

Bibliography

# Gamma Knife radiosurgery for a pediatric population

December 2017– December 2021 Gamma Knife radiosurgery in the management of hypothalamic glioma: A case report with long-term follow-up. Pediatr Neurosurg. 2021 Dec 30. DOI: 10.1159/000521732. Online ahead of print.

Jumah F, Abou-Al-Shaar H, Mallela AN, Wiley CA, Lunsford LD.

## Background

Optic pathway/hypothalamic gliomas are rare pediatric brain tumors. The management paradigm for these challenging tumors includes chemotherapy, radiotherapy, or surgical resection, but the optimal management strategy remains elusive. Gamma Knife radiosurgery (GKRS) has emerged as a promising treatment for such lesions as documented by a small number of cases in the literature.

## **Case Presentation**

Herein, we present a rare case of hypothalamic glioma in a 13-year-old girl who was referred to our service due to growth of a an incidentally diagnosed hypothalamic lesion following head injury at the age of 8 years. The lesion demonstrated hypointensity on T1 and hyperintensity on T2 without enhancement. Given the growth of the lesion on serial imaging, a stereotactic biopsy was performed demonstrating low-grade glioma. The patient underwent GKRS treatment with a marginal dose of 15 Gy at 50% isodose line for a tumor volume of 2.2 ml. Annual radiological surveillance over the next 17 years demonstrated a gradual shrinkage of the lesion until it completely disappeared. The patient is currently a healthy 31-year-old female without any visual, endocrine, or neurocognitive complaints.

## Conclusion

The outcome obtained after extended follow-up in our patient highlights the safety and efficacy of GKRS in the management of hypothalamic gliomas in pediatrics, which in turn can avoid potentially serious complications of surgery in this vulnerable patient population in this sensitive location.

Dosimetric parameters associated with the long-term oncological outcomes of Gamma Knife surgery for sellar and parasellar tumors in pediatric patients.

J Neurosurg Pediatr. 2021 Oct 22:1–9. DOI: 10.3171/2021.7.PEDS21312. Online ahead of print. Lee EJ, Lee JY, Kim JW, Phi JH, Kim YH, Kim SK, Chung HT, Wang KC, Kim DG.

## Objective

The authors aimed to investigate the dosimetric parameter and the minimally required dose associated with long-term control of sellar and parasellar tumors after Gamma Knife surgery (GKS) in children.

## Methods

A retrospective analysis was performed on pediatric patients younger than 19 years of age who were diagnosed with sellar and parasellar tumors and received GKS at the authors' institution from 1998 to 2019. Cox proportional hazards regression analyses were used to investigate the dosimetric parameters associated with treatment outcome. The Kaplan-Meier method was used to analyze tumor control rates after GKS.

## Results

Overall, 37 patients with 40 sellar and parasellar tumors, including 22 craniopharyngiomas and 12 pituitary adenomas, had a mean follow-up of 85.8 months. The gross target volume was 0.05 cm<sup>3</sup> to 15.28 cm<sup>3</sup>, and the mean marginal dose was 15.8 Gy (range 9.6-30.0 Gy). Ten patients experienced treatment failure at a mean of  $28.0 \pm 26.7$  months. The actuarial 5- and 10-year tumor control rates were 79.0% and 69.8%, respectively. D98% was an independent predictive factor of tumor control (HR 0.846 [95% CI 0.749-0.956], p = 0.007), with a cutoff value of 11.5 Gy for the entire cohort and 10 Gy for the craniopharyngioma group. Visual deterioration occurred in 2 patients with the maximum point dose of 10.1 Gy and 10.6 Gy to the optic apparatus.

## Conclusions

In pediatric patients, D98% was a reliable index of the minimum required dose for long-term control of sellar and parasellar tumors after GKS. The optimal D98% value for each tumor diagnosis needs to be elucidated in the future. Radiobiological evaluation of combined Gamma Knife radiosurgery and hyperthermia for pediatric neuro-oncology. Cancers (Basel). 2021 Jun 30;13(13):3277. DOI: 10.3390/cancers13133277.

Aram MG, Zanoli M, Nordstrom H, Toma-Dasu J, Blomgren K, Trefna HD.

Combining radiotherapy (RT) with hyperthermia (HT) has been proven effective in the treatment of a wide range of tumors, but the combination of externally delivered, focused heat and stereotactic radiosurgery has never been investigated. We explore the potential of such treatment enhancement via radiobiological modelling, specifically via the linear-quadratic (LQ) model adapted to thermoradiotherapy through modulating the radiosensitivity of temperature-dependent parameters. We extend this wellestablished model by incorporating oxygenation effects. To illustrate the methodology, we present a clinically relevant application in pediatric oncology, which is novel in two ways. First, it deals with medulloblastoma, the most common malignant brain tumor in children, a type of brain tumor not previously reported in the literature of thermoradiotherapy studies. Second, it makes use of the Gamma Knife for the radiotherapy part, thereby being the first of its kind in this context. Quantitative metrics like the biologically effective dose (BED) and the tumor control probability (TCP) are used to assess the efficacy of the combined plan.

