# Summary of glioblastoma brachytherapy study

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Summary and findings from: Chuck C, Teshome A, Lin A, Sayeed S, Wang E, Amaral-Nieves N, Taman M, Oldam J, Chen HC, Desai B, Kopecky A, Rivard MJ, Sarangi S, Elinzano H, Wong ET, Ciarelli CP, Chen CC. Redefining the therapeutic landscape of glioblastomas and brain metastasis through cesium brachytherapy and low-kV intra-operative radiation therapy (IORT). J Neurooncol. 2025 Nov 3;176(1):66. doi: 10.1007/s11060-025-05262-z. PMID: 41182498

Here is a detailed summary of the article by Carlin Chuck et al. (2025) titled "Redefining the therapeutic landscape of glioblastomas and brain metastasis through cesium brachytherapy and low-kV intra-operative radiation therapy (IORT)" in Journal of Neuro-Oncology. I've organized it into background, methods, key findings, strengths/limitations and implications — and given an annotated Vancouver-style reference at the end.

# **Background**

- The authors begin by noting that intracranial brachytherapy (i.e., placement of radiation sources directly in or at the tumor or resection cavity) has had cycles of enthusiasm and skepticism in neuro-oncology. PubMed +1
- · Two emerging platforms are highlighted:
  - 1. Brachytherapy using the radioisotope Cesium-131 (Cs-131)
  - 2. Low-kilovolt (low-kV) intra-operative radiation therapy (IORT) given at the time of resection. PubMed
- These approaches are attractive because they aim to deliver high-dose focal radiation immediately (or very early) in or near the surgical cavity, thereby
  minimizing delay between surgery and adjuvant therapy, and potentially improving local control. ResearchGate ±1
- The paper focuses on two patient populations: newly diagnosed or recurrent Glioblastoma (multiforme) (GBM) and patients with brain metastases (BM). These are areas of high unmet need in neuro-oncology given the poor outcomes with standard external beam radiotherapy alone.

#### Methods

- This is a **scoping literature review**, not a new prospective clinical trial. The authors reviewed the "historical landscape of brachytherapy, tracing influential studies, clinical adoption patterns, technological advancements, and ongoing trials" in neuro-oncology. PubMed
- They identify the key studies of Cs-131 brachytherapy and low-kV IORT in GBM and BM, summarizing safety profiles, local control outcomes, surgical
  morbidity, radiation necrosis rates and ongoing clinical trials. (The abstract notes that details such as volumetric dose coverage, cavity shrinkage, seed
  migration etc., are covered in prior literature and referenced.) PubMed +1
- They note that the data are heterogeneous (various platforms, isotopes, patient populations, prior irradiation or not) so their aim is to map out the "emerging therapeutic landscape" rather than perform a meta-analysis.

# Key Findings / Results

From the abstract and available summary, the main findings are:

- The safety profile of Cs-131 brachytherapy and low-kV IORT appears favourable: these techniques do not increase surgical morbidity or procedural
  complications significantly in GBM or BM settings.
- Rates of radiation necrosis remain rare in most GBM and BM cases treated with these modalities. PubMed
- Local control outcomes appear to be excellent, including in larger lesions (maximum diameter > 3.5 cm) in some published series. Consistently across
  available literature, these platforms appear to achieve good local tumour control.

  PubMed
- Given these emerging data, the authors argue that as the prospective clinical trials mature, Cs-131 brachytherapy and low-kV IORT are *poised to redefine* the therapeutic landscape for GBM and brain metastases. PubMed

The authors stress that these platforms may integrate into multimodal treatment strategies (surgery + immediate focal RT + systemic therapy) and potentially reduce the time gap between surgery and adjuvant therapy.

# Strengths and Limitations

# Strengths:

- The review succinctly captures the "renaissance" of intracranial brachytherapy and IORT in the era of more advanced surgical and radiotherapeutic techniques.
- It draws attention to newer isotopes (Cs-131) and low-kV IORT which may overcome some of the historical limitations of brachytherapy (e.g., long-half-life isotopes, seed migration, cavity shrinkage).
- · The paper provides a timely overview for neuro-oncology practitioners of emerging adjuncts beyond standard external beam RT.

#### Limitations:

 As a scoping review, the article is not a systematic review or meta-analysis; therefore, quantitative pooling of outcomes (e.g., median OS, median PFS) is not provided.

- The available literature is heterogeneous: different tumour types (GBM vs BM), different prior treatments, various brachytherapy and IORT platforms, different patient selection criteria making cross-study comparisons difficult. The authors themselves note that ongoing trials are required. PubMed
- For GBM in particular, given its diffuse infiltrative nature, even excellent local control may still not translate into major survival improvements unless systemic and margin strategies are simultaneously addressed. The authors implicitly acknowledge this challenge.
- · Because the review is based on published literature up to its cutoff, longer-term follow-up for newer IORT/ Cs-131 approaches may still be lacking.

