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GammaTile for Recurrent High-Grade Meningioma: Outcomes from a Multicenter Analysis

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Case Report

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Abstract

Purpose

GammaTile (GT), a form of brachytherapy utilizing cesium-131 seeds in a bioresorbable collagen tile, has gained popularity for recurrent intracranial tumors including high-grade meningioma. This study reports early experience utilizing GT in recurrent high-grade meningioma with a focus on perioperative safety and clinical applications.

Methods

The STaRT Registry (NCT04427384) was queried for patients receiving GT for WHO Grade II-III meningiomas from January 2021 to January 2026. Patient demographics, procedure details, overall survival, recurrence, and adverse events (AEs) were analyzed.

Results

Forty-nine tumors from 44 patients (mean age 58 years, SD ± 14.7) across 20 institutions were included. Prior radiation included fractionated stereotactic radiosurgery (SRS) in 20 patients (45%), single fraction SRS in 15 (34%), and whole-brain radiotherapy in one (2%). Median tumor diameter was 4.4cm (range 2.5–5.8). Gross total resection was achieved in 35 tumors (71%). One- and two-year overall survival (OS) were 86% and 54%, respectively. Karnofsky Performance Scale (KPS) < 80 was associated with shorter median OS ($p = 0.019$). Median time to local failure was 18 months, and tumor diameter < 3 cm was associated with local control ($p = 0.013$, 95% CI 0.031–0.661). Two patients (5%) developed asymptomatic adverse radiation effects (AREs), managed conservatively. Five AEs (11%) were reported, all CTCAE grade 3, with re-operations for surgical site infection. Three patients (7%) died from neurologic causes and five (11%) from systemic causes.

Conclusion

GT for recurrent high-grade meningioma demonstrates favorable local control and safety, with low AREs. Greater survival and local control were associated with higher KPS and smaller tumor size, respectively.

Introduction

Surgical resection remains the mainstay management of high-grade meningiomas[1]. In cases where residual disease, local progression, or recurrence is observed despite surgery, stereotactic radiosurgery (SRS) or fractionated intensity-modulated radiation therapy are frequently employed[2, 3]. However, therapeutic options are significantly limited for patients with aggressive meningiomas exhibiting local

progression following prior radiation therapy, as no standard-of-care systemic therapies have consistently demonstrated efficacy[4] and surgery alone is seldom curative in recurrent aggressive cases[5, 6]. Re-irradiation is associated with an elevated risk of radiation-induced injury, typically mitigated by lower radiation doses, potentially at the expense of reduced therapeutic efficacy[7, 8].

GammaTile (GT; GT Medical Technologies Inc.) is an FDA-approved brachytherapy platform that employs cesium-131 radiation seeds encapsulated within a collagen-based matrix. This device provides enhanced uniformity in radiation distribution, as the collagen matrix creates a 3-mm separation between the radiation seeds and targeted tissue[9, 10]. The structured collagen tiles ensure consistent seed positioning, minimizing dose heterogeneity, which could otherwise increase the risk of tumor recurrence due to insufficient radiation[11]. Furthermore, this stable seed arrangement mitigates localized radiation overdose from seed aggregation, a complication observed with other brachytherapy approaches, thus decreasing the incidence of radiation-induced necrosis[12].

In recent years, GT has gained popularity in the treatment of intracranial pathologies including recurrent meningioma, brain metastases, glioma and even upfront brain metastases[11, 13, 14]. Here we present the first cohort of survival following GT for recurrent high-grade meningioma.

Methods

Patient Selection and Data Collection

The STaRT Registry (NCT04427384) was queried for all patients with high-grade meningioma treated between January 2021 and January 2026. The registry is an IRB-approved prospectively enrolled multicenter database evaluating intracranial tumor resection outcomes with GammaTile brachytherapy. Deidentified clinical data was collected including demographic characteristics, surgical parameters, radiation dosimetry, local tumor control rates, and adverse events through standardized case report forms. All sensitive information was stored in a secured encrypted database adhering to HIPAA compliance standards. This study was approved by the Institutional Review Board.

