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Initial Outcomes of GammaTile Brachytherapy From a Single Institution: A Case Series

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Abstract

GammaTile (GT Medical Technologies, Inc., Tempe, AZ) is a bioresorbable, collagen-based brachytherapy device embedded with cesium-131 (Cs-131) seeds that is placed within the resection cavity at the time of surgery, delivering the majority of its dose before wound healing would otherwise delay external beam radiation. It has been increasingly adopted for newly diagnosed and recurrent malignant brain tumors, yet real-world experience across tumor types remains limited. We report a single-institution case series of four consecutive patients who underwent maximal safe resection followed by GammaTile implantation: a newly diagnosed glioblastoma, a human epidermal growth factor receptor 2-positive breast cancer brain metastasis, a pulmonary adenocarcinoma cerebellar metastasis, and a non-small cell lung carcinoma metastasis. All targets were prescribed 60 Gy at a 5 mm depth. In one patient, two lesions were treated concurrently with GammaTile and ZAP-X stereotactic radiosurgery, where tiles were deliberately arranged to spare the brainstem. In this limited series, outcomes varied widely and appeared to reflect baseline tumor biology rather than a uniform treatment effect. The two patients with newly diagnosed metastases achieved durable local control, including marked cavity regression at three months and radiographic stability through 13 months, with prompt resumption of systemic therapy. The glioblastoma demonstrated new nodular enhancement at one month that could not be distinguished from pseudoprogression on structural imaging, and the high-burden lung metastasis progressed with leptomeningeal dissemination despite combined-modality treatment. Adverse events, a pseudomeningocele and intraventricular hemorrhage with hydrocephalus, were manageable and largely attributable to surgery or disease. This series illustrates the feasibility, safety, and integration of GammaTile with chemoradiation and stereotactic radiosurgery, while highlighting the challenges of early post-implant imaging interpretation and the limits of local therapy in aggressive, disseminated disease.

Categories: Radiation Oncology, Medical Physics, Neurosurgery
Keywords: brachytherapy, brain metastasis, cesium-131, cesium tile, gammatile, glioblastoma, low-dose rate brachytherapy

Introduction

Malignant brain tumors with a high propensity for local recurrence remain a persistent source of morbidity and mortality despite advances in surgery and external beam radiation therapy (EBRT). Adjuvant radiation therapy following resection is the standard of care and is intended to achieve local control of the postoperative tumor cavity. However, the time required for wound healing between surgery and EBRT initiation allows an opportunity for proliferation of residual tumor cells, especially in glioblastoma and brain metastases. Brachytherapy addresses this delay by implanting radioactive sources directly within the resection cavity. GammaTile (GT Medical Technologies, Inc., Tempe, AZ) is a bioresorbable, collagen-based brachytherapy device consisting of 20 × 20 × 4 mm tiles embedded with four titanium-encapsulated cesium-131 (Cs-131) seeds spaced 10 mm apart and offset 3 mm from the tumor cavity surface. The 9.7-day half-life of Cs-131 allows the majority of the dose to be delivered early, before tile resorption or seed migration can occur. This geometry is intended to minimize the dosimetric “hot” and “cold” spots seen with freehand brachytherapy techniques [1].

GammaTile received United States Food and Drug Administration (FDA) clearance in 2018 for any recurrent brain tumor and an expanded clearance in 2020 for upfront use in any malignant brain tumor [1]. In the initial prospective trial at the Barrow Neurological Institute, patients with recurrent, previously irradiated glioblastoma treated with maximal safe resection and GammaTile placement achieved a median overall survival of 25 months from diagnosis with a 7% rate of symptomatic radiation necrosis [2]. Similar results have been reported for brain metastases, where GammaTile achieved a one-year local control rate of 91.6% in the previously irradiated setting, comparing favorably with the 61-68% one-year control historically reported after repeat stereotactic radiosurgery (SRS) alone [3]. In benign disease, 19 patients with 20 recurrent, previously irradiated meningiomas treated with resection and GammaTile achieved 89% progression-free survival at 18 months, compared with 50% following each patient’s most recent prior therapy [4].

Evidence in the newly diagnosed setting is also emerging. Multi-institutional case series and prospective registry data in newly diagnosed brain metastases have reported one-year local control of 84.7-100% with radiation necrosis rates of 0-8.4% [5-8]. A newly diagnosed glioblastoma case series reported a crude local control of 86% with no radiation necrosis [9]. Randomized comparison of resection plus GammaTile versus resection plus postoperative SRS for newly diagnosed brain metastases in the ROADS trial reported reduced 12-month cumulative incidence of surgical bed recurrence from 15.4% to 1.3% and improved surgical bed recurrence-free survival compared with resection followed by postoperative stereotactic radiotherapy, without an increase in grade 3 or higher treatment-related adverse events (20.0% versus 21.7%) or 12-month radiation necrosis (5.3% versus 5.7%) [10]. Nevertheless, real-world experience integrating GammaTile with concurrent chemoradiation and SRS across tumor types remains limited.

