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RESEARCH

Gamma knife radiosurgery in pediatric neuro-oncology: histology-specific outcomes and age-adapted procedural strategies

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Abstract

Purpose Gamma Knife radiosurgery (GKRS) is increasingly applied in pediatric neuro-oncology; however, integrated analyses of outcomes and procedural factors remain limited. This study evaluated histology-specific outcomes and technical considerations of GKRS for pediatric brain tumors.

Methods This study retrospectively analyzed 139 GKRS procedures performed in 108 pediatric patients (age 3–18 years) with brain tumors between 2002 and 2024. The clinical, radiological, dosimetric, and anesthetic data were analyzed. Progression-free survival (PFS) was estimated by Kaplan–Meier analysis and stratified by tumor histology.

Results The mean age at GKRS was 12.4 years (M: F ratio 1:1.16). The most common histologies were craniopharyngiomas (31 procedures), vestibular schwannomas (20), and pilocytic astrocytomas (16). The mean target coverage was 96.9% and the mean prescription dose was 18 Gy. Frameless mask fixation was feasible from age 6 and frame-based fixation from age 12. General anesthesia was required in 25.9%, predominantly in younger or uncooperative patients (8.5 vs 14.0 years, $p < 0.001$). Pediatric-type diffuse high-grade gliomas had the poorest outcomes (PFS 2.6 months, 100% mortality). Craniopharyngiomas showed high recurrence (48%) but a long failure interval (35.8 months) and low mortality (8%). Benign and low-grade tumors showed durable local control with a 5-year PFS exceeding 70%.

Conclusion GKRS provides durable local control in selected benign and low-grade pediatric brain tumors; however, outcomes remain poor in aggressive histologies, with high rates of progression and mortality. These findings highlight the importance of histology-based patient selection and integration of GKRS into multimodal treatment strategies. Age-adapted procedural approaches facilitate safe application in pediatric patients.

Keywords Pediatric · Radiosurgery · Neoplasm · Anesthesia · Progression · Mortality

Introduction

Pediatric brain tumors are the most common solid tumors in children and are a leading cause of cancer-related morbidity and mortality [1]. The anatomical complexity, histological heterogeneity, and vulnerability of the developing brain pose significant therapeutic challenges [2]. Although conventional treatments, such as maximal safe resection, chemotherapy, and radiotherapy, have improved survival, they carry substantial risks of long-term neurocognitive, endocrine, vascular, and secondary malignancy complications, particularly after high-dose or extended-field irradiation in young children [3, 4].

Stereotactic radiosurgery (SRS) offers a focused alternative that delivers high-dose radiation to a precisely defined target in one or a few sessions while minimizing exposure to the surrounding normal brain [5, 6]. Gamma Knife radiosurgery (GKRS), designed specifically for intracranial lesions, provides a highly conformal treatment using cobalt-60 sources and a collimator-based system [7, 8]. Although well established in adults, its use in children has been limited by concerns regarding anesthesia, skull development, and long-term radiation effects [7, 9]. Recent advances, including mask-based immobilization, volumetric planning, and image-guided verification, along with improved pediatric anesthetic techniques, have enhanced the feasibility and safety of GKRS in children [7, 10, 11].

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Nonetheless, most available data are derived from a small, single-pathology series with a short follow-up period and a heterogeneous methodology. In this study, we report a 20-year single-institution experience with GKRS for pediatric brain tumors, analyzing 139 GKRS procedures in 108 patients. This study analyzed patient characteristics, dosimetry, anesthetic strategies, and clinical outcomes to inform patient selection and optimize treatment planning for this population.

Methods

Study design and population

The database of patients who underwent GKRS from January 2002 to February 2024 at our institution was retrospectively queried. In total, 360 patients aged ≤ 18 years were identified. Among them, 108 patients who were diagnosed with brain tumors and underwent 139 GKRS procedures were included in the analysis. The patients' medical records, including clinical, pathological, neuroimaging, and GRKS-related data, were reviewed. Tumor histology was classified according to the 2021 World Health Organization (WHO) classification of tumors of the central nervous system (CNS) [12]. Data on the anesthetic methods were also collected.

For benign and low-grade tumors, GKRS was primarily performed for residual or recurrent lesions requiring local control. In contrast, for aggressive histologies such as high-grade glioma and medulloblastoma, GKRS was generally performed after prior standard therapies, including surgery, chemotherapy, and/or radiotherapy, and was applied for focal salvage, consolidation of residual disease, or palliative local control rather than as primary treatment.

This study was conducted in accordance with the Declaration of Helsinki and was reviewed and approved by the Institutional Review Board (IRB) of our institution. The requirement for informed consent was waived due to the retrospective design of the study.

GKRS technique

GKRS was performed using the Leksell Gamma Knife systems: Model C (2002–2010), Perfexion (2010–2015), and Icon (2015–2024; Elekta Instrument AB, Stockholm, Sweden). High-resolution contrast-enhanced magnetic resonance imaging (MRI) was performed within 24 h before treatment for stereotactic planning. Fixation has been achieved either by a stereotactic frame or a frameless thermoplastic mask since the Gamma Knife Icon was introduced. General anesthesia was administered to uncooperative or younger patients, while older children underwent procedures under local anesthesia or monitored anesthesia care (MAC).

