Brain/Spinal Cord

Protocol applies to all neoplasms of the brain/spinal cord. Excludes neoplasms of the pituitary gland.

Protocol revision date: January 2005
No AJCC/UICC staging system

Procedures
• Cytology (No Accompanying Checklist)
• Biopsy
• Resection

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Summary of Changes to Checklist(s)

Protocol revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.
Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2005
Applies to all brain/spinal cord neoplasms
Excludes neoplasms of the pituitary gland
No AJCC/UICC staging system

BRAIN/SPINAL CORD: Biopsy, Resection

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Open biopsy
___ Stereotactic needle core biopsy
___ Subtotal/partial resection
___ Total resection
___ Other (specify): ____________________________
___ Not specified

Specimen Size
Greatest dimension: ___ cm
*Additional dimensions: ___x___ cm

Tumor Site (check all that apply)
___ Cerebral meninges
___ Cerebrum (specify lobe[s], if known): ____________________________
___ Basal ganglia
___ Thalamus
___ Hypothalamus
___ Suprasellar
___ Pineal
___ Cerebellum
___ Cerebellopontine angle
___ Ventricle
___ Brain stem
___ Spinal cord
___ Nerve root
___ Other (specify): ____________________________
___ Not specified

* Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
Tumor Size
Largest dimension: ___ cm
*Additional dimensions: ___x___ cm
___ Cannot be determined (see Comment)

MICROSCOPIC

Histologic Type
___ Astrocytoma, not otherwise characterized
___ Astrocytoma, diffuse
___ Astrocytoma, pilocytic
___ Astrocytoma, pleomorphic xanthoastrocytoma
___ Astrocytoma, anaplastic
___ Astrocytoma, other (specify): ____________________________
___ Glioblastoma
___ Gliosarcoma
___ Oligodendroglioma, not otherwise characterized
___ Oligodendroglioma, anaplastic
___ Oligoastrocytoma, not otherwise characterized
___ Oligoastrocytoma, anaplastic
___ Ependymoma, not otherwise characterized
___ Ependymoma, tanycytic
___ Ependymoma, myxopapillary
___ Ependymoma, anaplastic
___ Ependymoma, other (specify): ____________________________
___ Subependymoma
___ Choroid plexus papilloma
___ Choroid plexus carcinoma
___ Gangliocytoma
___ Ganglioglioma
___ Dysembryoplastic neuroepithelial tumor
___ Desmoplastic infantile ganglioglioma/astrocytoma
___ Pineocytoma
___ Pineoblastoma
___ Pineal parenchymal tumor of intermediate differentiation
___ Medulloblastoma, not otherwise characterized
___ Medulloblastoma, desmoplastic
___ Medulloblastoma, large cell
___ Medulloblastoma, melanotic
___ Medulloblastoma, other (specify):
___ Primitive neuroectodermal tumor (PNET)
___ Neuroblastoma
___ Atypical teratoid/rhabdoid tumor
___ Schwannoma, not otherwise characterized
___ Schwannoma, cellular
___ Schwannoma, plexiform
___ Schwannoma, melanotic

* Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
Margins
___ Cannot be assessed
___ Not applicable
___ Margins uninvolved by tumor
___ Margin(s) involved by tumor
Specify which margin(s): ___________________________

*Additional Studies (check all that apply)
*___ None performed
*___ Electron microscopy
*___ Cytogenetics
*___ Molecular testing (specify): ___________________________
*___ Other (specify): ___________________________

*Additional Pathologic Findings
*Specify: ___________________________

*Comment(s)
Background Documentation

Protocol revision date: January 2005

I. Cytologic Material
A. Clinical Information
   1. Patient identification
      a. Name
      b. Identification number
      c. Age (birth date)
      d. Sex
   2. Responsible physician(s)
   3. Date of procedure
   4. Other clinical information
      a. Relevant history (Note A)
      b. Relevant findings (Note B)
      c. Clinical/imaging differential diagnosis
      d. Procedure (eg, percutaneous fine-needle aspiration)
      e. Anatomic site of specimen (Note C)

