Protocol for the Examination of Tumors of the Brain and Spinal Cord

Version: 1.0.0.1

Protocol Posting Date: September 2025

The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

The following tumor types should NOT be reported using this protocol:

Tumor type
Lymphoma (consider the Precursor and Mature Lymphoid Malignancies protocol)
Primary bone tumors (consider the Primary Bone Tumor protocol)
Metastatic tumors
Malignant peripheral nerve sheath tumor (consider the Soft Tissue Tumor protocol)

Version Contributors

Authors: Brent Harris, MD, PhD*, Carrie Mohila, MD, PhD*

Other Expert Contributors: Sarah Bach, MD, Nicole Becker, MD, Jennifer Cotter, MD, Brittany Dugger, PhD, Dibson Gondim, MD, Devon Jackson, MD, Karra Jones, MD, PhD, William McDonald, MD, Arie Perry, MD, Marie Rivera-Zengotita, MD, Cynthia Welsh, MD

* Denotes primary author.

For any questions or comments, contact: cancerprotocols@cap.org.

Glossary:

Author: Expert who is a current member of the Cancer Committee, or an expert designated by the chair of the Cancer Committee.

Expert Contributors: Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

Accreditation Requirements

The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.

Summary of Changes

v 1.0.0.1

- eCP only metadata and eCP only explanatory note electronic link updates

Reporting Template

Protocol Posting Date: September 2025
Select a single response unless otherwise indicated.
CASE SUMMARY: (CENTRAL NERVOUS SYSTEM)

CLINICAL

+History of Prior Therapy for this Neoplasm (Note A)
___ Not administered
___ Not known: _____
___ Administered
Select all that apply
+___ Chemotherapy
+___ Radiation therapy
+___ Corticosteroids
+___ Embolization
+___ Therapy performed, type not specified
+___ Other (specify): _____

+History of Previous Tumor and / or Familial Syndrome (not the current neoplasm) (Note A)
___ Not known: _____
___ Known (specify): _____
___ Not specified

+Neuroimaging Findings (Note B)
___ Specify: _____
___ Not available

SPECIMEN

Procedure (Note C) (select all that apply)
___ Open biopsy
___ Biopsy with intraoperative consultation
___ Stereotactic biopsy
___ Resection
___ Other (specify): _____
___ Not specified

Specimen Size, Gross Description (Note D)
For fragmented tissue, an aggregate size may be given
___ Greatest dimension in Centimeters (cm): _____ cm
+Additional Dimension in Centimeters (cm): ____ x ____ cm
___ Cannot be determined (explain): _____

TUMOR

Tumor Site (Note E) (select all that apply)
___ Skull / Bone
+Specify Precise Location, if known (select all that apply)
___ Frontal: _____
___ Parietal: _____
___ Temporal: _____
___ Occipital: _____
___ Other (specify): _____
___ Dura
+Specify Precise Location, if known (select all that apply)
___ Convexity / lobe (specify): _____
___ Falx
___ Tentorium
___ Posterior fossa
___ Sphenoid wing
___ Skull base
___ Spinal
___ Other (specify): _____
___ Leptomeninges
+Specify Precise Location, if known (select all that apply)
___ Cerebral convexity / lobe (specify): _____
___ Posterior fossa
___ Spinal
___ Other (specify): _____
___ Brain
Select all that apply
___ Cerebral lobes
+Specify Precise Location, if known (select all that apply)
___ Frontal: _____
___ Temporal: _____
___ Parietal: _____
___ Occipital: _____
___ Other (specify): _____
___ Deep grey matter
+Specify Precise Location, if known (select all that apply)
___ Basal ganglia
___ Thalamus
___ Hypothalamus
___ Ventricle
+Specify Precise Location, if known (select all that apply)
___ Lateral: _____
___ Third: _____
___ Fourth: _____

