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| <b>*Evolut</b>  |  |
| <b>Clinical guideline</b><br><b>CENTRAL NERVOUS SYSTEM - METASTASES</b> | <b>Original Date: June 2013</b>          |
| <b>Radiation Oncology</b>   | <b>Last Revised Date: May 2023</b>       |
| <b>Guideline Number: Evolut_CG_128-1</b>                                | <b>Implementation Date: January 2024</b> |

## 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 PATIENTS WITH METASTATIC CENTRAL NERVOUS SYSTEM TUMORS

### Metastatic Brain Tumors<sup>1-4</sup>

- For patients with favorable prognosis and limited brain metastases, routine adjuvant WBRT added to SRS is not recommended<sup>3</sup>
- For patients with favorable prognosis (estimated using a validated brain metastasis prognostic index) and brain metastases ineligible for surgery and/or SRS, WBRT (e.g., 3000cGy in 10 fractions) is recommended as primary treatment<sup>3</sup>
- SRS, WBRT, and the combination of SRS plus WBRT are all reasonable options for patients with more than four unresected brain metastases and better performance status (e.g., KPS > 70). SRS may be preferred for patients with better prognosis or where systemic therapy that is known to be active in the CNS is available<sup>2</sup>
- Whole Brain Radiation Therapy (WBRT) with 2D or 3D Conformal treatment is appropriate for treatment Metastatic Brain Tumors - Up to 15 Fractions
- Stereotactic Radiosurgery / Fractionated Stereotactic Radiosurgery (SRS/FSRT) up to 5 fractions is medically necessary if all the following criteria are met (excluding small-cell carcinoma):
  - Treatment for lesions ≤ 4cm
  - Controlled systemic disease or reasonable systemic treatment options
  - Eastern Cooperative Oncology Group (ECOG) rating of less than 3
  - 4 or less metastasis prior to procedure
    - For patients with an ECOG performance status of 0-2 and 5-10 intact brain metastases, SRS is conditionally recommended<sup>3</sup>

- Intensity Modulated Radiation Therapy will be reviewed on a case-by-case
  - IMRT for partial brain irradiation is approvable

### Post Metastasis Resection<sup>1</sup>

- For patients with intact brain metastases measuring > 4 cm in diameter, surgery is conditionally recommended<sup>3</sup>
- SRS, WBRT, and the combination of SRS plus WBRT are all reasonable options for patients with more than two resected brain metastases and better performance status (e.g., KPS ≥ 70). SRS may be preferred for patients with better prognosis or where systemic therapy that is known to be active in the CNS is available<sup>2</sup>
- For patients with resected brain metastases and limited additional brain metastases, SRS is recommended over WBRT to preserve neurocognitive function and patient-reported QoL<sup>3</sup>
- Stereotactic Radiosurgery/ Fractionated Stereotactic Radiosurgery (SRS/FSRT) post metastasis resection (up to 5 fractions)
  - SRS alone should be offered to patients with one to two resected brain metastases if the surgical cavity can be safely treated and considering the extent of remaining intracranial disease<sup>2</sup>

### Dose Guidelines

- WBRT 20-40Gy (20 fractions maximum)

### Pre-Metastasis Resection

- For patients whose brain metastasis is planned for resection, preoperative SRS is conditionally recommended as a potential alternative to postoperative SRS<sup>3</sup>

### Palliative

- For patients with poor prognosis and brain metastases, early introduction of palliative care for symptom management and caregiver support are recommended<sup>3</sup>
- For patients with poor predicated prognosis and with symptomatic brain metastases, standard WBRT of 20Gy in 5 fractions is a reasonable option
- Radiation therapy should not be offered to patients with asymptomatic brain metastases who have<sup>3</sup>:
  - Performance status Karnofsky Performance Status (KPS) < 50 or less, or
  - Performance status KPS < 70 and no systemic therapy options.

### Metastatic Spine Tumors<sup>1</sup>

- 2D/3D-CRT – 8-30Gy (maximum 10 fractions)
- Dose/fraction dependent on tumor type and performance status
- Stereotactic radiotherapy/IMRT may be appropriate for re-treatment
- Stereotactic radiotherapy may be appropriate for Oligometastatic Disease<sup>4</sup>:

- One (1) to five (5) metastatic lesions and
- Good performance status: ECOG less than 3 or Karnofsky Scale greater than or equal to 70% and stable systemic disease or reasonable systemic treatment options.