Here, we report four consecutive cases from a single institution that illustrate early clinical outcomes with GammaTile brachytherapy in newly diagnosed glioblastoma and brain metastases. The study protocol was reviewed and approved by the institutional review board (Pro2024-0029).

Case Presentation

Case 1

Patient 1 was a 53-year-old man with a history of hypertension who was hospitalized after acute-onset left-sided weakness and left peripheral vision loss. Neuroimaging revealed an intra-axial mass in the right parieto-occipital lobe measuring 6 × 5.4 × 5.8 cm. He underwent a right-sided craniotomy for tumor resection with GammaTile placement (Figure *1*, Panel A). Final molecular pathology confirmed glioblastoma, isocitrate dehydrogenase (IDH)-wildtype, central nervous system (CNS) World Health Organization (WHO) grade 4, O^6-methylguanine-DNA methyltransferase (MGMT)-unmethylated, with mutations in the telomerase reverse transcriptase (TERT) promoter and phosphatase and tensin homolog (PTEN), epidermal growth factor receptor (EGFR) and mouse double minute 2 (MDM2) amplification, combined +7/-10, and *CDKN2A/B* homozygous deletion. He subsequently began concurrent temozolomide-based chemoradiation with prophylactic sulfamethoxazole-trimethoprim and as-needed ondansetron.

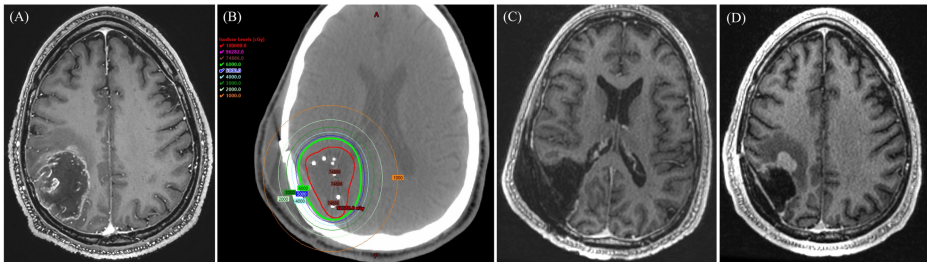


FIGURE 1: Right parieto-occipital lobe glioblastoma (A) preoperative MRI, (B) GammaTile postimplantation CT dose verification with GTV cavity contour in red, (C) postimplantation MRI, and (D) one-month postoperative MRI.

CT = computed tomography; GTV = gross target volume; MRI = magnetic resonance imaging

The gross target volume (GTV) for the cavity was 51.95 cm3. The prescription GammaTile dose was 60 Gy to a depth of 5 mm utilizing 44 seeds of 3.5 U/seed. MIM Symphony (MIM Software Inc., Cleveland, OH) was used to verify the delivered dose with postimplantation computed tomography (CT) and magnetic resonance imaging (MRI) (Figure *1*, Panels B and C). Dose calculation utilizes the methodology described in TG-43 [11,12]. The GTV and organ-at-risk (OAR) dose parameters are shown in Table *1*. Postoperatively, his left-sided weakness improved substantially. However, his left peripheral vision loss persisted unchanged. His early course was complicated by a pseudomeningocele which was managed with percutaneous aspiration and compressive wrapping. Cerebrospinal fluid cultures were negative, and the collection had fully resolved by six weeks postoperatively without further intervention. At his six-week follow-up, he was neurologically stable, and his incision had healed well.

Dosimetric parameter	Metric	GammaTile brachytherapy
GTV	V100% (%)	99.67%
	V150% (%)	95.61%
	D90% (cGy)	10,402.4 cGy
	D0.035cc (cGy)	97,879.2 cGy
Left optic nerve	D0.035cc (cGy)	77.9 cGy
Right optic nerve	D0.035cc (cGy)	102.6 cGy
Optic chiasm	D0.035cc (cGy)	280 cGy
Left cochlea	D0.035cc (cGy)	77.1 cGy
Right cochlea	D0.035cc (cGy)	383.6 cGy
Left lens	D0.035cc (cGy)	1.3 cGy
Right lens	D0.035cc (cGy)	1.4 cGy
Left eye	D0.035cc (cGy)	1.7 cGy
Right eye	D0.035cc (cGy)	1.7 cGy
Brainstem (excluding medulla)	D0.035cc (cGy)	1,310.9 cGy
Spinal cord (including medulla)	D0.035cc (cGy)	79.2 cGy
Skin	D0.035cc (cGy)	1,440.6 cGy
Brain - GTV	D5% (cGy)	7,209.7 cGy
Brain - GTV	V1,200cGy (cm^3)	234.943 cm^3

TABLE 1: Right parieto-occipital lobe glioblastoma GammaTile GTV and OAR dose parameters.