Treatment planning was conducted using Leksell GammaPlan software (Elekta Instrument AB, Stockholm, Sweden). Target volumes were manually delineated by a neurosurgeon. The prescription isodose volume (PIV) and line, most commonly the 50% line, were selected to achieve maximal coverage of the target volume. Marginal doses were determined based on the tumor histology, size, and proximity to critical structures. Dosimetric parameters, including tumor volume (TV), PIV, coverage rate (TV/PIV), and prescription dose (Gy), were recorded. For frame-based treatments, treatment was delivered immediately after planning on the same day, whereas mask-based treatments occasionally employed fractionation in selected cases with large TVs or lesions close to the eloquent structure. Post-treatment monitoring was performed in the recovery unit, and patients undergoing general anesthesia were routinely admitted overnight.

Outcome assessments

The clinical outcomes were assessed through clinical and radiological follow-ups. At each follow-up visit, a complete neurological examination was performed. Follow-up MRI was performed 3–6 months after GKRS, every 6 months for the first two years, and annually thereafter. Tumor response was evaluated on follow-up MRI, and local failure was defined as a ≥ 25% increase in TV at least 3 months after GKRS [13]. The primary outcomes included local control, progression-free survival (PFS), and mortality. PFS was defined as the interval from GKRS to radiographic progression at the treated site and was evaluated according to tumor histopathology using the Kaplan–Meier method. PFS was analyzed on a lesion-based basis, as GKRS is a focal treatment intended for local tumor control. In patients who underwent multiple GKRS procedures, each treated lesion was considered an independent treatment episode for local control analysis.

Statistical analysis

Statistical analyses were performed using the R Statistical Software (version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria). Kaplan–Meier survival curves were generated using the survival and survminer packages, and the results were reported with 95% confidence intervals (CIs). Continuous variables were summarized as medians and compared using the Mann–Whitney U test. A p-value < 0.05 was considered statistically significant. As analyses were performed per treated lesion, potential within-patient clustering effects in individuals who underwent

multiple GKRS procedures were not modeled separately, and findings should be interpreted in this context.

Results

Patient characteristics

In total, 139 GKRS procedures were performed in 108 pediatric patients with brain tumors (Table 1). The mean age at GKRS was 12.4 years (range, 3–18 years), with a male-to-female ratio of 1:1.16. Most patients (n = 91) underwent a single GKRS, whereas 17 patients underwent multiple procedures. The mean follow-up duration after GKRS was 83.8 months (range: 1.5–256.5 months). The most common histopathological diagnoses were sellar region tumors (n = 29 patients), followed by glioma, glioneuronal, and neuronal tumors (n = 28), cranial and paraspinal nerve tumors (schwannoma, n = 17), and ependymal tumors (n = 12) (Table 2). Among the six patients with meningiomas, three were diagnosed radiologically, and three were diagnosed histologically. Of the histologically confirmed cases, two were WHO grade 2 and one was WHO grade 1. Additionally, two patients had neurofibromatosis type 2 (NF2)-related schwannomatosis (SWN). Multiple GKRS were performed in patients with craniopharyngiomas, pilocytic astrocytomas, pediatric-type diffuse high-grade gliomas (PDHGGs), schwannomas, ependymal tumors, and meningiomas (Table 3).

Clinical outcomes according to histology

The mean TV was 3,768 mm^3, and the mean PIV was 3,447 mm^3, yielding a mean coverage (TV/PIV) of 96.9%. The mean prescription dose was 18 Gy, with variations according to tumor type and location. Meningiomas had the largest mean TV (9,903 mm^3), whereas pilocytic astrocytomas had the smallest (999 mm^3). Higher prescription doses were administered to pituitary neuroendocrine tumors (24 Gy) and medulloblastomas (23.5 Gy).

Seventeen patients underwent multiple treatments, comprising 48 GKRS sessions. Tumor progression occurred in 40 patients (37%), involving 62 GKRS sessions, with a mean time to treatment failure (TTF) of 26.3 months. Mortality was observed in 21 (19.4%) patients after 31 GKRS sessions. The highest progression rate was observed for PDHGGs (80%), followed by craniopharyngiomas (48%), ependymal tumors (41.7%), and pilocytic astrocytomas (28.6%). The shortest mean TTF was observed in PDHGGs (4.3 months), followed by ependymal tumors (8.9 months). Mortality was most frequent in patients with PDHGGs (100%), followed by medulloblastomas (50%), ependymal tumors (33%), and meningiomas (33%). PDHGGs showed the poorest prognosis, with the highest progression and mortality rates, and the shortest TTF. Ependymal tumors also have high progression and mortality rates; notably, two patients in this group underwent 13 GKRS sessions for multiple recurrences. Craniopharyngiomas demonstrated a high progression rate (48%), but had a relatively long mean TTF (35.8 months) and low mortality (8%). Benign tumors such as schwannomas and meningiomas exhibited slower progression (progression rates of 17.6% and 28.6%, respectively), longer mean TTF (51.0 and 22.3 months, respectively), and low mortality (5.9% and 0%, respectively). Representative cases demonstrate radiological responses to GKRS according to tumor histology (Fig. 1).

Kaplan–Meier analysis revealed significant differences in PFS among the histological subgroups (Fig. 2). PDHGGs showed a median PFS of 2.6 months and a 1-year PFS of 0%, with all patients dying during follow-up (Fig. 2-A). Craniopharyngiomas had a median PFS of 74.4 months and a 5-year PFS rate of 51.2% (Fig. 2-B). Ependymal tumors had a median PFS of 7.4 months, with 1-year and 5-year PFS rates of 49.3% and 26.3%, respectively (Fig. 2-C). Meningioma achieved durable control with a median PFS of 30.8 months, and 1-year and 5-year PFS rates of 85.7% and 42.9%, respectively (Fig. 2-D). Benign tumors, such as schwannomas and pilocytic astrocytomas, generally maintained long-term stability, with median PFS not reached; however, occasional progression was observed (5-year PFS of 75.3% and 75%, respectively) (Fig. 2-E, F). During the follow-up period, no grade ≥ 3 toxicities related to GKRS were observed based on the Common Terminology Criteria for Adverse Events.

