Protocol for the Examination of Specimens From Patients With Tumors of the Brain/Spinal Cord

Protocol applies to all primary neoplasms of the brain/spinal cord/peripheral nerve and pituitary. Metastatic tumors are not included.

No AJCC/UICC TNM Staging System
Protocol web posting date: November 2011

Procedures
- Biopsy/Resection

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CAP Brain/Spinal Cord Protocol Revision History

Version Code
The definition of the version code can be found at www.cap.org/cancerprotocols.

Version: Brain/Spinal Cord 3.0.1.0

Summary of Changes
The following changes have been made since the June 2008 release.

Biopsy/Resection

Tumor Site
“Cranial or peripheral nerve” was changed to “Peripheral nerve.”

Histologic Type and Grade

Tumors of Cranial and Paraspinal Nerves
“Malignant perineurioma (WHO grade III)” was added.

Mesenchymal (Nonmeningothelial) Tumors
“Osteoma” and “Malignant hemangiopericytoma” were added.

Tumors of the Sellar Region
“Craniopharyngioma (WHO grade I)” was added.

Important Note
This protocol should be applied to all primary neoplasms of the brain/spinal cord/peripheral nerve and pituitary, and it should be applied at initial biopsy/resection. Metastatic tumors are not included. There is no American Joint Committee on Cancer / International Union Against Cancer TNM classification system for primary nervous system neoplasms. The World Health Organization (WHO) grading system is recommended.
Surgical Pathology Cancer Case Summary

Protocol web posting date: November 2011

BRAIN/SPINAL CORD: Biopsy/Resection

Select a single response unless otherwise indicated.

+ History of Previous Tumor/Familial Syndrome (Note A)
  + ___ None known
  + ___ Known (specify, if known: _______________________)”
  + ___ Not specified

Specimen Type/Procedure (Note B)
  ___ Open biopsy
  ___ Resection
  ___ Stereotactic biopsy
  ___ Other (specify): _______________________
  ___ Not specified

Specimen Handling (select all that apply) (Note C)
  ___ Squash/smear/touch preparation
  ___ Frozen section
  ___ Tissue for electron microscopy
  ___ Frozen tissue
  ___ Unfrozen for routine permanent paraffin sections
  ___ Other (specify): _______________________
  ___ Not specified

+ Specimen Size (Note D)
  + ___ Greatest dimension: ___ cm
  + ___ Additional dimensions: ___x___ cm (for fragmented tissue, an aggregate size may be given)
  + ___ Cannot be determined (see Comment)

Laterality
  ___ Right
  ___ Left
  ___ Bilateral
  ___ Not specified
  ___ Not applicable

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Tumor Site (select all that apply) (Note E)

___ Skull
   + Specify further (eg, frontal, parietal, temporal, occipital), if known: ___________________

___ Dura
   + Specify further (eg, cerebral [convexity/lobe, falx, tentorium, sphenoid wing, skull base, other]; spinal or other), if known: ___________________

___ Leptomeninges
   + Specify further (eg, cerebral [convexity/lobe], spinal, or other), if known: ___________________

___ Brain/cerebrum
   + Specify lobe(s) (eg, frontal, temporal, parietal, occipital), if known: ___________________

___ Brain, other:
   ___ Basal ganglia
   ___ Thalamus
   ___ Hypothalamus
   ___ Pineal
   ___ Cerebellum
   ___ Cerebellopontine angle
   ___ Suprasellar
   ___ Sella
   ___ Other (specify, if known: ___________________

___ Cranial nerve
   + Specify I-XII, if known: ___________________

___ Ventricle
   + Specify lateral, third, fourth, cerebral aqueduct, if known: ___________________

___ Brainstem
   + Specify midbrain, pons, or medulla, if known: ___________________

___ Spine (vertebral column)
   + Specify bony level (eg, C5, T2, L3), if known: ___________________

___ Spinal Cord
   + Specify bony level (eg, C5, T2, L3), if known: ___________________
   + Specify spinal location (eg, extradural, intradural-extraduallary, intramedullary, conus medullaris, filum terminale), if known: ___________________