Impact of the skull size on the normal brain radiation dose during Gamma Knife radiosurgery: Results of a pilot study. Acta Neurochir Suppl. 2021;128:151–55. DOI: 10.1007/978-3-030-69217-9\_17.

Ma L, Fogh S, Braunstein SE, Auguste K, Theodosopoulos PV, McDermott MW, Sneed PK.

## Objective

The objective of the present study was evaluation of the interrelationships between changes in the skull size and variations in the normal brain radiation dose during Gamma Knife surgery (GKS).

#### Methods

With use of systematic modeling within Leksell GammaPlan<sup>®</sup> (Elekta AB; Stockholm, Sweden) in each of 15 analyzed cases, the skull was "expanded" and "contracted" by variation of its measurement values from 0 to  $\pm 3$  cm. The mean normal brain radiation dose was then computed for each variant of the adjusted skull size and compared with the original treatment plan. Variations in the maximum point dose delivered to selected critical anatomical structures were also investigated.

## Results

With changes in the skull radius within ±3 cm, the maximum absolute deviation in the mean normal brain radiation dose was 0.8%. As the skull radius increased, the mean normal brain radiation dose also increased linearly (confidence level >99%) with a positive slope of 0.2% per centimeter of radius length change. The maximum point dose deviations in all evaluated critical anatomical structures did not exceed 0.5%, with an overall trend toward a dose increase in parallel with an increase in the skull radius.

## Conclusion

The small skull size of pediatric patients may be associated with dosimetric advantages in terms of normal brain sparing during GKS.

Concise review of stereotactic irradiation for pediatric glial neoplasms: Current concepts and future directions. World J Methodol. 2021 May 20;11(3):61–74. DOI: 10.5662/wjm.v11.i3.61.

Sager O, Dincoglan F, Demiral S, Uysal B, Gamsiz H, Colak O, Ozcan F, Gundem E, Elcim Y, Dirican B, Beyzadeoglu M.

Brain tumors, which are among the most common solid tumors in childhood, remain a leading cause of cancerrelated mortality in pediatric population. Gliomas, which may be broadly categorized as low-grade glioma and high-grade glioma, account for the majority of brain tumors in children. Expectant management, surgery, radiation therapy (RT), chemotherapy, targeted therapy or combinations of these modalities may be used for management of pediatric gliomas. Several patient, tumor and treatment-related characteristics including age, lesion size, grade, location, phenotypic and genotypic features, symptomatology, predicted outcomes and toxicity profile of available therapeutic options should be considered in decision making for optimal treatment. Management of pediatric gliomas poses a formidable challenge to the physicians due to concerns about treatment induced toxicity. Adverse effects of therapy may include neurological deficits, hemiparesis, dysphagia, ataxia, spasticity, endocrine sequelae, neurocognitive and communication impairment,

deterioration in quality of life, adverse socioeconomic consequences, and secondary cancers. Nevertheless, improved understanding of molecular pathology and technological advancements may pave the way for progress in management of pediatric glial neoplasms. Multidisciplinary management with close collaboration of disciplines including pediatric oncology, surgery, and radiation oncology is warranted to achieve optimal therapeutic outcomes. In the context of RT, stereotactic irradiation is a viable treatment modality for several central nervous system disorders and brain tumors. Considering the importance of minimizing adverse effects of irradiation, radiosurgery has attracted great attention for clinical applications in both adults and children. Radiosurgical applications offer great potential for improving the toxicity profile of radiation delivery by focused and precise targeting of well-defined tumors under stereotactic immobilization and image guidance. Herein, we provide a concise review of stereotactic irradiation for pediatric glial neoplasms in light of the literature.

Safety and efficacy of primary hypofractionated Gamma Knife radiosurgery for giant hypothalamic hamartoma. Indian J Pediatr. 2021 Nov;88(11):1086–91. DOI: 10.1007/s12098-020-03637-w.

Tripathi M, Maskara P, Sankhyan N, Sahu JK, Kumar R, Kumar N, Ahuja CK, Kaur P, Kaur R, Batish A, Mohindra S.

#### Objective

To describe the feasibility, safety, efficacy, and complication profile of primary hypofractionated Gamma Knife radiosurgery (GKRS), and practical nuances of performing the same in pediatric patients.

## Method:

Three pediatric patients (age range 17–65 mo) underwent primary hypofractionated GKRS in 2-3 consecutive days with interfraction interval of 24 h. All patients had precocious puberty and were on GnRH analogue. Frame based GKRS done with 8.1-9.2 Gy radiation per fraction at 50% isodose in 2-3 fractions targeting the entire hamartoma volume. The mean target volume was 5.67 cc (4.45–7.39 cc). The authors followed these patients for clinical and endocrinological assessment at every 6 mo interval while the repeat MRI done at 6 mo and then annually. The seizure outcome analysis was done using Engel scale.

#### Results

At a mean follow up of 27 mo (24–30 mo), 2 patients became Engel class 3 while one achieved Engel class 1 control. 2 patients showed halted pubertal growth with no additional hormonal aberration. 2 patients showed significant volumetric reduction (48% and 32%) and patchy necrosis inside the hypothalamic hamartoma (HH). There was no deficit in visual function, memory, and cognition. One patient showed reduction in aggressiveness.

