

Radiation therapy for brain metastases: an ASTRO clinical practice guideline.

Guideline ID: 2802

Published: 2022 Jul-Aug

American Society for Radiation Oncology (ASTRO)

Gondi V, Bauman G, Bradfield L, et al. Radiation therapy for brain metastases: an ASTRO clinical practice guideline. *Pract Radiat Oncol.* 2022 Jul-Aug;12(4):265-282. [106 references] [PubMed](#)

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Overview

Guideline Objective

To provide updated recommendations on the management of patients with brain metastases, including advanced radiation therapy techniques such as stereotactic radiosurgery (SRS) and hippocampal avoidance whole brain radiation therapy, and the emergence of systemic therapies with central nervous system activity

Note:

- This guideline covers only the subjects specified in the Key Questions. The scope is limited to the radiotherapeutic management of intact (i.e., unresected) and resected brain metastases from nonhematologic solid tumors.
- Outside the scope of this guideline are many other important questions that may be subjects of other guidelines, including the appropriate role for central nervous system (CNS)-active systemic therapies and/or surgical intervention.

Patient Population

Adults with brain metastases

Recommendations

Recommendation Statements

Key Question (KQ) 1: What are the indications for stereotactic radiosurgery (SRS) alone for patients with intact brain metastases?

1. For patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 and up to 4 intact brain metastases, SRS is recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)
2. For patients with an ECOG performance status of 0-2 and 5-10 intact brain metastases, SRS is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Low**)
3. For patients with intact brain metastases measuring <2 cm in diameter, single-fraction SRS with a dose of 2000-2400 cGy is recommended. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

Implementation Remark: If multifraction SRS were chosen (e.g., V12 Gy >10 cm³ [see KQ4, below]), options include 2700 cGy in 3 fractions or 3000 cGy in 5 fractions.

4. For patients with intact brain metastases measuring ≥2 to <3 cm in diameter, single-fraction SRS using 1800 cGy or multifraction SRS (e.g., 2700 cGy in 3 fractions or 3000 cGy in 5 fractions) is conditionally recommended (see KQ4, below). (**Strength of recommendation: Conditional; Quality of evidence: Low**)
5. For patients with intact brain metastases measuring ≥3 to 4 cm in diameter, multifraction SRS (e.g., 2700 cGy in 3 fractions or 3000 cGy in 5 fractions) is conditionally recommended. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

Implementation Remark:

- If single-fraction SRS were chosen, doses up to 1500 cGy may be used (see KQ4, below).

- Multidisciplinary discussion with neurosurgery to consider surgical resection is suggested for all tumors causing mass effect, irrespective of tumor size.
6. For patients with intact brain metastases measuring >4 cm in diameter, surgery is conditionally recommended, and if not feasible, multifraction SRS is preferred over single-fraction SRS. (**Strength of recommendation: Conditional; Quality of evidence: Low**)

Implementation Remark: Given limited evidence, SRS for tumor size >6 cm is discouraged.

7. For patients with *symptomatic* brain metastases who are candidates for local therapy and central nervous system (CNS)-active systemic therapy, upfront local therapy is recommended. (**Strength of recommendation: Strong; Quality of evidence: Low**)
8. For patients with *asymptomatic* brain metastases eligible for CNS-active systemic therapy, multidisciplinary and patient-centered decision making is conditionally recommended to determine whether local therapy may be safely deferred. (**Strength of recommendation: Conditional; Quality of evidence: Expert Opinion**)

Implementation Remark: The decision to defer local therapy should consider factors such as brain metastasis size, parenchymal brain location, number of metastases, likelihood of response to specific systemic therapy, access to close neuro-oncologic surveillance, and availability of salvage therapies.

KQ 2: What are the indications for observation, preoperative SRS, or postoperative SRS or whole brain radiation therapy (WBRT) in patients with resected brain metastases?

1. For patients with resected brain metastases, radiation therapy (SRS or WBRT) is recommended to improve intracranial disease control. (**Strength of recommendation: Strong; Quality of evidence: High**)
2. For patients with resected brain metastases and limited additional brain metastases, SRS is recommended over WBRT to preserve neurocognitive function and patient-reported quality of life (QoL). (**Strength of recommendation: Strong; Quality of evidence: Moderate**)
3. For patients whose brain metastasis is planned for resection, preoperative SRS is conditionally recommended as a potential alternative to postoperative SRS. (**Strength**

KQ3: What are the indications for WBRT in patients with intact brain metastases?

1. 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., 3000 cGy in 10 fractions) is recommended as primary treatment (see KQ1, recommendations 7 and 8, above, for consideration of systemic therapy). (**Strength of recommendation: Strong; Quality of evidence: High**)
2. For patients with favorable prognosis and brain metastases receiving WBRT, hippocampal avoidance is recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

Implementation Remark: Hippocampal avoidance is not appropriate in cases of brain metastases in close proximity to the hippocampi or in cases of leptomeningeal disease.