#### Implications for Practice & Research

- For the neuro-oncology field (including your interest in gliomas and metastases): these data indicate that adding immediate focal radiation via Cs-131 brachytherapy or low-kV IORT at the time of resection may become a valuable adjunct to standard therapy (surgery + external beam RT + systemic therapy).
- Particularly in brain metastases, where local recurrence is common and surgery is increasingly used, such intra-operative radiation options may improve local control and reduce reliance on external beam radiotherapy (or shorten the window).
- For glioblastoma: although diffuse infiltration remains the major problem, if such focal treatments can safely provide improved local tumour bed control with minimal added morbidity, then they may allow further intensification at the margins or earlier systemic therapy.
- Ongoing and future prospective clinical trials will be critical: it will be important to define which patients benefit most (size of lesion, location, prior RT or not, primary tumour type for metastases), and whether survival (not just local control) can be improved.
- In the context of pediatric neuro-oncology (blood-brain barrier, drug delivery): while this review is focused on adult settings, the concept of immediate intraoperative radiation might eventually be adapted for selected high-risk paediatric tumours (though caution is required given developmental brain considerations and long-term toxicity).
- Also in the context of your interest in the BBB and drug delivery: combining intra-operative radiation with local delivery approaches (e.g., wafers, convection-enhanced infusion) could be an interesting future direction.

### **Summary Annotation for Your Bibliography**

Chuck C, Teshome A, Lin A, Sayeed S, Wang E, Amaral-Nieves N, Taman M, Oldam J, Chen HC, Desai B, Kopecky A, Rivard MJ, Sarangi S, Elinzano H, Wong ET, Ciarelli CP, Chen CC. Redefining the therapeutic landscape of glioblastomas and brain metastasis through cesium brachytherapy and low-kV intra-operative radiation therapy (IORT). J Neurooncol. 2025 Nov 3;176(1):66. doi:10.1007/s11060-025-05262-z. PMID:41182498.

In this scoping review the authors examine the emerging role of Cs-131 brachytherapy and low-kV IORT as adjuncts in the surgical management of glioblastoma and brain metastases. They report favourable safety profiles, low procedural morbidity and rare radiation necrosis in reported series. Local control outcomes appear encouraging (including for large lesions), and the authors argue that these technologies are poised to redefine focal radiotherapeutic paradigms in neuro-oncology. They call for maturation of prospective trials to clarify impact on survival and optimal integration into multimodal therapy.

If you like, I can pull out **specific numeric outcome data** (e.g., 1-year local control, radiation necrosis rates, survival) from the included studies of Cs-131 and low-kV IORT (where available) and compile a table of pros/cons and gaps for those modalities — would you like me to do that?

Yes

Great — I pulled numeric outcomes from the most-cited clinical series, reviews and institutional cohorts of Cs-131 intracavitary brachytherapy and low-kV IORT (INTRABEAM/LEX-IORT style) for glioblastoma (GBM) and brain metastases (BM) and compiled them into a concise table with the key outcome numbers you asked for (local control, radiation-necrosis rates, median OS where reported). I list the primary sources under the table so you can inspect the originals.

### Key studies — numeric outcomes (summary table)

Study (author, year)	Population (tumour)	n (patients / lesions)	Treatment (dose / platform)	FU (median/mean)	Local control (crude or 1- yr)	Radiation necrosis (RN)	Median overall survival (OS)	Notes
Wernicke et al., 2017 (prospective). Int J Radiat Oncol Biol Phys.	Large resected brain metastases (≥2.0 cm)	42 pts / 46 lesions	Intra-op permanent Cs-131 stranded seeds (prescribed per protocol)	median follow- up 11.9 mo	Local FFP 100% (all sizes); 1-yr regional FFP 89% (for >3.0 cm: 80%). PubMed	0% RN reported in study. <u>PubMed</u>	Median OS 15.1 mo; 1-yr OS 58%. PubMed	Prospective single-arm trial; strong for large lesions. <u>PubMed</u>
Wernicke et al., 2020. Brachytherapy (recurrent GBM series)	Recurrent glioblastoma (previous RT)	20 pts	Intra-op <b>Cs-</b> <b>131</b> ; 80 Gy to 0.5 cm from cavity surface	median FU 19 mo	Crude LC 85% at median FU. <u>PubMed</u>	0% RN (no RN observed). PubMed	Median OS 9 mo (range 5– 26). PubMed	Many patie also receive bevacizume (salvage setting). PubMed
Bander et al. / Weill Cornell retrospective (Bander/Bander- style review), 2023	Mixed brain tumors (BrM, gliomas, meningiomas)	119 pts (Cs-131 series)	Cs-131 adjuvant intracavitary brachytherapy after resection	median FU 11.8 mo (IQR 4.7– 23.6)	1-yr LC: BrM 84.7%, gliomas 34.1%, meningiomas 83.3%. PubMed	RN 8.4% (10/119 radiographic RN). PubMed	1-yr survival: BrM 53.3%; gliomas 45.9% (estimates reported). PubMed	Larger heterogene institutional cohort; RN higher than some small trials but sti acceptable PubMed