## Conclusion

Giant HH are exceptionally difficult neurological diseases. Primary hypofractionated GKRS may be an alternative approach as mono/multitherapy with promising results and minimal complication.

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## Long-term outcomes of pediatric arteriovenous malformations: the 30-year Pittsburgh experience.

J Neurosurg Pediatr. 2020 May 15;26(3):275–82. DOI: 10.3171/2020.3.PEDS19614.

McDowell MM, Agarwal N, Mao G, Johnson S, Kano H, Lunsford LD, Greene S.

## Objective

The study of pediatric arteriovenous malformations (pAVMs) is complicated by the rarity of the entity. Treatment choice has often been affected by the availability of different modalities and the experience of the providers present. The University of Pittsburgh experience of multimodality treatment of pAVMs is presented.

## Methods

The authors conducted a retrospective cohort study examining 212 patients with pAVM presenting to the University of Pittsburgh between 1988 and 2018, during which patients had access to surgical, endovascular, and radiosurgical options. Univariate analysis was performed comparing good and poor outcomes. A poor outcome was defined as a modified Rankin Scale (mRS) score of  $\geq$  3. Multivariate analysis via logistic regression was performed on appropriate variables with a p value of  $\leq$  0.2. Seventy-five percent of the cohort had at least 3 years of follow-up.

## Results

Five patients (2.4%) did not receive any intervention, 131 (61.8%) had GKRS alone, 14 (6.6%) had craniotomies alone, and 2 (0.9%) had embolization alone. Twenty-two (10.4%) had embolization and Gamma Knife radiosurgery (GKRS); 20 (9.4%) had craniotomies and GKRS; 8 (3.8%) had embolization and craniotomies; and 10 (4.7%) had embolization, craniotomies, and GKRS. Thirty-one patients (14.6%) were found to have poor outcome on follow-up. The multivariate analysis performed in patients with poor outcomes was notable for associations with no treatment (OR 18.9, p = 0.02), hemorrhage requiring craniotomy for decompression alone (OR 6, p = 0.03), preoperative mRS score (OR 2.1, p = 0.004), and Spetzler-Martin score (OR 1.8, p = 0.0005). The mean follow-up was 79.7 ± 62.1 months. The confirmed radiographic obliteration rate was 79.4% and there were 5 recurrences found on average 9.5 years after treatment.

## Conclusions

High rates of long-term functional independence (mRS score of < 2) can be achieved with comprehensive multimodality treatment of pAVMs. At this center there was no difference in outcome based on treatment choice when accounting for factors such as Spetzler-Martin grade and presenting morbidity. Recurrences are rare but frequently occur years after treatment, emphasizing the need for long-term screening after obliteration.

Skull base aneurysmal bone cyst presenting with hydrocephalus: progressive residuum obliterated by Gamma Knife stereotactic radiosurgery in a pediatric patient.

J Neurosurg Pediatr. 2020 Apr 3;26(1):76–81. DOI: 10.3171/2020.2.PEDS19755.

Tse GH, Jiang FY, Radatz MWR, Sinha S, Zaki H.

Aneurysmal bone cysts (ABCs) are an uncommon entity predominantly encountered in the pediatric population. The skull is rarely involved, but these cysts have been reported to arise in the skull base. Traditional treatment has been with surgery alone; however, there is a gathering body of literature that reports alternative treatments that can achieve long-term disease-free survival. However, these therapies are predominantly directed at peripheral skeletal lesions. To the authors' knowledge, this report is the first to describe long-term follow-up of the efficacy of Gamma Knife stereotactic radiosurgery for treatment of ABC residuum in the skull base that resulted in long-term patient stability and likely ABC obliteration. Clinical outcomes of stereotactic radiosurgery for cerebral arteriovenous malformations in pediatric patients: Systematic review and meta-analysis.

Neurosurgery. 2019 Oct 1;85(4):E629-40. DOI: 10.1093/neuros/nyz146.

Borcek AO, Celtikci E, Aksogan Y, Rousseau MJ.

### Background

Arteriovenous malformations (AVMs) in pediatric patients exhibit remarkable differences in terms of management and outcomes. Owing to a paucity of relevant data pertaining to AVMs in pediatric patients, special interest and investigation are required for an improved understanding of the available evidence by clinicians.

## Objective

To determine the clinical outcomes of single-session stereotactic radiosurgery (SRS) for AVMs in pediatric patients.

## Methods

A systematic literature review was performed to identify studies that reported the outcomes of SRS for AVMs in pediatric patients. Data pertaining to variables such as obliteration rate, post-SRS new hemorrhage rate, post-SRS new neurological deficit rate, and mortality rate were extracted and analyzed using meta-analysis techniques.

