*Evolent	
Clinical guideline **CENTRAL NERVOUS SYSTEM – PRIMARY NEOPLASM AND METASTATIC TUMORS**	**Original Date: June 2013**
Radiation Oncology	**Last Revised Date: May 2023**
Guideline Number: Evolent_CG_128	**Implementation Date: January 2024**

GENERAL INFORMATION

- *It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- *Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines and state/national recommendations.*

INDICATIONS FOR RADIATION THERAPY FOR PRIMARY CNS NEOPLASMS

3D, IMRT and SRS/FSRT techniques may be used as appropriate, depending on the tumor location and stage of disease.

Gliomas[1, 2]

- **Oligodendroglioma, IDH-mutant, and 1p/19q codeleted**
  - For patients with oligodendroglioma, IDH-mutant, 1p/19q codeleted, WHO grade 2, < 4-6 cm tumor, with gross total resection (defined as < 1 cm residual tumor on MRI) and age < 40 y, close surveillance alone is recommended
  - For patients with oligodendroglioma, IDH-mutant, 1p/19q codeleted, WHO grade 2, with high-risk features (subtotal resection, age ≥ 40 y, tumor size ≥ 4-6 cm, tumor crosses midline, refractory seizures, or presurgical neurologic symptoms from tumor), either RT with sequential chemotherapy or RT with concurrent/sequential chemotherapy is conditionally recommended
  - For patients with oligodendroglioma, IDH-mutant, 1p/19q codeleted, WHO grade 3, with any extent of surgery, either RT with sequential chemotherapy or RT with concurrent/sequential chemotherapy is recommended
- **Astrocytoma, IDH-mutant**
  - For patients with astrocytoma, IDH-mutant, WHO grade 2, < 4-6 cm tumor, with gross total resection (defined as < 1 cm residual tumor on MRI), and age < 40 y, close surveillance alone is conditionally recommended
  - For patients with astrocytoma, IDH-mutant, WHO grade 2, with high-risk features (subtotal resection, age ≥ 40 y, tumor size ≥ 4-6 cm, tumor crosses midline, refractory

seizures, or presurgical neurologic symptoms from tumor), either RT with sequential chemotherapy or RT with concurrent/sequential chemotherapy is conditionally recommended
    - For patients with astrocytoma, IDH-mutant, WHO grade 3, with any extent of surgery, either RT with sequential chemotherapy or RT with concurrent/sequential chemotherapy is recommended

Dosage Guidelines

- Oligodendroglioma, IDH-mutant, 1p/19q codeleted
    - WHO grade 2: 45-54Gy up to 30 fractions
    - WHO grade 3: 59.4cGy up to 33 fractions
- Astrocytoma, IDH-mutant
    - WHO grade 2: 45-54Gy up to 30 fractions
    - WHO grade 3: 59.4-60Gy up to 33 fractions
- High Grade Tumors – Grade III or IV
    - Post-operative/biopsy: up to 33 fractions
    - In poorly performing patients or elderly patients, a hypofractionated accelerated course over 2–4 weeks should be considered
        - 34Gy/10 fractions of 3D-CRT
        - 40.05Gy/15 fractions of 3D-CRT
        - 25Gy/5 fractions of 3D-CRT
- IDH-mutant WHO grade 2/3 Diffuse Glioma
    - Consider proton therapy
- Recurrence
    - Low Grade: Up to 33 fractions
    - High Grade: 35Gy in 10 fractions of 3D-CRT
    - SRS/FSRT: up to 5 fractions
    - Consider reirradiation on select cases. Proton Beam Therapy may be considered.

Ependymoma – High (Anaplastic) or Low Grade[1]

- Brain and/or spine: up to 33 fractions

Meningiomas[1]

- WHO Grade 1
    - 50–50.4Gy up to 28 fractions
    - SRS/FSRT (up to 5 fractions)
- WHO Grade 2
    - 54-60Gy up to 30 fractions

- SRS/FSRT (up to 5 fractions)

- WHO Grade 3
  - 59.4–60Gy up to 30 fractions
  - SRS/FSRT (up to 5 fractions)

CNS Lymphoma[1]

- Complete response to chemotherapy
  - Low-dose WBRT should be limited to 23.4Gy (up to 13 fractions of 3D-CRT)
- Less than complete response to chemotherapy, or not candidates for chemotherapy
  - WBRT up to 20 fractions with or without Limited field boost 3D/IMRT (up to 25 fractions)

Medulloblastoma/Supratentorial PNET (Adult)[1]

Craniospinal radiation with brain primary site boost – 3D-CRT/IMRT/PBT up to 31 fractions

Primary Spinal Cord[1]

- 3D-CRT/IMRT (up to 28 fractions)
  - Tumor below conus medullaris 3D-CRT/IMRT (up to 33 fractions)
- SRS/FSRT – (up to 5 fractions)

INDICATIONS FOR PROTON BEAM THERAPY

Treatment of the following in children less than 21 years of age:

- Primary, metastatic, or benign solid tumors when sparing of surrounding normal tissues cannot be achieved with photon therapy

Treatment at any age

- Spinal tumors (primary or metastatic) where spinal cord has previously been treated with radiation or where the spinal cord tolerance may be exceeded with conventional treatment
- Tumors at the base of skull (chordoma, chondrosarcoma)
- Re-irradiation cases (where cumulative critical structure dose would exceed tolerance dose)
- Malignant and benign primary CNS tumors: Consider proton therapy for patients with good long-term prognosis (grade 2 and 3 IDH-mutant diffuse glioma and 1p19q codeleted tumors)
- Craniospinal RT: To reduce toxicity from CSI in adults, consider the use of IMRT or protons if available (for patients with positive CSF or known metastatic disease)[3]

Requests for Proton Beam Radiation Therapy beyond the indications listed above will be reviewed on a case-by-case basis as outlined below to determine medical necessity.