___ Spinal nerve root(s)
   + Specify bony level (eg, C5, T2, L3), if known: ___________________
   + Specify location (eg, intradural, foramen), if known: ___________________

___ Peripheral nerve
   + Specify site, if known: ___________________

___ Ganglion
   + Specify site, if known: ___________________

___ Other (specify): ___________________
___ Not specified

Histologic Type and Grade (applicable World Health Organization [WHO] classification and grade)
(select all that apply) (Note F, Note G)

Astrocytic Tumors
___ Pilocytic astrocytoma (WHO grade I)
___ Pilomyxoid astrocytoma (WHO grade II)
___ Subependymal giant cell astrocytoma (WHO grade I)
___ Pleomorphic xanthoastrocytoma (WHO grade II)
___ Pleomorphic xanthoastrocytoma with anaplastic features (WHO grade not assigned)

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Diffuse astrocytoma (WHO grade II)
  - Fibrillary astrocytoma (WHO grade II)
  - Protoplasmic astrocytoma (WHO grade II)
  - Gemistocytic astrocytoma (WHO grade II)
Anaplastic astrocytoma (WHO grade III)
Glioblastoma (WHO grade IV)
Giant cell glioblastoma (WHO grade IV)
Gliosarcoma (WHO grade IV)
Gliomatosis cerebri (usually WHO grade III; diagnosis requires clinical-pathological correlation)
Astrocytoma, not otherwise characterized (WHO grades I-IV)

Oligodendroglial Tumors
  - Oligodendrogioma (WHO grade II)
  - Anaplastic oligodendrogioma (WHO grade III)

Oligoastrocytic Tumors (mixed glioma)
  - Oligoastrocytoma (WHO grade II)
  - Anaplastic oligoastrocytoma (WHO grade III)

Ependymal Tumors
  - Subependymoma (WHO grade I)
  - Myxopapillary ependymoma (WHO grade I)
  - Ependymoma (WHO grade II)
    - Cellular ependymoma (WHO grade II)
    - Papillary ependymoma (WHO grade II)
    - Clear cell ependymoma (WHO grade II)
    - Tanycytic ependymoma (WHO grade II)
  - Anaplastic ependymoma (WHO grade III)

Choroid Plexus Tumors
  - Choroid plexus papilloma (WHO grade I)
  - Atypical choroid plexus papilloma (WHO grade II)
  - Choroid plexus carcinoma (WHO grade III)

Other Neuroepithelial Tumors
  - Astroblastoma (WHO grade not assigned)
  - Chordoid glioma of the third ventricle (WHO grade II)
  - Angiocentric glioma (WHO grade I)

Neuronal and Mixed Neuronal-Glial Tumors
  - Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos) (WHO grade I)
  - Desmoplastic infantile astrocytoma/ganglioglioma (WHO grade I)
  - Dysembryoplastic neuroepithelial tumor (WHO grade I)
  - Gangliocytoma (WHO grade I)
  - Ganglioglioma (WHO grade I)
  - Anaplastic ganglioglioma (WHO grade III)
  - Central neurocytoma (WHO grade II)
  - Extraventricular neurocytoma (WHO grade II)
  - Cerebellar liponeurocytoma (WHO grade II)
  - Papillary glioneuronal tumor (PGNT) (WHO grade I)
  - Rosette-forming glioneuronal tumor of the fourth ventricle (RGNT) (WHO grade I)
  - Paraganglioma of the spinal cord (WHO grade I)

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Tumors of the Pineal Region

Pineal parenchymal tumors
- Pineocytoma (WHO grade I)
- Pineal parenchymal tumor of intermediate differentiation (WHO II-III)
- Pineoblastoma (WHO grade IV)
- Papillary tumor of the pineal region (WHO grade II-III)