GammaTile Specifications and Technique

Intra-operatively, the resection cavity was lined with a single layer of bioresorbable collagen tiles measuring 20 × 20 × 4 mm following tumor removal. Each tile contained four titanium-encapsulated cesium-131 (Cs-131) sources emitting an initial dose rate of 3.5 cGy·cm²/h with a 9.7-day radioactive half-life. The geometrically arranged radiation sources (10 mm apart from neighboring seeds and 3 mm from the cavity surface), create a rapid dose falloff gradient, typically delivering 60 Gy to a 5-mm depth from the resection margin, with variations based on cavity morphology and tile deployment density[10].

The biologically-effective dose (BED) was calculated using the linear-quadratic model with $\alpha/\beta = 10$ for early-responding tissues. At 60 Gy prescription dose, the BED of 51.5 Gy was comparable to

hypofractionated stereotactic regimens (30 Gy in 5 fractions, BED 48.0 Gy)[15, 16]. Subsequent dosimetric analyses revealed GammaTile provided equivalent or superior BED compared to CyberKnife, GammaKnife, and proton therapy within 3 mm of cavity margins[17].

Follow-up

Local progression was determined by application of the Response Assessment in Neuro-Oncology (RANO) criteria and defined as recurrent disease within 1.5 cm of the original resection cavity, confirmed either histopathologically via subsequent surgery or radiographically through new nodular enhancement patterns unresponsive to corticosteroid therapy.

Radiographic follow-up was achieved via postoperative MR images and non-contrast thin-cut CT scans (0.8-1.2 mm slice thickness) within 24 hours of surgical intervention for dosimetric verification. Researchers performed radiation dose calculations through BrachyVision treatment planning software (Varian Medical Systems), analyzing spatial distribution of cesium-131 sources relative to critical anatomical structures.

Toxicity was assessed during follow-up using the Common Terminology Criteria for Adverse Events (CTCAE v5.0)[18]. Wound breakdown was defined as sterile dehiscence lacking clinical evidence of infection, while wound infection required microbiological confirmation or systemic inflammatory markers, independent of dehiscence status. For intracranial radiation-related adverse effects, clinicians integrated symptomatic presentation with serial contrast-enhanced MRI demonstrating either progressive perilesional edema exceeding preoperative baselines or non-nodular operative bed enhancement responsive to corticosteroid therapy.

Statistical Analysis

Utilizing the Kaplan-Meier technique, we calculated overall survival and local control times. Univariate cox regression was performed to identify predictors of local control with $p<0.05$ considered statistically significant. All statistical analyses were performed using Stata Version 19.0 (StataCorp LP).

Statements and Declarations

As a retrospective study with minimal risk, thus Human Ethics and Consent to Participate declarations: not applicable. Clinical trial number: not applicable. The authors declare no sources of funding was used for this study. The study was reviewed and approved by the central Institutional Review Board WCG-IRB.

Results

Study population

Forty-four patients with 49 tumors from 20 institutions were included in the analysis. Five patients had two tumors (WHO Grade II in three patients and WHO Grade III in two patients). The mean age was 58

years, with 17 patients (39%) being female (**Table 1**). The overwhelming majority of patients presented with an underlying symptom, most frequently focal neurological deficit (59%), followed by headache (30%) and seizure (30%). Overall, the majority of patients (77%) presented to surgery and GT placement with Karnofsky Performance Scale (KPS) of 80 or greater. All 49 tumors were implanted with Cs-131 tiles at the time of surgical resection. WHO grade at the time of surgery was WHO Grade II in 26 tumors (53%), and WHO Grade III in 23 tumors (47%). The prior treatment of meningioma in our cohort was most frequently fractionated SRS, followed by single fraction SRS, 45% and 34%, respectively **(Figure 1)**. Eight patients (18%) had prior surgical resection of their tumors.

Treatment Efficacy

Overall survival (OS) rates from the time of surgery at one and two years were 86% and 54%, respectively **(Figure 2)**. Maximum follow-up at present is 36 months and at the time of analysis, 36 patients (82%) were alive. A preoperative KPS <80 was associated with significantly shorter overall median survival compared to KPS ≥80 (p=0.019). Three patients (7%) were deceased due to CNS-related disease and five patients (11%) due to systemic deterioration or other non-CNS related causes.

Gross total resection was achieved in 35 tumors (71%) and near gross total resection in 10 patients (20%). Post-operatively, local control was achieved in 35 patients (80%) overall. Median local failure was 18 months (**Figure 3)**. Using the cox proportional hazard model, tumor size <3cm in diameter was associated with increased local control (HR 0.143, 95% CI 0.031-0.661, p=0.013). Extent of resection and number of tiles used during surgery were not associated with local control, p=0.854 and p=0.688, respectively.