GTV = gross target volume; OAR = organ at risk; V100% = percentage of volume receiving 100% prescription dose; V150% = percentage of volume receiving 150% prescription dose; D90% = dose received by 90% of the volume; D0.035cc = dose received by 0.035 cm^3 of the volume; D5% = dose received by 5% of the volume; V1,200cGy = volume receiving 1,200 cGy

A one-month post-treatment MRI demonstrated the expected postsurgical cavity with cystic encephalomalacia, chronic blood products, and GammaTile seed artifact in addition to an overlying subdural collection that decreased in size on sequential imaging. There was moderately increased T2/fluid-attenuated inversion recovery (FLAIR) hyperintensity surrounding the surgical cavity with increased local mass effect. New nodular enhancement measuring 18 × 12 mm was also noted along the anterosuperior margin of the cavity (Figure *1*, Panel D). There was no acute hemorrhage, infarct, midline shift, or hydrocephalus. These findings raised concern for early tumor recurrence versus treatment-related pseudoprogression, a distinction that could not be resolved on structural imaging. Perfusion MRI or amino acid positron emission tomography (PET) would be needed for definitive differentiation, and monitoring was chosen over reoperation.

Case 2

Patient 2 was a 56-year-old female with a history of estrogen receptor weakly positive, progesterone receptor negative, human epidermal growth factor receptor 2 (HER2)-positive invasive breast cancer with axillary lymph node involvement. This patient had been treated with six cycles of docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) completed in March 2025, followed by mastectomy. In January 2026, she developed a transient, hour-long episode of expressive aphasia. She described her words as “being filtered” and an unusual affective indifference to the event, features concerning for a focal seizure. An outside CT head showed left temporal lobe edema, prompting transfer to Jersey Shore University Medical Center (JSUMC). MRI of the brain with and without contrast demonstrated a 1.4 × 1.4 cm enhancing nodular lesion in the left temporal lobe adjacent to the language cortex, suspicious for malignancy (Figure *2*, Panel A).

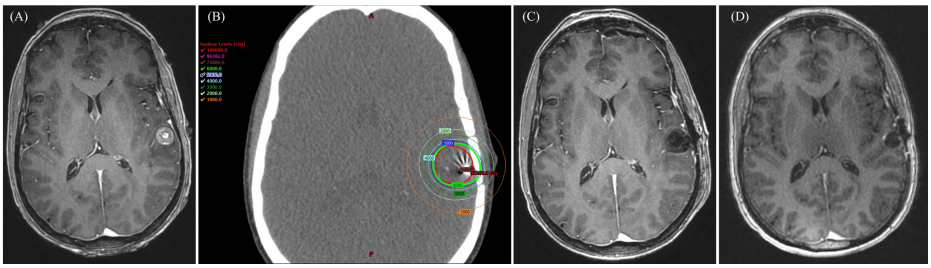


FIGURE 2: Left temporal lobe metastatic mammary carcinoma (A) preoperative MRI, (B) GammaTile postimplantation CT dose verification with GTV cavity contour in red, (C) postimplantation MRI, and (D) three-month postoperative MRI.

CT = computed tomography; GTV = gross target volume; MRI = magnetic resonance imaging

She underwent a left temporal craniotomy for gross total resection with placement of GammaTile brachytherapy in January 2026. Final pathology demonstrated metastatic mammary carcinoma with immunohistochemistry positive for GATA3, focal mammaglobin, focal (1%) estrogen receptor, with HER2 scored 3+, and negative for progesterone receptor, glial fibrillary acidic protein (GFAP), and thyroid transcription factor 1 (TTF-1). Next-generation sequencing identified mutations in the following genes: *TP53*, *PIK3R1*, *AKT2*, *ATM*, and *NF1*, among others.

The GTV for the cavity was 5.64 cm^3. The prescription GammaTile dose was 60 Gy to a depth of 5 mm utilizing eight seeds of 3.5 U/seed. MIM Symphony was used to verify the delivered dose with postimplantation CT and MRI (Figure *2*, Panels B and C). The GTV and OAR dose parameters are shown in Table *2*.

Dosimetric parameter	Metric	GammaTile brachytherapy
GTV	V100% (%)	99.32%
	V150% (%)	80.79%
	D90% (cGy)	7,810.3 cGy
	D0.035cc (cGy)	79,483.4 cGy
Left optic nerve	D0.035cc (cGy)	100.3 cGy
Right optic nerve	D0.035cc (cGy)	44 cGy
Optic chiasm	D0.035cc (cGy)	167.3 cGy
Left cochlea	D0.035cc (cGy)	55.1 cGy
Right cochlea	D0.035cc (cGy)	43.6 cGy
Left lens	D0.035cc (cGy)	1 cGy
Right lens	D0.035cc (cGy)	1 cGy
Left eye	D0.035cc (cGy)	40 cGy
Right eye	D0.035cc (cGy)	20 cGy
Brainstem (excluding medulla)	D0.035cc (cGy)	474.6 cGy
Spinal cord (including medulla)	D0.035cc (cGy)	40 cGy
Skin	D0.035cc (cGy)	1,122.3 cGy
Brain - GTV	D5% (cGy)	1,021.5 cGy
Brain - GTV	V1,200cGy (cm^3)	55.359 cm^3

TABLE 2: Left temporal lobe metastatic mammary carcinoma GammaTile GTV and OAR dose parameters.