___ Cerebral Aqueduct: _____
___ Other (specify): _____
___ Cerebellum
___ Brain stem
+Specify Precise Location, if known (select all that apply)
___ Midbrain: _____
___ Pons: _____
___ Medulla: _____
___ Other (specify): _____
___ Other (specify): _____
___ Cerebellopontine angle
___ Sellar / Suprasellar / Pituitary
___ Pineal
___ Cranial nerve
+Specify I-XII, if known (select all that apply)
___ I
___ II
___ III
___ IV
___ V
___ VI
___ VII
___ VIII
___ IX
___ X
___ XI
___ XII
___ Spine / Bone (vertebral column)
+Specify Precise Location, if known (select all that apply)
___ C1
___ C2
___ C3
___ C4
___ C5
___ C6
___ C7
___ T1
___ T2
___ T3
___ T4
___ T5
___ T6
___ T7
___ T8
___ T9
___ T10

___ T11
___ T12
___ L1
___ L2
___ L3
___ L4
___ L5
___ Sacrum
___ Coccyx
___ Other (specify): _____
___ Spinal cord
+Specify Precise Location, if known (select all that apply)
___ C1
___ C2
___ C3
___ C4
___ C5
___ C6
___ C7
___ T1
___ T2
___ T3
___ T4
___ T5
___ T6
___ T7
___ T8
___ T9
___ T10
___ T11
___ T12
___ L1
___ L2
___ L3
___ L4
___ L5
___ Sacral
___ Coccygeal
___ Other (specify): _____
___ Spinal nerve root(s)
+Specify Precise Location, if known (select all that apply)
___ C1
___ C2
___ C3
___ C4
___ C5

___ C6
___ C7
___ T1
___ T2
___ T3
___ T4
___ T5
___ T6
___ T7
___ T8
___ T9
___ T10
___ T11
___ T12
___ L1
___ L2
___ L3
___ L4
___ L5
___ Sacral
___ Coccygeal
___ Other (specify): _____
___ Other (specify): _____
___ Not specified

Tumor Laterality (Note E)
___ Right
___ Left
___ Midline
___ Bilateral
___ Other (specify): _____
___ Not specified

+Tumor Focality (Note E)
___ Unifocal
___ Multifocal (specify number of lesions): _____
___ Cannot be determined: _____

Integrated Diagnosis (CNS WHO 2021) (Notes F, G)
___ Gliomas, glioneuronal tumors, and neuronal tumors
Adult-type diffuse gliomas
___ Astrocytoma, IDH-mutant
___ Oligodendroglioma, IDH-mutant and 1p/19q-codeleted
___ Glioblastoma, IDH-wildtype
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
___ 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
Circumscribed astrocytic gliomas
___ Pilocytic astrocytoma
___ High-grade astrocytoma with piloid features
___ Pleomorphic xanthoastrocytoma
___ Subependymal giant cell astrocytoma
___ Chordoid glioma
___ Astroblastoma, MN1-altered
Glioneuronal and neuronal tumors
___ Ganglioglioma
___ Gangliocytoma
___ Desmoplastic infantile ganglioglioma
___ Desmoplastic infantile astrocytoma
___ Dysembryoplastic neuroepithelial tumor
___ Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters
___ Papillary glioneuronal tumor
___ Rosette-forming glioneuronal tumor
___ Myxoid glioneuronal tumor
___ Diffuse leptomeningeal glioneuronal tumor
___ Multinodular and vacuolating neuronal tumor
___ Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)
___ Central neurocytoma
___ Extraventricular neurocytoma
___ Cerebellar liponeurocytoma
Ependymal tumors
___ Supratentorial ependymoma
___ Supratentorial ependymoma, ZFTA fusion-positive
___ Supratentorial ependymoma, YAP1 fusion-positive
___ Posterior fossa ependymoma
___ Posterior fossa group A (PFA) ependymoma
___ Posterior fossa group B (PFB) ependymoma
___ Spinal ependymoma
___ Spinal ependymoma, MYCN-amplified
___ Myxopapillary ependymoma
___ Subependymoma
___ Choroid plexus tumors
___ Choroid plexus papilloma
___ Atypical choroid plexus papilloma
___ Choroid plexus carcinoma
___ Medulloblastoma