Adverse events

Overall, 2 of the 49 tumors treated (4%) exhibited local adverse radiation effects (ARE), both cases were asymptomatic and managed with close observation. ARE occurred at 6 months post-operatively in one patient and at 13 months in the other. The number of tiles was not significantly associated with ARE (p=0.484).

Table 2 summarizes treatment complications, including the CTCAE grade. In total, 5 patients (11%) reported adverse events (AEs) over the duration of study follow-up, all characterized as possibly attributable to GT and none as definitely attributable to GT placement. In the initial 7-day post-operative period, one patient developed an intracerebral hemorrhage that was treated medically and did not require surgical evacuation. Surgical site infection occurred in two patients, within the first 30 days post-operatively in one and at 3-months following wound dehiscence in the other. Both cases required hospitalization with antibiotics and surgical wound washout. Another patient reported seizures at one year following surgery that was medically managed. Lastly, one patient was identified to have a subacute lacunar ischemic infarct more than 15 months after surgery and managed medically.

Discussion

High-grade meningiomas, comprising WHO grade 2 (atypical) and WHO grade 3 (anaplastic) tumors, account for approximately 5-10% and 1-5% of all meningiomas respectively, and have been associated with significantly increased recurrence rates, morbidity, and mortality compared to benign meningiomas[19, 20]. These tumors demonstrate more aggressive biological behavior, resulting in substantially reduced progression-free survival and overall survival despite maximal surgical resection and adjuvant radiotherapy[19-21]. Even among high-grade meningiomas, prognosis varies considerably with median overall survival of 14.7 years for WHO Grade 2 versus significantly worse prognosis for WHO Grade 3[21-23].

In this study, we explored patient characteristics, survival outcomes and local control with GT placement for aggressive recurrent high-grade meningioma. This series introduces two novel aspects: first, it represents the largest published application of Cs-131 seed brachytherapy in high-grade meningioma treatment; second, data on safety, survival and adverse effects are reported.

By integrating GT directly into the surgical cavity following meningioma resection, radiation can commence immediately postoperatively when residual tumor burden is minimized, bypassing the typical 3–4 week wait for postoperative healing before stereotactic radiosurgery[24]. Unlike standard postoperative SRS, which mandates expanded margins to account for uncertain cavity geometry, the conformable Cs-131 tiles deliver highly localized radiation precisely to the resection bed[25-27]. This intraoperative approach eliminates the need for multiple outpatient radiotherapy sessions, thereby reducing logistical barriers—such as transportation, repeat imaging, and insurance approvals—thus ensuring 100% treatment compliance[28, 29].

No reliably effective treatment modality currently exists for aggressive meningiomas that progress following primary irradiation. In salvage scenarios, re-irradiation is typically delivered via fractionated external beam radiation therapy (EBRT) or SRS, employed either as adjuvant therapy following surgical resection or as definitive monotherapy[30-32].

Currently, the highest level of evidence for EBRT in WHO grade 2 meningiomas is reported by the RTOG 0539 and EORTC 22042 trials[33, 34]. Following complete surgical resection, 60 Gy postoperative EBRT achieved a 3-year progression-free survival rate of 88.7% in EORTC 22042[33], while intermediate-risk meningioma patients treated with 54 Gy in 30 fractions achieved a 3-year progression-free survival of 93.8% in RTOG 0539[34].

While extensively studied for benign meningiomas, the application of SRS to WHO grade 2 and 3 tumors lacks robust evidence. High-grade meningiomas treated with radiosurgery exhibit failure rates comparable to those seen after fractionated radiotherapy, with progression occurring both within and beyond treatment volumes. The combination of microscopic dural infiltration characteristic of aggressive meningiomas and the reduced margins typical of radiosurgical planning contributes to limited durability, reflected in 5-year progression-free survival of 34-56%[35-39]. A significant proportion of

failures occur in untreated regions of the surgical cavity[40]. Nevertheless, in heavily pretreated patient populations, the spatial precision of SRS mitigates the substantial risks of wound dehiscence and radiation-induced tissue injury that accompany large-volume irradiation strategies.