Embryonal Tumors
- Medulloblastoma, not otherwise characterized (WHO grade IV)
- Desmoplastic/nodular medulloblastoma (WHO grade IV)
- Medulloblastoma with extensive nodularity (WHO grade IV)
- Anaplastic medulloblastoma (WHO grade IV)
- Large cell medulloblastoma (WHO grade IV)
- Central nervous system (CNS) primitive neuroectodermal tumor (PNET) (WHO grade IV)
- Medulloepithelioma (WHO grade I)
- Neuroblastoma (WHO grade IV)
- Ganglioneuroblastoma (WHO grade IV)
- Ependymoblastoma (WHO grade IV)
- Atypical teratoid/rhabdoid tumor (WHO grade IV)

Tumors of Cranial and Paraspinal Nerves
- Schwannoma (WHO grade I)
- Cellular (WHO grade I)
- Plexiform (WHO grade I)
- Melanotic (WHO grade I)
- Neurofibroma (WHO grade I)
- Plexiform (WHO grade I)
- Perineurioma (WHO grade I)
- Intraneural perineurioma (WHO grade I)
- Soft tissue perineurioma (WHO grade I)
- Malignant perineurioma (WHO grade III)
- Ganglioneuroma (WHO grade I)
- Malignant peripheral nerve sheath tumor (MPNST) (WHO grade II-IV) (Note H, Note I)
- Epithelioid (WHO grade II-IV)
- MPNST with divergent mesenchymal and/or epithelial differentiation (WHO grade II-IV)

Tumors of the Meninges/Meningothelial Cells
- Meningioma (WHO grade I)
- Meningothelial (WHO grade I)
- Fibrous (fibroblastic) (WHO grade I)
- Transitional (mixed) (WHO grade I)
- Psammomatous (WHO grade I)
- Angiomatous (WHO grade I)
- Microcystic (WHO grade I)
- Secretory (WHO grade I)
- Lymphoplasmacyte-rich (lymphoplasmacytic) (WHO grade I)
- Metaplastic (WHO grade I)
- Atypical meningioma (WHO grade II)
- Clear cell meningioma (WHO grade II)
- Chordoid meningioma (WHO grade II)
- Anaplastic meningioma (WHO grade III)

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Central Nervous System • Brain/Spinal Cord
Brain/Spinal Cord 3.0.1.0

___ Papillary meningioma (WHO grade III)
___ Rhabdoid meningioma (WHO grade III)
___ Other (specify): _______________________

Mesenchymal (Nonmeningothelial) Tumors (Note I)
___ Lipoma
___ Angiolipoma
___ Hibernoma
___ Liposarcoma (intracranial)
___ Solitary fibrous tumor
___ Fibrosarcoma
___ Malignant fibrous histioscytoma
___ Leiomyoma
___ Leiomyosarcoma
___ Rhabdomyoma
___ Rhabdomyosarcoma
___ Chondroma
___ Chondrosarcoma
___ Osteoma
___ Osteosarcoma
___ Osteochondroma
___ Hemangioma
___ Epithelioid hemangioendothelioma
___ Hemangiopericytoma
___ Malignant hemangiopericytoma
___ Angiosarcoma
___ Kaposi sarcoma
___ Chordoma
___ Mesenchymal, nonmeningothelial tumor, other (specify type, if possible): _______________________
___ Sarcoma, primary CNS (specify type, if possible): _______________________

Primary Melanotic Tumors
___ Diffuse melanocytosis
___ Melanocytoma
___ Malignant melanoma
___ Meningeal melanomatosis

Tumors of Uncertain Histogenesis
___ Hemangioblastoma (WHO grade I)

Lymphoma and Hematopoietic Tumors
___ Malignant lymphoma (specify type, if possible): _______________________
___ Plasmacytoma
___ Granulocytic sarcoma
___ Hematopoietic neoplasm, other (specify type, if possible): _______________________