3. For patients with favorable prognosis and brain metastases receiving WBRT or hippocampal avoidance WBRT, addition of memantine is recommended. (**Strength of recommendation: Strong; Quality of evidence: Low**)
4. For patients with favorable prognosis and limited brain metastases, routine adjuvant WBRT added to SRS is **not** recommended. (**Strength of recommendation: Strong; Quality of evidence: High**)

Implementation Remark: To maximize intracranial control and/or when close imaging surveillance with additional salvage therapy is not feasible, adjuvant WBRT may be offered in addition to SRS.

5. For patients with poor prognosis and brain metastases, early introduction of palliative care for symptom management and caregiver support are recommended. (**Strength of recommendation: Strong; Quality of evidence: Moderate**)

Implementation Remark:

- Supportive care only (with omission of WBRT) should be considered.
- If WBRT is used, brief schedules (e.g., 5 fractions) are preferred.

KQ4: What are the risks of symptomatic radionecrosis with WBRT and/or SRS for patients with brain metastases?

1. For patients with brain metastases, limiting the single-fraction $V_{12\text{Gy}}$ to brain tissue (normal brain *plus* target volumes) to $\leq 10 \text{ cm}^3$ is conditionally recommended.
(**Strength of recommendation: Conditional; Quality of evidence: Low**)

Implementation Remark: Any brain metastasis with an associated tissue $V_{12\text{Gy}} > 10 \text{ cm}^3$ may be considered for fractionated SRS to reduce risk of radionecrosis (see KQ1, above).

Evidence Rating Scheme

ASTRO Recommendation Grading Classification System

Overall Quality of Evidence (QoE) Grade	Type and Quality of Study	Evidence Interpretation
High	• 2 or more well-conducted and highly-generalizable randomized controlled trials (RCTs) or meta-analyses of such trials.	The true effect is very likely to lie close to the estimate of the effect based on the body of evidence.
Moderate	• 1 well-conducted and highly-generalizable RCT or a meta-analysis of such trials OR • 2 or more RCTs with some weaknesses of procedure or generalizability OR	The true effect is likely to be close to the estimate of the effect based on the body of evidence, but it is possible that it is substantially different.

	• 2 or more strong observational studies with consistent findings.	
Low	• 1 RCT with some weaknesses of procedure or generalizability OR • 1 or more RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes OR • 2 or more observational studies with inconsistent findings, small sample sizes, or other problems that potentially confound interpretation of data.	The true effect may be substantially different from the estimate of the effect. There is a risk that future research may significantly alter the estimate of the effect size or the interpretation of the results.
Expert Opinion*	• Consensus of the panel based on clinical judgment and experience, due to absence of evidence or limitations in evidence.	Strong consensus ($\geq 90\%$) of the panel guides the recommendation despite insufficient evidence to discern the true magnitude and direction of the net effect. Further research may better inform the topic.

* A lower quality of evidence, including expert opinion, does not imply that the recommendation is conditional. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials but there still may be consensus that the benefits of a treatment or diagnostic test clearly outweigh its risks and burden.

Recommendation Rating Scheme

ASTRO Recommendation Grading Classification System

Strength of Recommendation	Definition	Overall QoE Grade	Recommendation Wording
Strong	• Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh benefits. • All or almost all informed people would make the recommended choice.	Any (usually high, moderate, or expert opinion)	"Recommend/Should"
Conditional	• Benefits are finely balanced with risks and burden or appreciable uncertainty exists about the magnitude of benefits and risks. • Most informed people would choose the recommended course of action, but a substantial number would not. • A shared decision-making approach regarding patient values and preferences is	Any (usually moderate, low, or expert opinion)	"Conditionally recommend"

	particularly important.		
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Related Content

Supporting Documents

- [Appendix E1. Peer Reviewers and Disclosures \(Comprehensive\).](#)
- [Appendix E2. Abbreviations.](#)
- [Appendix E3. Evidence Table.](#)
- [Radiation Therapy for Brain Metastases: A Systematic Review; 2021 Sep 1.](#)
 - [Online Appendix.](#)
- [Radiation Therapy for Brain Metastases. Comparative Effectiveness Review No. 242; 2021 Jun.](#)
- [ASTRO Clinical Practice Guideline Methodology Guide; 2019 May.](#)
- [ASTRO Guideline Development Process Overview.](#)

Implementation Tools

- [Slide Set; 2022 Jul-Aug.](#)
- [Podcast.](#)
- [Patient Advice to Radiation Oncologist; 2022 May.](#)
- The [Original Guideline](#) includes the following:
 - [Figure 1. Limited Brain Metastases Treatment Algorithm \(p. 276\)](#)
 - [Figure 2. Extensive Brain Metastases Treatment Algorithm \(p. 277\)](#)

Patient Education

No patient education materials available.

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TRUST Scorecard

Composition of Guideline Development Group (GDG)

Multidisciplinary GDG Members

Yes

Methodologist Involvement

Yes

Incorporation of Patient and Public Perspective



Systematic Review of Evidence

Literature Search



Study Selection



Evidence Synthesis



Foundations for Recommendations

Strength of Evidence Grade



Description of Benefits and Harms of Recommendations



Summary of Evidence Supporting Recommendations



Strength of Recommendations Rating



Clear Articulation of Recommendations



Funding Source

Yes

Disclosure and Management of Financial Conflicts of Interests



External Review



Updating