Among the patients with tumor progression after GKRS, subsequent management was tailored according to tumor histology. In craniopharyngiomas (n = 12), treatment included surgery (n = 6), repeat GKRS (n = 4), and combined surgery with repeat GKRS (n = 2). Schwannoma recurrences (n = 3) were managed with surgery

Table 1 Baseline characteristics and clinical variables related to GKRS (n = 139 GKRS in 108 patients)

Baseline characteristics	Measurement
Male: Female	50: 58 (1: 1.16)
Age at GKRS, yrs (mean, range)	12.4 (3–18)
Number of GKRS per patient	
1	91
2	12
3	2
5	2
8	1
Post-GKRS follow-up period, mos (mean, range)	83.8 (1.5–256.5)

GKRS Gamma Knife radiosurgery, *yr* Year, *mo* Month

Table 2 Histopathological diagnosis of pediatric brain tumors

Histopathologic diagnosis	Number of patients ($n=108$)	Number of GKRS ($n=139$)	Age at GKRS, years (median, range)
Tumors of the sellar region	***n* = 29**	***n* = 35**	
Adamantinomatous craniopharyngioma	25	31	12.0 (3—18)
Pituitary neuroendocrine tumor	4	4	14.5 (12—18)
Glioma, glioneuronal, and neuronal tumors	***n* = 28**	***n* = 31**	
Circumscribed astrocytic gliomas	19	21	
Pilocytic astrocytoma	14	16	12.5 (8—16)
Subependymal giant cell astrocytoma	3	3	11.0 (7—15)
Pleomorphic xanthoastrocytoma	2	2	14.5 (13—16)
Pediatric-type diffuse high-grade gliomas	5	6	15.0 (4—18)
Pediatric-type diffuse low-grade gliomas	2	2	10.5 (7—14)
Glioneuronal and neuronal tumors	2	2	
Central neurocytoma	1	1	17.0
Rosette-forming glioneuronal tumor	1	1	9.0
Cranial and paraspinal nerve tumors	***n* = 17**	***n* = 20**	
Schwannoma	17	20	15.5 (7—18)
Ependymal tumors	***n* = 12**	***n* = 23**	
Ependymal tumors	12	23	9.0 (5—18)
Embryonal tumors	***n* = 6**	***n* = 6**	
Medulloblastoma	4	4	11.0 (9—16)
Atypical teratoid rhabdoid tumor	1	1	17.0
CNS embryonal tumor	1	1	12.0
Meningioma	***n* = 6**	***n* = 14**	
Meningioma	6	14	15.5 (4—18)
Mesenchymal, non-meningothelial tumors	***n* = 3**	***n* = 3**	
Solitary fibrous tumor	1	1	18
Hemangiopericytoma	1	1	12
Chordoma	1	1	6.0
Germ cell tumors	***n* = 2**	***n* = 2**	
Germ cell tumors	2	2	12.5 (11—14)
Metastases to the CNS	***n* = 2**	***n* = 2**	
Metastases	2	2	17.0 (16—18)
Choroid plexus tumors	***n* = 1**	***n* = 1**	
Choroid plexus papilloma	1	1	18.0
Pineal tumors	***n* = 1**	***n* = 1**	
PPID	1	1	15.0
Hypothalamic hamartomas	***n* = 1**	***n* = 1**	
Hypothalamic hamartoma	1	1	16

GKRS Gamma Knife radiosurgery, *CNS* Central nervous system, *PPID* Pineal parenchymal tumor with intermediate differentiation

(n = 1) or repeat GKRS (n = 2). Pilocytic astrocytomas (n = 4) were treated with surgery (n = 2) or repeat GKRS (n = 2), while all recurrent meningiomas (n = 3) underwent repeat GKRS. Among ependymomas (n = 5), management included surgery (n = 1), repeated GKRS (n = 1), combined surgery and repeat GKRS (n = 1), and multimodal therapy including surgery and radiotherapy (n = 2). In high-grade gliomas (n = 4), three patients received multimodal therapy and one received palliative care. The single patient with medulloblastoma progression was managed with palliative care.

GKRS methods in pediatric patients

Among the 139 GKRS procedures performed in pediatric patients, 39 (28.1%) were conducted using frameless thermoplastic mask fixation, whereas 100 (71.9%) employed stereotactic frame fixation (Table 4). General anesthesia was required for 36 procedures