B. Macroscopic Examination
   1. Specimen
      a. Unfixed/fixed (specify fixative) (Note D)
      b. Number of slides received, if appropriate
      c. Cytologic preparation of tissue specimen (touch or squash/smear preparation)
   2. Material submitted for microscopic evaluation (eg, smear of fluid, other liquid based cytology preparations, cell block) (Note E)
   3. Special studies (eg, cytochemistry, immunocytochemistry, microbiology, flow cytometry, genetic and molecular testing) (Note F)

C. Microscopic Evaluation
   1. Adequacy of specimen for diagnostic evaluation (if unsatisfactory or limited, specify reason)
   2. Tumor
      a. Histologic type, if possible (Note G)
   3. Other pathologic findings
   4. Results/status of special studies (specify)
   5. Comments
      a. Correlation with intraprocedural consultation
      b. Correlation with other specimens
      c. Correlation with clinical information (Note H)

II. Biopsy
A. Clinical Information
   1. Patient identification
      a. Name
      b. Identification number
      c. Age (birth date)
      d. Sex
   2. Responsible physician(s)
   3. Date of procedure
4. Other clinical information
   a. Relevant history (Note A)
   b. Relevant findings (Note B)
   c. Clinical/imaging differential diagnosis
   d. Procedure (e.g., stereotactic needle core biopsy, open biopsy)
   e. Anatomic site of specimen (Note C)

B. Macroscopic Examination
   1. Specimen
      a. Unfixed/fixed (specify fixative) (Note D)
      b. Size (number of cores or size of biopsy in dimensions or approximate volume)
      c. Descriptive features (grossly obvious meninges, gray matter or white matter, color, texture, cut surface, mucinous, fibrous, bloody, necrotic, gritty)
      d. Recognition of gross and microscopic correlates is helpful in correct interpretation of microscopic findings and is also helpful in selecting cores for frozen section analysis
   2. Special studies (Note F)
      a. Frozen sections, if requested
      b. Squash, touch, or scrape preparations
      c. Histochemistry
      d. Immunohistochemistry, including proliferation markers
      e. Electron microscopy (EM)
      f. Other (microbiology, flow cytometry, cytogenetics, molecular diagnostics)
      g. Was a portion of tissue frozen for later potential studies?
   3. Tissue submitted for microscopic evaluation. The specimen is usually totally submitted after removing tissue for frozen sections, EM, or other special studies as indicated in Note F. Try to orient at right angles to surface.