## **TREATMENT OPTIONS (WILL BE REVIEWED ON A CASE-BY-CASE BASIS)**

### **Intensity Modulated Radiation Therapy (IMRT)<sup>1</sup>**

Intensity Modulated Radiation Therapy (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.

### **Hippocampal Sparing Whole Brain Intensity Modulated Radiation Therapy<sup>1, 5-7</sup>**

- Hippocampal sparing whole brain IMRT (plus memantine) is considered medically necessary for metastatic brain lesions in individuals with all of the following:
  - 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, lymphoma or unknown
- Dosage Guidelines
  - Standard doses vary between 30Gy and 37.5Gy in 10-15 fractions.

## **INDICATIONS FOR PROTON BEAM THERAPY**

- Proton Beam Radiation Therapy for central nervous system lesions adjacent to the brain stem, spinal cord, or optic nerve will be reviewed on a case-by-case basis. A treatment plan with a comparison to conventional IMRT/SRS may be required
- Requests for Proton Beam Radiation Therapy beyond the indications listed above will be reviewed on a case-by-case basis.

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

- Metastatic central nervous system 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, chondrosarcomas)

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

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## **BACKGROUND**

Metastatic tumors for the Central Nervous System (CNS) start in other organs, e.g., lung, breast, or colon, and spread to the brain and spinal cord. In adults, these are more common than primary CNS/brain tumors. Both primary and metastatic brain tumors can readily spread through the brain or spinal cord, destroying and compressing normal brain tissue. Metastatic brain tumors occur at some point in 20 to 40% of persons with cancer and are the most common type of brain tumor. Prognosis is dependent on several factors including the type of tumor, location, response to treatment, an individual's age, and overall health status.

Surgery, radiation therapy and chemotherapy are the primary modalities used to treat CNS tumors, either alone or in combination. There are many different approaches in delivering radiation therapy to CNS tumors, including fractionated radiation therapy, stereotactic fractionated radiotherapy, stereotactic radiosurgery, brachytherapy, and proton beam irradiation. Fractionated conformal beam irradiation is the most common approach.

Radiation therapy may be delivered following surgical resection, debulking or biopsy procedures. It may also be used to treat recurrences in patients whose initial treatment was surgery alone. The value of radiation therapy lies in its ability to cure some patients and to prolong disease-free survival for others. Combined modality approaches that include chemotherapy may also contribute to prolonged disease-free survival in pediatric patients with medulloblastoma, germ cell tumors and gliomas.

The dose and fractionation of radiation depends not only on the tumor type, but also in the curative/palliative setting.

## REFERENCES

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**POLICY HISTORY**

| <b>Date</b>  | <b>Summary</b>  |
|--------------|---|
| May 2023     | <ul style="list-style-type: none"> <li>• Clarified/updated Metastatic Brain Tumors</li> <li>• Clarified updated Post Metastasis Resection</li> <li>• Added Pre-Metastasis Resection</li> <li>• Added Palliative section</li> <li>• Clarified/updated Metastatic Spine Tumors</li> <li>• Clarified/updated Hippocampal Sparing Whole Brain IMRT</li> <li>• Removed Stereotactic Radiosurgery (SRS) or Fractionated Stereotactic Radiosurgery (FSRT)</li> <li>• Removed Proton Beam Radiation Therapy (Added to INDICATIONS FOR PROTON BEAM THERAPY)</li> <li>• Removed Small Cell from: “Whose primary histology is not germ cell, lymphoma or unknown” under hippocampal avoidance</li> <li>• Updated references</li> <li>• Deleted Additional Resources</li> <li>• Removed “physician review” language</li> </ul>      |
| January 2022 | <ul style="list-style-type: none"> <li>• Under Hippocampal Sparing Whole Brain Intensity Modulated Radiation Therapy:               <ul style="list-style-type: none"> <li>○ Clarified that IMRT is considered medically necessary for metastatic brain lesions in individuals with all of the following:                   <ul style="list-style-type: none"> <li>▪ Good performance status: ECOG rating is less than 3</li> <li>▪ Who have a prognosis of at least 4 months</li> <li>▪ No metastases within 5mm of the hippocampi</li> <li>▪ Have not had prior WBRT or external beam radiation to the brain</li> <li>▪ Do not have leptomeningeal disease</li> <li>▪ Whose primary histology is not germ cell, small cell, lymphoma or unknown</li> </ul> </li> <li>○ Added Dosage Guidelines</li> </ul> </li> </ul> |

## Reviewed / Approved by Clinical Guideline Committee

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