Table 3 Dosimetric parameters and treatment outcomes

	Total (139 GKRS in 108 Patients)	Craniopharyngioma (31 in 25)	Schwannoma (20 in 17)	Pilocytic astrocytoma (16 in 14)	Ependymal tumor (23 in 12)	Meningioma (14 in 6)	PHGG (6 in 5)	PitNet (4 in 4)	Medulloblastoma (4 in 4)
Mean age at GKRS, yrs	12.4 (3—18)	11 (3—18)	14.7 (7—18)	12.3 (8—16)	10.5 (5—18)	14.4 (4—18)	12.8 (4—18)	14.8 (12—18)	11.8 (9—16)
M: F	50:58	16:9	6:11	4:10	4:8	2:4	3:2	2:2	3:1
Mean TV, mm^3	3,768.2 (34—26,100)	2,133.7 (125.6—9,753)	3,215.8 (113—9,429)	999.0 (242.4—2,000)	4,194.6 (475—10,193)	9,903.3 (890.5—26,100)	4,797.5 (1,300—11,600)	6,102.3 (2,201—13,703)	4,150.9 (34—14,676)
Mean PIV, mm^3	3446.8 (34—16,261)	2,061.3 (122.5—9,698)	3,176.4 (112—9,408)	969.0 (231.3—2,000)	4,227.1 (472—10,049)	7,368.5 (883.4—16,261)	4,620.8 (1,300—11,200)	6,046.4 (2,149—13,631)	4,053.5 (34—14,287)
Mean coverage (PIV/TV), %	96.9 (49—100)	96.9 (85—100)	98.3 (92—100)	97.9 (95—100)	97.6 (93—100)	89.4 (49—100)	97.5 (96—99)	98.3 (98—99)	99 (97—100)
Mean prescription dose, Gy	18.0 (9—35)	15.6 (9—25)	15.7 (11—24)	17.1 (13—24)	20.6 (11.5—35)	15.5 (10—20)	16.2 (13—20)	24 (20—30)	23.5 (20—25)
Multiple GKRS	48 GKRS in 17 patients	12 GKRS in 6 patients	6 GKRS in 2 patients	4 GKRS in 2 patients	13 GKRS in 2 patients	12 GKRS in 4 patients	2 GKRS in 1 patient	None	None
Progression, %	40 patients (62 GKRS), 37%	12 patients (14 GKRS), 48%	3 patients (5 GKRS), 17.6%	4 patients (5 GKRS), 28.6%	5 patients (15 GKRS), 41.7%	3 patients (9 GKRS), 50%	4 patients (5 GKRS), 80%	None	1 patient (1 GKRS), 25%
Mean time to Tx failure, mos	26.3 (1.9—114.7)	35.8 (3.5—106.3)	51.0 (7.2—114.6)	22.3 (4.5—65.1)	8.9 (1.9—30.7)	27.8 (4.9—85.2)	4.3 (2.0—11.4)	None	None
Mortality, %	21 patients (31 GKRS), 19.4%	2 patients (2 GKRS), 8%	1 patient (2 GKRS), 5.9%	None	4 patients (8 GKRS), 33.3%	2 patients (6 GKRS), 33.3%	5 patients (6 GKRS), 100%	None	2 patients (2 GKRS), 50%
Mean follow-up, mos	83.8 (1.5—256.5)	98.7 (3.3—256.5)	99.2 (7.3—243.9)	95.6 (24.8—218.8)	52.8 (3.2—249.7)	133.0 (62.2—165.0)	15.7 (1.5—64.0)	81.0 (13.5—225.7)	52.5 (9.9—160)

GKRS Gamma Knife radiosurgery, *PHGG* Pediatric-type diffuse high-grade glioma, *PitNET* Pituitary neuroendocrine tumor, *yr* Years, *M* Male, *F* Female, *TV* Tumor volume, *PIV* Prescription isodose volume, *Gy* Gray, *Tx* Treatment, *mo* Month

Table 4 Anesthetic method for GKRS according to patient age ($n = 139$)