C. Microscopic Evaluation
   1. Tumor
      a. Histologic type (Note I)
      b. Histologic grade (Note J)
      c. Additional features, if present
         (1) hemosiderin deposition
         (2) calcification
         (3) microcyst formation
         (4) mitotic activity
         (5) pleomorphism
         (6) presence of gemistocytes
         (7) vascular proliferation
         (8) necrosis
         (9) eosinophilic granular bodies
      d. Findings in smear/squash, touch, or scrape preparations (Note K)
   2. Status/results of special studies (specify)
   3. Comments
      a. Correlation with intraoperative consultation
      b. Correlation with previous specimens
      c. Correlation with clinical and radiographic information (Note H)
III. Resection
A. Clinical Information
1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (Note A)
   b. Relevant findings (Note B)
   c. Clinical/imaging differential diagnosis
   d. Procedure (total, subtotal, or partial resection)
   e. Operative findings
   f. Anatomic site of specimen (Note C)
B. Macroscopic Examination
1. Specimen
   a. Unfixed/fixed (specify fixative) (Note D)
   b. Number of pieces with combined aggregate dimensions (the extent of resection can have prognostic significance) (Note A)
   c. Descriptive features (grossly obvious meninges, gray matter or white matter, color, texture, cut surface, mucinous, fibrous, bloody, necrotic, gritty)
   d. Recognition of gross and microscopic correlates is helpful in correct interpretation of microscopic findings and is also helpful in selecting cores for frozen section analysis
   e. Margins, as appropriate. For the majority of central nervous system (CNS) neoplasms, margins are not evaluated because specimens are fragmented. Exceptions would be some meningeal or metastatic tumors.
   f. Results of intraoperative consultation
2. Tissue submitted for microscopic evaluation. The specimen is usually totally submitted after removing tissue for frozen sections, EM, or special studies as suggested in Note F.
3. Special studies (Note F)
   a. Frozen sections, if requested
   b. Squash/smear, touch, or scrape preparations
   c. Histochemistry
   d. Immunohistochemistry, including proliferation markers
   e. Electron microscopy (EM)
   f. Receptor analysis
   g. Other (microbiology, flow cytometry, cytogenetics, molecular diagnostics)
   h. Was a portion of tissue frozen for later potential studies?
C. Microscopic Evaluation
1. Tumor
   a. Histologic type (Note I)
   b. Histologic grade (Note J)
   c. Local extension (eg, bony or soft tissue invasion, subarachnoid spread) (Note K)
   d. Additional features, if present
      (1) hemosiderin deposition
      (2) calcification
(3) microcyst formation
(4) mitotic activity
(5) pleomorphism
(6) presence of gemistocytes
(7) vascular proliferation
(8) necrosis
(9) eosinophilic granular bodies
e. Findings in squash, touch, or scrape preparations (Note K)

2. Status/results of special studies (specify)

3. Comments
   a. Correlation with intraoperative consultation
   b. Correlation with previous specimens
   c. Correlation with clinical and radiographic information (Note H)

Explanatory Notes

A. Relevant History

Patient Age
Most central nervous system (CNS) tumors show an age predilection, and patient age has been shown to predict survival in many malignant CNS neoplasms. With diffusely infiltrating astrocytic tumors, age followed by histologic grade represent the 2 strongest prognostic indicators for patient outcome, with patient age of greater than 50 years and high-grade tumors serving as negative indicators.1-4

Duration of Symptoms (Acute or Chronic)
A long clinical history of CNS symptoms or seizures prior to the diagnosis of a CNS tumor favors a slowly growing neoplasm that is more likely to be benign. A rapidly progressive neurological deficit of sudden onset is more consistent with, but not always indicative of, a high-grade malignant tumor.5

Extent of Resection
For most CNS tumors, the amount of tumor removed (total, subtotal, or partial resection) is an important predictor of patient outcome.3,4,6 The extent of resection can be estimated by recording the gross dimensions of the aggregate pieces. In most operating rooms, a suction device is frequently used in conjunction with gross debulking to remove tumors. The tissue in the suction bags generally liquefies and is not usually adequate for surgical pathology submission. However, when possible, we recommend that the surgical team be encouraged to submit the suction specimen to surgical pathology. This will serve to better estimate the extent of resection, and the tissue present in the suction specimen might be critical in making the correct diagnosis.

Tumor Location and Size
The extent of surgical resection possible is determined by tumor location and size.

Previous Diagnoses
Knowledge of the presence or absence of extracranial disease, ie, a history of immunosuppression or a history of a primary malignant neoplasm outside the CNS, can be critical in the correct interpretation of biopsy material.5 If a metastatic tumor is included in the differential diagnosis, it is helpful to have slides of the primary tumor available.
Previous CNS Biopsies
Previous slides should be obtained whenever possible for comparison.

History of Radiation or Radiosurgery
Knowledge of prior radiation therapy or radiosurgery can help in interpreting specimens in which there are large areas of radiation change (eg, coagulative necrosis, gliosis, vascular hyalinization). CNS tumors noted to arise in a field of prior irradiation include meningiomas, meningeal sarcomas, astrocytomas, primitive neuroectodermal tumors, and gliosarcomas. Radiation therapy of diffusely infiltrating astrocytomas has been shown to increase survival.