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Germ Cell Tumors
__ Germinoma
__ Embryonal carcinoma
__ Yolk sac tumor
__ Choriocarcinoma
__ Teratoma, mature
__ Teratoma, immature
__ Teratoma with malignant transformation
__ Malignant mixed germ cell tumor (specify components, eg, germinoma, embryonal, yolk sac, choriocarcinoma, teratoma): __________________________

Tumors of the Sellar Region
__ Craniopharyngioma (WHO grade I)
__ Craniopharyngioma, adamantinomatous (WHO grade I)
__ Craniopharyngioma, papillary (WHO grade I)
__ Granular cell tumor (WHO grade I)
__ Pituicytoma (WHO grade I)
__ Spindle cell oncocytoma (WHO grade I)
__ Pituitary adenoma (specify nonfunctional or hormone expression, if known): __________________________
__ Pituitary carcinoma
__ Pituitary hyperplasia
__ Other (specify): __________________________

Other/Nonclassifiable
__ Other(s) (specify): __________________________
__ Malignant neoplasm, type cannot be determined

Histologic Grade (WHO histologic grade) (Note G)
__ Not applicable
__ Cannot be determined
__ WHO grade I
__ WHO grade II
__ WHO grade III
__ WHO grade IV
__ WHO grade not assigned
__ Other (specify): __________________________

Margins (for resections of malignant peripheral nerve sheath tumors only) (Note H)
__ Cannot be assessed
__ Margins not involved by tumor
__ Margins involved by tumor
  + Specify, if possible: __________________________
Ancillary Studies (select all that apply)
+ ___ None performed
+ ___ Immunohistochemistry (specify): __________________________
+ ___ Electron microscopy
+ ___ Molecular genetic studies (specify): __________________________ (Note J)
  + ___ 1p deletion identified
  + ___ 1p deletion not identified
  + ___ 19q deletion identified
  + ___ 19q deletion not identified
  + ___ Other (specify): __________________________
+ ___ Other (specify): __________________________

Additional Pathologic Findings
+ Specify: __________________________

Comment(s): __________________________
Explanatory Notes

A. Relevant History

Patient Age
Patient age may be critically important for predicting tumor behavior. For example, patient age is predictive of survival in many malignant CNS neoplasms. For diffusely infiltrating astrocytomas, age and histologic grade are the two strongest predictors of patient outcome, with patient age greater than 50 years and high-grade histologic features serving as negative indicators.14

Duration of Symptoms
A long clinical history of CNS symptoms or seizures prior to the diagnosis of a CNS tumor is suggestive of origin from a slowly growing neoplasm. Alternatively, a sudden onset of clinical symptoms or a rapidly progressive neurological deficit may be indicative of a high-grade tumor, hemorrhage, infarct, active demyelinating disease, or edema associated with some other benign or low-grade lesion.

Previous Diagnoses or CNS Biopsies
Knowledge of the presence or absence of previous intracranial or extracranial disease (eg, immunosuppression, 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.

Preoperative Treatment
Knowledge of preoperative treatment, including radiation therapy, corticosteroid therapy, chemotherapy, and other therapy, is helpful for specimen interpretation. In particular, prior radiation therapy or radiosurgery may alter the interpretation of specimens in which there are increased cellular atypia, decreased proliferative activity, or large areas of radiation-induced change (eg, coagulative [nonpalisading] necrosis, vascular hyalinization, and gliosis).

Family History of Cancer or Primary CNS Tumors
Several genetic conditions/syndromes are associated with an increased predisposition to the development of certain brain neoplasms (eg, neurofibromatosis types 1 and 2, Turcot/Lynch, tuberous sclerosis, von Hippel-Lindau, Cowden, Li-Fraumeni, and Gorlin syndromes).