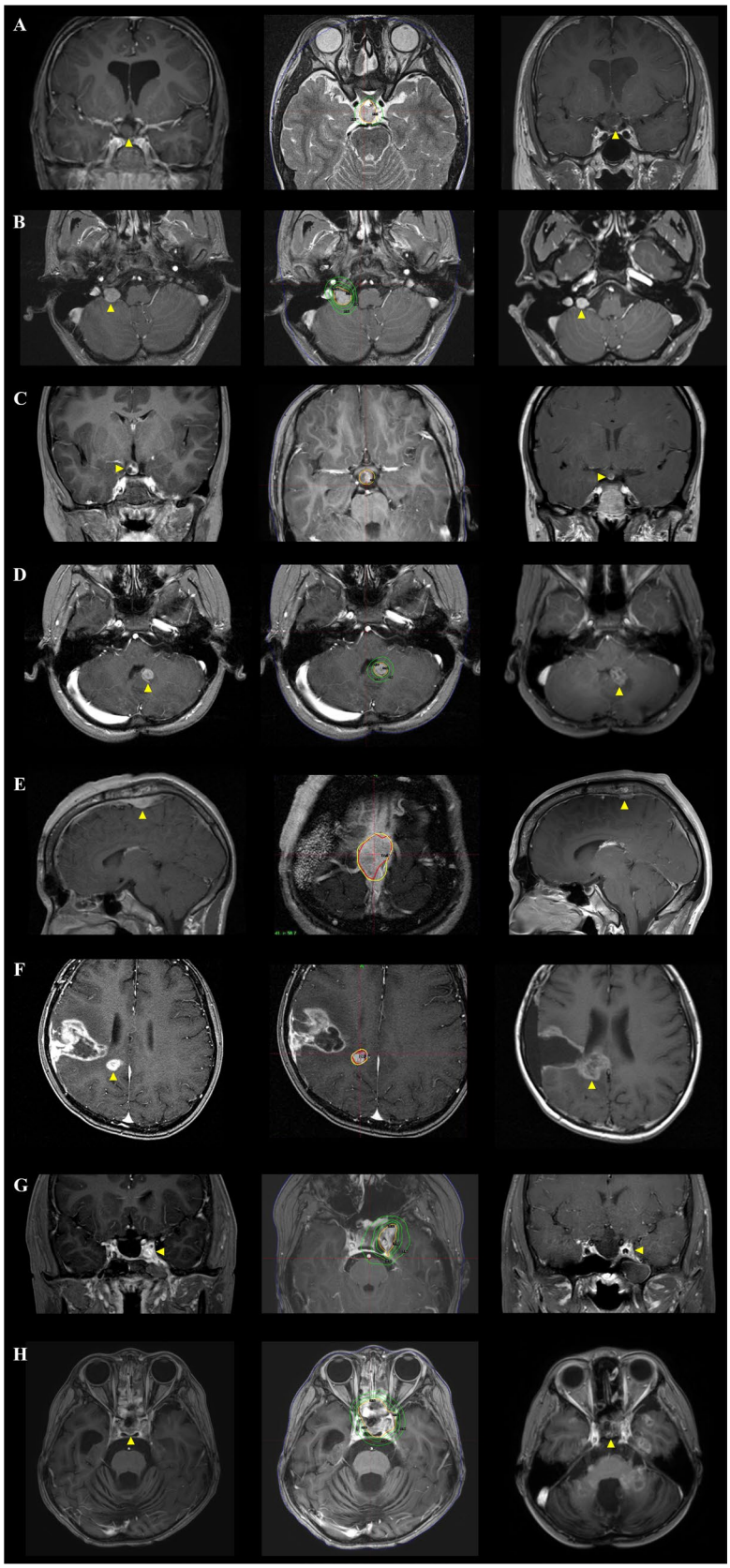
Baseline characteristics	Number of GKRS	Age at GKRS, years (median, range)
Method of fixation		
Mask	n = 39 (28.1%)	
General anesthesia	1	3
Local anesthesia	38	12.0 (6—18)
Frame	n = 100 (71.9%)	
General anesthesia	35	9.0 (3—16)
MAC	2	12.5 (11—14)
Local anesthesia	63	15.0 (12—18)
Method of GKRS		
General anesthesia	36 (25.9%)	8.5 (3—16)
MAC	2 (1.4%)	12.5 (11—14)
Local anesthesia	101 (72.7%)	14.0 (6—18)

GKRS Gamma Knife radiosurgery, *MAC* Monitored anesthesia care

(25.9%), MAC for two procedures (1.4%), and local anesthesia for 101 procedures (72.7%). The median age of patients treated under local anesthesia was 14.0 years (range, 6–18 years), compared to 8.5 years (range, 3–16 years) for those requiring general anesthesia. The median age was significantly higher in the local anesthesia group compared with the general anesthesia group (14.0 vs. 8.5 years, $p < 0.001$). Mask fixation was feasible in cooperative children aged 6 years, whereas awake frame fixation was generally tolerated only in children aged ≥ 12 years. No acute procedural complications related to fixation or anesthesia were observed.

Discussion

This study evaluated 139 GKRS procedures performed on 108 pediatric patients with brain tumors. The analysis integrated histology-specific outcomes with procedural and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◂**Fig. 1** Representative magnetic resonance imaging (MRI) obtained before Gamma Knife radiosurgery (GKRS), at the time of treatment planning, and at last follow-up in pediatric patients with various brain tumor histologies. (**A**) Recurrent adamantinomatous craniopharyngioma after surgical resection. GKRS was performed with a marginal dose of 9 Gy at the 50% isodose line (coverage 98%). At 8-year follow-up, a small residual enhancing lesion attached to the optic nerve remains radiologically stable. (**B**) Right NF2-related vestibular schwannoma. GKRS was delivered with 14 Gy at the 50% isodose line (coverage 98%). At 7 years and 6 months of follow-up, the tumor decreased in size and remained stable, with no hearing deterioration. (**C**) Biopsy-proven pilocytic astrocytoma of the pituitary stalk. GKRS was performed with 13 Gy at the 50% isodose line (coverage 100%). At 6 years and 6 months of follow-up, the lesion shows volume reduction and radiological stability. (**D**) Posterior fossa ependymoma type A (WHO grade 3) recurring after surgery and radiotherapy, presenting as a nodular enhancing mass in the fourth ventricle. GKRS was performed with 15 Gy at the 50% isodose line (coverage 99%). Radiological progression was observed at 1 year and 4 months after treatment. (**E**) NF2-related parasagittal meningioma. GKRS was delivered with 17 Gy at the 50% isodose line (coverage 99%). At 9-year follow-up, the tumor decreased in size and remained stable. (**F**) Pediatric high-grade glioma with corpus callosum recurrence after surgery, chemotherapy, and radiotherapy. GKRS was performed with 20 Gy at the 50% isodose line (coverage 98%). Radiological progression was noted at 3-month follow-up. (**G**) Nonfunctioning pituitary neuroendocrine tumor with left cavernous sinus invasion and postoperative remnant. Fractionated GKRS was delivered (5 Gy×4 fractions at the 50% isodose line; coverage 98%). At 1 year and 6 months of follow-up, no radiological evidence of residual tumor is observed. (**H**) Medulloblastoma with distant sellar recurrence after surgery, chemotherapy, and radiotherapy. Fractionated GKRS was delivered (6 Gy×4 fractions at the 50% isodose line; coverage 97%). At 8-month follow-up, local control was achieved at the treated site; however, diffuse intracranial progression developed

anesthetic considerations within a large single-institution cohort. The findings demonstrated that GKRS was associated with durable local control in selected benign and low-grade tumors, whereas outcomes were limited in aggressive histologies, particularly PDHGGs. The absence of acute procedural complications supports the safety of GKRS in children when anesthesia and fixation are tailored to age and cooperation level. This study highlights the potential role of repeat GKRS in the management of indolent or recurrent lesions, emphasizing the importance of histology-specific treatment planning within a multidisciplinary framework.