Family History of Cancer or Primary CNS Tumors
Approximately 16% of patients with brain tumors have a family history of cancer. Several genetic conditions/syndromes are associated with an increased predisposition to the development of certain brain neoplasms. Neurofibromatosis type 2 is associated with acoustic neuromas, multiple meningiomas, and spinal cord ependymomas. Tuberous sclerosis is associated with subependymal giant cell astrocytomas. Von Hippel-Lindau is associated with hemangioblastomas of the cerebellum while Turcot syndrome is associated with medulloblastomas and glioblastomas. Therefore, knowledge of presence of such conditions is important in reaching a proper diagnosis.

B. Relevant Findings
Imaging Features
- Density
- Enhancement pattern
- Well-circumscribed or infiltrative borders
- Cyst formation
- Calcification
- Location (intraventricular; white matter, gray matter, or both)

Recognition of characteristic imaging patterns and locations of CNS tumors is important in correct interpretation of biopsy specimens, eg, low-grade infiltrating astrocytomas usually do not enhance, whereas high-grade ones do. Tumor enhancement and peritumoral edema in infiltrating astrocytomas are associated with a worse prognosis, and diffuse tumors have been shown to have a poorer prognosis than focal ones.

C. Anatomic Site of Specimen
Cytologic Material
- Cerebrospinal fluid (CSF) (ventricular, lumbar, cisternal)
- Cyst fluid
- Fine-needle aspiration
- Percutaneous (specify site)
- Stereotactic computer tomography (CT)-guided
- Other (eg, external shunt drain canisters)

Biopsy or Resection
- Dura (convexity, falx, tentorium, sphenoid wing, skull base)
- Leptomeninges
- Cerebrum (specify lobe: frontal, parietal, temporal, occipital)
- Basal ganglia
- Thalamus
For Information Only

Central Nervous System • Brain/Spinal Cord

Hypothalamus
Pituitary
Suprasellar area
Pineal
Cerebellum (specify lobe: right or left hemisphere, midline or lateral)
Cerebellopontine angle
Ventricle (third, lateral, fourth)
Brain stem (midbrain, pons, or medulla)
Spine (extradural, intradural/extradural, intradural/intradural, conusmedullaris, filum terminale)
Nerve root(s)/canal (extradural, intradural, anterior root or posterior root)

D. Specimen Unfixed/Fixed

Cytologic Material
Cytologic preservation in cerebrospinal fluid (CSF) depends on the time interval before processing, especially for hematopoietic and some neuroepithelial cells. Refrigerate if delayed more than 30 to 45 minutes. Record the time interval to aid in interpretation.

Biopsy or Resection
Cellular detail is very important for interpreting CNS neoplasms, and previously frozen tissue is suboptimal, especially for grading and subclassifying gliomas. Recommendations for optimally freezing and cutting frozen sections from tissue from the brain and spinal cord have been made in a previously published paper. Make every attempt to retain tissue that has not been previously frozen for permanent sections. Avoid using sponges in cassettes because they produce angular defects, which resemble vascular/luminal spaces in the final sections. Wrapping small biopsies in lens paper prior to placing them in cassettes is recommended.

E. Cytologic Material Submitted for Microscopic Evaluation
Cytospin slides or liquid-based monolayer cytology, both air-dried Romanowsky-stained and fixed Papanicolaou-stained slides, as well as unstained slides, should be prepared from fluid specimens, especially CSF, meningeal, and tumoral cyst fluid.

