-Methyltransferase**

Code	Description
0	MGMT methylation absent/not present, unmethylated MGMT
1	MGMT methylation present, low level Hypomethylated Partial methylated
2	MGMT methylation present, high level Hypermethylated
3	MGMT Methylation present, level unspecified
6	Benign or borderline tumor
7	Test ordered, results not in chart
8	Not applicable: Information not collected for this case (If this item is required by your standard setter, use of code 8 will result in an edit error.)
9	Not documented in medical record Cannot be determined by the pathologist MGMT not assessed or unknown if assessed

Brain & CNS Neoplasm Treatment Options

- Biopsy & Genetic Testing
- Imaging – MRI, CT and PET
- Surgical Resection – Transsphenoidal; Craniotomy, Neuroendoscopy
  - Depends on Tumor Location, Grade, 'Histology' and Resectable or Not
- Surgical Debulking
- Radiation Therapy
  - External Beam – Proton Beam
  - Stereotactic Radiosurgery or Stereotactic Body Radiation Therapy
  - Brachytherapy
- Chemotherapy – Temodar, Afinitor, Carmustine, Temozolamide
- Targeted Drugs – Bavacizumab, Naxitamab
- Steroids and Ancillary Drugs – treat symptoms, edema, intracranial pressure, etc.

Surgery, Radiation & New Targeted Therapies

- Benign Tumors may be treated with surgery when large.
- Benign Tumors more often are treated by gamma knife or other stereotactic radiosurgery techniques
- Surgery is the treatment of choice for malignant tumors – particularly if good margins can be achieved. If any tumor remains, the patient is at high risk for progression which may be called recurrence.
- Radiation Therapy to treat remaining tumor using IMRT, 3D-CRT or Proton Beam – stereotactic radiosurgical techniques for benign tumors and SBRT/SABR for malignant
- Chemotherapy to treat microscopic remaining tumor
- Everolimus (Afinitor) for subependymal giant cell astrocytoma or SEGA that cannot be completely resected
- Temodar also used frequently as have become the gliadel wafers coated with BCNU

NEW Surgery of Primary Site Codes – Brain/CNS

IMPORTANT

Changes to Surgery of Primary Site Codes for ALL Site-Specific Surgery Codes in 2023

BRAIN

Meninges C70.0–C70.9, Brain C71.0–C71.9,

Spinal Cord, Cranial Nerves and Other Parts of Central Nervous System C72.0–C72.9

Do not code laminectomies for spinal cord primaries.

Codes

A000 None; no surgery of primary site; autopsy ONLY

A100 Tumor destruction, NOS

No specimen sent to pathology from surgical event A100.

Do not record stereotactic radiosurgery (SRS), Gamma knife, Cyber knife, or Linac radiosurgery as surgical tumor destruction. All of these modalities are recorded in the radiation treatment fields.

A200 Local excision of tumor, lesion or mass; excisional biopsy

A210 Subtotal resection of tumor, lesion or mass in brain

A220 Resection of tumor of spinal cord or nerve

A300 Radical, total, gross resection of tumor, lesion or mass in brain

A400 Partial resection of lobe of brain, when the surgery cannot be coded as 20-30.

A550 Gross total resection of lobe of brain (lobectomy)

Codes A300-A550 are not applicable for spinal cord or spinal nerve primary sites.

Specimen sent to pathology from surgical events A200–A550.

A900 Surgery, NOS

A990 Unknown if surgery performed; death certificate ONLY

Comparison of Surgery of Primary Site Codes – Brain/CNS

BRAIN
Meninges C70.0–C70.9, Brain C71.0–C71.9,
Spinal Cord, Cranial Nerves and Other Parts of Central Nervous System C72.0–C72.9

Do not code laminectomies for spinal cord primaries.

Codes

00 None; no surgery of primary site; autopsy ONLY

10 Tumor destruction, NOS

No specimen sent to pathology from surgical event 10.

Do not record stereotactic radiosurgery (SRS), Gamma knife, Cyber knife, or Linac radiosurgery as surgical tumor destruction. All of these modalities are recorded in the radiation treatment fields.

20 Local excision of tumor, lesion or mass; excisional biopsy
21 Subtotal resection of tumor, lesion or mass in brain
22 Resection of tumor of spinal cord or nerve

30 Radical, total, gross resection of tumor, lesion or mass in brain

40 Partial resection of lobe of brain, when the surgery cannot be coded as 20-30.

55 Gross total resection of lobe of brain (lobectomy)

Codes 30 - 55 are not applicable for spinal cord or spinal nerve primary sites.

Specimen sent to pathology from surgical events 20–55.

90 Surgery, NOS

99 Unknown if surgery performed; death certificate ONLY

BRAIN

Meninges C70.0–C70.9, Brain C71.0–C71.9,

Spinal Cord, Cranial Nerves and Other Parts of Central Nervous System C72.0–C72.9

Do not code laminectomies for spinal cord primaries.

Codes

A000 None; no surgery of primary site; autopsy ONLY

A100 Tumor destruction, NOS

No specimen sent to pathology from surgical event A100.

Do not record stereotactic radiosurgery (SRS), Gamma knife, Cyber knife, or Linac radiosurgery as surgical tumor destruction. All of these modalities are recorded in the radiation treatment fields.