GKRS outcomes according to tumor histology

Several studies have evaluated GKRS in pediatric brain tumors [8, 10, 11, 14–18]. Benign tumors, such as meningiomas and vestibular schwannomas, showed favorable local control, which is consistent with our findings (5-year PFS, 42.9% and 75.3%, respectively). In one study of 20 meningiomas and 17 vestibular schwannomas, only 1.6% showed progression after GKRS during 6–48 months of follow-up [8]. Another study that included 40 tumors (25% meningioma, 75% schwannoma) in 26 patients (13 with NF2-related SWN) reported that all tumors either regressed or remained stable during a mean follow-up period of 51 months [14]. Tumor regression was more frequent in sporadic lesions than in NF2-associated tumors (100% vs. 69%; $p=0.036$). In our cohort, meningioma outcomes appeared slightly less favorable than those in previous reports, which may be attributable to the higher proportion of WHO grade 2 meningiomas and NF2-related SWN cases. Low-grade gliomas also showed favorable outcomes, with a 5-year PFS of 75% in our cohort, comparable to previous reports (PFS 83%, median follow-up 74 months) [10, 11]. Craniopharyngiomas exhibited frequent progression (48%), but with a relatively long mean TTF (35.8 months) and low mortality (8%). These outcomes are comparable to those of a large series that reported 5- and 10-year tumor control rates of 70–80% and 60–70%, respectively [16]. In this study, the recurrence rate was 32% and the mean TTF was 34.3 months during the mean follow-up period of 92.9 months. Ependymomas demonstrated variable results, with 41.7% progression in this study, and some patients required multiple GKRS sessions (up to 13). A previous study on 40 intracranial ependymomas reported a 2-year cumulative local failure rate of 25% and a 5-year overall survival rate of 52% [17]. Another study evaluating 48 tumors (28% ependymomas) reported a 2-year cumulative local failure rate of 12.8% [6].

Malignant tumors such as medulloblastoma and PDHGGs had a poor prognosis, with mortality rates exceeding 50%. PDHGG, newly defined in the 2021 WHO CNS classification, showed a median PFS of 2.6 months and a 100% mortality rate in our cohort. Previous studies have reported a median PFS of 11 months for medulloblastoma and 12 months for anaplastic astrocytoma/glioblastoma, with 3-year local control rates of 57% and 60%, respectively [15]. PDHGGs in our cohort showed minimal benefit from GKRS, although the interpretation should be made with caution, given the small sample size.

Overall, the data and prior literature support GKRS as an effective, minimally invasive modality for benign and low-grade pediatric brain tumors, with a role as salvage or adjuvant therapy for craniopharyngioma and selected ependymomas. However, its role in malignant tumors, particularly in PDHGG, remains limited. Histology-specific patient selection, integration into multimodal treatment strategies, and prospective multicenter studies incorporating molecular profiling are needed to refine the indications and improve outcomes in this challenging population.

GKRS methodology in pediatric patients

Technical factors, including the fixation method and anesthesia, are critical determinants of the feasibility and safety of pediatric radiosurgery. In our cohort, frameless mask fixation was used in 39 patients (28.1%) and stereotactic