Treatment efficacy

In this study we reported the largest cohort to date of recurrent high-grade meningioma treated with GT radiotherapy. The median OS reported in this series is on par with previously reported prognosis in similar cohorts[41, 42]. Repeat irradiation for meningioma recurrences poses significant challenges due to the necessity of treating extensive and irregular target volumes. Given that patients may experience prolonged survival following recurrence, the potential for late-onset toxicities plays a critical role in selecting the optimal salvage approach.

While the idea of utilizing brachytherapy to treat intracranial neoplasms dates back to Harvey Cushing, few studies have rigorously studied the outcomes of such modality[43]. Recent studies have explored the utility of I-125 seeds in the operative bed after resection for recurrent atypical and malignant meningioma. The largest of these studies was reported by *Magill et* al., a 25-year retrospective series of 42 patients demonstrating median progression-free survival of 20.9 months for atypical meningiomas and 11.4 months for malignant meningiomas, with median overall survival after diagnosis of 11.1 years and 9.1 years, respectively[44]. Despite a 16% rate of radiation necrosis, the study supports brachytherapy as a salvage option for heavily pretreated aggressive meningiomas, with 85% of patients having received prior radiation therapy.

More recently, utilization of Cs-131 seeds for the treatment of high-grade meningioma reported increased biological safety and efficacy. Cs-131 demonstrates significantly better dosimetric characteristics compared to Iodine-125 with superior homogeneity and conformity indices indicating more uniform dose distribution that more precisely matches the clinical target volume[45].

Comparative Local Control: GammaTile Versus External Beam Radiotherapy and Radiosurgery

The majority of patients in the present series had already failed cranial irradiation, and the appropriate comparison for such a cohort is the salvage literature rather than the upfront adjuvant trials. In our series, actuarial local control was 94% and 75% at 6 and 12 months, with a median time to local failure of 18 months, figures that compare favorably with published salvage outcomes.

The most methodologically informative comparisons are those in which patients serve as their own controls or are matched to contemporaneous cohorts. Mooney et al. evaluated 27 recurrent high-grade meningiomas that had exhausted external beam options and found that brachytherapy with planned gross total resection significantly improved tumor control relative to prior treatment, with 6- and 12-month progression-free survival (PFS) of 92.3% and 84.6%[46]. Brachman et al. demonstrated the same effect using Cs-131 collagen tiles: across 20 previously irradiated meningiomas, 18-month PFS rose from 50% after the most recent prior therapy to 89% after implantation in the same tumors[11]. Our 6- and

12-month local control falls within this range and closely matches the initial multi-institutional report from this registry (94.4% and 78.3%)[47].

Where direct comparison with radiosurgery has been undertaken, it favors brachytherapy. In a matched-pair analysis of resected brain metastases, Julie et al. observed significantly greater freedom from local recurrence after Cs-131 than after postoperative SRS (p=0.027), with radiation necrosis in 3.3% versus 10.0%[48]. The advantage is attributed to the interval between resection and SRS, during which repopulation may occur, and to the reduced conformality of radiosurgery for large cavities—both directly relevant to the large tumors treated here. In salvage meningioma series, radiosurgery achieves comparable control at considerably greater costs. Peng et al. reported adverse radiation effects in 33.8% after repeat radiosurgery with 3-year PFS of 43.8%, and Desideri et al. a 3-year second PFS of 51.5% across 181 re-irradiated recurrences, against an adverse radiation effect rate of 4% in our cohort[8, 49].

Fractionated EBRT benchmarks derive from a different population. RTOG 0539 and EORTC 22042-26042 enrolled radiation-naïve patients[29,30], and even in the high-risk stratum—the closest analogue to our cohort—3-year local control was 68.9%, with essentially all progression occurring in-field[33, 34, 50]. That failure pattern argues for dose intensification at the margin. Escalation to ≥66 Gy EQD2 improved PFS and reduced local failure among high-grade meningiomas, and the FIRESTORM meta-analysis confirmed superior 3-year PFS with the equivalent biologically effective dose of ≥79.2 Gy at $\alpha/\beta = 10$ (86.4% versus 55.6%)[51, 52]. Such escalation is rarely feasible after prior irradiation. GT offers a different form of intensification: the steep falloff of low-energy Cs-131 concentrates dose within the first few millimeters of the cavity, where physical doses reach 80–120 Gy, while the prescription dose at 5 mm (BED 51.5 Gy) remains comparable to hypofractionated stereotactic regimens, limiting exposure of previously irradiated parenchyma and scalp, and is delivered without the six-week course or treatment delay that fractionated therapy requires[11, 27, 53].