Select all that apply
Must select both molecularly defined and histologically defined subtypes
Molecularly Defined Medulloblastomas
___ Medulloblastoma, WNT-activated
___ Medulloblastoma, SHH-activated and TP53-wildtype
___ Medulloblastoma, SHH-activated and TP53-mutant
___ Medulloblastoma, non-WNT / non-SHH
Histologically Defined Medulloblastomas
___ Classic medulloblastoma
___ Desmoplastic / nodular medulloblastoma
___ Medulloblastoma with extensive nodularity
___ Large cell / anaplastic medulloblastoma
___ Other CNS embryonal tumors
___ Atypical teratoid / rhabdoid tumor
___ Cribriform neuroepithelial tumor
___ Embryonal tumor with multilayered rosettes
___ CNS neuroblastoma, FOXR2-activated
___ CNS tumor with BCOR internal tandem duplication
___ CNS embryonal tumor, NEC / NOS
___ Pineal tumors
___ Pineocytoma
___ Pineal parenchymal tumor of intermediate differentiation
___ Pineoblastoma
___ Papillary tumor of the pineal region
___ Desmoplastic myxoid tumor of the pineal region, SMARCB1-mutant
___ Cranial and paraspinal nerve tumors
___ Schwannoma
___ Neurofibroma
___ Plexiform neurofibroma
___ Perineurioma
___ Hybrid nerve sheath tumor (specify subtype(s), if known): _____
___ Malignant melanotic nerve sheath tumor
___ Malignant peripheral nerve sheath tumor
___ Cauda equina neuroendocrine tumor (previously paraganglioma)
___ Meningioma (specify subtype(s), if known): _____
___ Mesenchymal, non-meningothelial tumors involving the CNS
Fibroblastic and myofibroblastic tumors
___ Solitary fibrous tumor
Vascular tumors
___ Hemangioma
___ Cavernous malformation
___ Arteriovenous malformation
___ Capillary telangiectasia
___ Hemangioblastoma
Skeletal muscle tumors
___ Embryonal rhabdomyosarcoma
___ Alveolar rhabdomyosarcoma

___ Rhabdomyosarcoma, pleomorphic type
___ Spindle cell rhabdomyosarcoma
Tumors of uncertain differentiation
___ Intracranial mesenchymal tumor, FET::CREB fusion-positive
___ CIC-rearranged sarcoma
___ Primary intracranial sarcoma, DICER1-mutant
___ Ewing sarcoma
Chondrogenic tumors
___ Mesenchymal chondrosarcoma
___ Chondrosarcoma
___ Dedifferentiated chondrosarcoma
Notochordal tumors
___ Chordoma
___ Melanocytic tumors
Diffuse meningeal melanocytic neoplasms
___ Meningeal melanocytosis
___ Meningeal melanomatosis
Circumscribed meningeal melanocytic neoplasms
___ Meningeal melanocytoma
___ Meningeal melanoma
___ Hematolymphoid tumors involving the CNS
CNS Lymphomas
___ Primary diffuse large B-cell lymphoma of the CNS
___ Immunodeficiency-associated CNS lymphoma
___ Lymphomatoid granulomatosis
___ Intravascular large B-cell lymphoma
Miscellaneous rare lymphomas in the CNS
___ MALT lymphoma of the dura
___ Other low-grade B-cell lymphomas of the CNS (specify subtype(s), if known): _____
___ Anaplastic large cell lymphoma (ALK+ / ALK-)
___ T-cell lymphoma
___ NK / T-cell lymphoma
Histiocytic tumors
___ Erdheim-Chester disease
___ Rosai-Dorfman disease
___ Juvenile xanthogranuloma
___ Langerhans cell histiocytosis
___ Histiocytic sarcoma
___ Germ cell tumors
___ Mature teratoma
___ Immature teratoma
___ Teratoma with somatic-type malignancy
___ Germinoma
___ Embryonal carcinoma
___ Yolk sac tumor
___ Choriocarcinoma
___ Mixed germ cell tumor (specify subtype(s), if known): _____

___ Tumors of the sellar region
  ___ Adamantinomatous craniopharyngioma
  ___ Papillary craniopharyngioma
  ___ Pituicytoma
  ___ Granular cell tumor of the sellar region
  ___ Spindle cell oncocytoma
  ___ Pituitary adenoma / pituitary neuroendocrine tumor (PitNET)
  ___ Pituitary blastoma
___ Other (e.g., NEC, NOS) (specify): _____
___ Cannot be determined: _____
___ Pending
  Specify Histologic Type: _____
  +Histologic Type Comments: _____