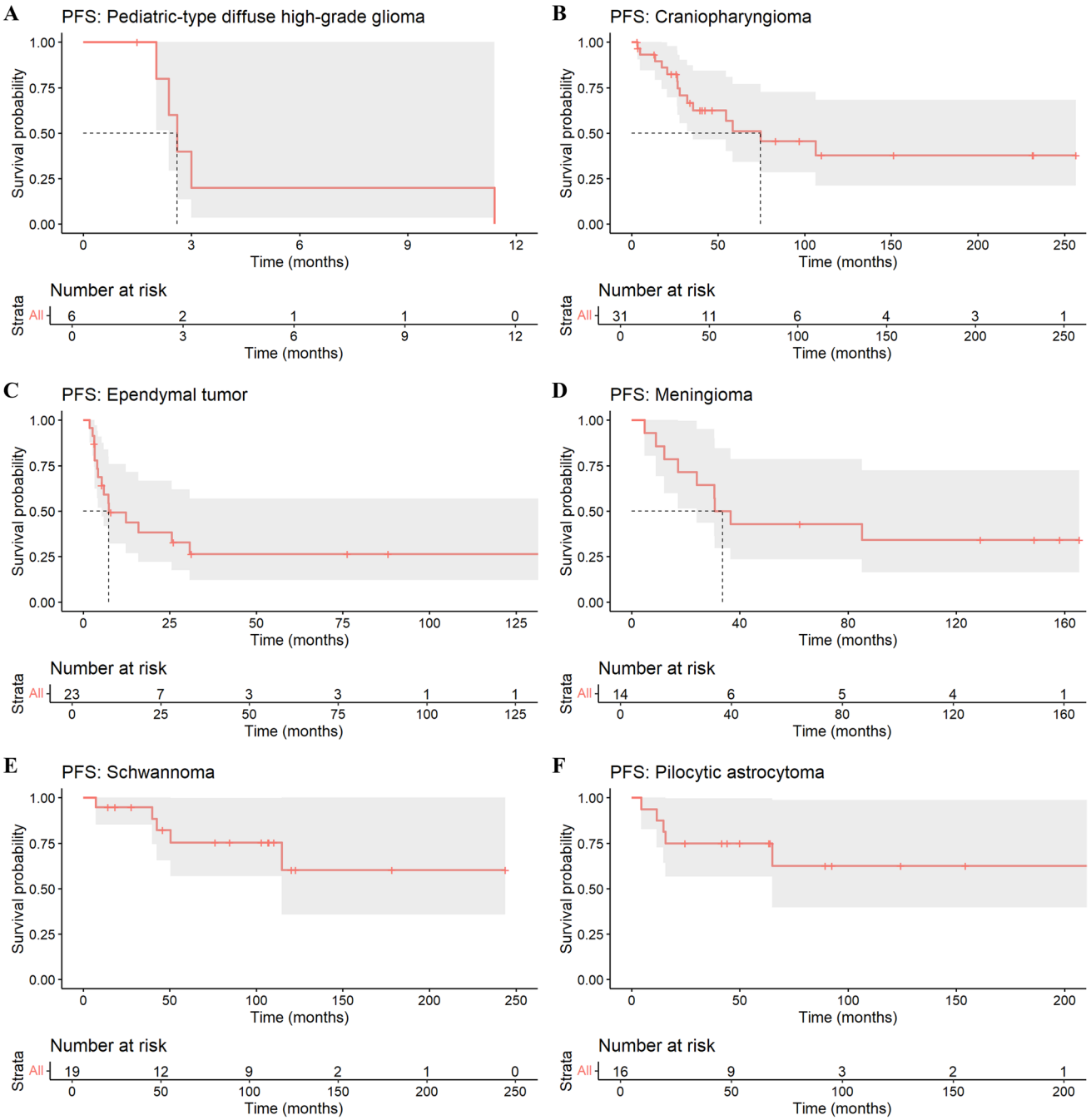

Fig. 2 Kaplan–Meier curve showing the progression of tumors after gamma knife radiosurgery according to histopathological diagnosis. (**A**) Median progression-free survival (PFS) of pediatric-type diffuse high-grade glioma is 2.6 months (95% confidence interval, CI: 2.1—3.1). The 3-month and 1-year PFS rates are 20% and 0%, respectively. (**B**) Median PFS of craniopharyngioma is 74.4 months (95% CI: 16.4–132.4). The 1-, 3-, and 5-year PFS rates are 93.2%, 62.6%, and 51.2%, respectively. (**C**) Median PFS of ependymal tumor is 7.4 months (95% CI: 0–16.2). The 1-, 3-, and 5-year PFS rates are 49.3%, 26.3%, and 26.3%, respectively. (**D**) Median PFS of meningioma is 30.8 months (95% CI: 19.6–42.0). The 1-, 3-, and 5-year PFS rates are 85.7%, 50%, and 42.9%, respectively. (**E**) Median PFS for schwannoma is not reached during the follow-up period. The 1-, 3-, and 5-year PFS rates are 94.7%, 94.7%, and 75.3%, respectively. (**F**) Median PFS for pilocytic astrocytomas is not reached during the follow-up period. The 1-, 3-, and 5-year PFS rates are 87.5%, 75%, and 75%, respectively