TREATMENT OPTIONS REQUIRING ADDITIONAL CLINICAL REVIEW

Intensity modulated radiation therapy (IMRT)

If IMRT is not indicated as a standard treatment option, a peer review will be indicated. IMRT may be appropriate for limited circumstances in which radiation therapy is indicated and 3D conformal radiation therapy (3D-CRT) techniques cannot adequately deliver the radiation prescription without exceeding normal tissue radiation tolerance, the delivery is anticipated to contribute to potential late toxicity, or tumor volume dose heterogeneity is such that unacceptable hot or cold spots are created.

Clinical rationale and documentation for performing IMRT rather than 2D or 3D-CRT treatment planning and delivery will need to:

- Demonstrate how 3D-CRT isodose planning cannot produce a satisfactory treatment plan (as stated above) via the use of patient-specific dose volume histograms and isodose plans.
- Provide tissue constraints for both the target and affected critical structures

Stereotactic Radiosurgery (SRS) or Fractionated Radiosurgery (FSRT)[1, 4]

- If SRS or FSRT is not indicated as a medically necessary treatment option, a peer review will be required.

Proton Beam Radiation Therapy[3, 5]

Requests for Proton Beam Radiation Therapy will be reviewed on a case-by-case basis (See Proton Beam Guideline).

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BACKGROUND

There are many different types of brain tumors. Because brain tumors are located at the control center for thought, emotion, and movement, their effects on an individual's physical and cognitive abilities can be devastating. Prognosis or expected outcome is dependent on several factors including the type of tumor, location, response to treatment, an individual's age, and overall health status. The most common CNS tumors are astrocytomas and glioblastomas, followed by meningiomas and a variety of other less common tumors. Metastatic brain tumors start in other organs, e.g., lung, breast, or colon and spread to the brain. In adults, these are more common than primary brain tumors. Both primary and metastatic brain tumors can readily spread through the brain or spinal cord, destroying and compressing normal brain tissue.

Surgery, radiation therapy and chemotherapy are the primary modalities used to treat CNS tumors, either alone or in combination. The first step in brain tumor treatment is usually surgical resection, with two primary goals: (1) removing as much of the tumor as possible while preserving neurological function and (2) establishing a histologic diagnosis. If the tumor cannot be completely removed, subtotal resection, (debulking) can increase the effectiveness of other treatments. Deep-seated tumors of the brain stem, e.g., pontine gliomas, are generally diagnosed and treated based on clinical and imaging evidence.

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Central Nervous System Cancers

Version 2.2022. National Comprehensive Cancer Network (NCCN). Updated September 29, 2022. Accessed December 13, 2022. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf
2. Halasz LM, Attia A, Bradfield L, et al. Radiation Therapy for IDH-Mutant Grade 2 and Grade 3 Diffuse Glioma: An ASTRO Clinical Practice Guideline. *Pract Radiat Oncol*. Sep-Oct 2022;12(5):370-386. doi:10.1016/j.prro.2022.05.004 https://doi.org/10.1016/j.prro.2022.05.004
3. Brown AP, Barney CL, Grosshans DR, et al. Proton beam craniospinal irradiation reduces acute toxicity for adults with medulloblastoma. *Int J Radiat Oncol Biol Phys*. Jun 1 2013;86(2):277-84. doi:10.1016/j.ijrobp.2013.01.014
4. American Society for Radiation Oncology. Model Policies: Stereotactic Body Radiation Therapy. American Society for Radiation Oncology (ASTRO). Updated June 2020. Accessed December 13, 2022,
5. Shih HA, Sherman JC, Nachtigall LB, et al. Proton therapy for low-grade gliomas: Results from a prospective trial. *Cancer*. May 15 2015;121(10):1712-9. doi:10.1002/cncr.29237

POLICY HISTORY

Date	Summary
May 2023	• Updated/Clarified Gliomas, ependymoma, meningioma, CNS lymphoma, and primary spinal cord • Removed Hippocampal Sparing Whole Brain Intensity Modulated Radiation Therapy • Added indications for proton beam therapy • Deleted Additional Resources • Removed “physician review” language

January 2022	• Under Indications for Proton Beam Therapy (Treatment at any age)
	  ○ Added: Malignant and benign primary CNS tumors, consider for patients with good long-term prognosis (grade 3 IDH-mutant tumors and 1p19q co-deleted tumors)
	  ○ Added: craniospinal RT to reduce toxicity from CSI in adults, consider use of IMRT or protons if available (for patients with positive CSF or known metastatic disease)
	• Under Hippocampal Sparing Whole Brain Intensity Modulated Radiation Therapy, added that all of the following must be met:
	  ○ Good performance status: ECOG rating is less than 3
	  ○ Who have a prognosis of at least 4 months
	  ○ No metastases within 5mm of the hippocampi
	  ○ Have not had prior WBRT or external beam radiation to the brain
	  ○ Do not have leptomeningeal disease
	  ○ Whose primary histology is not germ cell, small cell, lymphoma or unknown
	• Added: Dosage Guidelines under Hippocampal Sparing Whole Brain Intensity Modulated Radiation Therapy

Reviewed / Approved by Clinical Guideline Committee

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