GTV = gross target volume; OAR = organ at risk; V100% = percentage of volume receiving 100% prescription dose; V150% = percentage of volume receiving 150% prescription dose; D90% = dose received by 90% of the volume; D0.035cc = dose received by 0.035 cm^3 of the volume; D5% = dose received by 5% of the volume; V1,200cGy = volume receiving 1,200 cGy

Postoperative MRI confirmed gross total resection with expected postsurgical changes. A staging PET scan in February 2026 showed no fluorodeoxyglucose (FDG)-avid disease elsewhere, and she was started on trastuzumab deruxtecan for systemic and CNS-directed Anti-HER2 targeted therapy. She had one additional brief focal seizure in January 2026 and was admitted in March 2026 for continuous video electroencephalography (EEG) monitoring to facilitate antiepileptic medication.

Follow-up MRI of the brain performed approximately three months after surgery demonstrated marked interval improvement of the treated lesion. The surgical cavity had decreased in size from 1.6 × 1.7 × 1.6 cm to 1.0 × 1.3 × 1.0 cm, with complete resolution of previous vasogenic edema (Figure *2*, Panel D). Linear foci of low T1/T2 signal within the cavity were consistent with residual GammaTile seed artifact. Perfusion imaging showed no abnormal cerebral blood volume, new enhancement, or evidence of additional metastatic disease.

Case 3

Patient 3 was a 59-year-old female with a history of prediabetes and hyperlipidemia who was transferred to JSUMC after several weeks of nausea, weakness, unintentional weight loss, and gait instability. Imaging revealed a large right cerebellar mass with effacement of the fourth ventricle and acute obstructive hydrocephalus. MRI of the brain confirmed a 2.6 × 3.8 × 3.0 cm enhancing mass in the right cerebellar hemisphere with surrounding vasogenic edema (Figure *3*, Panel A). A concurrent CT of the chest identified a right upper lobe subpleural nodule measuring 1.0 cm.

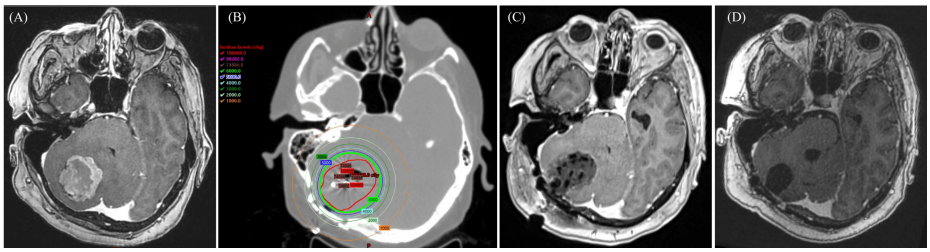


FIGURE 3: Right cerebellar metastatic adenocarcinoma (A) preoperative MRI, (B) GammaTile postimplantation CT dose verification with GTV cavity contour in red, (C) postimplantation MRI, and (D) 13-month postoperative MRI.

CT = computed tomography; GTV = gross target volume; MRI = magnetic resonance imaging

The patient underwent a right suboccipital craniotomy for resection of the right cerebellar mass with GammaTile placement. Final molecular pathology confirmed metastatic adenocarcinoma with papillary features consistent with pulmonary origin, positive for CAM5.2, AE1/3, CK7, TTF-1, and Napsin A, and negative for GATA3, CK20, and PAX8. She was subsequently diagnosed with metastatic right upper lobe lung adenocarcinoma.

The GTV for the cavity was 21.38 cm^3. The prescribed GammaTile dose was 60 Gy to a depth of 5 mm utilizing eight seeds of 3.5 U/seed. MIM Symphony was used to verify the delivered dose with postimplantation CT and MRI (Figure *3*, Panels B and C). The GTV and OAR dose parameters are shown in Table *3*.

Dosimetric parameter	Metric	GammaTile brachytherapy
GTV	V100% (%)	99.85%
	V150% (%)	94.02%
	D90% (cGy)	9,955.6 cGy
	D0.035cc (cGy)	97,872.2 cGy
Left optic nerve	D0.035cc (cGy)	106.7 cGy
Right optic nerve	D0.035cc (cGy)	121.2 cGy
Optic chiasm	D0.035cc (cGy)	340.6 cGy
Left cochlea	D0.035cc (cGy)	237.1 cGy
Right cochlea	D0.035cc (cGy)	779.4 cGy
Left lens	D0.035cc (cGy)	1.1 cGy
Right lens	D0.035cc (cGy)	1.1 cGy
Left eye	D0.035cc (cGy)	1.3 cGy
Right eye	D0.035cc (cGy)	1.3 cGy
Brainstem (excluding medulla)	D0.035cc (cGy)	2,909 cGy
Spinal cord (including medulla)	D0.035cc (cGy)	916.1 cGy
Skin	D0.035cc (cGy)	1,029 cGy
Brain - GTV	D5% (cGy)	3,202 cGy
Brain - GTV	V1,200cGy (cm^3)	169.855 cm^3

TABLE 3: Right cerebellar metastatic adenocarcinoma GammaTile GTV and OAR dose parameters.