### Results

Based on pooled data from 20 studies with 1212 patients, single-session SRS resulted in complete obliteration in 65.9% (95% confidence interval [CI], 60.5%-71.1%; 12 = 66.5%) patients. Overall complication rate (including new hemorrhage, new neurodeficit, and mortality) was 8.0% (95% CI, 5.1%-11.5%; 12 = 66.4%). Post-SRS new neurological deficit rate was 3.1% (95% CI, 1.3%-5.4%; 12 = 59.7%), and post-SRS hemorrhage rate was 4.2%(95% CI, 2.5%-6.3%; 12 = 42.7%). There was no significant difference between studies disaggregated by treatment method (Gamma Knife [Elekta AB] vs other), treatment year (before year 2000 vs after year 2000), median AVM volume reported ( $\ge 3$  vs <3 cm3), median dose reported ( $\ge 20$  vs <20 Gy), or follow-up period ( $\ge 36$  vs <36 mo).

## Conclusion

Single-SRS is a safe treatment alternative that achieves high obliteration rates and acceptable complication rates for AVMs in pediatric patients.

Twenty-three years follow-up after low-dose Gamma Knife surgery of a brainstem juvenile pilocytic astrocytoma: a case report and review of the literature.

Childs Nerv Syst. 2019 Jul;35(7):1227-30. DOI: 10.1007/s00381-019-04147-7.

Liu JS, Foo D, Yeo TT, Ho KH, Nga VDW, Karlsson B.

Juvenile pilocytic astrocytoma (JPA) is a World Health Organization (WHO) grade I tumor that is the commonest to occur in the 0-19 age group, with an excellent prognosis of 96% 10-year survival in pediatric patients. Complete resection is the treatment of choice for JPAs. However, this is not always feasible due to the location of certain tumors, and the management following subtotal resection is controversial. Fractionated radiotherapy, chemotherapy, radiosurgery, and observation have all been used to treat tumor remnants. We report a young patient with good tumor control 23 years following low-dose Gamma Knife surgery (GKS) of a subtotally resected brainstem JPA and recommend that GKS may be a feasible treatment option to achieve long-term tumor control when subtotal resection cannot be achieved, even if the GKS prescription dose must be significantly reduced due to large tumor volume or proximity to critical structures sensitive to radiation. Long-term outcomes for pediatric patients with brain arteriovenous malformations treated with Gamma Knife radiosurgery, Part 2: The incidence of cyst formation, encapsulated hematoma, and radiation-induced tumor. World Neurosurg. 2019 Jun;126:e1526–36. DOI: 10.1016/j.wneu.2019.03.177.

Hasegawa T, Kato T, Naito T, Tanei T, Torli J, Ishii K, Tsukamoto E, Hatanaka KC, Sugiyama T.

## Objective

Long-term data about the incidence of late adverse radiation effects (AREs) in pediatric brain arteriovenous malformations (AVMs) treated with Gamma Knife radiosurgery (GKRS) are lacking. This study addresses the incidence of late AREs, including cyst formation (CF), chronic encapsulated hematoma (CEH), and radiation-induced tumor, in pediatric patients with AVM treated with GKRS.

## Methods

This is a single-institutional study involving pediatric patients with AVM who underwent GKRS between 1991 and 2014. Among 201 pediatric patients with AVM (age  $\leq$ 15 years), 189 who had at least 12 months of follow-up were assessed in this study. The median treatment volume was 2.2 cm<sup>3</sup>, and the median marginal dose was 20 Gy.

## Results

The mean follow-up period was 136 months. During the follow-up period, symptomatic radiation-induced perilesional edema was found in 5 patients (3%), CFs in 7 patients (4%), CEHs in 7 patients (4%), and radiation-induced tumors in 2 patients (1%). The cumulative incidences of late AREs including CF, CEH, and radiation-induced tumor were 1.2% at 5 years, 5.2% at 8 years, 6.1% at 10 years, 7.2% at 15 years, and 17.0% at 20 years. In the multivariate analysis, treatment volume alone was a significant factor for late AREs (P < 0.001; hazard ratio, 1.111).

## Conclusions

GKRS is a reasonable treatment option for pediatric AVMs to prevent future intracranial hemorrhages, particularly in the eloquent regions. However, considerable attention should be paid to late AREs such as CFs, CEHs, and radiation-induced tumors because of longer life expectancy in pediatric patients.

## Long-term outcomes for pediatric patients with brain arteriovenous malformations treated with Gamma Knife radiosurgery, Part 1: Analysis of nidus obliteration rates and related factors World Neurosurg. 2019 Jun;126:e1518–25. DOI: 10.1016/j.wneu.2019.03.176.

Hasegawa T, Kato T, Naito T, Tanei T, Toril J, Ishii K, Tsukamoto E.

## Objective

Little is known about long-term outcomes for pediatric brain arteriovenous malformations (AVMs) treated with Gamma Knife radiosurgery (GKRS). This study investigated annual hemorrhage rates and nidus obliteration rates, and the factors affecting them, in pediatric AVMs treated with GKRS.

## Methods

We examined 189 pediatric AVM patients (age  $\leq$ 15 years) who underwent GKRS and had at least 12 months of follow-up. The Spetzler-Martin (S-M) grade was I in 29 patients (15%), II in 57 (30%), III in 82 (43%), IV in 16 (9%), and V in 5 (3%). The median treatment volume was 2.2 cm<sup>3</sup>, and the median marginal dose was 20 Gy.