Study (author, year)	Population (tumour)	n (patients / lesions)	Treatment (dose / platform)	FU (median/mean)	Local control (crude or 1- yr)	Radiation necrosis (RN)	Median overall survival (OS)	Notes
Kahl et al., 2024 (Augsburg Univ. cohort) — INTRAOP low- kV IORT	Resected brain metastases	105 pts / 117 resections	INTRABEAM 50 kV IORT; median dose 20 Gy (to applicator surface)	mean FU 14 mo; median MRI FU for alive pts 9 mo	Observed LC 90.5%; estimated 1-yr LC 84.2%. SpringerLink	RN 2.6% (observed). <u>SpringerLink</u>	Median OS 18.2 mo; estimated 1-yr OS 57.7%. SpringerLink	Large singl center "rou practice" dataset; lov RN and hig LC. <u>SpringerL</u>
Ylanan et al., 2021 (systematic review — IORT in GBM)	Glioblastoma cohorts (various IORT techniques)	pooled (small studies)	Electron / photon / low- kV IORT (varied doses)	variable	Median time to local recurrence 9.9–16 mo; IORT improved LC in multiple small series. PubMed	Reported RN range across studies 2.8%–33% (heterogeneous reporting). PubMed	Reported median OS ranges: 13–18.0 mo (electron/photon cohorts). PubMed	Review highlights heterogene in technique and reportir suggests IC may offer comparable OS and improved L in some series. PubMed
Palmisciano et al., 2023 (review — Cs-131 for BM)	Resected brain metastases (review)	multiple studies pooled qualitatively	Cs-131 intracavitary brachytherapy	varied	Reviews report improved loco-regional control vs historical SRS/Cavity RT and consistently low RN. PubMed	Generally low RN in most Cs- 131 series; better safety profile than historical I-125. PubMed	Not a primary OS dataset — reviews suggest favorable outcomes in selected cohorts. PubMed	

# Quick synthesis / practical takeaways

- Local control: Both Cs-131 intracavitary brachytherapy and low-kV IORT report high local control for resected brain metastases (1-yr LC ~80–100% in major series) and promising LC in selected GBM/recurrent GBM series. Key prospective Cs-131 trial reported 100% local freedom from progression (Wernicke 2017) for large BM. PubMed +1
- Radiation necrosis (RN): RN rates are low but variable across reports many small prospective trials reported 0% RN (Wernicke), larger institutional series report ~2–8% RN (Kahl 2024 2.6%; Bander cohort 8.4%). Systematic reviews show a broad reported RN range (2.8–33%) reflecting heterogeneity in prior RT, dose, patient selection and imaging criteria. PubMed +3 SpringerLink +3
- Overall survival: OS is heavily confounded by diagnosis (BM vs GBM), extracranial disease, and systemic therapy. Typical median OS in BM cohorts treated with intra-op focal RT is in the ~15–18 mo range in several series; GBM median OS after IORT or Cs-131 salvage varies but generally falls in the ~9–18 mo window depending on context (newly diagnosed vs recurrent). PubMed +3 PubMed +3 PubMed +3
- Heterogeneity & selection: Studies differ in patient selection (new vs recurrent disease, previous RT), isotope/platform (Cs-131 stranded seeds vs INTRABEAM low-kV spherical applicators vs electron IORT), doses prescribed, and follow-up imaging criteria this explains variability in RN and LC reporting. Systematic reviews caution that direct comparisons are limited. PubMed ±1

# Limitations of the extracted data

- Many series are single-center, retrospective or small prospective single-arm trials; randomised data comparing cavity SRS / fractionated SRT vs Cs-131 or IORT are limited.
- Definitions of radiation necrosis differ (radiographic vs symptomatic vs histologic confirmation), and imaging follow-up schedules vary this inflates variability in reported RN rates.
- GBM behaves diffusely excellent local control does not necessarily equate to major survival gains unless systemic/field strategies are also addressed.
   PubMed

# Sources (primary ones I used for numbers above)

- Wernicke AG et al. Clinical outcomes of large brain metastases treated with neurosurgical resection and intraoperative Cs-131 brachytherapy: results of a prospective trial. Int J Radiat Oncol Biol Phys. 2017. <u>PubMed</u>
- Wernicke AG et al. Cs-131 brachytherapy for patients with recurrent glioblastoma combined with bevacizumab avoids radiation necrosis while maintaining local control. Brachytherapy. 2020. PubMed
- Bander ED et al. Safety and efficacy of Cesium-131 brachytherapy for brain tumors (Weill Cornell retrospective review), 2023. PubMed
- Kahl KH et al. Intraoperative radiotherapy after neurosurgical resection of brain metastases update of the oncological outcome from a single center cohort after 117 procedures. J Neurooncol. 2024. <a href="SpringerLink">SpringerLink</a>

- Ylanan AMD et al. Intraoperative radiotherapy for glioblastoma: systematic review. 2021. PubMed
- Palmisciano P et al. Cesium-131 brachytherapy for the treatment of brain metastases: current status and future perspectives. 2023. PubMed