GTV = gross target volume; OAR = organ at risk; V100% = percentage of volume receiving 100% prescription dose; V150% = percentage of volume receiving 150% prescription dose; D90% = dose received by 90% of the volume; D0.035cc = dose received by 0.035 cm^3 of the volume; D5% = dose received by 5% of the volume; V1,200cGy = volume receiving 1,200 cGy

Postoperatively, the patient recovered without new neurologic deficit. MRI at three, seven, and nine months postoperatively demonstrated a stable resection cavity without evidence of recurrent tumor. At her nine-month follow-up, she remained neurologically intact with an Eastern Cooperative Oncology Group (ECOG) performance score of 1-2 and proceeded with EBRT to the right lung, nine months post-GammaTile. Follow-up MRI approximately 13 months postoperatively continued to show a stable surgical cavity with a faint rim of enhancement that had decreased compared with the prior study (Figure *3*, Panel D). These findings are consistent with postoperative change rather than recurrence.

Case 4

Patient 4 was a 69-year-old male with a history of hypertension, hyperlipidemia, and a 40-pack-year smoking history. He presented with two days of confusion, memory loss, and headache in addition to six months of ataxia and word-finding difficulty. Neuroimaging revealed a 3.4 × 3.3 × 3.5 cm, partially hemorrhagic mass involving the left temporo-occipital lobe and extending into the left lateral ventricle (Figure *4*, Panel A). Prominent surrounding edema and a 0.3 cm rightward midline shift were noted. A separate, smaller enhancing lesion measuring 1.3 × 1.0 × 1.2 cm was also identified in the right inferior temporal gyrus (Figure *4*, Panel E). CT of the chest, abdomen, and pelvis showed mediastinal and right hilar lymphadenopathy concerning for metastatic non-small cell lung carcinoma.

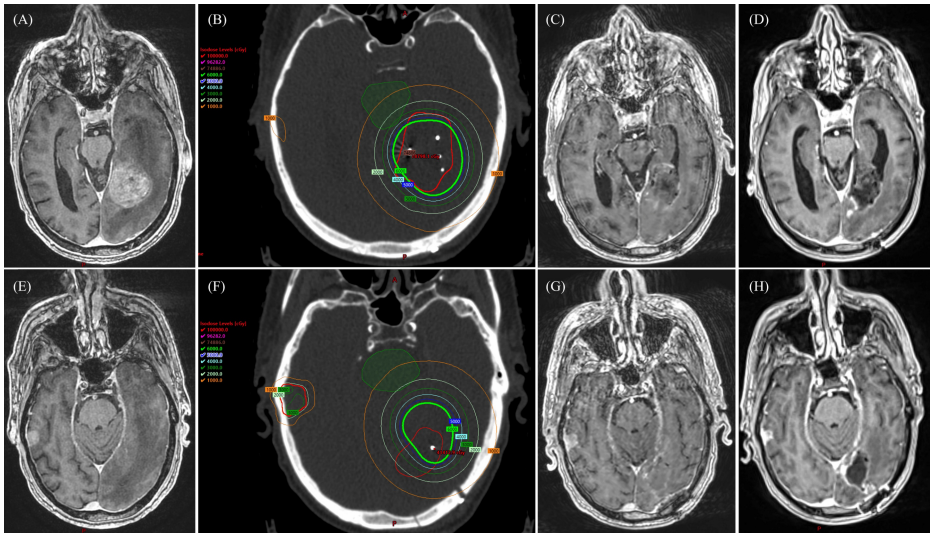


FIGURE 4: Metastatic non-small cell lung carcinoma (A) left temporo-occipital lobe/lateral ventricle preoperative MRI, (B) GammaTile postimplantation CT dose verification with GTV cavity contour in red, (C) postimplantation MRI, (D) six-week postoperative MRI, (E) right inferior temporal gyrus preoperative MRI, (F) ZAP-X treatment planning CT delivering a prescription dose of 22 Gy in one fraction with PTV contour in red, (G) postimplantation MRI, and (H) six-week postoperative MRI.

CT = computed tomography; GTV = gross target volume; MRI = magnetic resonance imaging; PTV = planning target volume

The patient underwent a left-sided craniotomy for resection of the dominant left temporo-occipital mass with GammaTile placement followed by ZAP-X SRS (ZAP Surgical Systems, Inc., San Carlos, CA) to the right inferior temporal gyrus lesion five days later. Final molecular pathology confirmed metastatic poorly differentiated carcinoma compatible with lung adenocarcinoma positive for CK7, TTF-1, and Napsin, while being negative for CK20, CDX2, NKX3.1, SOX10, and p40. His postoperative course was complicated by intraventricular hemorrhage and obstructive hydrocephalus that required extraventricular drain placement. He remained confused with inconsistent mental status, although he gradually began speaking in longer sentences before the drain was removed.