Safety and adverse effects

In our cohort, GT placement for high-grade meningiomas demonstrated to be safe with only 4% of tumors exhibiting ARE, all of which asymptomatic, discovered on follow-up radiographic surveillance and required no intervention. Despite their aggressive neoplastic nature, the tumors in our cohort demonstrated below average rates of radiation necrosis, compared with previously reported rates of 10% with GT therapy[11]. Similarly, *Peng et al.* published a recent series of 112 patients that underwent SRS to recurrent high-grade meningiomas. The reported rates of radiation necrosis in this cohort were 20%, and were largely asymptomatic[49]. We believe the lower rates of radiation necrosis with Cs-131 compared to external radiation sources is attributable its low-energy 30 keV x-rays, which together with the precipitous dose attenuation inherent to brachytherapy delivery, result in substantially reduced irradiation of normal intracranial structures. Furthermore, the intracavitary placement of these low-energy sources preferentially spares extraneural tissues in the surgical field, notably the scalp wound and reconstructed

cranium. With increased familiarity with the technology and careful patient selection, rates of radiation necrosis have been kept to a minimum.

In our cohort, two patients that were colonized with MRSA developed post-operative superficial tissue infection necessitating antibiotics and surgical washout. Notably, the tile carriers were retained during wound washout, and the infection had fully resolved by the six-month follow-up without further complications, implying that removal of the GT seeds is unnecessary when the infectious process is confined to the superficial tissue. These rates of infection are below those reported by Koch et al., with up to 40% of patients requiring reoperations from surgical site infections and local wound complications following Cs-131 and I-125 brachytherapy for high grade meningiomas[54]. Prior literature indicates that complication rates for craniotomy for tumor resection is 7%, which may increase to 31% when postoperative nausea and vomiting are incorporated into reporting metrics[55, 56]. The adverse event rate observed with GT implantation demonstrates equivalence to these benchmarks. In our series, tension-free flap closure and adherence to institutional guidelines and principles of wound handling such as maximizing viability of the skin edges maintained low rates of local wound complications.

Limitations

Our study has limitations. The retrospective cohort study is constrained by evolving treatment protocols over the study period, which complicates consistent assessment of patient follow-up and therapeutic outcomes. Furthermore, the absence of a control group limits interpretation of survival and local control, as some tumors may have achieved local control due to the repeat surgery alone. Lastly, variations across institutions including techniques in tile placement and handling, interpretation of follow-up imaging and collection of patient information limit the generalizability of the results. Prospective clinical trials are therefore required to validate the effects of GT in high-grade meningioma on these clinical endpoints.

Conclusion

In the modern era of cranial tumor surgery, GammaTile brachytherapy demonstrated favorable local control and survival outcomes in patients with recurrent high-grade meningioma, with minimal treatment-related toxicity observed across the cohort. Higher baseline KPS and smaller tumor diameter were associated with increased OS and local control, respectively.

Declarations

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Tables

Table 1
Patient and Treatment Characteristics

Characteristic	**N = 44[1] Patients**
Tumors Implanted (n)	49
Mean Age, (SD)	58 (± 14.7)
Sex (n, %)	
Male	27 (61%)
Female	17 (39%)
Race (n, %)	
Black	8 (18%)
White	29 (66%)
Asian	7 (16%)
BMI, median (range)	26 (23–31)
Presenting Symptom	
Headache	13 (30%)
Seizure	13 (30%)
Focal neurological deficit	26 (59%)
Confusion	7 (16%)
Asymptomatic	4 (9%)
Meningioma Grade	
WHO Grade II	26 (53%)
WHO Grade III	23 (47%)
Median Follow Up, months (range)	7 (3–16)
Median Tumor Diameter, cm (range)	4.4 (2.5–5.8)
Prior Treatment	
Fractionated SRS (2–5 fractions)	20 (45%)
Single fraction SRS	15 (34%)
WBRT	1 (2%)

[1] Mean (SD); n (%); Median (Interquartile Range)