F. Special Studies
It may be necessary to divide biopsy/resection tissue into portions for the following procedures:

1. Squash/smear, touch, or scrape preparations
2. Unfrozen permanent paraffin sections
3. Frozen sections, if requested
4. Electron microscopy (EM) (retain a small portion in 3% glutaraldehyde or "embed and hold" for EM, if necessary)
5. Other (microbiology, flow cytometry, cytogenetics, molecular diagnostics)
6. Frozen tissue, if requested (freeze fresh tissue as soon as possible and store at -70°C), especially for possible future molecular diagnostic studies

When the tissue is a biopsy and the tissue sample is small, the order of priority for processing tissue for the procedures outlined above is as listed. It is imperative to have unfrozen tissue for diagnosis, since freezing artifact may make accurate diagnosis very difficult or impossible. Recommendations for optimally freezing and cutting frozen sections from tissue from the brain and spinal cord have been made in a previously published paper. If biopsy frozen and permanent sections are nondiagnostic, tissue that
was retained in 3% glutaraldehyde could be submitted for EM or for additional paraffin sections, depending on the amount of tissue available, with the hope of making a diagnosis. Some pathologists may choose to examine semi-thin or 1-micron-thick stained sections with toluidine blue instead.

Squash preparations (also referred to as smear preparations by some experts) are prepared by placing a tiny (1- to 2-mm) fragment of tissue onto a glass slide, placing another glass slide over it, pressing the slides together, squashing the tissue between them, then sliding the 2 slides past each other, dragging squashed tissue across each slide. Slides are then rapidly placed into fixative in the same rack used for frozen sections and stained as for frozen sections.  

Squash preparations are recommended for most CNS lesions. Touch preparations are recommended for pituitary adenomas, oligodendrogliomas, meningiomas, metastatic carcinomas, and lymphomas. Scrape preparations, in which tissue is scraped with a scalpel blade and scrapings applied to glass slides and stained similar to squash and touch preparations, are recommended for desmoplastic tumors, such as dural metastases that cannot be squashed or do not shed well on touch preparations.

If infectious etiologies are suspected, a portion of fresh tissue can be sent to the microbiology laboratory in a sterile container to be processed for bacterial, fungal, or viral cultures. Tissue from patients with symptoms suggestive of transmissible spongiform encephalopathy (Creutzfeldt-Jakob disease [CJD]) requires special handling. The infectious agent of CJD may be inactivated by immersing formalin-fixed tissue in 50 to 100 mL of pure formic acid for 1 hour, followed by reimmersion in fresh formalin. While the clinical diagnosis of transmissible spongiform encephalopathy encompasses a spectrum of neurologic dysfunction, rapidly progressive dementia and myoclonus are especially suggestive of this diagnosis.

If a lymphoproliferative disorder is suspected, a portion of fresh tissue can be sent to the surgical pathology laboratory where it will be placed in appropriate holding media (RPMI) for flow cytometry and cytogenetics. Refer to a previously published protocol for processing specimens from patients with non-Hodgkin lymphoma. Molecular diagnostic testing is playing an increasingly important role in the diagnosis, staging, and treatment of tumors. Tissue that has been frozen shortly after arrival in the laboratory and stored at -70°C will be suitable for these studies. Paraffin-embedded tissue can also occasionally be used.

G. Cytopathology: Histologic Type
Tumor cells, especially those of glial lineage, are often altered by time in fluid/CSF and are difficult to interpret unless cell clusters or tissue fragments are available. Choroid plexus and ependymal cells are quite similar, with the latter showing more "degenerative" cytologic features and fewer cellular clusters. Therefore, the designation "choroid-ependymal" cells is appropriate. Ependymomas and choroid plexus papillomas generally appear cytologically benign or bland. It is helpful to prepare squash preparations routinely during intraoperative consultations to develop or keep a sharp "cytologic eye" for CNS neoplasms.
H. Comments
Correlation of clinical and radiographic information should be critically reviewed before final sign-out of the biopsy diagnosis.\textsuperscript{20}

I. Histologic Type
The World Health Organization (WHO) classification of tumors of the central nervous system is shown below.\textsuperscript{21}

**WHO Histologic Typing of Tumors of the Nervous System**

Tumors of Neuroepithelial Tissue

Astrocytic tumors
- Diffuse astrocytoma
- Fibrillary astrocytoma
- Protoplasmic astrocytoma
- Gemistocytic astrocytoma
- Anaplastic astrocytoma
- Glioblastoma
  - Giant cell glioblastoma
  - Gliosarcoma
- Pilocytic astrocytoma
- Pleomorphic astrocytoma
- Pleomorphic xanthoastrocytoma
- Subependymal giant cell astrocytoma