The GTV for the GammaTile cavity was 30.71 cm^3. The prescription GammaTile dose was 60 Gy to a depth of 5 mm utilizing 20 seeds of 3.5 U/seed. MIM Symphony was used to verify the delivered dose with postimplantation CT and MRI (Figure *4*, Panels B, C, G). Tiles were placed in the cavity to reduce brainstem dose, resulting in 70.49% prescription dose coverage of the GTV (V100%). The deliberate reduction of V100% for brainstem protection is a dosimetric compromise. The ZAP-X GTV was 1.91 cm^3, and a 1 mm margin was added for a planning target volume (PTV) of 3.07 cm^3. The prescription ZAP-X dose was 22 Gy to the 57% isodose line in one fraction utilizing seven isocenters, 161 beams, an average collimator size of 9 ± 3 mm, and a path complexity of 6 for gantry movement (Figure *4*, Panel F). Combined forward- and inverse-planning was performed using a 0.5 mm dose grid, limiting the dose to the eyes, lens, optic nerves, optic chiasm, cochleae, brainstem, spinal cord, and whole brain based on Timmerman OAR and Milano et al. recommendations [13,14]. Plan quality was evaluated for conformality and dose fall-off using conformity index (CI) and gradient index (GI). The CI was defined as the ratio of the prescription isodose volume to the target volume [15]. The GI was defined as the ratio of the volume receiving half the prescription dose to the prescription isodose volume [16]. Plan quality constraints followed the Radiation Therapy Oncology Group Protocol 0813 [17]. The GTV/PTV and OAR dose parameters are shown in Table *4* for GammaTile and Table *5* for ZAP-X.

Dosimetric parameter	Metric	GammaTile brachytherapy
GTV	V100% (%)	70.49%
	V150% (%)	56.16%
	D90% (cGy)	2,901 cGy
	D0.035cc (cGy)	88,329.9 cGy
Left optic nerve	D0.035cc (cGy)	137.7 cGy
Right optic nerve	D0.035cc (cGy)	84.9 cGy
Optic chiasm	D0.035cc (cGy)	423 cGy
Left cochlea	D0.035cc (cGy)	447.4 cGy
Right cochlea	D0.035cc (cGy)	137.1 cGy
Left lens	D0.035cc (cGy)	1.1 cGy
Right lens	D0.035cc (cGy)	1.1 cGy
Left eye	D0.035cc (cGy)	1.1 cGy
Right eye	D0.035cc (cGy)	1.1 cGy
Brainstem (excluding medulla)	D0.035cc (cGy)	3,061.2 cGy
Spinal cord (including medulla)	D0.035cc (cGy)	424 cGy
Skin	D0.035cc (cGy)	964.8 cGy
Brain - GTV	D5% (cGy)	3,415 cGy
Brain - GTV	V1,200cGy (cm^3)	216.504 cm^3

TABLE 4: Left temporo-occipital lobe/lateral ventricle GammaTile GTV and OAR dose parameters.

GTV = gross target volume; OAR = organ at risk; V100% = percentage of volume receiving 100% prescription dose; V150% = percentage of volume receiving 150% prescription dose; D90% = dose received by 90% of the volume; D0.035cc = dose received by 0.035 cm^3 of the volume; D5% = dose received by 5% of the volume; V1,200cGy = volume receiving 1,200 cGy

Dosimetric parameter	Metric	Constraint	ZAP-X SRS
PTV	V100 (%)	≥95%	98.65%
	CI	≤1.2–1.5	1.116
	GI	≤3.697–4.19	2.62
Left optic nerve	D0.035 (cGy)	≤1,000 cGy	60.2 cGy
	V800 (cm^3)	≤0.2 cm^3	0 cm^3
Right optic nerve	D0.035 (cGy)	≤1,000 cGy	72.9 cGy
	V800 (cm^3)	≤0.2 cm^3	0 cm^3
Optic chiasm	D0.035 (cGy)	≤1,000 cGy	133.1 cGy
	V800 (cm^3)	≤0.2 cm^3	0 cm^3
Left cochlea	D0.035 (cGy)	≤900 cGy	38.9 cGy
Right cochlea	D0.035 (cGy)	≤900 cGy	75.6 cGy
Left lens	D_{max} (cGy)	≤100–200 cGy	24.2 cGy
Right lens	D_{max} (cGy)	≤100–200 cGy	22.5 cGy
Left eye	D_{max} (cGy)	≤100–200 cGy	13.9 cGy
Right eye	D_{max} (cGy)	≤100–200 cGy	13.1 cGy
Brainstem (excluding medulla)	D0.035 (cGy)	≤1,500 cGy	279.8 cGy
	V1,000 (cm^3)	≤0.5 cm^3	0 cm^3
Spinal cord (including medulla)	D0.035 (cGy)	≤1,000 cGy	157.5 cGy
	V2200 (cm^3)	≤0.35 cm^3	0 cm^3
Skin	D0.035 (cGy)	≤2,750 cGy	1,428.7 cGy
	V2,550 (cm^3)	≤10 cm^3	0 cm^3
Brain - GTV	V1,200 (cm^3)	≤10 cm^3	2.823 cm^3

TABLE 5: Right inferior temporal gyrus ZAP-X PTV and OAR dose parameters.