Characteristic	N = 44[1] Patients
Surgical resection	8 (18%)
KPS at Surgery (%)	
80 or above	34 (77%)
Below 80	10 (23%)
Extent of Resection	
Gross Total Resection (%)	35 (71%)
Near Gross Total Resection	10 (20%)
Subtotal Resection	4 (9%)
Number of Tiles Placed, median (range)	6 (2–9)
KPS at Last Follow-Up (%)	
80 or above	29 (66%)
Below 80	15 (34%)
Cause of Death	
Neurologic	3 (7%)
Non-neurologic	5 (11%)
[1] Mean (SD); n (%); Median (Interquartile Range)	

Table 2

Adverse Events Reported in Patients Who Received GammaTile for Grade II-III Meningioma

Patient	Time after surgery (days)	AE CTCAE Grade	Type	Action Taken	Related to Surgery? (Definite, Probable, Possible)	Related to GT? (Definite, Probable, Possible)
1	463	3	Subacute lacunar infarct	Medication	Possible	Possible
2	387	3	Seizure	Medication	Possible	Possible
3	93	3	Wound dehiscence	Surgical Intervention	Definite	Possible
4	6	3	Intracerebral hemorrhage	Medication	Possible	Possible
5	22	3	Wound dehiscence	Surgical Intervention	Definite	Possible