Integrated Histologic Molecular Grade (CNS WHO 2021) (Note H)
___ CNS WHO grade 1
___ CNS WHO grade 2
___ CNS WHO grade 3
___ CNS WHO grade 4
___ Pending
___ Other (specify): _____
___ Not applicable: _____
___ Cannot be assessed: _____

+Treatment Effect (histological evidence of prior therapy) (Note I)
___ Not identified
___ Present: _____
  +Specify Percentage of Tumor that is Necrotic: _____ %
___ Cannot be determined: _____

ADDITIONAL FINDINGS

+Additional Pathologic Findings (specify): _____

SPECIAL STUDIES

+Molecular Information (Note J) (select all that apply)
___ Specify test(s) and results: _____
___ Pending (specify test(s)): _____
___ Not performed: _____
___ Not applicable: _____

+Designate Block(s) for Future Studies: _____

CAP Approved CentralNervousSystem.Bx.Res_1.0.0.1.REL_CAPCP

COMMENTS

Comment(s): _____

Explanatory Notes

A. Relevant History

Previous Therapy for CNS Tumors

Surgery, radiation, and chemotherapy are standard therapeutic options for brain tumors. However, these therapies pose neurotoxicity risks with long-term complications including radiation necrosis, chemotherapy-associated leukoencephalopathy, and secondary neoplasms. A tissue diagnosis remains the gold standard to assess for treatment response and treatment-related changes. Treatment-associated changes such as cytologic atypia, inflammation, vasculopathy, and tumor necrosis can create diagnostic challenges, so providing a detailed therapy history is essential for adequate specimen interpretation.[1]

Previous Diagnoses or CNS Biopsies

Knowledge of the presence or absence of previous intracranial or extracranial disease (e.g., immunosuppression or previous CNS or other primary neoplasm) is essential for specimen interpretation. If a previous tumor is included in the differential diagnosis, it is useful to have microscopic slides of the lesion available for review and comparison.[2]

Family History of Cancer or Primary CNS Tumors

Several genetic conditions/syndromes are associated with an increased predisposition to the development of specific forms of CNS neoplasms (e.g., neurofibromatosis types 1 and 2, constitutional mismatch repair syndrome, Lynch syndrome, tuberous sclerosis, von Hippel-Lindau, Cowden, Li-Fraumeni, and Gorlin syndromes).[3]

References

1. Bette Kleinschmidt-DeMasters, Tarik Tihan, Fausto Rodriguez. *Diagnostic Pathology: Neuropathology*. 2nd ed, Philadelphia: Elsevier; 2016.
2. Perry A, Brat DJ. *Practical Surgical Pathology: A Diagnostic Approach*. 2nd ed. Philadelphia: Elsevier; 2018.
3. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*, 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.

B. Neuroimaging Findings

Knowledge of neuroimaging features is extremely helpful in specimen interpretation.[1,2,3] A differential diagnosis may be generated based on patient age, tumor location, and neuroimaging features. Neuroimaging also can be helpful in providing correlation with or highlighting discrepancies with pathologic diagnosis (e.g., contrast enhancement with hypocellularity). A close collaboration with the neuroradiologist and neurosurgeon is essential.

References

1. Vincentelli C, Hwang SN, Holder CA, Brat DJ. The use of neuroimaging to guide the histologic diagnosis of central nervous system lesions. *Adv Anat Pathol*. 2012; 19:97-107.
2. Glastonbury CM, Tihan T. Practical neuroimaging of central nervous system tumors for surgical pathologists. *Surg Pathol Clin*. 2015 Mar;8(1):1-2.

3. Jaimes C, Poussaint TY. Primary Neoplasms of the Pediatric Brain. *Radiol Clin North Am.* 2019 Nov;57(6):1163-1175.

C. Procedure
It is useful to know if the specimen was procured by open craniotomy or stereotactic biopsy. Since tumors may be heterogeneous, adequate sampling is an issue. The reliability of the prognostic information derived from such specimens may vary depending on how the specimen was obtained.