Oligodendrogial tumors
- Oligodendroglioma
  - Anaplastic oligodendroglioma
- Mixed gliomas
  - Oligoastrocytoma
  - Anaplastic oligoastrocytoma

Ependymal tumors
- Ependymoma
  - Cellular
  - Papillary
  - Clear cell
  - Tanycytic
- Anaplastic ependymoma
- Myxopapillary ependymoma
- Subependymoma

Choroid plexus tumors
- Choroid plexus papilloma
- Choroid plexus carcinoma

Glial tumors of uncertain origin
- Astroblastoma
- Gliomatosis cerebri
- Chordoid glioma of the third ventricle

Neuronal and mixed neuronal-glial tumors
- Gangliocytoma
- Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
- Desmoplastic infantile astrocytoma/ganglioglioma
- Dysembryoplastic neuroepithelial tumor
Ganglioglioma
Anaplastic ganglioglioma
Central neurocytoma
Cerebellar liponeurocytoma
Paraganglioma of the filum terminale

Neuroblastic tumors
Olfactory neuroblastoma (esthesioneuroblastoma)
Olfactory neuroepithelioma
Neuroblastomas of the adrenal gland and sympathetic nervous system

Pineal parenchymal tumors
Pineocytoma
Pineoblastoma
Pineal parenchymal tumor of intermediate differentiation

Embryonal tumors
Medulloepithelioma
Ependymoblastoma
Medulloblastoma
  Desmoplastic medulloblastoma
  Large cell medulloblastoma
  Medullomyoblastoma
  Melanotic medulloblastoma
Supratentorial primitive neuroectodermal tumor (PNET)
  Neuroblastoma
  Ganglioneuroblastoma
  Atypical teratoid/rhabdoid tumor

Tumors of Peripheral Nerves
Schwannoma (Neurilemmoma, Neurinoma)
  Cellular
  Plexiform
  Melanotic

Neurofibroma
  Plexiform

Perineurioma
  Intraneural perineurioma
  Soft tissue perineurioma

Malignant Peripheral Nerve Sheath Tumor (MPNST)
  Epithelioid
  MPNST with divergent mesenchymal and/or epithelial differentiation
  Melanotic
  Melanotic psammomatous

Tumors of the Meninges
Tumors of meningothelial cells
Meningioma
  Meningothelial
  Fibrous (fibroblastic)
  Transitional (mixed)
  Psammomatous
  Angiomatous
  Microcystic
Secretory
Lymphoplasmacyte-rich
Metaplastic
Clear cell
Chordoid
Atypical
Papillary
Rhabdoid
Anaplastic meningioma

Mesenchymal, non-meningothelial tumors
Lipoma
Angiolipoma
Hibernoma
Liposarcoma (intracranial)
Solitary fibrous tumor
Fibrosarcoma
Malignant fibrous histiocytoma
Leiomyoma
Leiomyosarcoma
Rhabdomyoma
Rhabdomyosarcoma
Chordroma
Chondrosarcoma
Osteoma
Osteosarcoma
Osteochondroma
Haemangioma
Epithelioid haemangioendothelioma
Haemangiopericytoma
Angiosarcoma
Kaposi sarcoma

Primary melanocytic lesions
Diffuse melanocytosis
Melanocytoma
Malignant melanoma
Meningeal melanomatosis

Tumors of uncertain histogenesis
Haemangioblastoma

Lymphomas and Haemopoietic Neoplasms
Malignant lymphomas
Plasmacytoma
Granulocytic sarcoma

Germ Cell Tumors
Germinoma
Embryonal carcinoma
Yolk sac tumor (endodermal sinus tumor)
Choriocarcinoma
Teratoma
  Mature
  Immature
  Teratoma with malignant transformation
Mixed germ cell tumors

Tumors of the Sellar Region
Craniopharyngioma
  Adamantinomatous
  Papillary
Granular cell tumor

Metastatic Tumors

J. Histologic Grade
The WHO grading system (malignancy scale) of CNS tumors is shown below. There is no formal TNM-based classification and staging system for the central nervous system at this time.