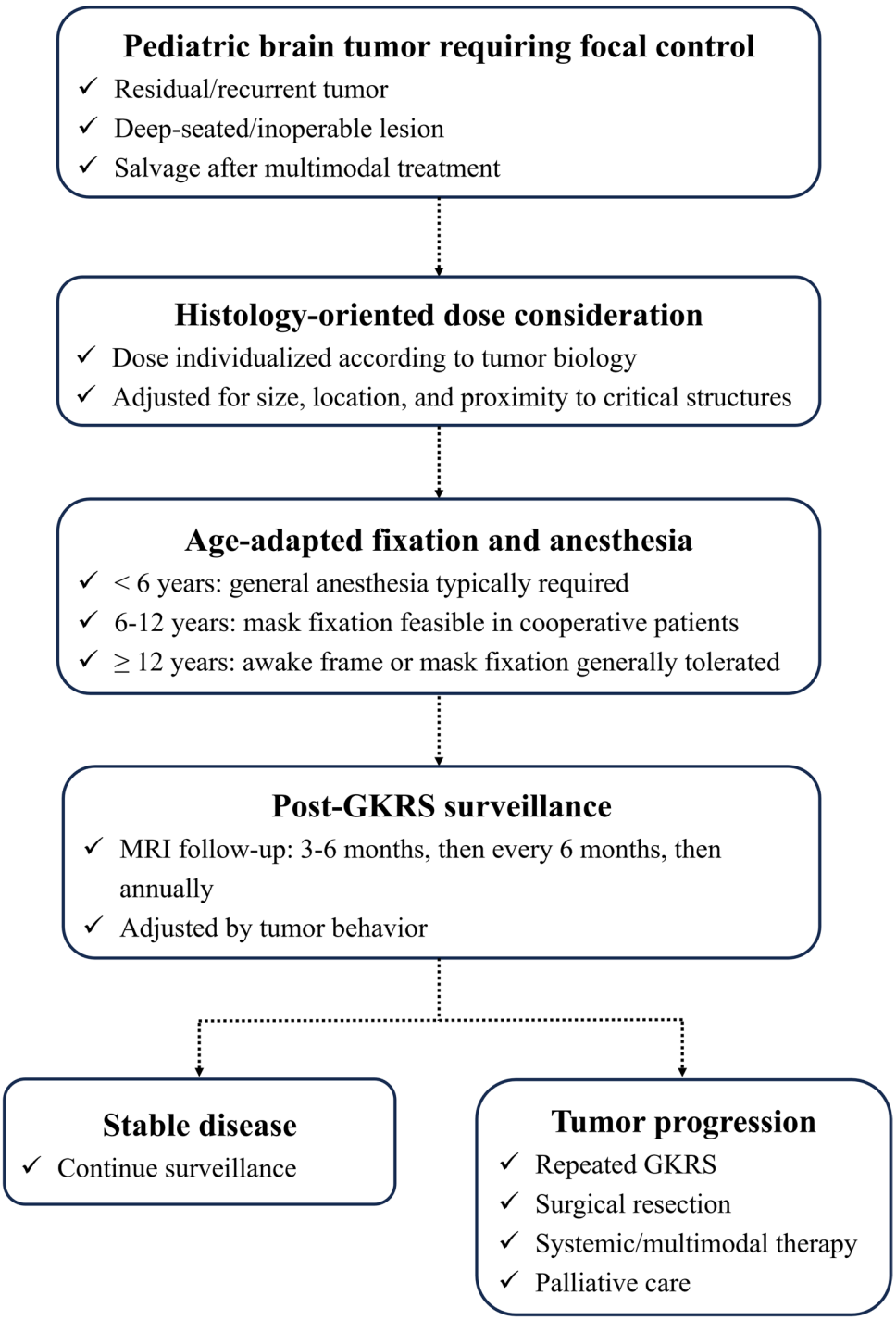

Fig. 3 Conceptual framework for Gamma Knife radiosurgery (GKRS) in pediatric brain tumors. The diagram summarizes histology-based dose considerations, age-adapted procedural strategies, and follow-up pathways. Treatment decisions are individualized according to tumor biology, size, location, and prior therapies rather than applied as a uniform protocol

frame fixation in 100 patients (71.9%). Frameless mask fixation is feasible in cooperative patients as young as six years, whereas awake frame fixation is generally tolerated at approximately 12 years of age. This finding is consistent with earlier reports that frame-based GKRS can be safely performed under local anesthesia in older children but typically requires general anesthesia in younger patients due to cooperation and anxiety issues [7, 19]. Since the introduction of the Gamma Knife Icon, mask-based fixation has been increasingly adopted, allowing for noninvasive immobilization and fractionated treatments when indicated [20].

Anesthesia requirements are strongly dependent on age. General anesthesia was required for 36 procedures (25.9%), MAC for 2 (1.4%), and local anesthesia for 101 (72.7%). Patients undergoing local anesthesia were significantly older than those requiring general anesthesia (median age 14.0 vs.

8.5 years, $p < 0.001$). Prior studies have similarly recommended general anesthesia for children unable to tolerate frame placement or closed treatment environments [9, 21]. Notably, no acute complications related to fixation or anesthesia were observed, confirming that both approaches are safe when appropriately selected [9, 20]. Overall, mask fixation can be safely applied in younger children when cooperation is sufficient. Anesthesia choices should be individualized based on age and anxiety levels.

Taken together, these findings support an individualized approach that considers both tumor biology and procedural factors. To provide a practical summary of our institutional strategy, we present a schematic framework outlining histology-based dose considerations, age-adapted procedural strategies, and follow-up pathways (Fig. 3).

Limitations

This study had several limitations. Its retrospective, single-institution design introduced inherent selection bias and limited causal inferences. The inclusion of heterogeneous histologies and variable follow-up durations may have influenced survival estimates, and the relatively small sample size within each histological subgroup limited the statistical power to detect outcome differences. Multivariable analysis across the entire cohort was not performed due to limited subgroup sizes and potential model instability, and therefore the findings should be interpreted as descriptive rather than inferential. The clinical indications for GKRS also differed according to tumor histology. While GKRS was primarily used for durable local control in benign and low-grade tumors, it was generally applied in the salvage or palliative setting in aggressive histologies after prior multimodal therapy. Accordingly, differences in treatment intent and prior therapeutic exposure should be considered when interpreting survival outcomes across tumor subgroups. Molecular classification was not uniformly available throughout the study period, and the heterogeneous histologies with relatively small subgroup sizes precluded meaningful molecular stratification. Furthermore, the lack of systematic assessment of long-term neurocognitive, endocrine, and functional outcomes restricts the evaluation of the effects of late treatment.

Nevertheless, this study has several important strengths. This represents one of the largest single-institution pediatric GKRS cohorts with a comprehensive analysis of fixation methods, anesthetic strategies, and histology-specific outcomes. The integration of detailed dosimetric parameters with survival analyses provides evidence for the safe and effective use of GKRS in children. Future prospective multicenter studies incorporating molecular profiling, standardized dosimetric protocols, and systematic long-term follow-up are warranted to refine patient selection criteria and the role of GKRS in multidisciplinary pediatric neuro-oncology care.

Conclusions

In this series of 139 GKRS procedures in 108 patients with pediatric brain tumors, outcomes varied substantially according to tumor histology. Benign and low-grade tumors were associated with durable local control, whereas aggressive histologies, particularly PDHGG, demonstrated poor progression-free survival and high mortality. These findings emphasize the importance of careful histology-based patient selection and integration of GKRS within multimodal treatment strategies. Age-adapted fixation and anesthesia approaches allowed safe implementation in appropriately selected pediatric patients.

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Data availability Data is available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

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