PTV = planning target volume; OAR = organ at risk; GTV = gross target volume; SRS = stereotactic radiosurgery; V100% = percentage of volume receiving 100% prescription dose; CI = conformity index; GI = gradient index; D0.035cc = dose received by 0.035 cm^3 of the volume; V800cGy = volume receiving 800 cGy; D_{max} = maximum point dose; V1,000cGy = volume receiving 1,000 cGy; V2,200cGy = volume receiving 2,200 cGy; V2,550cGy = volume receiving 2,550 cGy; V1,200cGy = volume receiving 1,200 cGy

Follow-up MRI five weeks postoperatively demonstrated increased thickness, nodular rim enhancement along the resection cavity, and the ependymal surface of the left lateral ventricle, concerning for leptomeningeal spread. An MRI six weeks postoperatively confirmed new hemorrhage within the third ventricle and further tumor progression with nodular intraventricular growth along the frontal horn and septum pellucidum of the left lateral ventricle (Figure *4*, Panel D). The right inferior temporal gyrus lesion was reduced in size, measuring 0.7 × 0.9 × 0.7 cm (Figure *4*, Panel H). Given his ECOG 3 performance status and evidence of disease progression, he was transitioned to palliative radiotherapy and care, with plans for spinal MRI to evaluate leptomeningeal disease and PET/CT for systemic staging.

Discussion

This single-institution series illustrates the breadth of contemporary GammaTile application, spanning upfront treatment of newly diagnosed glioblastoma, treatment-naïve brain metastases from breast and lung primaries, and a large dominant metastasis managed with combined brachytherapy and SRS. The radiobiologic rationale for the device rests on the physical properties of Cs-131, which front-loads the majority of its dose within the first month after implantation and thereby allows local radiation to begin at

the time of resection without the wound-healing delay that precedes external beam therapy or postoperative SRS [1]. Consistent with this mechanism, outcomes in the present series were heterogeneous and tracked underlying tumor biology and disease burden more closely than the modality itself.

The two patients with newly diagnosed brain metastases achieved durable local control. In Case 2, an HER2-positive breast metastasis demonstrated marked interval regression of the resection cavity with complete resolution of vasogenic edema at three months and no evidence of recurrence on perfusion imaging, while Case 3, a cerebellar metastasis from pulmonary adenocarcinoma, remained radiographically stable through 13 months of follow-up. These outcomes are concordant with contemporary series of Cs-131 collagen-tile brachytherapy for newly diagnosed metastases, which have reported one-year local control approaching 84.7-100% with radiation necrosis rates of roughly 0-8.4% [5,6], and with a larger retrospective experience in which one-year local control for brain metastases was 84.7% and was highest among non-small cell lung carcinoma histologies (90.8%) [7]. Case 2 also exemplifies a practical advantage of the platform: because local radiation was delivered at the time of resection, systemic HER2-directed therapy with trastuzumab deruxtecan could be resumed promptly for concurrent extracranial and CNS disease control.

Case 1 highlights a central interpretive challenge of intracavitary brachytherapy. New nodular enhancement measuring 18 × 12 mm along the anterosuperior cavity margin at one month could not be distinguished from treatment-related pseudoprogression on structural MRI. Because Cs-131 delivers most of its dose early and this patient concurrently received temozolomide-based chemoradiation, early treatment-related change is both expected and difficult to separate from true progression; advanced techniques such as perfusion imaging or amino acid PET, or short-interval follow-up, are frequently required to resolve the distinction [18]. This uncertainty should be weighed against the natural history of high-grade disease. In a prospective series of GammaTile for recurrent glioblastoma, 12-month local control was approximately 81% with median overall survival of 20 months in MGMT-unmethylated and 37.4 months in MGMT-methylated tumors [19], and a systematic review for high-grade gliomas estimated a mean overall survival of 27.3 months and progression-free survival of 8.8 months [20]. Notably, brachytherapy dosimetric parameters, including D90%, V100%, and V150%, did not correlate with progression-free survival in that recurrent glioblastoma cohort [19], underscoring that early enhancement and coverage metrics alone are insufficient to guide management decisions.

