Protocol for the Examination of Specimens from Patients with Primary Tumors of the Brain and Spinal Cord

Protocol applies to all primary neoplasms of the brain and spinal cord. This protocol does not apply to metastatic tumors and primary bone tumors, lymphoma, malignant peripheral nerve sheath tumor or mesenchymal tumors.

Based on:

No AJCC/UICC TNM Staging System
CAP Cancer Protocol version: Brain/Spinal Cord 4.0.0.0
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Revision History:

None

Summary of Changes:

This protocol is updated to the 8th Edition AJCC Cancer Staging Manual and the current version of the CAP Cancer Protocol CNS 4.0.0.0.

Procedures Covered in this Protocol:

- Open Biopsy
- Craniotomy for Resection of Tumor
- Stereotactic Biopsy

Authors:

Edgar B. Masmila, PA(ASCP)CM*, MBA
School of Medicine, Department of Pathology, University of California, San Diego, La Jolla, CA
Heidi Cheek, PA(ASCP)CM
Mayo Clinic, Rochester, MN
Jennifer Davidson, PA(ASCP)CM
Mayo Clinic, Rochester, MN
Chelsea Graun, MHS, PA(ASCP)CM
Department of Pathology, MD Anderson Cancer Center, Houston, TX
Liz Hamir, PA(ASCP)CM
Spectrum Medical Group, South Portland, ME
Jodi Hilderbrand, PA(ASCP)CM
Mayo Clinic, Rochester, MN
Courtney Hyland, PA(ASCP)CM
Mayo Clinic, Rochester, MN
Monica Kendall, PA(ASCP)CM
Mayo Clinic, Rochester, MN
Darryl Kinnear, PA(ASCP)CM
Department of Pathology, Baylor College of Medicine, Houston, TX
John Lehman, PA(ASCP)CM
Mayo Clinic, Rochester, MN
Leo Limuaco, PA(ASCP)CM
Self Employed Contractor, Las Vegas, NV
Stephanie Miller, PA(ASCP)CM
Providence Health & Services, Portland, OR
Tina Rader, PA(ASCP)CM
Drexel University College of Medicine, Philadelphia, PA

Dan Soderberg, PA(ASCP)[CM]
Mayo Clinic, Rochester, MN
Mike Sovocool, MHA, PA(ASCP)[CM]
Pathology Associates of Syracuse, Syracuse, NY
Dennis Strenk, PA(ASCP)[CM]
Wisconsin Diagnostic Laboratories, Milwaukee, WI
Connie Thorpe, PA(ASCP)[CM]
Department of Pathology, Saint Louis University, St. Louis, MO
Jon Wagner, PA(ASCP)[CM]
Department of Pathology, Sutter Roseville Medical Center, Roseville, CA

*Denotes primary author. All other contributing authors are listed alphabetically.

Previous Contributors:
None

The purpose of the Protocols is to support Laboratory Personnel engaged in the macroscopic examination of cancer resection specimens. The Protocols are based on specified relevant source documents, drafted by pathologists' assistant experts, and supported by information provided by the College of American Pathologists (CAP) and the American Joint Committee on Cancer (AJCC). These Protocols are intended to serve patients by ensuring that the macroscopic examination of cancer resection specimens is compliant with CAP Cancer Protocols, the AJCC Cancer Staging Manual, and provide optimization of the pre-analytic steps necessary to promote appropriate molecular studies.

The AAPA cautions that the use of the Protocols in practice may require the use of additional considerations that are beyond the scope of the Protocols. The AAPA does not offer medical advice or diagnoses, or engage in the practice of medicine. The information provided in the Protocols is not intended or implied to be a substitute for the Laboratory Personnel's own training, professional medical opinion, diagnosis, or treatment advice. All content, including text, graphics, images and information contained in the Protocols are for the above stated purposes only. Laboratory Personnel are encouraged to confirm any information provided in these Protocols with other sources. The inclusion of a product name, organization, or service in an AAPA publication, including without limitation the Protocols, should not be construed as an endorsement of such product, organization, or service, nor is failure to include the name of a product, organization or service to be construed as disapproval.

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Molecular Considerations:

In the updated 2016 WHO Classification of Tumours of the Central Nervous System, molecular information is now integrated into some of the tumor diagnostic entities. In such cases, including diffuse gliomas and embryonal tumors, the final diagnosis should reflect the integration of both histologic and molecular information.

- For molecular diagnostic studies, snap freeze tissue as soon as possible, and store at -70 degrees Celsius.
- For cases of possible or suspected lymphoma, consider triaging the sample for flow cytometric analysis.

For more information on molecular studies, please refer to the ICCR Dataset for CNS Tumors.

http://www.iccr-cancer.org/getattachment/Datasets/Published-Datasets/Central-Nervous-System/Tumours-of-the-Central-Nervous-System-CNS/ICCR-CNS-Molecular-Information-Bookmarked-guide-1st-edition.pdf

PROCEDURES AND GENERAL ANATOMIC CONSIDERATIONS:

- **Procedures Covered by this Protocol:**

  - Open biopsy
  - Resection
  - Stereotactic biopsy
  - Other: specify

- **Specimen Size:**

  - Record three dimensions in cm.
  - For fragmented tissue, an aggregate measurement may be given.

  NOTE: Staging and grading of CNS tumors is not based on size, but the differences in the gross appearance of the specimen may play a role in determining the heterogeneity of the tumor in relation to the total size of the specimen.