D. Specimen Size
For most CNS tumors, specimen size is not used for grading. However, in heterogeneous lesions, tissue sampling may become important, and the size of the biopsy relative to the overall size of the lesion provides useful information concerning whether the sample is representative of the overall lesion. The total specimen size may not correspond to the tumor size within the specimen, and this discrepancy should be noted. The protocol may not be applicable to a biopsy specimen if the tissue sample is limited.

E. Primary Tumor Site, Laterality, and Focality
Since the anatomic site of a neoplasm may correlate with tumor type and prognosis, it should be recorded, if known.

- For skull location, specify bone involved, such as frontal, parietal, temporal, occipital, etc., if known. The College of American Pathologists (CAP) cancer protocol for bone should be used for primary tumors of bone.[1]
- For dural location, indicate cerebral convexity/lobe, falx, tentorium, posterior fossa, sphenoid wing, skull base, spinal, or other, if known.
- For leptomeningeal location, indicate cerebral convexity/lobe, posterior fossa, spinal, or other, if known.
- For cerebral lobe location, indicate frontal, temporal, parietal, or occipital lobe, if known.
- For a deep gray matter location, indicate basal ganglia, thalamus, or hypothalamus.
- For an intraventricular location, indicate lateral, third, fourth, or cerebral aqueduct, if known.
- For a brain stem location, indicate midbrain, pons, or medulla, if known.
- For spine (vertebral bone), spinal cord, spinal root or spinal ganglion, indicate level (e.g., C5, T2, L3), if known. The CAP cancer protocol for bone should be used for primary tumors of bone.[1]

The laterality of a neoplasm should be indicated as involving the left or right side of the CNS structure. In some instances, such as tumors arising in the pineal, pituitary, third ventricle, or other locations, the tumor will be situated in the midline. A tumor would be considered bilateral if it involved both sides of the brain, such as glioblastoma extending across the corpus callosum to involve the left and right hemispheres. The focality of a lesion should be indicated, if possible. Multifocality implies that multiple, noncontiguous lesions are noted on neuroimaging, such as might be seen in primary CNS lymphoma. A solitary lesion would be considered unifocal.

Margins
Resection margins provide no prognostic information and generally are not required for most CNS neoplasms.[2]

References
1. Laurini JA. Protocol for the examination of resection specimens from patients with primary tumors of bone. 2021. Available at www.cap.org/cancerprotocols.
2. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*, 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.

F. Integrated Diagnosis

Historically, the diagnosis and classification of CNS tumors have been based exclusively on the histologic appearance of the tumor. In recent decades, however, our knowledge of the molecular basis of many of these tumors has increased significantly. In the 5th edition of the WHO Classification of Tumours of the Central Nervous System,[1] molecular information is now integrated into many of the tumor diagnostic entities. In such cases, including the diffuse gliomas and embryonal tumors, the final diagnosis should reflect the integration of both histologic and molecular information.

One optional method of reporting the histologic and molecular information is through a “layered” report format with the tumor site as follows:[2]

Layer 1: Integrated diagnosis (combined tissue-based histological and molecular diagnosis)
Layer 2: Histopathological classification
Layer 3: CNS WHO grade
Layer 4: Molecular Information

At centers where molecular testing is not available, an NOS (not otherwise specified) designation is available for tumor entities that include molecular alterations as part of the definitions. The NOS designation implies that insufficient information is available to provide a more specific integrated diagnosis and may occasionally be used for tumors that do not precisely fit into one of the defined tumor categories. A designation of NEC (not elsewhere classified) can be added when necessary diagnostic testing was successfully performed but the results do not readily permit a WHO diagnosis. Both NOS and NEC can be used for all tumor types.

References
1. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*, 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.
2. Louis DN, Perry A, Burger P, et al. International Society of Neuropathology-Haarlem Consensus guidelines for nervous system tumor classification and grading. *Brain Pathol.* 2014; 24:429-435.

G. Histologic Type

Classification should be made according to the WHO classification of tumors of the nervous system and the WHO classification of tumors of the endocrine organs whenever possible.[1,2] Table 1 listed in Note H (Histologic Grade) contains WHO 2021 diagnostic entities for which the Central Nervous System (CNS) Cancer Protocol is recommended.

References
1. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*, 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.

2. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Endocrine and Neuroendocrine Tumours,* 5th Edition, Volume 9. Lyon, France: IARC Press; 2022.