Relevant Radiographic Imaging Features
Knowledge of neuroimaging features is extremely helpful in specimen interpretation. 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 discrepancy with pathologic diagnosis (eg, contrast enhancement with hypocellularity). A close collaboration with the neuroradiologist and neurosurgeon is essential.

B. Specimen Type/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.

C. Specimen Handling, Triage, and Special Procedures
It may be necessary to divide biopsy/resection tissue into portions for the following procedures:
- Squash/smear/touch preparations
- Frozen sections
- Unfrozen routine permanent paraffin sections (essential to avoid artifacts)
- Electron microscopy (retain a small portion in glutaraldehyde, or "embed and hold" for electron microscopy, if necessary)
• Frozen tissue, for possible molecular diagnostic studies (freeze fresh tissue as soon as possible and store)
• Other (microbiology, flow cytometry, cytogenetics, molecular diagnostics)

Since cellular details are very important in interpreting CNS neoplasms, previously frozen tissue with its inherent artifacts is suboptimal, especially for subclassifying and grading gliomas. Recommendations for optimally freezing and cutting frozen sections from tissue from the brain and spinal cord have been published. It is imperative to retain tissue that has not been previously frozen for permanent sections. Avoid using sponges in cassettes because they produce angular defects that resemble vascular/luminal spaces in the final sections. Wrapping small biopsies in lens paper, or placement into agar or into tissue sacs prior to submitting in cassettes, is recommended. If biopsy frozen and permanent sections are nondiagnostic, tissue that was retained in glutaraldehyde may be submitted for additional paraffin sections.

If touch preparations are used, the presence of cells with delicate processes on smear/squash preparations is suggestive of a primary CNS neoplasm. The formation of processes and cytoplasmic fibrillarity may be seen in reactive astrocytosis. The identification of macrophages is important since a macrophage-rich lesion is more likely a subacute infarct or demyelination, rather than a neoplasm.

If an infectious etiology is suspected, the neurosurgeon should be alerted to submit a fresh sample to microbiology to be processed for bacterial, fungal, and/or viral cultures.

If a lymphoproliferative disorder is suspected and sufficient tissue is available, a portion of fresh tissue should be set aside for appropriate workup.

D. Specimen Size
For most CNS tumors, specimen size is of limited significance, with optimal preservation and processing of greater importance. In heterogeneous lesions, issues of tissue sampling may become important.

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

F. Histologic Type
Classification of tumors should be made according to the WHO classification of tumors of the nervous system whenever possible.

G. Histologic Grade
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.
Table 1. WHO Grading System for some of the More Common Tumors of the CNS

<table>
<thead>
<tr>
<th>Tumor Group</th>
<th>Tumor Type</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrocytic tumors</td>
<td>Diffuse astrocytoma</td>
<td>X</td>
<td></td>
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<tr>
<td></td>
<td>Anaplastic astrocytoma</td>
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<td>Glioblastoma</td>
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<td>Pilocytic astrocytoma</td>
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<td>Subependymal giant cell astrocytoma</td>
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<td>Pleomorphic xanthoastrocytoma</td>
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<td>Oligodendrogliomas</td>
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<td>Anaplastic oligodendroglioma</td>
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<tr>
<td>Oligoastrocytomas</td>
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<td></td>
<td>Anaplastic oligoastrocytoma</td>
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<td>Ependymal tumors</td>
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<td>Anaplastic ependymoma</td>
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<td>Subependymoma</td>
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<td>Myxopapillary ependymoma</td>
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<td>Choroid plexus tumors</td>
<td>Choroid plexus papilloma</td>
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<td>Atypical choroid plexus papilloma</td>
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<td>Choroid plexus carcinoma</td>
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<td>X</td>
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<td>Other neuroepithelial tumors</td>
<td>Angiocentric glioma</td>
<td>X</td>
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<td>Chordoid glioma of the third ventricle</td>
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<td>Neuronal-glia tumors</td>
<td>Gangliocytoma</td>
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<td>Desmoplastic infantile ganglioglioma/ astrocytoma</td>
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<td>Dysembryoplastic neuroepithelial tumor (DNET)</td>
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<td>Anaplastic ganglioglioma</td>
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<td>Central neurocytoma</td>
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<td>Extraventricular neurocytoma</td>
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<td>Cerebellar liponeurocytoma</td>
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<td>Rosette-forming glioneuronal tumor of the fourth ventricle (RGNT)</td>
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<td>X</td>
</tr>
<tr>
<td></td>
<td>Paraganglioma of the spinal cord</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
### Table: Tumor Types and Grades