- **Specimen Handling, Triage, and Special Procedures**:

  Divide the tissue into portions for the following procedures if adequate tissue is obtained and if indicated:

  - Squash / smear / touch preparations
  - Frozen section(s) – avoid freezing entire specimen
    - Retain tissue that has not been previously frozen for permanent sections.
  - Routine, permanent paraffin sections
  - Electron microscopy (small portion in glutaraldehyde or embed and hold for electron microscopy, if necessary)
  - Frozen tissue for possible molecular diagnostic studies (snap freeze tissue as soon as possible and store at -70 degrees C)
  - Other (sterile tumor for microbiology cultivation, flow cytometric analysis, cytogenetic analysis, molecular diagnostics)

  NOTE: The macroscopic examination plays an important role in choosing the correct diagnostic tissue for processing. Tissue that is colored differently from the surrounding normal brain tissue and hemorrhagic tissue most commonly represents viable tumor tissue. Keep the specimen moist with sterile saline until processed appropriately.

  Since the cytological details play an important role in interpreting CNS tumors, do not use sponges in cassettes to avoid angular defects that may resemble vascular/luminal spaces in the final sections. It is recommended to wrap small biopsies in lens paper or place into tissue sacs.

TUMOR ("T" of TNM)

- **Tumor Site(s):**

  Tumor site is important in determining the effect on the functional status of the patient before and after surgical, radiological or chemotherapeutic treatment and to determine if the tumor is unifocal or multifocal.

  Common brain tumor site guidelines (must be provided by the surgeon):

  - Skull (CAP Cancer protocol for bone should be used for primary tumors of bone)
    - Frontal, parietal, temporal, occipital, or other
  - Dura
    - Cerebral convexity/lobe, falx, tentorium, posterior fossa, sphenoid wing, skull base, spinal, or other
  - Leptomeninges
    - Cerebral convexity/lobe, posterior fossa, spinal, or other
  - Brain
    - Cerebral lobes
      - Frontal, temporal, parietal, or occipital lobe
    - Deep gray matter
      - Basal ganglia, thalamus, or hypothalamus
    - Cerebellum
    - Cerebellopontine angle
  - Ventricle
    - Lateral, third, fourth, or cerebral aqueduct, if known
  - Brain stem
    - Midbrain, pons, or medulla
  - Sellar/Suprasellar/Pituitary
  - Pineal
  - Cranial nerve (specify I-XII, if known)
  - Spine (vertebral bone), spinal cord, spinal nerve root(s) or spinal ganglion, indicate level, if known (CAP Cancer protocol for bone should be used for primary tumors of bone)

- **Tumor Laterality:**

  - Right
  - Left
  - Midline
  - Bilateral
  - Other (specify)

- **Tumor Focality:**

  - Unifocal
  - Multifocal (specify number of lesions) *

  *Multifocality implies that multiple, noncontiguous lesions are noted on neuroimaging, such as might be seen in primary CNS lymphoma.

- **Margins:**

  Resection margins do not provide prognostic value and generally are not required for CNS neoplasms with the exception of the malignant peripheral nerve sheath tumors and some meningiomas.

- **Relevant History:**

  - Patient Age
    - Most powerful predictor of prognosis and treatment outcome.
  - Duration of Symptoms
    - Slow growing tumor is indicated by long or chronic history of CNS symptoms or seizure.
    - Sudden or acute onset of CNS symptoms including neurologic deficit indicates a high-grade tumor, hemorrhage, infarct, or active demyelinating disease.
  - Previous Diagnoses or CNS Biopsies
    - Includes previous histories of intracranial and extracranial results that are relevant for the Pathologists to make an accurate histologic diagnosis.
    - Slides from previous biopsies will be helpful for review and comparison.
  - Family History of Cancer or Primary CNS Tumors
    - Includes history of genetic conditions or syndromes that are predisposed to the development and progression of brain tumor.
  - Neuroimaging Findings
    - Neuroimaging features, age, and tumor location are helpful in narrowing down the differential diagnosis.
    - Correlate with the pathologic diagnosis.
    - Should be collaborated with neuroradiologist and neurosurgeon.
  - Preoperative treatment
    - Some histologic findings may be caused by preoperative treatment including coagulative (nonpalisading) necrosis, vascular hyalinization and gliosis.
    - Preoperative treatments are helpful in making a diagnosis, including:
      - Radiation therapy
      - Chemotherapy
      - Corticosteroid therapy
      - Embolization therapy
      - Radiosurgery
  - Primary Tumor size
    - Primary tumor size is usually included on the imaging report and should be recorded.

- **Explanatory Notes:**

  Some laboratories or institutions require the dictation of clinical history. A short clinical history that includes the above relevant history will be very beneficial to the Pathologists in helping them to make an accurate histologic or microscopic diagnosis. If the clinical information is not included with the pathology requisition, include pertinent information from the patient's medical record.

- **Histologic Grade/WHO grading System:**

There is no American Joint Committee on Cancer or International Union Against Cancer TNM grading system for primary tumors of the Central Nervous System. It is recommended to use the World Health Organization grading system:

WHO Grade	Grade Definition
I	Circumscribed tumors of low proliferative potential associated with the possibility of cure following resection
II	Infiltrative tumors with low proliferative potential with increased risk of recurrence
III	Tumors with histologic evidence of malignancy, including nuclear atypia and mitotic activity, associated with an aggressive clinical course
IV	Tumors that are cytologically malignant, mitotically active, and associated with rapid clinical progression and potential for dissemination

METASTASIS ("M" of TNM)

- Central nervous system tumors rarely develop extraneural metastases as the brain does not have a well-developed lymphatic drainage system.
- Certain tumors spread through cerebrospinal fluid, which can have a major and negative impact on survival.
- Tumor dissemination through the CSF is a hallmark of childhood brain tumors such as PNET.
- Primary lymphomas of the central nervous system may spread along the craniospinal axis and may exhibit intraocular dissemination.

REFERENCE REVIEW:

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