H. Histologic Grade

Below is a list of possible WHO grades for CNS tumors. The WHO grading of some of the more common CNS tumors is shown in Table 1. There is no formal TNM-based classification and staging system for CNS tumors.

CNS WHO Grades for CNS Tumors
CNS WHO grade 1
CNS WHO grade 2
CNS WHO grade 3
CNS WHO grade 4
CNS WHO grade not assigned

Table 1. CNS WHO Grading System for Some of the More Common Tumors of the CNS[1,2]

Group	Type	Grade 1	Grade 2	Grade 3	Grade 4
Adult-type diffuse gliomas	Astrocytoma, IDH-mutant		X	X	X
	Oligodendroglioma, IDH-mutant and, 1p/19q co-deleted		X	X	
	Glioblastoma, IDH-wildtype				X
Pediatric-type diffuse low-grade gliomas	Diffuse glioma, MYB- or MYBL1-altered	X			
	Angiocentric glioma	X			
	Polymorphous low-grade neuroepithelial tumor of the young	X			
	Diffuse low-grade glioma, MAPK pathway-altered*				
Pediatric-type diffuse high-grade gliomas	Diffuse midline glioma, H3 K27-altered				X
	Diffuse hemispheric glioma, H3 G34-mutant				X
	Diffuse pediatric-type high-grade glioma, H3/IDH-wildtype				X
	Infant-type hemispheric glioma*				
Circumscribed astrocytic gliomas	Pilocytic astrocytoma	X			
	High-grade astrocytoma with piloid features*				
	Pleomorphic xanthoastrocytoma		X	X	
	Subependymal giant cell astrocytoma	X			

	Chordoid glioma		X		
	Astroblastoma, MN1-altered*				
Glioneuronal and neuronal tumors	Ganglioglioma	X			
	Gangliocytoma	X			
	Desmoplastic infantile ganglioglioma/astrocytoma	X			
	Dysembryoplastic neuroepithelial tumor	X			
	Papillary glioneuronal tumor	X			
	Rosette-forming glioneuronal tumor	X			
	Myxoid glioneuronal tumor	X			
	Diffuse leptomeningeal glioneuronal tumor		X	X	
	Diffuse glioneuronal tumor with oligodendroglioma features and nuclear clusters*				
	Multinodular and vacuolating neuronal tumor	X			
	Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)	X			
	Central neurocytoma		X		
	Extra-ventricular neurocytoma		X		
	Cerebellar liponeurocytoma		X		
Ependymal tumors	Supratentorial ependymoma		X	X	
	Supratentorial ependymoma, *ZFTA* fusion-positive		X	X	
	Supratentorial ependymoma, *YAP1* fusion-positive		X	X	
	Posterior fossa ependymoma		X	X	
	Posterior fossa ependymoma, group PFA		X	X	
	Posterior fossa ependymoma, group PFB		X	X	
	Spinal ependymoma		X	X	
	Spinal ependymoma, *MYCN*-amplified*				
	Myxopapillary ependymoma		X		
	Subependymoma	X			
Choroid plexus tumors	Choroid plexus papilloma	X			
	Atypical choroid plexus papilloma		X		

	Choroid plexus carcinoma			X	
Embryonal Tumors	Medulloblastoma, WNT-activated				X
	Medulloblastoma, SHH-activated and *TP53*-wildtype				X
	Medulloblastoma, SHH-activated and *TP53*-mutant				X
	Medulloblastoma, non-WNT/non-SHH				X
	Medulloblastomas, histologically defined				X
	Atypical teratoid/rhabdoid tumor				X
	Embryonal tumor with multilayered rosettes				X
	CNS neuroblastoma, *FOXR2*-activated				X
	CNS tumor with *BCOR* internal tandem duplication*				
	CNS embryonal tumor, NEC/NOS			X	X
Pineal parenchymal tumors	Pineocytoma	X			
	Pineal parenchymal tumor of intermediate differentiation		X	X	
	Pineoblastoma				X
	Papillary tumor of the pineal region		X	X	
	Desmoplastic myxoid tumor of the pineal region, SMARCB1-mutant*				
Cranial and peripheral nerve tumors	Schwannoma	X			
	Neurofibroma	X			
	Perineurioma	X			
	Hybrid nerve sheath tumor	X			
	Malignant melanotic nerve sheath tumor*				
	Malignant peripheral nerve sheath tumor*				
Meningiomas	Meningioma	X	X	X	
	Atypical meningioma		X		
	Clear cell meningioma		X		
	Chordoid meningioma		X		
	Anaplastic meningioma			X	
	Papillary meningioma	X	X	X	
	Rhabdoid meningioma	X	X	X	