Figures

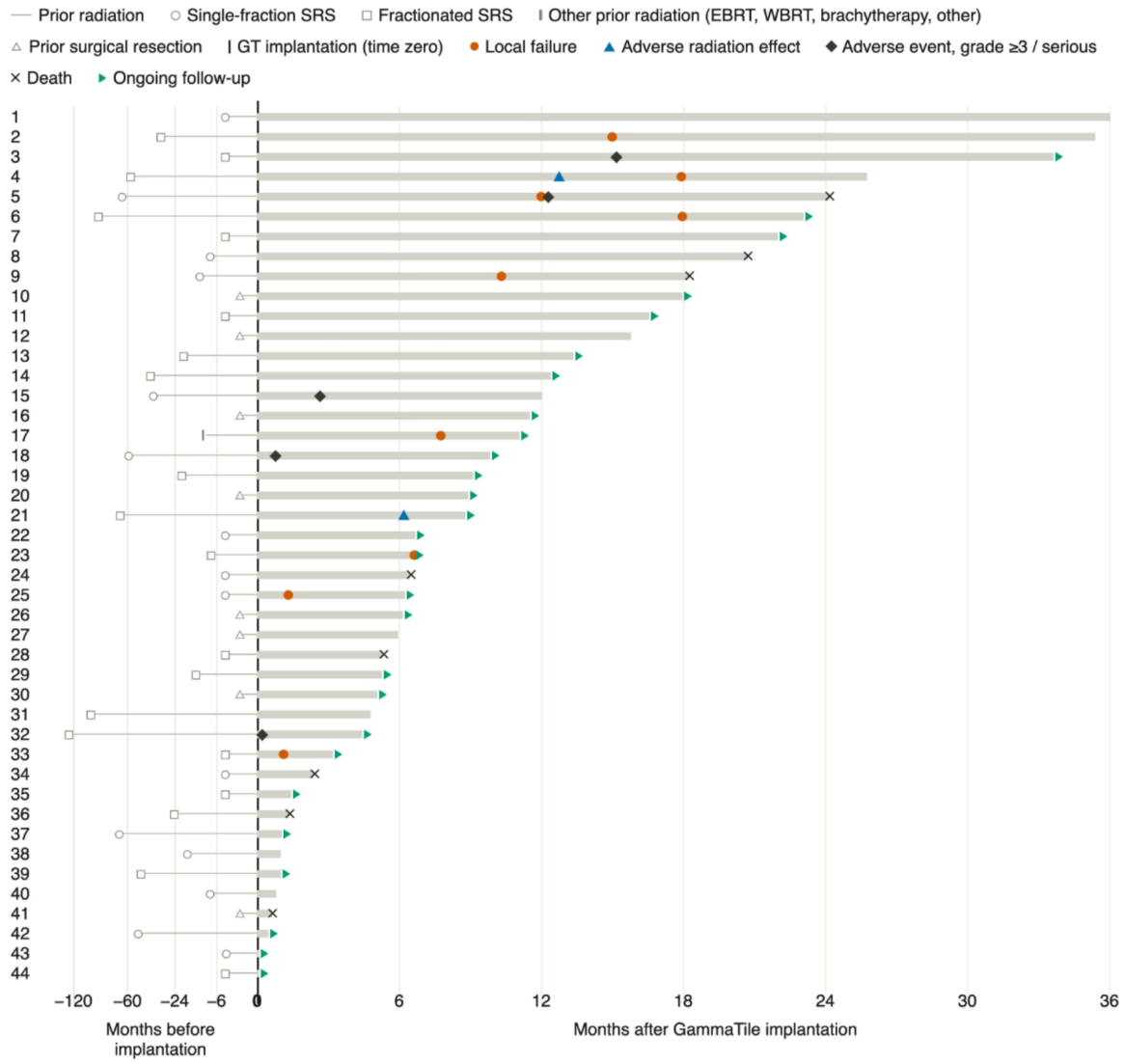


Figure 1

Patient-level timelines of prior treatment and post-implantation outcomes

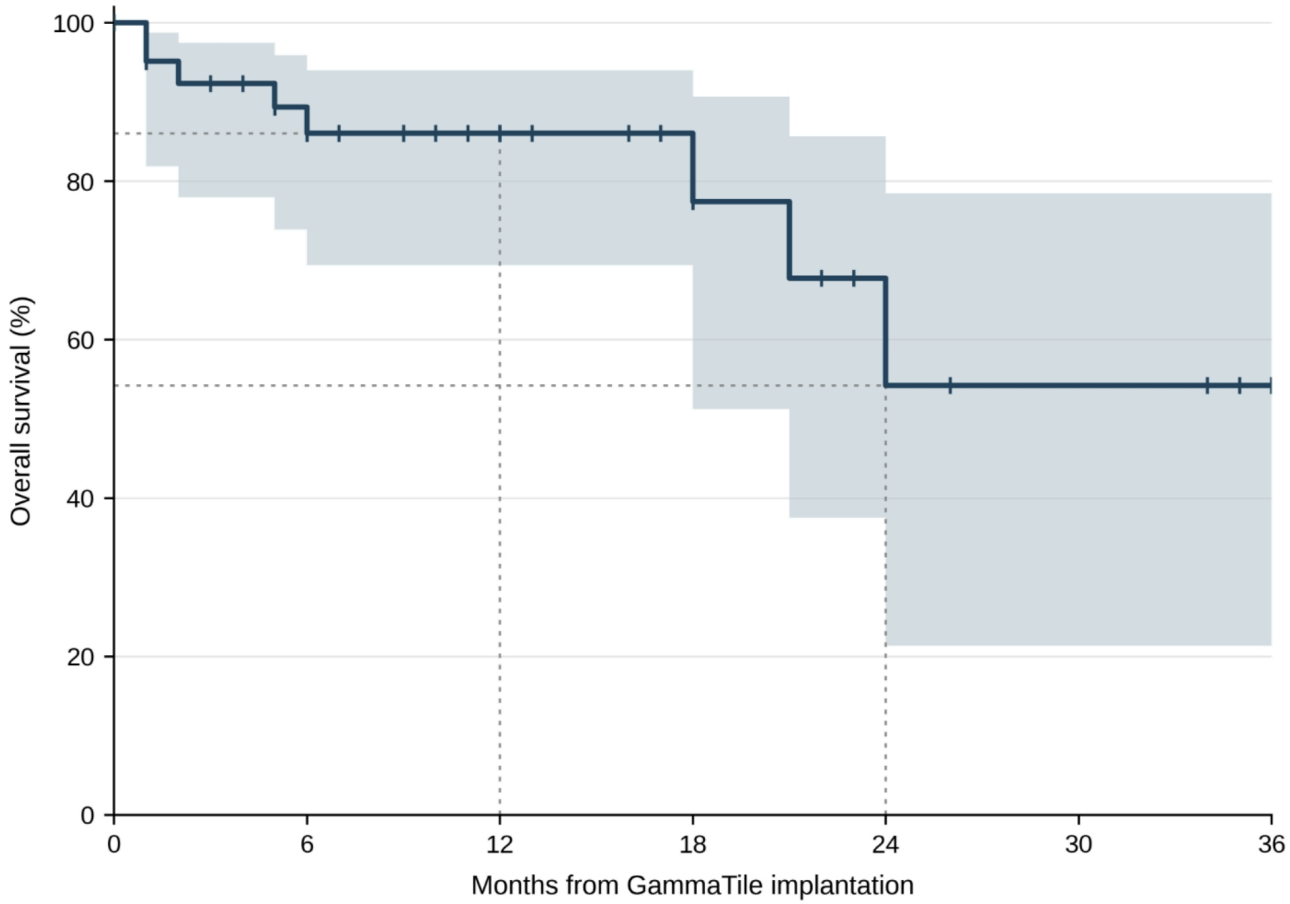


