Intracranial Metastases Recurrence

- Population-Based Real-World Outcomes of Post-Operative Adjuvant Brain Cavity Radiotherapy Versus Observation
- Cesium-131 collagen tile brachytherapy for salvage of recurrent intracranial metastases
- Multi-institutional Outcomes after Stereotactic Radiosurgery for Gastrointestinal Brain Metastases
- Gyroscopic radiosurgery-based lattice therapy for intracranial tumors: A dosimetric study
- Minimally Invasive and Cost-Effective Access to Deep-Seated Intracranial Lesions Using 19F Peel-Away Sheath Introducer and "Dynamic" Retraction: Technical Note and a Case Series
- Radiation therapy in the treatment of pancreatoblastoma: a narrative review
- Advances in minimally invasive surgery for brain metastases
- Case Report: The price of intraoperative cell salvage? - implantation metastases of meningioma in both lungs and left cubital fossa

---

Suppree et al. conducted a systematic review and meta-analysis to investigate the brain metastases local recurrence rate following surgical resection of brain metastases without adjuvant therapy. The analysis included four studies with a total of 235 cases. It was found that the rate of local recurrence by 12 months was 48.1% (95% CI 41.2-58.9). These findings underscore the high rate of patients who will experience local recurrence within 12 months of surgery, emphasizing the need for vigilant surveillance when omitting adjuvant radiotherapy in favor of systemic treatments with potential but unproven CNS penetrance. The analysis highlights unmet needs in this patient population [1)]

The benefits of adding upfront post-operative radiation therapy, either whole brain radiotherapy for intracranial metastases or cavity, have been debated, particularly due to the long-term sequalae post radiation. Bolem et al. searched various biomedical databases from 1983 to 2018, for eligible randomized controlled trials (RCT). Outcomes studied were local recurrence (LR), overall survival (OS) and serious (Grade 3 +) adverse events. They used the random effects model to pool outcomes. Methodological quality of each study was assessed using the Cochrane Risk of Bias tool. They employed the GRADE approach to assess the certainty of evidence.

They included 5 RCTs comprising of 673 patients. The pooled odds ratio (OR) for LR is 0.26 (95% confidence interval (CI) 0.19-0.37, P < 0.001, GRADE certainty high), strongly supporting the use of post-operative radiation. Meta-regression analysis done comparing cavity and WBRT, did not show any difference in LR. The pooled hazard ratio (HR) for overall survival (OS) is 1.1 (95% CI 0.90-1.34, P = 0.37, GRADE certainty high). The treatment-related toxicities could not be pooled; the 2 studies which reported this did not find differences between the approaches. The risk of bias across the included studies was low.

The analysis confirms that upfront post-operative radiation significantly reduces the risk of LR. However, the lack of improvement in overall survival suggests that local control alone may not impact survival. Balancing local control, and neuro-cognitive effects of WBRT, cavity radiation seems to be a safe and effective option [2)].

Stereotactic radiosurgery (SRS) has become a first-line treatment option for brain metastases, both as a boost following whole-brain radiation therapy (WBRT), and as stand-alone treatment. When SRS is used as a single modality treatment, the local and distant brain recurrence rates range from 73 to 76.4%. When used in combination with WBRT, recurrence rates range from 27 to 46.8%. As systemic therapies improve, the number of patients who develop new or recurrent brain metastases after SRS is likely to increase. The evidence regarding the safety and efficacy of salvage therapies is very limited, making options for treatment unclear and controversial. Potential therapeutic strategies include repeated SRS, surgical resection, WBRT, fractionated stereotactic radiosurgery, chemotherapy, and supportive care [3) 4)].

Stereotactic radiosurgery is an effective and relatively safe treatment for recurrent solitary metastases and is an appealing technique for the initial management of deep-seated lesions as a boost to whole brain radiotherapy [5)]

Results suggest that initial management approach for recurrent brain metastases after upfront SRS does not affect the rate of radiation necrosis (RN). However, the risk of RN significantly increases when patients are treated with both repeat SRS and salvage WBRT. Methods to improve prediction of toxicity and optimize patient selection for salvage treatments are needed [6)]

1)
Suppree JS, Kannan S, Hughes DM, Jenkinson MD, Zakaria R. Letter: Estimating the baseline local recurrence rate for a brain metastasis after neurosurgical resection. Clin Exp Metastasis. 2024 Feb 14. doi: 10.1007/s10585-024-10274-6. Epub ahead of print. PMID: 38353933.
2)
Bolem N, Soon YY, Ravi S, Dinesh N, Teo K, Nga VDW, Lwin S, Yeo TT, Vellayappan B. Is there any survival benefit from post-operative radiation in brain metastases? A systematic review and meta-analysis of randomized controlled trials. J Clin Neurosci. 2022 Mar 24;99:327-335. doi: 10.1016/j.jocn.2022.03.024. Epub ahead of print. PMID: 35339853.
3)
Stockham AL, Suh JH, Chao ST, Barnett GH. Management of recurrent brain metastases after radiosurgery. Prog Neurol Surg. 2012;25:273-86. doi: 10.1159/000331200. Epub 2012 Jan 6. PMID: 22236688.
4)
Chidambaram S, Pannullo SC, Schwartz TH, Wernicke AG. Reirradiation of Recurrent Brain Metastases: Where Do We Stand? World Neurosurg. 2019 May;125:156-163. doi: 10.1016/j.wneu.2019.01.182. Epub 2019 Feb 8. PMID: 30738931.
5)
Loeffler JS, Kooy HM, Wen PY, Fine HA, Cheng CW, Mannarino EG, Tsai JS, Alexander E 3rd. The treatment of recurrent brain metastases with stereotactic radiosurgery. J Clin Oncol. 1990 Apr;8(4):576-82. doi: 10.1200/JCO.1990.8.4.576. PMID: 2179476.
6)
Rae A, Gorovets D, Rava P, Ebner D, Cielo D, Kinsella TJ, DiPetrillo TA, Hepel JT. Management approach for recurrent brain metastases following upfront radiosurgery may affect risk of subsequent radiation necrosis. Adv Radiat Oncol. 2016 Aug 24;1(4):294-299. doi: 10.1016/j.adro.2016.08.007. PMID: 28740900; PMCID: PMC5514163.