## Results

The mean follow-up period was 136 months. During a cumulative latency period to nidus obliteration of 813 years, 23 hemorrhages occurred, resulting in an annual post-GKRS hemorrhage rate of 2.8%. The cumulative hemorrhage rates after GKRS were 3.3%, 8.5%, and 11.9% at 3, 5, and 10 years, respectively. Higher S-M grade was significantly associated with intracranial hemorrhages during the latency period (P < 0.001). The actuarial nidus obliteration rates with repeated GKRS were 64% and 81% at 5 and 10 years, respectively. Absence of pre-GKRS embolization (P = 0.023) and higher marginal dose (P = 0.029) were significant factors predicting nidus obliteration.

## Conclusions

GKRS is a reasonable treatment option in pediatric AVMs to prevent future hemorrhages. Because higher S-M grade AVMs are more likely to hemorrhage during the latency period, a combined therapy with endovascular embolization should be considered to prevent AVM rupture. Outcomes after Gamma Knife stereotactic radiosurgery in pediatric patients with cushing disease or acromegaly: A multi-institutional study.

## World Neurosurg. 2019 May;125:e1104–13. DOI: 10.1016/j.wneu.2019.01.252.

Shrivastava A, Mohammed N, Xu Z, Liscak R, Kosak M, Krsek M, Karim KA, Lee CC, Marinez-Moreno N, Vance ML, Lunsford LD, Sheehan JP.

## Objective

Pituitary adenomas comprise about 3% of all intracranial tumors in pediatric patients. This study examines the role of stereotactic radiosurgery in the management of pediatric acromegaly or patients with Cushing disease (CD).

## Methods

From an international consortium, we retrospectively collected treatment and outcome data on pediatric adrenocorticotrophic hormone and growth hormonesecreting pituitary adenomas treated with Gamma Knife radiosurgery (GKRS). There was a total of 36 patients including 24 with CD and 12 with acromegaly. The data were analyzed to assess outcomes including tumor control, endocrine remission, and adverse effects. Statistical analysis was performed to determine correlation between clinical/ treatment parameters and outcomes.

## Results

At the last follow-up after GKRS, endocrine remission rates for CD and acromegaly were 80% and 42%, respectively. Tumor control was achieved in 87.5% of patients with CD and in 42% of patients with acromegaly. New pituitary hormone deficiency occurred in 7 of the 36 patients at a median time of 18 months after GKRS (range, 12-81 months). The predictive factors for endocrine remission were age <15 years (P = 0.015) and margin dose (P = 0.042). The median endocrine follow-up was 63.7 months (range, 7-246 months).

## Conclusions

GKRS affords reasonable rates of endocrine remission and tumor control in most pediatric patients with functioning adenomas. The most common post-GKRS complication was hypopituitarism, although this occurred in only a few patients. Given the larger at-risk period for pediatric patients, further study is required to evaluate for delayed recurrences and hypopituitarism.

Radiosurgical treatment of arteriovenous malformations in a retrospective study group of 33 children: The importance of radiobiological scores.

Childs Nerv Syst. 2019 Feb;35(2):301-08. DOI: 10.1007/s00381-018-4008-2.

Capitanio JF, Panni P, Gallotti AL, Gigliotti CR, Scomazzoni F, Acerno S, Del Vecchio A, Mortini P.

## Purpose

Arteriovenous malformations' (AVMs) obliteration depends on several factors; among the many factors that must be considered to obtain a high rate of obliteration and a low rate of complications, Flickinger-Pollock Score (FPS) seems to have an important role but still have to be validated in the pediatric population while Paddick-Conformity Index (PCI) still has no demonstration of its utility on the outcome and is considered only as a treatment quality marker.

## Methods

We retrospectively analyzed 33 consecutive children (2-18 years) with an AVM, treated with stereotactic radiosurgery Gamma Knife (SRS-GK) from 2001 to 2014 in our institution. We assess angiographic (DSA) Obliteration Rate (OR) as well FPS and PCI to draw conclusions.

## Results

DSA-OR was 60.6% with a rate of hemorrhage of 0%. median target volume (TV) was 3.60 cc (mean  $4.32 \pm 3.63$ ; range 0.15-14.2), median PD was 22 Gy (mean  $21.4 \pm 2.6$ ; range 16.5-25). Median percentage of coverage was 98% (mean 97  $\pm$  3; range 84-100). The median modified FPS was 0.78 (mean 0.89  $\pm$  0.52; range 0.21-2.1) and highly correlate with OR (p = 0.01). The median PCI was 0.65 (mean 0.65  $\pm$  0.14; range 0.34-0.95) A PCI lower than 0.57 highly correlates with final OR (p = 0.02).

## Conclusion

SRS-GK was safe and gradually effective in children. A prescription dose-like that used in adult population (i.e. > 18 and between 20 and 25 Gy) is essential to achieve obliteration. A PD of 23 Gy and 22 Gy did impact OR, respectively (p = 0.02) and (p = 0.05). FPS and PCI are valuable scores that seem to correlate with the OR also in the pediatric population although further prospective studies are needed to confirm these observations.