Figure 2

Kaplan-Meier Curve for Overall Survival

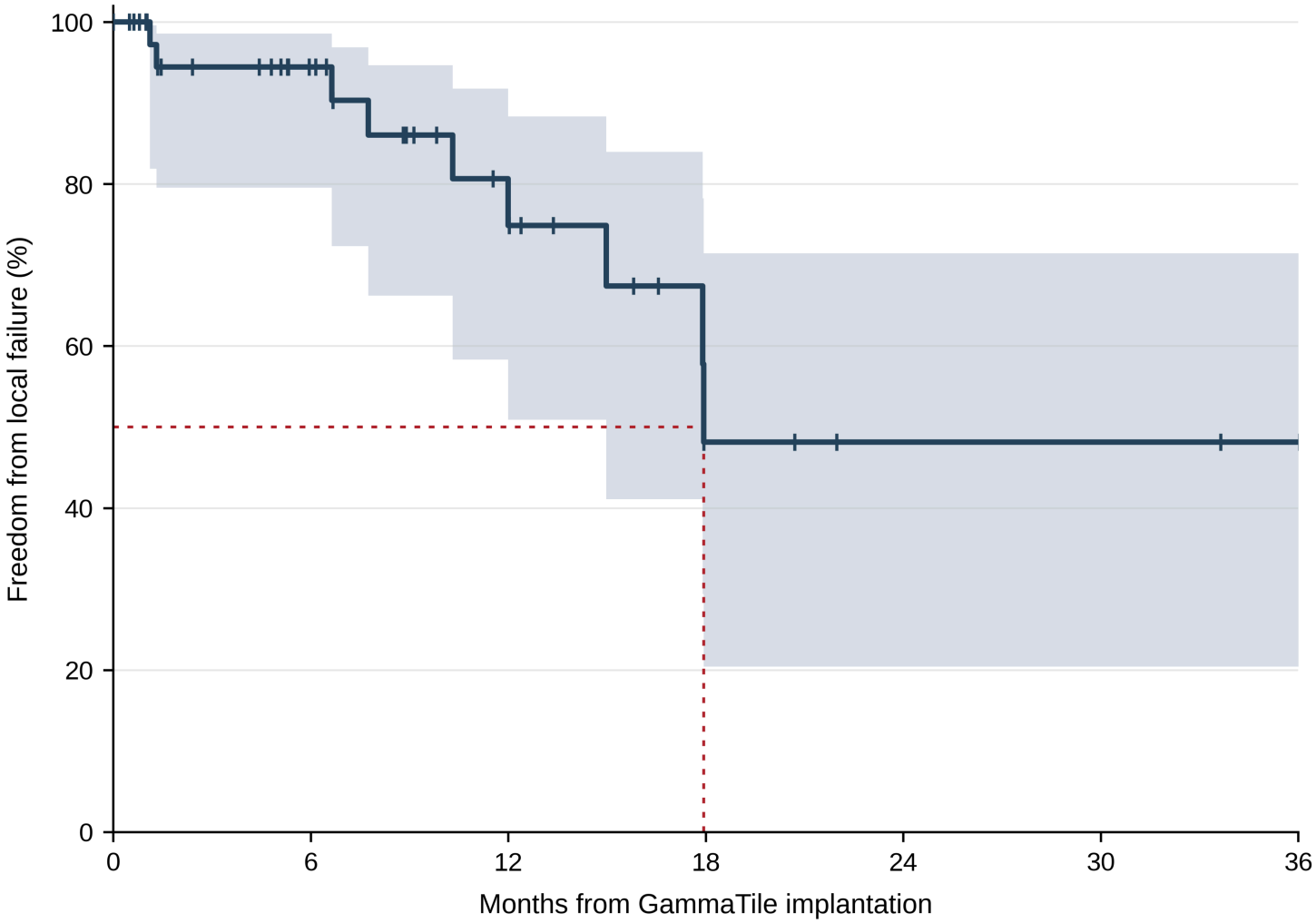


Figure 3

Kaplan-Meier Curve for Local Control