<table>
<thead>
<tr>
<th>Tumor Group</th>
<th>Tumor Type</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pineal parenchymal tumors</td>
<td>Pineocytoma</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pineal parenchymal tumor of intermediate differentiation</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pineoblastoma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Papillary tumor of the pineal region</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embryonal tumors</td>
<td>Medulloblastoma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CNS primitive neuroectodermal tumor</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Medulloepithelioma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuroblastoma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ganglioneuroblastoma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ependymoblastoma</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Atypical teratoid/rhabdoid tumor</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cranial and peripheral nerve tumors</td>
<td>Schwannoma</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurofibroma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perineurioma</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Malignant peripheral nerve sheath tumors (MPNST)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Meningeal tumors</td>
<td>Meningioma</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atypical meningioma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clear cell meningioma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td></td>
<td>Chordoid meningioma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td></td>
<td>Anaplastic meningioma</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Papillary meningioma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rhabdoid meningioma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Mesenchymal tumors</td>
<td>(Named as soft tissue counterpart)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Hemangiopericytoma</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Tumors of uncertain histogenesis</td>
<td>Hemangioblastoma</td>
<td>X</td>
<td></td>
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</tr>
</tbody>
</table>

After patient age, tumor histology and grade have been shown to be the strongest predictors of clinical course in selected CNS astrocytomas. Several grading systems for diffusely infiltrating astrocytomas are based on their ability to define distinct groups with significantly different survivals. The WHO uses a 3-tiered grading system (modified St. Anne-Mayo) for diffuse astrocytomas (Table 2).
Table 2. WHO Grading System for Diffuse Infiltrating Astrocytomas

<table>
<thead>
<tr>
<th>WHO Grade</th>
<th>WHO Designation</th>
<th>Histologic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Diffuse astrocytoma</td>
<td>1 criterion: usually nuclear atypia</td>
</tr>
<tr>
<td>III</td>
<td>Anaplastic astrocytoma</td>
<td>2 criteria: usually nuclear atypia and mitoses</td>
</tr>
<tr>
<td>IV</td>
<td>Glioblastoma</td>
<td>3 criteria: usually nuclear atypia, mitoses, and endothelial proliferation and/or necrosis</td>
</tr>
</tbody>
</table>

H. Margins
With the exception of malignant peripheral nerve sheath tumors, resection margins provide no prognostic information and generally are not required for most CNS neoplasms.

I. Mesenchymal Tumors
Mesenchymal tumors vary widely in grade, from benign tumors (WHO grade I) to highly malignant sarcomas (WHO grade III to IV). The classification and grading of these lesions is performed as for the corresponding tumor of soft tissue and bone, as detailed in the WHO monograph, *Tumours of Soft Tissue and Bone*,8 and the College of American Pathologists bone and soft tissue cancer protocol.9

J. Molecular Genetic Studies
Recent studies have shown that combined 1p and 19q deletions in oligodendrogliaomas are associated with enhanced chemoresponsiveness and improved survival.10-12 In addition, several other rapidly emerging molecular markers are providing useful diagnostic and prognostic information. For example, *EGFR* amplification may be useful in distinguishing high-grade astrocytoma from anaplastic oligodendrogliaoma; *n-Myc* amplification has prognostic significance in medulloblastomas; and *INI1* studies are useful in the diagnosis of atypical teratoid/rhabdoid tumor.

References