## A giant solid cavernous hemangioma mimicking sphenoid wing meningioma in an adolescent: A case report.

Medicine (Baltimore). 2018 Nov;97(44):e13098. DOI: 10.1097/MD.00000000013098.

Lan Z, Richard SA, Li J, Xu J, You C.

## Rationale

Central nervous system (CNS) solid cavernous hemangiomas are rare extra-axial anomalies that may sometimes resemble meningiomas. Due to their complex vascular nature, accurate preoperative diagnosis is important to avoid disastrous hemorrhage during operation. To the best of our knowledge this is the first case in an adolescent since all middle cranial fossa hemangioma cases reported in literature are adults in their 40s or 50s and all the pediatric cases are cystic.

## Patient concerns

We present a case of a 14-year-old girl with headache and dizziness for 3 months. She occasionally experienced nausea and vomiting but denied visual disturbances and loss of smell.

## Diagnoses

MRI revealed a lesion that extends to the greater wing of the sphenoid bone as well as the pituitary fossa. Our initial diagnosis was a sphenoid wing meningioma but interestingly, histopathology revealed solid cavernous hemangioma.

## Interventions

The residual tumor was completely removed with 2 sessions of Gamma Knife radiotherapy after surgery.

## Outcomes

We were confronted with excessive bleeding during surgery, so we attained subtotal resection. However, the patient recovered well with no recurrence of the tumor.

## Lessons

Our case shows that space occupying lesions involving the cavernous sinus and sphenoid ridged could be easily misdiagnosed as sphenoid wing meningiomas in children and adolescents and even adults therefore great care must be exercised when confronted with this kind of presentation.

## Primary central nervous system germ cell tumors: A review and update. Med Res Arch. 2018 Mar;6(3):1719. DOI: 10.18103/mra.v6i3.1719. Fetcko K, Dey M.

## Importance

Primary central nervous system (CNS) germ cell tumors (GCT) are a heterogeneous group of tumors that are still poorly understood. In North America, GCTs comprise approximately 1% of primary brain tumors in pediatric and young adult patients. GCTs can occur as pure or mixed subtypes; they are divided into germinomas, which are the most common subtype, and non-germinomatous germ cell tumors (NGGCTs), which consist of approximately one-third of GCTs and include teratomas, embryonal carcinomas, choriocarcinomas, and yolk sac tumors.

## Observations

While the etiology of primary CNS GCT is not entirely clear, the various subtypes are lineage-related and may involve progenitor germ cells that fail to migrate and become trapped in midline locations. Primary CNS GCT most commonly arises in the pineal region but also occur in other areas. Presenting symptoms can include headache, Parinaud syndrome, diabetes insipidus, precocious puberty, ataxia, or hemiparesis. Diagnosis of primary CNS GCTs can be difficult and is often delayed. Various imaging studies and tumor markers can assist in specific diagnosis. Treatment plans differ depending on the subtype of GCT and may vary among physicians and institutions. Germinomas have a favorable prognosis with a greater than 90% overall survival, while NGGCTs only have survival rates ranging from 40–70%.

## Conclusions and relevance

Germinomas seem to be most effectively treated with chemotherapy and radiation, while NGGCT usually require surgical resection, chemotherapy, and radiation with the exception of mature teratomas frequently curable with surgery alone. Gamma knife radiosurgery is a promising treatment that may be an effective additional treatment option. Cytogenic and molecular analyses are attempting to further specify the different GCT subtypes and are helping to direct the development of distinct therapeutic targets to improve treatment and prognosis.

## Stereotactic radiosurgery for pediatric versus adult brain arteriovenous malformations. Stroke. 2018 Aug;49(8):1939–45. DOI: 10.1161/STROKEAHA.118.022052.

Chen CJ, Ding D, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Grills IS, Barnett G, Lunsford LD, Sheehan JP, International Gamma Knife Research Foundation.

## **Background and Purpose**

The aim of this international, multicenter, retrospective matched cohort study is to directly compare the outcomes after stereotactic radiosurgery (SRS) for brain arteriovenous malformations (AVM) in pediatric versus adult patients. Methods- We performed a retrospective review of patients with AVM who underwent SRS at 8 institutions participating in the International Gamma Knife Research Foundation from 1987 to 2014. Patients were categorized into pediatric (<18 years of age) and adult (≥18 years of age) cohorts and matched in a 1:1 ratio using propensity scores. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiationinduced changes.

## Results

From a total of 2191 patients who were eligible for inclusion in the overall study cohort, 315 were selected for each of the matched cohorts. There were no significant differences between matched pediatric versus adult cohorts with respect to the rates of favorable outcome (59% versus 58%; P=0.936), AVM obliteration (62% versus 63%; P=0.934), post-SRS hemorrhage (9% versus 7%; P=0.298), radiological radiationinduced changes (26% versus 26%; P=0.837), symptomatic radiation-induced changes (7% versus 9%; P=0.383), or permanent radiation-induced changes (2% versus 3%; P=0.589). The all-cause mortality rate was significantly lower in the matched pediatric cohort (3% versus 10%; P=0.003).