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<th>Tumor Type</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
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<td>Tumor Type</td>
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<tr>
<td></td>
<td>Other primitive neuroectodermal tumors</td>
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<td></td>
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<tr>
<td></td>
<td>Neuroblastoma</td>
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<td>Ependymoblastoma</td>
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<td></td>
<td>Atypical teratoid / rhaboid tumor</td>
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<td>Cranial and nerve sheath tumors</td>
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<td>Malignant peripheral nerve sheath tumors</td>
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### Tumor Group

<table>
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<th>Tumor Group</th>
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<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
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<td>Clear cell meningioma</td>
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<td>Chordoid meningioma</td>
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<td>Anaplastic meningioma</td>
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<td></td>
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<tr>
<td></td>
<td>Hemangiopericytoma</td>
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</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 have been proposed based on their ability to define distinct patient groups with significantly different survival curves. Both 3-tiered and 4-tiered systems are currently in use and have been reviewed. Two examples of popular grading systems are shown below. For a complete review and comparison of these systems, including the 3-tiered system, such as Ringertz system and modifications thereof, the reader is referred to the review by McLendon et al.

### Comparison of the WHO and St. Anne/Mayo Grading Systems for Astrocytomas

<table>
<thead>
<tr>
<th>WHO Grade</th>
<th>WHO Designation</th>
<th>St. Anne/Mayo Designation</th>
<th>Histologic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Pilocytic astrocytoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Astrocytoma (low-grade)</td>
<td>Astrocytoma, grade 2</td>
<td>1 criterion, usually nuclear atypia</td>
</tr>
<tr>
<td>III</td>
<td>Anaplastic astrocytoma</td>
<td>Astrocytoma, grade 3</td>
<td>2 criteria, usually nuclear atypia and mitoses</td>
</tr>
<tr>
<td>IV</td>
<td>Glioblastoma multiforme</td>
<td>Astrocytoma, grade 4</td>
<td>3 criteria, usually nuclear atypia, mitoses, and endothelial proliferation and/or necrosis</td>
</tr>
</tbody>
</table>

### K. Other Pathologic Features

Hemosiderin deposition, calcification, and microcyst formation are nonspecific findings that occur in both malignant and benign CNS neoplasms. However, in general, calcification usually favors a slowly growing neoplasm, which is more likely to be benign.
In non-pilocytic neoplasms, the presence of gemistocytes, vascular proliferation, and necrosis represent negative prognostic indicators, and the latter 2 histologic changes are diagnostic of high-grade astrocytomas.\textsuperscript{10,26-28} By contrast, eosinophilic granular bodies typically occur in low grade neoplasms (pilocytic astrocytoma, ganglion cell tumors, and pleomorphic xanthoastrocytoma).\textsuperscript{4}

**Findings in Touch, Squash, or Scrape Preparations**

The presence of process-forming cells is suggestive of a primary CNS neoplasm. Extreme fibrillarity may represent reactive astrocytosis.\textsuperscript{4} Touch or squash preparations are also of value in evaluating specimens for the presence of macrophages. A macrophage-rich lesion is more consistent with a subacute infarct or demyelinating lesion, rather than a tumor.

Local extension, rapid growth, invasion of adjacent structures, and CNS spread via the ventricular system or subarachnoid space are often suggestive of, but not always diagnostic of, malignancy. Low-grade neoplasms, such as meningioma and pilocytic astrocytoma, may also exhibit this type of spread, but at a slower rate of growth than most malignant tumors. Malignant and atypical meningeal tumors often invade brain substance.\textsuperscript{29}

**References**


Bibliography