A200 Local excision of tumor, lesion or mass; excisional biopsy

A210 Subtotal resection of tumor, lesion or mass in brain

A220 Resection of tumor of spinal cord or nerve

A300 Radical, total, gross resection of tumor, lesion or mass in brain

A400 Partial resection of lobe of brain, when the surgery cannot be coded as 20-30.

A550 Gross total resection of lobe of brain (lobectomy)

Codes A300-A550 are not applicable for spinal cord or spinal nerve primary sites.

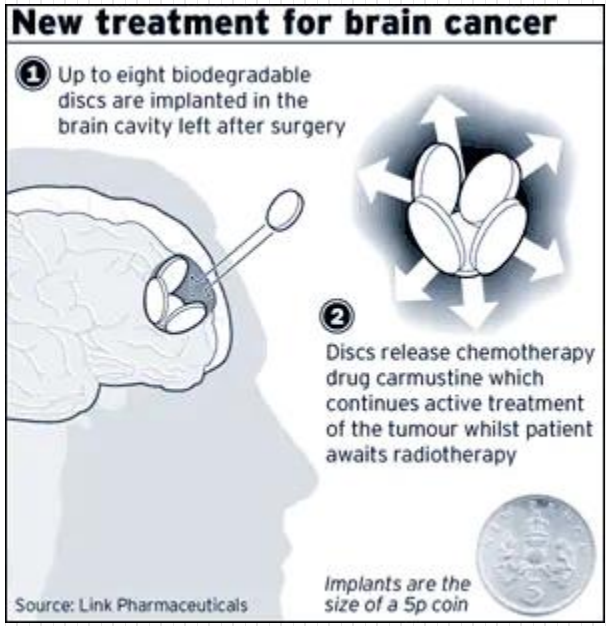
Specimen sent to pathology from surgical events A200–A550.

A900 Surgery, NOS

A990 Unknown if surgery performed; death certificate ONLY

Anti-neoplastic Agents Approved for Brain Tumors

- Afinitor (Everolimus)
- Afinitor Disperz (Everolimus)
- Alymsys (Bevacizumab)
- Avastin (Bevacizumab)
- Belzutifan
- Bevacizumab
- BiCNU (Carmustine)
- Carmustine
- Carmustine Implant
- Danyelza (Naxitamab-gqgk)
- Everolimus
- Gliadel Wafer (Carmustine Implant)
- Lomustine
- Mvasi (Bevacizumab)
- Naxitamab-gqgk
- Temodar (Temozolomide)
- Temozolomide
- Welireg (Belzutifan)
- Zirabev (Bevacizumab)



Additional Resources

- **The WHO Classification of Tumors of the Central Nervous System, 5th ed, Vol 6**, World Health Organization, Lyon, France, 2021
- **The 2021 WHO classification of tumors, 5th edition, central nervous system tumors: the 10 basic principles;** Brain Tumor Pathology (2022) 39:47–50; https://doi.org/10.1007/s10014-022-00428-3
- **A Summary of the Inaugural WHO Classification of Pediatric Tumors: Transitioning from the Optical into the Molecular Era; American Association for Cancer Registries, Cancer Discovery,** 2022;12:331–55, **February 2022, doi: 10.1158/2159-8290.CD-21-1094**
- **5th edition WHO Brain Tumor Classification in a Nutshell;** Kanhu Charan Patro, Mahatma Gandi Cancer Hospital, India; January 9, 2022
- **Central Brain Tumor Registry of the United States (CBTRUS)**, cbtrus.org, 2022
- **CBTRUS Statistical Report**, 2022, Neurooncology, 24(S5), v1–v95, 2022 | https://doi.org/10.1093/neuonc/noac202
- **Genetics of Common Pediatric Brain Tumors,** Pediatric Neurology, Vol 104, March 2020, pages 3-12
- **Molecular biomarkers and integrated pathological diagnosis in the reclassification of gliomas;** Molecular and Clinical Oncology 15: 150, 2021
- **Imaging diagnosis and treatment selection for brain tumors in the era of molecular therapeutics;** Vagvala et al. Cancer Imaging (2022) 22:19; https://doi.org/10.1186/s40644-022-00455-5
- **American Cancer Society Cancer Facts and Figures, 2022**
- **American Brain Tumor Association (ABTA),** abta.org, 2022 – About Brain Tumors and Brain Tumor Dictionary
- **NCI Physician Data Query – Adult Brain and Pediatric Brain**
- **Site-Specific Data Items Manual and Grade Coding Manual – NAACCR, 2022**
- **ICD-O-3 Updates – NAACCR, 2023**
- **Solid Tumor Rules and Manual**, SEER 2023
- **STORE Manual – 2023**
- **NCCN Evidence Based Treatment Guidelines**, nccn.org, 2022 – Central Nervous System Cancers and Pediatric Central Nervous System Cancers
- **Radiation Oncology Clinical Appropriateness Guidelines – November 7, 2021**
- **AJCC Cancer Staging Manual**, 8th ed., AJCC, 2017
- **SEER Summary Staging Manual 2022**
- **Data collection of primary central nervous system tumors. National Program of Cancer Registries Training Materials.** Department of Health and Human Services, Centers for Disease Control and Prevention. Atlanta, Georgia, 2004.

QUESTIONS

NCRA CEU# is 2022-160

Pinky and the Brain