## Conclusions

The outcomes after SRS for comparable AVMs in pediatric versus adult patients were not found to be appreciably different. SRS remains a reasonable treatment option for appropriately selected pediatric patients with AVM, who harbor a high cumulative lifetime hemorrhage risk. Age seems to be a poor predictor of AVM outcomes after SRS.

## Comparison of the long-term efficacy and safety of Gamma Knife radiosurgery for arteriovenous malformations in pediatric and adult patients.

Neurol Med Chir (Tokyo). 2018 Jun 15;58(6):231-239. DOI: 10.2176/nmc.st.2018-0008.

Hasegawa H, Hankita S, Shin M, Kawashima M, Takahashi W, Ishikawa O, Koizumi S, Nakatomi H, Saito N.

It is debated whether the efficacy and long-term safety of gamma knife radiosurgery (GKRS) for arteriovenous malformations (AVMs) differs between adult and pediatric patients. We aimed to clarify the long-term outcomes of GKRS in pediatric patients and how they compare to those in adult patients. We collected data for 736 consecutive patients with AVMs treated with GKRS between 1990 and 2014 and divided the patients into pediatric (age < 20 years, n = 144) and adult (age  $\geq$  20 years, n = 592) cohorts. The mean follow-up period in the pediatric cohort was 130 months. Compared to the adult patients, the pediatric patients were significantly more likely to have a history of hemorrhage (P < 0.001). The actuarial rates of post-GKRS nidus obliteration in the pediatric cohort were 36%, 60%, and 87% at 2, 3, and 6 years, respectively. Nidus obliteration occurred earlier in the pediatric cohort than in the adult cohort (P = 0.015). The actuarial rates of post-GKRS hemorrhage in the pediatric cohort were 0.7%, 2.5%, and 2.5% at 1, 5, and 10 years, respectively. Post-GKRS hemorrhage was marginally less common in the pediatric cohort than in the adult cohort (P = 0.056). Cyst formation/encapsulated hematoma were detected in seven pediatric patients (4.9%) at a median post-GKRS timepoint of 111 months, which was not significantly different from the rate in the adult cohort. Compared to adult patients, pediatric patients experience earlier therapeutic effects from GKRS for AVMs, and this improves long-term outcomes.

Clinical outcomes and radiosurgical considerations for pediatric arteriovenous malformation: Influence of clinical features on obliteration rate.

Childs Nerv Syst. 2017 Dec;33(12):2137-45. DOI: 10.1007/s00381-017-3579-7.

Park CK, Choi SK, Lee SH, Choi MK, Lim YJ.

## Purpose

Gamma knife radiosurgery (GKRS) is an established treatment modality for brain arteriovenous malformation (AVM), but there have been few published studies examining the relationship between clinical features of AVM and successful obliteration with GKRS in pediatric patients. In the current study, we investigate the outcomes of GKRS for pediatric patients with brain AVM and analyze the variables that influence obliteration.

#### Methods

We analyzed 68 pediatric patients (≤ 18 years) with a mean follow-up period of 61.9 months (range 6-215 months). The following parameters were analyzed to determine their influence on obliteration of AVM treated by GKRS: age, sex, target volume, irradiation dose, prior treatment, location of AVM, nidus structure, velocity of AVM, location of venous drainage, number of feeding arteries, and initial presenting symptoms. Also, we estimated clinical factors which should be considered during the follow-up period.

## Results

Of the 68 patients, complete obliteration was confirmed in 26 (38.2%) by cerebral angiography. The response rate of AVM for GKRS was 92.6%. No significant association was observed between any of the parameters investigated and the obliteration of AVM, with the exception of number of feeding arteries, which exhibited a statistically significant difference by univariate analysis (p = 0.003). However, on multivariate analysis, nidus structure (p = 0.007), velocity of the main arterial phase (p = 0.013), velocity of the feeding arteries (p = 0.004), and the number of feeding arteries (p = 0.018) showed statistical significance.

## Conclusion

GKRS yielded good long-term clinical outcomes in most pediatric patients. Multiple arterial feeding vessels, diffuse nidus structure, and fast flow of AVM were specific factors associated with a low rate of obliteration in pediatric AVMs.

Does stereotactic radiosurgery positively impact the local control of atypical teratoid rhabdoid tumors? World Neurosurg. 2017 Aug;104:612-618. DOI: 10.1016/j.wneu.2017.04.132.

Spina A, Gagliardi F, Boari N, Bailo M, Mortini P.

## Background

Atypical teratoid rhabdoid tumors (ATRTs) are rare and aggressive tumors, usually affecting patients younger than 3 years of age, that are characterized by a poor prognosis. Nowadays multimodal management, including surgery, chemotherapy, and radiation therapy (RT), is advocated depending on the patients' age and tumor stage, even if no consensus exists regarding the best treatment modality. Local RT seems to be the most effective treatment in prolonging progression-free and overall survival rates, although RT might not be used on younger children because of the risk of neurocognitive and endocrine sequelae. Stereotactic radiosurgery (SRS) is a valuable alternative therapeutic option to conventional RT because of the more conformal dose delivery. The aim of this study was to review the available literature on SRS in the management of ATRT.