Case 4 illustrates the limits of local therapy in high-burden, biologically aggressive disease. To protect the adjacent brainstem, tiles were deliberately positioned to reduce brainstem dose, resulting in prescription-dose coverage (V100%) of only 70.49% of the GTV, and a synchronous right inferior temporal lesion was treated in the same setting with ZAP-X SRS (22 Gy in a single fraction), demonstrating the feasibility of integrating brachytherapy with frameless SRS during a single multimodal course. The combined modality (brachytherapy+SRS) is novel, and the approach is not yet validated. It is presented here as a proof of concept. Dose-response data for collagen-tile brachytherapy are sparse and derive from recurrent glioblastoma rather than metastases. In a 22-patient recurrent glioblastoma cohort, D90%, V100%, and V150% did not correlate with progression-free survival [19], whereas a subsequent dosimetric analysis from the same institution (20 patients, 21 lesions) found that D90% to the high-risk clinical target volume was associated with local recurrence at six months ($p = 0.026$) and reported a trend toward longer local recurrence-free survival when D90% was at or above the cohort median of 56 Gy ($p = 0.048$) [21]. In a 10-patient metastasis pilot with a mean D90% of 51.2 Gy (range = 22.4-80.8 Gy), by contrast, no local recurrence was detected at a median follow-up of 6.2 months [8]. The D90% in Case 4 fell below the lowest value in the glioblastoma dosimetric series (31.7 Gy) [19,21], and a coverage threshold for durable control of metastases has not been validated. We therefore regard the coverage in this case as a deliberate but substantial compromise whose contribution to the early cavity-margin enhancement cannot be separated from the underlying disease biology. The patient also developed nodular ependymal enhancement, intraventricular hemorrhage, and progressive leptomeningeal spread within six weeks. Tumor contact with the ventricle in brain metastases [22] and with the ependyma in high-grade glioma [23] is a recognized risk factor for leptomeningeal dissemination after resection. In a prospective registry, leptomeningeal disease occurred in 7.8% of patients after resection and GammaTile placement, with 3-, 6-, and 12-month leptomeningeal disease-free rates of 97.4%, 94.1%, and 88.5%, respectively [6]; an event at five to six weeks therefore lies within the reported experience but at its early margin. More fundamentally, the dose from intracavitary Cs-131 tiles is prescribed to a depth of 5 mm and falls off steeply beyond the cavity wall [1], so that, similar to postoperative stereotactic radiotherapy, the implant treats the cavity margin and does not address tumor cells already seeded along the ependyma or into the cerebrospinal fluid pathways. After resection and cavity-directed SRS, leptomeningeal disease developed in a median of 16.1% of patients across 13 surgical series (386 of 2,105 patients), with proximity of the metastasis to cerebrospinal fluid spaces and ventricular violation during surgery among the reported risk factors [24], and in a seven-center analysis, 57% of these recurrences were nodular and arose at a median of 5.6 months after radiosurgery [25]. For metastases that breach the ventricle, cavity-directed local therapy of any modality should therefore be regarded as insufficient on its own [22-24]. Once the five-week MRI raised concern for leptomeningeal spread, spinal imaging was planned to complete evaluation of the neuraxis, consistent with European Association of Neuro-Oncology (EANO)-European Society for Medical Oncology (ESMO) guidance that suspected leptomeningeal metastasis be evaluated with cerebrospinal MRI and cerebrospinal fluid studies [26]; whether routine cerebrospinal MRI surveillance benefits asymptomatic patients at high risk has not been evaluated [26]. On balance, the clinical trajectory was most consistent with disseminated disease biology

rather than an isolated local failure of the device, with the acknowledgment that reduced coverage may have contributed.

Across the series, adverse events were manageable and largely attributable to surgery or disease rather than to the implant. Case 1 developed a pseudomeningocele that resolved with percutaneous aspiration and compressive wrapping, and Case 4 experienced intraventricular hemorrhage with obstructive hydrocephalus requiring external ventricular drainage; no patient experienced a wound-healing failure that precluded subsequent therapy. This safety profile is consistent with larger experiences reporting radiation necrosis rates of approximately 0-8.4% and wound complication rates of 2.8-11.8% [5-8], and reflects a practical strength of the platform: initiation of local radiation at the time of resection with a prompt return to systemic therapy.

Several limitations temper these observations. The series comprises only four consecutive patients treated at a single institution with a retrospective design, short and heterogeneous follow-up, mixed histologies, and no comparator arm or pathologic confirmation of equivocal imaging findings. These features preclude any conclusion regarding comparative efficacy, and the report is best regarded as hypothesis-generating. Maturing prospective data, including the multicenter STaRT Registry [27] and randomized trials such as ROADS [10] and GESTALT [28], will be needed to define optimal patient selection and to clarify the role of GammaTile relative to postoperative SRS or SRT and external beam reirradiation.

Conclusions

GammaTile brachytherapy is technically feasible and safe in a single-institution setting, and when combined with concurrent chemoradiation or SRS, it offers a practical means to deliver immediate local therapy. However, given the small sample, mixed histologies, and short follow-up, these observations are hypothesis-generating and must be interpreted alongside emerging multi-institutional and randomized data.

Additional Information

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All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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