Mesenchymal tumors					
	Solitary fibrous tumor	X	X	X	
	Hemangioma*				
	Hemangioblastoma	X			
	Rhabdomyosarcoma*				
	Intracranial mesenchymal tumor, FET::CREB fusion-positive*				
	CIC-rearranged sarcoma				X
	Primary intracranial sarcoma, DICER1-mutant*				
	Ewing sarcoma				X
	Mesenchymal chondrosarcoma*				
	Chondrosarcoma	X	X	X	
	Chordoma*				
Melanocytic tumors	Meningeal melanocytosis and meningeal melanomatosis*				
	Meningeal melanocytoma and meningeal melanoma*				
Tumors of the sellar region	Adamantinomatous craniopharyngioma	X			
	Papillary craniopharyngioma	X			
	Pituicytoma, granular cell tumor and spindle cell oncocytoma*				
	Pituitary adenoma/PitNET*				
	Pituitary blastoma*				
*WHO does not currently grade these tumor types					

References

1. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*, 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.
2. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Endocrine and Neuroendocrine Tumours,* 5th Edition, Volume 9. Lyon, France: IARC Press; 2022.

I. Preoperative Treatment and Treatment Effect

Knowledge of preoperative treatment, including radiation therapy, chemotherapy, corticosteroid therapy, embolization, and other therapy, is helpful for specimen interpretation.[1,2,3] In particular, prior radiation therapy or radiosurgery may alter the interpretation of specimens in which there is increased cellular atypia, decreased proliferative activity, or large areas of radiation-induced change (e.g., coagulative [nonpalisading] necrosis, vascular hyalinization, and gliosis). The addition of chemotherapy to radiation may further alter histomorphological appearance. For patients with malignant gliomas, the presence and degree of radiation necrosis appear to be of prognostic significance. Tumors that show evidence of radiation necrosis are associated with a longer survival, and the degree of necrosis appears to be prognostically significant.[1,2,3] Corticosteroid treatment can alter the pathologic features of some CNS

diseases. In particular, the treatment of primary CNS lymphoma with corticosteroids can be associated with widespread tumor cell dropout and infiltration by macrophages, which may limit or misguide interpretation. Embolization of certain tumor types, especially meningiomas, may introduce histologic changes in the neoplasm.

References
1. Perry A, Brat DJ. *Practical Surgical Pathology: A Diagnostic Approach.* 2nd ed. Philadelphia: Elsevier; 2018.
2. Bette Kleinschmidt-DeMasters, Tarik Tihan, Fausto Rodriguez. *Diagnostic Pathology: Neuropathology.* 2nd ed, Philadelphia: Elsevier; 2016.
3. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System,* 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.

J. Biomarker Studies

Immunohistochemical and molecular genetic studies are often performed to assist with diagnosis, prognosis, or to predict therapeutic response.[1] The most recent update of the World Health Organization's Classification of Tumours of the Central Nervous System has incorporated many of these biomarkers into this formal diagnostic classification system, thereby formally encouraging their use in the evaluation of these neoplasms. Currently, the 2021 WHO Classification of Tumours of the Central Nervous System and the 2022 (WHO) Endocrine and Neuroendocrine Tumours incorporate molecular genetic studies into many entities while the diagnoses of some CNS tumors remain largely morphologic.[1,2] As our understanding of the pathobiology of CNS tumors is ever expanding, the list of entities requiring molecular genetic studies will continue to grow. New methodologies of biomarker tests must be accompanied with careful validation studies to support their use.

References
1. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*, 5th Edition, Volume 6. Lyon, France: IARC Press; 2021.
2. WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Endocrine and Neuroendocrine Tumours,* 5th Edition, Volume 9. Lyon, France: IARC Press; 2022.