### Methods

The authors carried out a systematic review of PubMed, Web of Science, and Google Scholar for clinical reports dealing with SRS for the management of ATRT.

#### Results

Nine studies describing 12 patients treated with SRS for ATRT were included in the analysis. Patient's clinical features, radiosurgical treatment characteristics, and follow-up data of the pertinent literature were reviewed critically. SRS represents a feasible and effective therapeutic option in the management of ATRT. Local control has been reported in 66.7% of cases; however, 33.3% of patients experienced poor survival because of craniospinal tumor dissemination.

#### Conclusion

SRS should be considered in the multimodal treatment of ATRT, and future studies should focus on a better definition of the role played by SRS in their management.

## Stereotactic radiosurgery for pediatric high-grade brain arteriovenous malformations: Our experience and review of literature.

## World Neurosurg. 2017 Jun;102:613-22. DOI: 10.1016/j.wneu.2017.03.064.

Patibandla MR, Ding D, Xu A, Sheehan JP.

## Introduction

Although high-grade AVMs pose a particularly high lifetime hemorrhage risk to pediatric patients (age <18 years), little is known about the treatment outcomes. Therefore, the aim of this retrospective cohort study was to evaluate the outcomes after single-session stereotactic radiosurgery (SRS) for pediatric high-grade AVMs.

## Methods

We reviewed baseline and treatment outcomes data from pediatric patients aged less than 18 years with Spetzler-Martin grade IV AVMs treated with SRS in a single session at our institution. The study cohort comprised 28 pediatric patients with Spetzler-Martin grade IV AVMs, with a mean age of 12.1 years. Statistical analyses were performed to determine predictors of obliteration and compare the outcomes of patients with versus without previous AVM hemorrhage.

## Results

The mean nidus volume, radiosurgical margin dose, and follow-up duration were  $5.9 \text{ cm}^3$ , 19.4 Gy, and 116 months, respectively. The actuarial obliteration rates at 3, 5, 7, and 10 years were 11%, 19%, 29%, and 35%, respectively. Older age was significantly associated with obliteration in the univariate Cox proportional regression analysis (P = 0.01). During the latency period before obliteration, the annual post-SRS hemorrhage rate was 3.2%. Symptomatic and permanent radiation-induced changes were detected in 7.1% and 3.5%, respectively. A favorable outcome was achieved in 35.7%, and it was more frequently achieved for those with ruptured AVMs (P = 0.0484).

## Conclusions

The efficacy of single-session SRS for the treatment of highgrade AVMs in the pediatric population is limited, particularly for those with unruptured nidi. Multimodal therapies should be considered in the management of selected pediatric high-grade AVMs. However, further prospective analyses are warranted to define the optimal management strategy for these challenging vascular malformations.

Pediatric infratentorial meningiomas: A series of 19 cases and review of the literature. Childs Nerv Syst. 2017 May;33(5):777–86. DOI: 10.1007/s00381-017-3362-9. Liu H, Luo W, Li J, Yang J, Xu Y.

## Purpose

Pediatric infratentorial meningiomas are extremely rare. In this article, we present a series of 19 cases operated at our institution in the last 8 years.

## Methods

During the 8-year period from January 2008 to December 2015, we encountered 21 cases suffered from infratentorial meningiomas. Two patients were excluded. The clinical profiles, radiological features, surgical procedures, intraoperative findings, and outcomes were extracted from the patient records and neuroimaging data.

## Results

The 19 cases with pediatric infratentorial meningiomas account for about 12.8% of all pediatric intracranial meningiomas. The age distribution of the patients ranged from 7 to 18 years. There were 9 male and 10 female patients. Cranial nerve defects were the first common signs and symptoms found in most cases (n = 14). One meningioma localized in cerebellum, one originated in jugular foramen. Meningioma involving internal auditory canal was only seen in one of the six patients with CPA meningioma. One tumor was totally ossified. In all, total resection was achieved in 14 patients, subtotal resection in 5 patients. Gamma knife was used for the recurrent and subtotally resected tumors. Conventional radiotherapy was applied for high-grade meningiomas (WHO grade II and WHO grade III).

## Conclusion

Pediatric infratentorial meningiomas are different from supratentorial ones in many aspects, such as onset age, gender ratio, and neuroradiological characteristics. Surgical excision is challenging. According to the locations of tumors, different surgical approaches would be chosen to maximally resect the lesions without damage to brain stem and cranial nerves. Gamma knife and conventional radiotherapy could be used as postoperative adjuvant therapies. Long-term clinical follow-up and serial imaging are recommended. As a leader in precision radiation therapy, Elekta is committed to ensuring every patient has access to the best cancer care possible. We openly collaborate with customers to advance sustainable, outcome-driven and cost-efficient solutions to meet evolving patient needs, improve lives and bring hope to everyone dealing with cancer. To us, it's personal, and our global team of 4,700 employees combine passion, science, and imagination to profoundly change cancer care.

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